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EDITORIAL

Three-dimensional printing in paediatric orthopaedic surgery

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Abstract

Three-dimensional (3D) printing is a rapidly evolving and promising field to improve outcomes of orthopaedic surgery. The use of patient-specific 3D-printed models is specifically interesting in paediatric orthopaedic surgery, as limb deformity corrections often require an individual 3D treatment. In this editorial, various operative applications of 3D printing in paediatric orthopaedic surgery are discussed. The technical aspects and the imaging acquisition with computed tomography and magnetic resonance imaging are outlined. Next, there is a focus on the intraoperative applications of 3D printing during paediatric orthopaedic surgical procedures. An overview of various upper and lower limb deformities in paediatrics is given, in which 3D printing is already implemented, including post-traumatic forearm corrections and proximal femoral osteotomies. The use of patient-specific instrumentation (PSI) or guiding templates during the surgical procedure shows to be promising in reducing operation time, intraoperative haemorrhage and radiation exposure. Moreover, 3D-printed models for the use of PSI or patient-specific navigation templates are promising in improving the accuracy of complex limb deformity surgery in children. Lastly, the future of 3D printing in paediatric orthopaedics extends beyond the intraoperative applications; various other medical applications include 3D casting and prosthetic limb replacement. In conclusion, 3D printing opportunities are numerous, and the fast developments are exciting, but more evidence is required to prove its superiority over conventional paediatric orthopaedic surgery.

Key Words: Three-dimensional printing; Paediatric; Orthopaedic surgery; Intraoperative; Patient-specific instrumentation; Guiding

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Core Tip: Three-dimensional (3D) printing for intraoperative use in paediatric orthopaedic surgery is a relatively novel field. Research has shown that 3D anatomic models can be used for patient-specific instrumentation and patient-specific templates, that possibly allow the orthopedic surgeon to perform complex surgery more accurately. Based on the latest scientific evidence, this editorial provides an overview of the overall role of 3D printing in intraoperative applications of upper and lower limb surgery in paediatric orthopaedics.

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INTRODUCTION

Over the last decade, three-dimensional (3D) printing–or additive/layer manufacturing-has become a more and more interesting application in medicine. It has been used in various surgical specialties, including neurosurgery, oral and maxillofacial surgery, plastic surgery and cardiothoracic surgery[1-3]. Also in the field of orthopaedic surgery the interest and use of 3D printing has grown over the years, since it started in 1999 in a case of complex spinal surgery[4].

In the orthopaedic field, 3D technology can be used in three different sections: Including preoperative planning, 3D-printed models and 3D printing for patient-specific instrumentation (PSI). A recent meta-analysis reported that the use of 3D-printed models in preoperative planning significantly reduced the operative time, intraoperative blood loss and fluoroscopy use during orthopedic trauma surgery[5]. These outcomes may be the result of a better understanding of the pathological anatomy in complex cases. Moreover, 3D printing helps the surgeon in preoperative planning of the surgical procedure by means of fracture reduction and the sizes and positioning of plates and screws for internal fixation. This could possibly reduce operation time and the amount of dissection of surrounding tissues and therefore blood loss[5]. In addition to trauma surgical applications, PSI allows the surgeon to perform precise osteotomies for deformity correction[5-8], which is specifically interesting for paediatric patients[9].

Correcting limb deformities in children is a challenging and complex type of surgery. Therefore, novel technologies such as 3D printing are increasingly applied, aiming to achieve more accurate corrections and improved outcomes[9]. The use of patient-specific 3D-printed models is specifically interesting and promising in paediatric orthopaedic surgery, as limb deformity corrections require [sh6] an individual 3D treatment. For example, the use of 3D printing in preoperative planning of hip preservation surgery created an improvement in trainee and patient education for understanding the abnormality of the patient's disorder[6]. However, due to its novelty, evidence on the use of 3D printing in pediatric orthopedics is still limited.

This editorial provides an overview of the various intraoperative applications of 3D printing in pediatric orthopedic surgery and assesses the overall role, challenges and future of this relatively novel technique.

TECHNICAL ASPECTS OF 3D PRINTING

3D printing, or additive layer manufacturing, is a technique to create a 3D object from a digital model. It is an advanced, computer-controlled technology that deposits successive layers of materials (*e.g.*, metals or plastic) to create an object. In contrast to traditional subtractive manufacturing processes that take away or shape material, 3D printing has the advantage to create complex structures by adding hundreds of miniscule layers that are fused together. Another advantage of 3D printing is the

possibility to create shapes of different materials including plastic, rubber, metals or ceramics[7,10].

The process of creating 3D-printed models for medical applications starts with high-resolution imaging (Figure 1)[7,8,10-12]. Multi-row detecting computed tomography (MDCT) and magnetic resonance imaging (MRI) are frequently used in orthopedics for diagnostics of complex anatomy or severe deformities[7,11-13]. MDCT is a high-contrast computed tomography (CT) that produces thin-section slices of less than 1 mm and therefore highly suitable for analysing bony structures. After acquiring the clinical dataset, MDCT images are stored according to a universal data format; standardized digital imaging and communications in medicine (DICOM). Post-processing software extracts these DICOM files[7,8,14]. This extraction process is called segmentation. It separates the outlines of different anatomical structures in each individual 2D image (slice) by using colour contrast to create separate objects. In the next phase, computer-aided design (CAD) software (*e.g.*, MIMICS or InPrint) combines all the individual 2D images (slices) and creates a virtual 3D initial object (Mesh creation)[7,8,10,14]. This makes it possible to see depth, angulation and diameters of the anatomical structure or pathology. Next, the 3D object is transformed into a file that is ready for printing. In some cases, the resolution of the radiology is suboptimal, or the 3D object has no clear boundaries. In these cases, a manual reconstruction of a 3D object can be performed (*i.e.*, ReplicatorG software) and anatomical corrections of the model can be made in this CAD software[7,8,14]. It also provides control of the filling of the model, with possibilities between 0% filling (shell alone) to 100% filling and makes the model more suitable for 3D printing or material of preference[7,8,10,14]. Once the CAD model is finalised, it is converted into a common 3D file format, stereolithography (SLA) file and sent to the appropriate 3D printer[2,7,8,14]. Post process, the materials first need to cool down before they can be used and consequently sterilization is required for intraoperative use[12].

Different types of 3D printing techniques have been used over the last years, including printers that use powder, melted polymers, gel, liquids, or a combination of these substances[7,8]. In the past, Fused Deposition Modeling (FDM) was used as a 3D printing technique, in which a movable nozzle places long, thin wire of thermoplastic material on top of each other. A 3D object is created layer by layer. It is a relatively cheap and fast production method to create anatomical models. However, the shape of a FDM print differs greatly in quality from a professional 3D printer[7,8,15,16]. Therefore, different 3D printing procedures are used for the production of patient-specific models and patient-specific surgical guides at this moment. Selective laser sintering (SLS) is a powder-based fusion technology that uses a laser beam to locally sinter polymer powder to build 3D objects layer by layer[7,8,15,16]. SLS uses bio-based polyamide materials and metals for 3D printing. Other 3D printing techniques are SLA and digital light processing (DLP) that use UV laser and a liquid bath containing a UV-sensitive liquid polymer[8,10,12,17]. This liquid is illuminated layer by layer by the laser where the liquid has to cure. The surface cures into a solid state and subsequently the surface raises one layer. The next layer is then exposed and cured. 3D-printed objects that are generated SLS, DLP and SLA can be sterilized and therefore can be used in the operating room.

INTRAOPERATIVE APPLICATIONS OF 3D PRINTING IN PEDIATRIC ORTHOPEDIC SURGERY

Intraoperative applications of 3D printing in pediatric orthopedics involve the creation of PSI to perform more accurate complex surgery or correct deformities. There are increasingly interesting and promising applications in both upper limb and lower limb deformities.

Upper limb

Currently, the most commonly described application of 3D printing in the upper extremity is the forearm, usually rotational impairment after malunited forearm fractures. Byrne *et al*[18] used 3D-printed patient-specific osteotomy guides and custom-made plates for multiplanar corrective osteotomies in 5 patients with posttraumatic malunion of the forearm. An angular correction of the ulna and radius of 9.9° and 10.0° was planned, respectively. They reported mean postoperative corrections of 10.1° and 10.8°, respectively. Forearm pronation improved from 68° to 87° and supination improved from 47° to 89°. Furthermore, a significant improvement in pain relief and grip strength was seen. Another prospective study enrolled 16

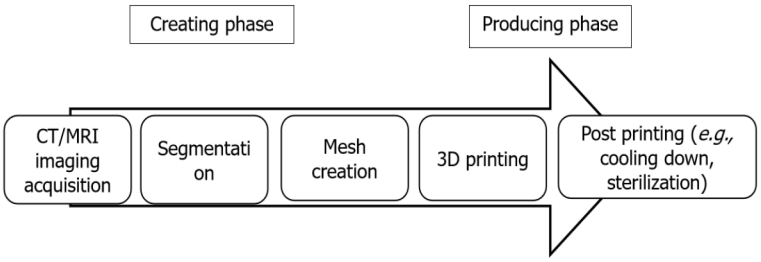


Figure 1 The process of three-dimensional printing. A high-resolution computed tomography (CT) or magnetic resonance imaging (MRI) scan is required for the data acquisition of the limb deformity. The data are used for the segmentation process where each anatomical structure is processed as an individual entity. Mesh creation uses this data to generate the process from the segmented anatomy models into a model that only retains the specific structures that must be used for three-dimensional (3D) printing. Then, the 3D-printed model is manufactured. The post-printing process includes cooling down the created model or sterilization for the use in the operating room. CT: Computed tomography; MRI: Magnetic resonance imaging; 3D: Three-dimensional.

patients with a total of 17 bone deformities, including distal radial malunion, distal humeral malunion and forearm diaphyseal malunion[19]. They reported that the use of 3D patient-matched instruments for corrective osteotomies showed a significant deformity improvement of 22.2°. Also, in patients treated for distal radial malunion and diaphyseal malunion, the flexion, extension and pronation of the forearm were significantly improved. Clinical implications as pain, range of motion, and grip strength were also significantly improved compared to the preoperative situation. Another study used 3D-printed templates to guide the osteotomy orientation in a posttraumatic forearm malunion of a 15-year-old female[3]. The authors reported that 3D-printed templates made it possible to achieve near-anatomical reduction close to 1° residual deformity in all three planes and a recovery to full function within 3 mo. One of our own cases presented with decreased rotational range of motion after sustaining a forearm fracture as a child, without improvement after extensive rehabilitation. 3D analysis determined the deformity and optimal planes of correction (Figure 2). Patient-specific osteotomy guides with predrilling of the screw holes were designed, and hardware for fixation was selected (Figure 2). The surgical procedure was then completed according to plan, which resulted in a vast improvement in range of motion and high patient satisfaction. In the period 2014-2020, 42 cases were operated using this technique, of which 16 were malunited forearms with rotational impairment. Most patients had a severe supination deficit (mean -10 degrees), which improved to a mean supination of +60 degrees. Pronation limitation was much less severe (mean +45 degrees) with a mean improvement to +55 degrees. We experienced one complication due to a transient posterior interosseous nerve paralysis, which recovered spontaneously within the first 6 wk after surgery. Thus, in deformities of the forearm due to malunion, the use of 3D PSI shows improvement in correction angles as well as in clinical outcomes as grip strength and pain relief[1,18,19]**.** Nevertheless, it is important to realize that the studies mentioned above are low-grade evidence and therefore the results need to be analysed with a critical view.

Cubitus varus deformities are sometimes seen after elbow fractures in children. Correction of this deformity is a complex surgical procedure and requires a 3D approach. Hu *et al*[20] included 35 patients and assigned them into two different groups comparing traditional surgery to surgery using an intraoperative patient-specific 3D-printed navigation template. All patients underwent similar surgery with wedge osteotomy of the lateral distal humerus. The 3D-printed patient-specific template significantly reduced the operation time with a mean of 11 min and significantly improves the accuracy of the correction by a mean of 3°. However, the question remains whether and accuracy of 3° is clinically relevant. Another study analysed 25 patients with cubitus varus deformity and compared a group of patient-specific 3D-printed osteotomy guides with a traditional group[21]. The 3D guiding template procedure resulted in a significant decrease of the operation time (almost 30 min), less intraoperative blood loss (17.5 mL) and higher satisfaction. However, the most important achievement of correcting deformities in pediatric orthopedics is recovery of function.

Lower limb

For lower limb paediatrics, 3D printing has been used for various complex techniques, including femoral and pelvic osteotomies and tarsal coalition resection[15,22]. Femoral and pelvic osteotomies with use of 3D guides have been applied for late sequelae of

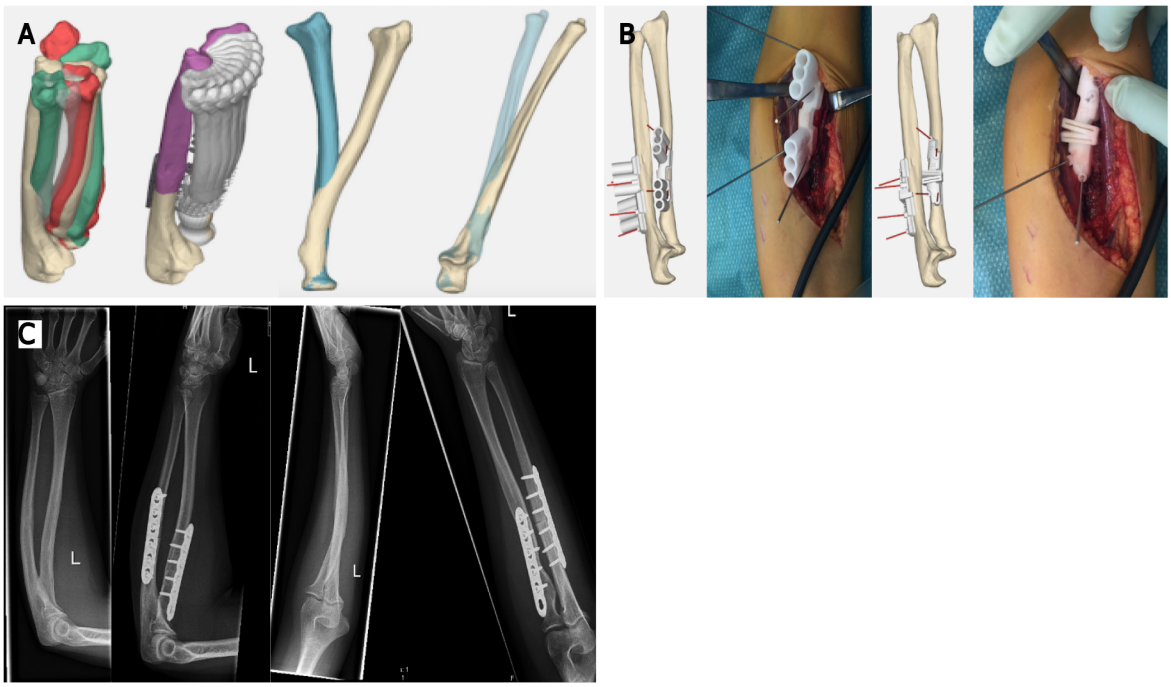


Figure 2 Three-dimensional-printed guides in posttraumatic rotational impairment of the forearm. This patient suffered from a decreased rotational range of motion due to malunion after a forearm fracture. The three-dimensional (3D) deformity in both bones of the forearm was assessed with 3D analysis. During this analysis the optimal planes of correction were determined, and potential gains were calculated with simulation of rotation of the forearm comparing the preoperative and postoperative situation. Patient-specific guides to perform the desired osteotomies with predrilling of the screw holes for the radius and ulna are shown here. The surgical procedure was completed as planned and resulted in a vast improvement in range of motion. A: Preoperative planning; B: Intraoperative use of 3D-printed patient specific guides; C: Preoperative and postoperative radiographs, showing correction of the flexion deformity of the ulna to an ulna with a normalized proximal ulna dorsal angulation, as well as correction of an S-shaped radial shaft to a normalized bowing configuration of the radial shaft.

developmental dysplasia of the hip (DDH), slipped capital femoral epiphysis (SCFE) and Legg-Calvé-Parthes (LCP) disease[15].

Severe DDH can lead to hip deformity that may require surgical correction. Zheng *et al*[23] compared 12 cases of femoral corrective osteotomy after DDH using patient-specific 3D navigation templates with 13 cases using conventional approaches[23]. No differences in varus and angles were reported. However, significantly decreased operation time (26 min) and fluoroscopy were reported in favour of the 3D-printed model group.

SCFE leads to a posterior and inferior displacement of the femoral head, giving an altered mobility of the hip joint and a syphon-shaped femoral neck after consolidation. A 3D sub- or intertrochanteric osteotomy can be performed for correction of the varus, internal rotation and flexion of the hip and thereby restoring its function. Cherkasskiy *et al*[24] used 3D models for proximal femoral osteotomy following SCFE and also found decreased operation and fluoroscopy times. We have used a CT-based 3D-printed model to plan and perform a complex osteotomy in a previously pinned SCFE case, with favourable results with regard to osteotomy precision, positioning of the implant, surgical time and use of the image intensifier (Figure 3). In this case the patient had a pre-operative externally rotated right hip of 40 degrees. Post-operatively, she was able to internally rotate the hip 10 degrees, compared to 20 degrees of internal rotation on the contralateral left side (Figure 3).

LCP disease can lead to deformity of the femoral head and an adaptive deformity of the acetabulum. Six patients with LCP disease were treated with a 3D-printed patient-specific osteotomy model[25]. The model allowed the surgeon to correct the femoral head almost identical to the contralateral healthy side[25].

A recent review confirmed that use of PSI for the above indications has led to improved accuracy and precision, decreased procedure times, and decreased intra-operative imaging requirements, compared to conventional methods of performing femoral or pelvic osteotomy[15].

3D techniques have also been used in pediatric foot orthopaedics. De Wouters *et al* [22] used 3D-printed PSI to guide the surgeon in removal of talocalcaneal and calcaneonavicular coalitions. It helped to orientate the saw blade for the resection of the bone bridge at the correct depth, which resulted in complete resections with no

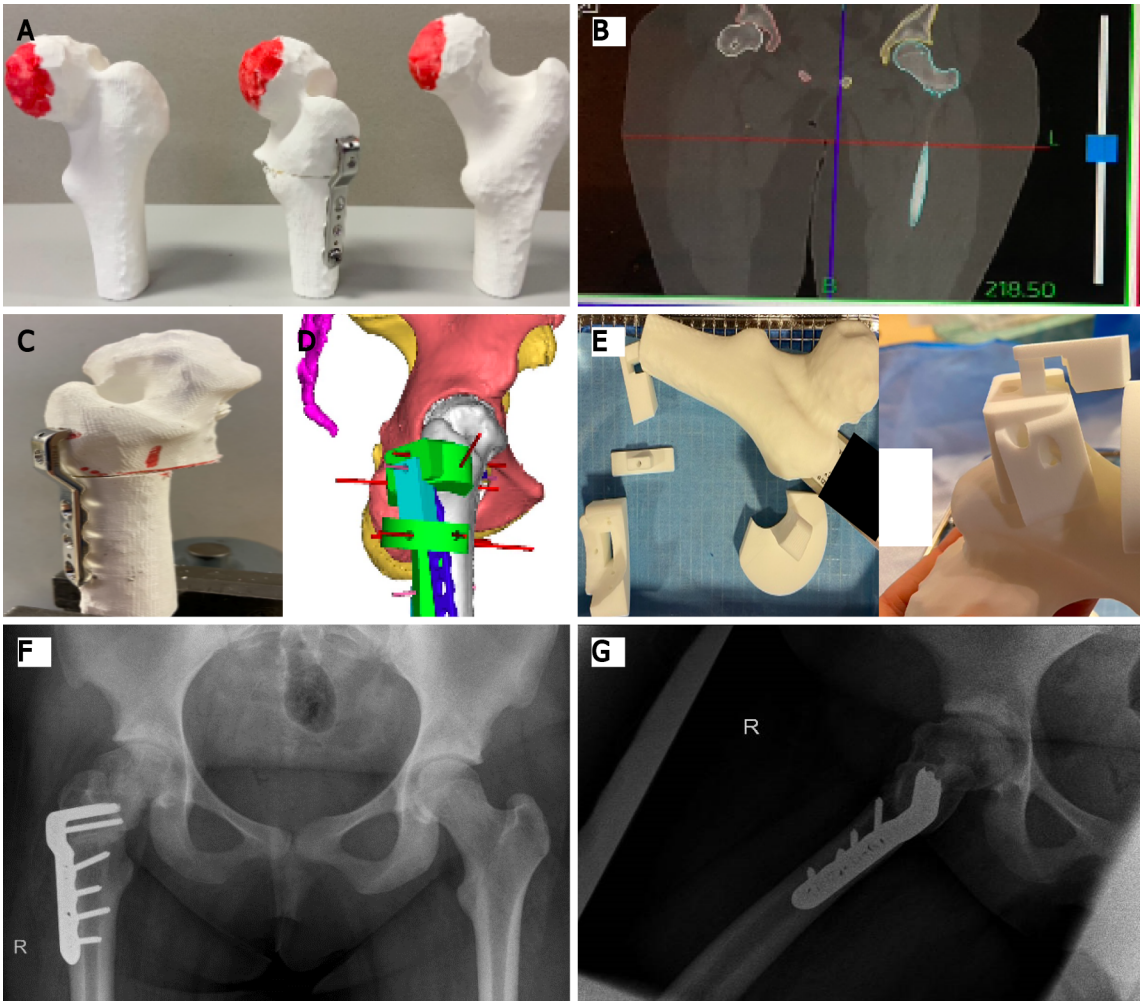


Figure 3 Three-dimensional printing for grade 3 slipped capital femoral epiphysis. This figure shows different steps required in a case of grade 3 slipped capital femoral epiphysis where three-dimensional (3D)-based templates for positioning of the implant were used, and guidance of the osteotomy during the surgical procedure was performed. A: Preoperative 3D-printed model of the deformed femoral head; B: High-resolution computed tomography scan for exact preoperative planning of deformity correction; C: Preoperative 3D-printed model of the deformed femoral head after correction; D: Analysis of the unique blade plate through 3D-computed view; E: The 3D-printed unique locking system; F: Postoperative anteroposterior radiograph; G: Postoperative lateral radiograph.

recurrence after a mean follow-up period of 18 mo. We have promising experience with 3D-guided resection of a calcaneonavicular coalition based on preoperative MRI (Figure 4).

ADDITIONAL APPLICATIONS OF 3D PRINTING IN PAEDIATRIC ORTHOPAEDICS

Over the last years, 3D printing has been successfully introduced in pediatric orthopaedics. Because of its seemingly endless possibilities, this relatively novel technique expands further than surgical applications alone.

In the technology of prosthetic limbs, 3D printing is increasingly used. Traditional prostheses for children with upper extremity amputees have been considered to be too heavy or too expensive to be a true benefit for a child[22]. In addition, children outgrow prostheses and may damage them[26]. In 3D printed prostheses, there is the possibility to replace a part of the prosthesis instead of the complete device[13]. Children are also allowed to choose the design and colour schemes, which make 3D-printed model prostheses more tailored to a child's choices. Therefore, children may be more self-confident, as described in various studies of 3D-printed upper limb replacement[13,27-29].

In the conservative treatment of paediatric fractures, two studies described the treatment of nondisplaced forearm fractures with a 3D-printed device compared to a traditional plaster cast[30,31]. The results showed an improvement of wrist function

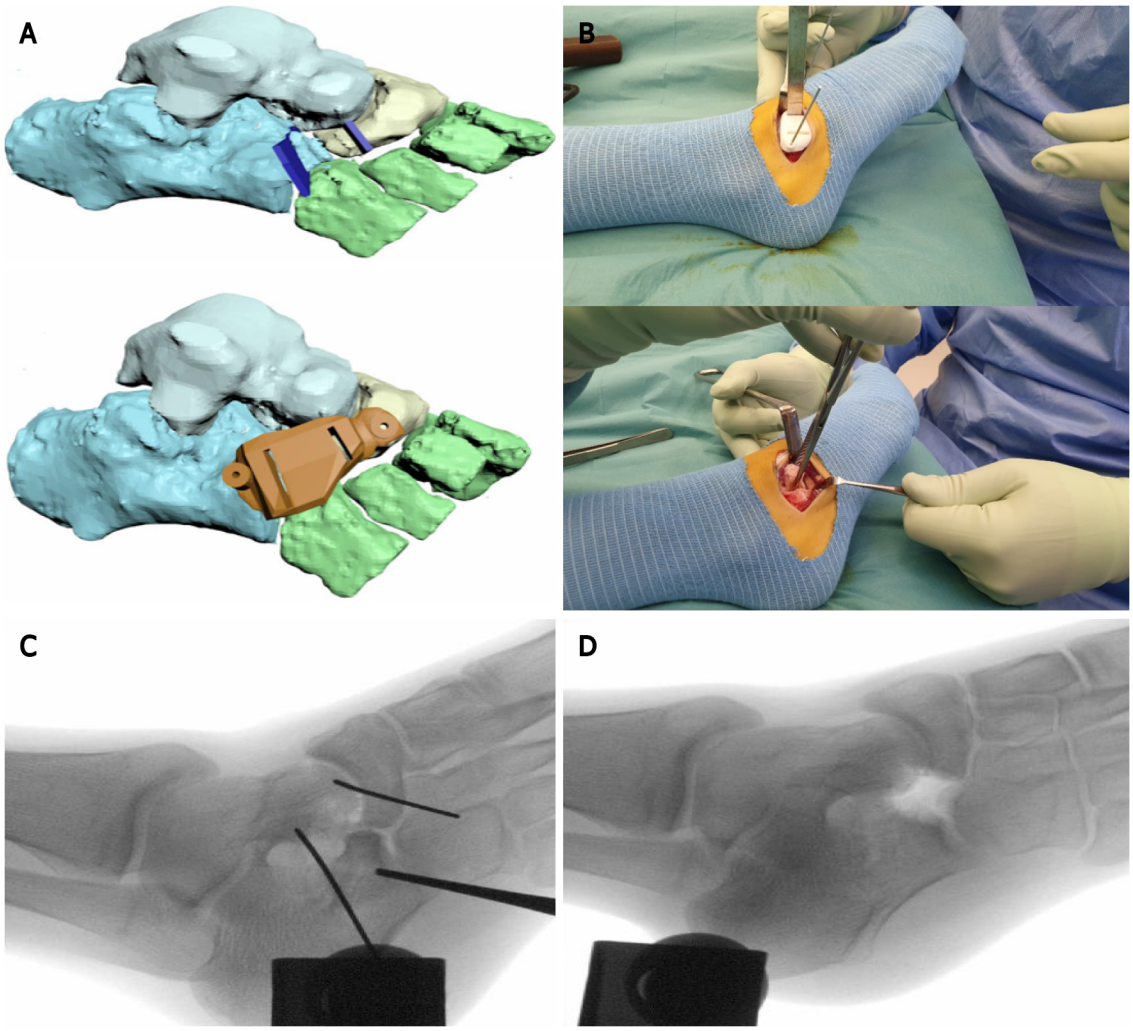


Figure 4 Preoperative planning and intraoperative use of three-dimensional-printing for a calcaneonaviculair coalition in a 14-year-old girl. A preoperative magnetic resonane imaging scan was used to manufacture a three-dimensional (3D)-printed osteotomy guide for removal of a calcaneonavicular coalition. A: Preoperative 3D-planning; B: Intraoperative use of the manufactured 3D-printed guide and coalition resection; C: Intraoperative fluoroscopy shows the position of K-wires to hold the 3D-printed guide; D: Intraoperative fluoroscopy shows the resected bone.

after immobilization with a 3D-printed device. Moreover, activities of everyday life, patient satisfaction and patient comfort during the immobilization were improved compared to the traditional cast group. In addition, the 3D-printed devices were reported to be lighter than traditional casts and removable, which make them more patient-friendly (*e.g.* when taking a shower). This suggests that a 3D device can also be an effective alternative approach in the conservative treatment of fractures in paediatric orthopaedics.

CHALLENGES AND FUTURE OF 3D PRINTING IN PAEDIATRIC ORTHOPAEDIC SURGERY

As outlined, 3D printing seems to have great potential in numerous paediatric orthopaedic applications. However, there are several challenges in this field that need further investigation and improvement.

Although the production time of a 3D product has decreased since it was invented, preparation and production of PSI still take at least several days[32]. Therefore, the application in the acute setting is challenging (*e.g.*, for fractures). However, research and development in 3D printing is a growing field of interest, resulting in new upcoming materials with better biomechanical and biocompatible characteristics. Furthermore, the development of 3D printers that can create models within hours is very promising.

Another challenge is reduction of radiation exposure. Although the use of fluoroscopy during the surgical procedure is reduced by using 3D PSI or 3D-printed model guiding templates[23,33], the total dose of radiation might not be decreased *per* case. A preoperative high-resolution CT scan is usually obtained to produce a 3D image, which is additional radiation exposure to the child[16,32]. Instead, the use of MRI would help reduce the radiation exposure, with the possible additional advantage of a more detailed image of the paediatric anatomic structures (*e.g.*, physeal bar, periosteum and soft tissue)[10]. However, the process of undergoing an MRI scan is more difficult for very young children (under the age of 5), because of the necessity of sedation, motion reduction and/or accelerated imaging[7,8,17,34,35]. Moreover, studies using MRI for preoperative imaging acquisition in 3D processes are scarce. Our case shows the potential of MRI to produce surgical 3D guides (Figure 4).

In addition, 3D printing requires advanced technology and financial resources, which may not be available in developing countries[32]. However, printing costs seem to decrease over time[36] and costs of 3D printing may be outweighed by saving operation time. A cost analysis showed that using 3D-printed models saved a mean operating time of 62 min, translated to $3720 *per* case compared to conventional techniques[37]. Due to the ambiguity in evidence on the cost-savings of using 3D-printed models in paediatric orthopaedic surgery, an in-depth cost analysis is required of production costs *vs* potential savings obtained by improved intraoperative results [5].

Finally, more scientific evidence is required on the use of 3D techniques in paediatric orthopaedic surgery. Despite the fact that the current literature shows promising results for various indications as discussed, randomized trials on 3D printing compared to conventional methods are still lacking. It is likely to expect that 3D printing will be mainly beneficial for complex surgical cases.

CONCLUSION

3D printing is a promising technique for numerous upper and lower limb surgical applications in paediatric orthopaedics. In upper limb surgery, 3D has been most frequently used in posttraumatic deformities. In lower limb surgery, 3D-printed models are mostly used to correct congenital and developmental deformities of the hip. Other applications of 3D-printed models include limb prostheses and non-surgical treatment of fractures. Future possibilities of this exciting technique are numerous.

The affordability of 3D printers has increased over the years, and literature shows that using 3D-printed models for PSI or intraoperative guiding reduces the operating time and radiation exposure. Moreover, an improved accuracy of deformity correction is attained. However, most studies have a low level of evidence. Moreover, using 3D-printed models in pediatric orthopaedic surgery is complex due to growth of children and therefore, the moment of planning *vs* the timing of the surgery is also a challenge to overcome. All in all, more research, preferably randomized controlled studies, is required to compare conventional approaches and the intraoperative use of 3D-printed models. Nevertheless, the use of 3D-printed models as an intraoperative tool seems to have great future potential in complex pediatric orthopaedic surgical procedures.

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REFERENCES

1 **Chae MP**, Rozen WM, McMenamin PG, Findlay MW, Spychal RT, Hunter-Smith DJ. Emerging Applications of Bedside 3D Printing in Plastic Surgery. *Front Surg* 2015; **2**: 25 [PMID: 26137465 DOI: 10.3389/fsurg.2015.00025]

2 **Giannopoulos AA**, Steigner ML, George E, Barile M, Hunsaker AR, Rybicki FJ, Mitsouras D. Cardiothoracic Applications of 3-dimensional Printing. *J Thorac Imaging* 2016; **31**: 253-272 [PMID: 27149367 DOI: 10.1097/RTI.0000000000000217]

3 **Jeuken RM**, Hendrickx RPM, Schotanus MGM, Jansen EJ. Near-anatomical correction using a CT-guided technique of a forearm malunion in a 15-year-old girl: A case report including surgical

technique. *Orthop Traumatol Surg Res* 2017; **103**: 783-790 [PMID: 28428034 DOI: 10.1016/j.otsr.2017.03.017]

4 **D'Urso PS**, Askin G, Earwaker JS, Merry GS, Thompson RG, Barker TM, Effeney DJ. Spinal biomodeling. *Spine (Phila Pa 1976)* 1999; **24**: 1247-1251 [PMID: 10382253 DOI: 10.1097/00007632-199906150-00013]

5 **Morgan C**, Khatri C, Hanna SA, Ashrafian H, Sarraf KM. Use of three-dimensional printing in preoperative planning in orthopaedic trauma surgery: A systematic review and meta-analysis. *World J Orthop* 2020; **11**: 57-67 [PMID: 31966970 DOI: 10.5312/wjo.v11.i1.57]

6 **Bockhorn L**, Gardner SS, Dong D, Karmonik C, Elias S, Gwathmey FW, Harris JD. Application of three-dimensional printing for pre-operative planning in hip preservation surgery. *J Hip Preserv Surg* 2019; **6**: 164-169 [PMID: 31660202 DOI: 10.1093/jhps/hnz023]

7 **Garcia J**, Yang Z, Mongrain R, Leask RL, Lachapelle K. 3D printing materials and their use in medical education: a review of current technology and trends for the future. *BMJ Simul Technol Enhanc Learn* 2018; **4**: 27-40 [PMID: 29354281 DOI: 10.1136/bmjstel-2017-000234]

8 **Wong KC**. 3D-printed patient-specific applications in orthopedics. *Orthop Res Rev* 2016; **8**: 57-66 [PMID: 30774470 DOI: 10.2147/ORR.S99614]

9 **Ma L**, Zhou Y, Zhu Y, Lin Z, Wang Y, Zhang Y, Xia H, Mao C. 3D-printed guiding templates for improved osteosarcoma resection. *Sci Rep* 2016; **6**: 23335 [PMID: 26997197 DOI: 10.1038/srep23335]

10 **Starosolski ZA**, Kan JH, Rosenfeld SD, Krishnamurthy R, Annapragada A. Application of 3-D printing (rapid prototyping) for creating physical models of pediatric orthopedic disorders. *Pediatr Radiol* 2014; **44**: 216-221 [PMID: 24202430 DOI: 10.1007/s00247-013-2788-9]

11 **Jovičić MŠ**, Vuletić F, Ribičić T, Šimunić S, Petrović T, Kolundžić R. Implementation of the three-dimensional printing technology in treatment of bone tumours: a case series. *Int Orthop* 2021; **45**: 1079-1085 [PMID: 32901331 DOI: 10.1007/s00264-020-04787-4]

12 **Parthasarathy J**, Krishnamurthy R, Ostendorf A, Shinoka T. 3D printing with MRI in pediatric applications. *J Magn Reson Imaging* 2020; **51**: 1641-1658 [PMID: 31329332 DOI: 10.1002/jmri.26870]

13 **Zuniga JM**, Young KJ, Peck JL, Srivastava R, Pierce JE, Dudley DR, Salazar DA, Bergmann J. Remote fitting procedures for upper limb 3d printed prostheses. *Expert Rev Med Devices* 2019; **16**: 257-266 [PMID: 30661413 DOI: 10.1080/17434440.2019.1572506]

14 **Tack P**, Victor J, Gemmel P, Annemans L. 3D-printing techniques in a medical setting: a systematic literature review. *Biomed Eng Online* 2016; **15**: 115 [PMID: 27769304 DOI: 10.1186/s12938-016-0236-4]

15 **Baraza N**, Chapman C, Zakani S, Mulpuri K. 3D - Printed Patient Specific Instrumentation in Corrective Osteotomy of the Femur and Pelvis: A Review of the Literature. *3D Print Med* 2020; **6**: 34 [PMID: 33170384 DOI: 10.1186/s41205-020-00087-0]

16 **Furlow B**. Radiation protection in pediatric imaging. *Radiol Technol* 2011; **82**: 421-439 [PMID: 21572064]

17 **Jaimes C**, Gee MS. Strategies to minimize sedation in pediatric body magnetic resonance imaging. *Pediatr Radiol* 2016; **46**: 916-927 [PMID: 27229508 DOI: 10.1007/s00247-016-3613-z]

18 **Byrne AM**, Impelmans B, Bertrand V, Van Haver A, Verstreken F. Corrective Osteotomy for Malunited Diaphyseal Forearm Fractures Using Preoperative 3-Dimensional Planning and Patient-Specific Surgical Guides and Implants. *J Hand Surg Am* 2017; **42**: 836.e1-836.e12 [PMID: 28709790 DOI: 10.1016/j.jhsa.2017.06.003]

19 **Oka K**, Tanaka H, Okada K, Sahara W, Myoui A, Yamada T, Yamamoto M, Kurimoto S, Hirata H, Murase T. Three-Dimensional Corrective Osteotomy for Malunited Fractures of the Upper Extremity Using Patient-Matched Instruments: A Prospective, Multicenter, Open-Label, Single-Arm Trial. *J Bone Joint Surg Am* 2019; **101**: 710-721 [PMID: 30994589 DOI: 10.2106/JBJS.18.00765]

20 **Hu X**, Zhong M, Lou Y, Xu P, Jiang B, Mao F, Chen D, Zheng P. Clinical application of individualized 3D-printed navigation template to children with cubitus varus deformity. *J Orthop Surg Res* 2020; **15**: 111 [PMID: 32192482 DOI: 10.1186/s13018-020-01615-8]

21 **Zhang YW**, Xiao X, Gao WC, Xiao Y, Zhang SL, Ni WY, Deng L. Efficacy evaluation of three-dimensional printing assisted osteotomy guide plate in accurate osteotomy of adolescent cubitus varus deformity. *J Orthop Surg Res* 2019; **14**: 353 [PMID: 31706346 DOI: 10.1186/s13018-019-1403-7]

22 **de Wouters S**, Tran Duy K, Docquier PL. Patient-specific instruments for surgical resection of painful tarsal coalition in adolescents. *Orthop Traumatol Surg Res* 2014; **100**: 423-427 [PMID: 24793905 DOI: 10.1016/j.otsr.2014.02.009]

23 **Zheng P**, Yao Q, Xu P, Wang L. Application of computer-aided design and 3D-printed navigation template in Locking Compression Pediatric Hip Plate™ placement for pediatric hip disease. *Int J Comput Assist Radiol Surg* 2017; **12**: 865-871 [PMID: 28190127 DOI: 10.1007/s11548-017-1535-3]

24 **Cherkasskiy L**, Caffrey JP, Szewczyk AF, Cory E, Bomar JD, Farnsworth CL, Jeffords M, Wenger DR, Sah RL, Upasani VV. Patient-specific 3D models aid planning for triplane proximal femoral osteotomy in slipped capital femoral epiphysis. *J Child Orthop* 2017; **11**: 147-153 [PMID: 28529664 DOI: 10.1302/1863-2548-11-170277]

25 **Fürnstahl P**, Casari FA, Ackermann J, Marcon M, Leunig M, Ganz R. Computer-assisted femoral head reduction osteotomies: an approach for anatomic reconstruction of severely deformed Legg-Calv é-Perthes hips. A pilot study of six patients. *BMC Musculoskelet Disord* 2020; **21**: 759 [PMID: 33208124 DOI: 10.1186/s12891-020-03789-y]

26 **Aimar A**, Palermo A, Innocenti B. The Role of 3D Printing in Medical Applications: A State of the Art. *J Healthc Eng* 2019; **2019**: 5340616 [PMID: 31019667 DOI: 10.1155/2019/5340616]

27 **Gálvez JA**, Gralewski K, McAndrew C, Rehman MA, Chang B, Levin LS. Assessment and Planning for a Pediatric Bilateral Hand Transplant Using 3-Dimensional Modeling: Case Report. *J Hand Surg Am* 2016; **41**: 341-343 [PMID: 26810827 DOI: 10.1016/j.jhsa.2015.12.010]

28 **Gurnaney HG**, Fiadjoe JE, Levin LS, Chang B, Delvalle H, Gálvez J, Rehman MA. Anesthetic management of the first pediatric bilateral hand transplant. *Can J Anaesth* 2016; **63**: 731-736 [PMID: 26951450 DOI: 10.1007/s12630-016-0625-y]

29 **Tanaka KS**, Lightdale-Miric N. Advances in 3D-Printed Pediatric Prostheses for Upper Extremity Differences. *J Bone Joint Surg Am* 2016; **98**: 1320-1326 [PMID: 27489324 DOI: 10.2106/JBJS.15.01212]

30 **Chen Y**, Lin H, Yu Q, Zhang X, Wang D, Shi L, Huang W, Zhong S. Application of 3D-Printed Orthopedic Cast for the Treatment of Forearm Fractures: Finite Element Analysis and Comparative Clinical Assessment. *Biomed Res Int* 2020; **2020**: 9569530 [PMID: 32775455 DOI: 10.1155/2020/9569530]

31 **Guida P**, Casaburi A, Busiello T, Lamberti D, Sorrentino A, Iuppariello L, D'Albore M, Colella F, Clemente F. An alternative to plaster cast treatment in a pediatric trauma center using the CAD/CAM technology to manufacture customized three-dimensional-printed orthoses in a totally hospital context: a feasibility study. *J Pediatr Orthop B* 2019; **28**: 248-255 [PMID: 30768580 DOI: 10.1097/BPB.0000000000000589]

32 **Iobst CA**. New Technologies in Pediatric Deformity Correction. *Orthop Clin North Am* 2019; **50**: 77-85 [PMID: 30477708 DOI: 10.1016/j.ocl.2018.08.003]

33 **Zheng P**, Xu P, Yao Q, Tang K, Lou Y. 3D-printed navigation template in proximal femoral osteotomy for older children with developmental dysplasia of the hip. *Sci Rep* 2017; **7**: 44993 [PMID: 28322290 DOI: 10.1038/srep44993]

34 **Barnea-Goraly N**, Weinzimer SA, Ruedy KJ, Mauras N, Beck RW, Marzelli MJ, Mazaika PK, Aye T, White NH, Tsalikian E, Fox L, Kollman C, Cheng P, Reiss AL; Diabetes Research in Children Network (DirecNet). High success rates of sedation-free brain MRI scanning in young children using simple subject preparation protocols with and without a commercial mock scanner--the Diabetes Research in Children Network (DirecNet) experience. *Pediatr Radiol* 2014; **44**: 181-186 [PMID: 24096802 DOI: 10.1007/s00247-013-2798-7]

35 **de Bie HM**, Boersma M, Wattjes MP, Adriaanse S, Vermeulen RJ, Oostrom KJ, Huisman J, Veltman DJ, Delemarre-Van de Waal HA. Preparing children with a mock scanner training protocol results in high quality structural and functional MRI scans. *Eur J Pediatr* 2010; **169**: 1079-1085 [PMID: 20225122 DOI: 10.1007/s00431-010-1181-z]

36 **Hoang D**, Perrault D, Stevanovic M, Ghiassi A. Surgical applications of three-dimensional printing: a review of the current literature & how to get started. *Ann Transl Med* 2016; **4**: 456 [PMID: 28090512 DOI: 10.21037/atm.2016.12.18]

37 **Ballard DH**, Mills P, Duszak R Jr, Weisman JA, Rybicki FJ, Woodard PK. Medical 3D Printing Cost-Savings in Orthopedic and Maxillofacial Surgery: Cost Analysis of Operating Room Time Saved with 3D Printed Anatomic Models and Surgical Guides. *Acad Radiol* 2020; **27**: 1103-1113 [PMID: 31542197 DOI: 10.1016/j.acra.2019.08.011]

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REVIEW

Regional anesthesia for orthopedic procedures: What orthopedic surgeons need to know

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Abstract

Regional anesthesia is an integral component of successful orthopedic surgery. Neuraxial anesthesia is commonly used for surgical anesthesia while peripheral nerve blocks are often used for postoperative analgesia. Patient evaluation for regional anesthesia should include neurological, pulmonary, cardiovascular, and hematological assessments. Neuraxial blocks include spinal, epidural, and combined spinal epidural. Upper extremity peripheral nerve blocks include interscalene, supraclavicular, infraclavicular, and axillary. Lower extremity peripheral nerve blocks include femoral nerve block, saphenous nerve block, sciatic nerve block, iPACK block, ankle block and lumbar plexus block. The choice of regional anesthesia is a unanimous decision made by the surgeon, the anesthesiologist, and the patient based on a risk-benefit assessment. The choice of the regional block depends on patient cooperation, patient positing, operative structures, operative manipulation, tourniquet use and the impact of post-operative motor blockade on initiation of physical therapy. Regional anesthesia is safe but has an inherent risk of failure and a relatively low incidence of complications such as local anesthetic systemic toxicity (LAST), nerve injury, falls, hematoma, infection and allergic reactions. Ultrasound should be used for regional anesthesia procedures to improve the efficacy and minimize complications. LAST treatment guidelines and rescue medications (intralipid) should be readily available during the regional anesthesia administration.

Key Words: Orthopedic surgery; Regional anesthesia; Spinal; Epidural; Combined spinal epidural; Peripheral nerve blocks; Neuraxial blocks; Upper extremity; Lower extremity; Interscalene; Supraclavicular; Infraclavicular; Axillary; Femoral; Fascia iliaca; Popliteal; Sciatic; Saphenous; Adductor canal; Lumbar plexus; Brachial plexus; Ankle; iPACK; Complication; Local anesthetic systemic toxicity; Nerve injury; Block failure; Continuous nerve block catheters

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Core Tip: Understanding the fundamentals of regional anesthesia techniques for orthopedic surgery is essential for superior clinical outcomes and optimal patient safety. The choice of a regional technique requires a well-informed shared decision making process that encompass the anatomical coverage of the block, density of the block, duration of the block, patient positioning considerations, existing comorbidities, side effects, complications, advantages, disadvantages, positioning and impact on postoperative recovery. A risk-benefit analysis that achieves superior clinical outcomes can be only performed if the perioperative team has a profound understanding of the fundamentals of regional anesthesia administration.

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INTRODUCTION

Orthopedic surgery is one of the most rapidly growing surgical specialties in the world. A total of 22.3 million orthopedic surgical procedures were performed worldwide in 2017. The number of annual orthopedic procedures is forecasted to increase 4.9% annually, approaching 28.3 million surgeries by the year 2022[1]. Anesthetic techniques for orthopedic surgical procedures include general and regional anesthesia techniques. Over the past decades, regional anesthesia has become the anesthetic technique of choice for many orthopedic procedures. Regional anesthesia entails the injection of local anesthetic solution to interrupt signal transmission in peripheral nerves or spinal nerve roots that provide sensory and motor supply to operative structures.

The use of regional anesthesia for orthopedic procedures mitigates some of the complications associated with general anesthesia such as nausea, vomiting, airway trauma, hypoxia, respiratory depression, and the risk of pulmonary aspiration[2,3]. Advantages of regional anesthesia for orthopedic surgeries include superior postoperative pain control, reduction in opioid consumption, reduced opioid-associated side effects[4-12], shorter hospital stay[7,8,11-13], early initiation of physical therapy[7,11], reduced hospital readmission rate[14], higher patient satisfaction[4,11], faster recovery[15], reduced unanticipated admissions due to uncontrolled pain[16], improved intraoperative muscle relaxation, decreased intraoperative blood loss[11,12], and a reduction in postoperative urinary retention and ileus formation[8].

Although regional blocks are often administered by the anesthesiologist, it is important for the orthopedic surgeon to have an understanding of the relevant clinical aspects of the blocks in order to optimize patient safety, maximize perioperative efficiency, and improve clinical outcomes. In this article, we review the techniques of regional anesthesia used for orthopedic procedures.

TYPES OF REGIONAL ANESTHESIA

Regional anesthesia can be broadly divided into two categories: neuraxial anesthesia [spinal, epidural, combined spinal epidural (CSE)], and peripheral nerve blocks (upper and lower extremity blocks).

Neuraxial anesthesia

Neuraxial anesthesia (NA) is the process of placing a needle or a catheter between the vertebrae and injecting medications into the epidural (epidural anesthesia) or subarachnoid space (spinal anesthesia). The target of NA is the spinal nerve root. Medication injected neuraxially is primarily local anesthetics with adjuncts such as preservative free opioids. NA is commonly used for abdominal and lower extremity surgeries. The sensory level required for a specific surgery is determined by the extent

of surgical incision and surgical manipulation. Total hip arthroplasty (THA), open reduction and internal fixation of femur, and hip fractures require a sensory level of T10, whereas knee procedures require a sensory level of L1.

Spinal anesthesia is typically administered as a single injection, while epidural anesthesia is usually administered *via* an indwelling catheter for continuous infusion. CSE anesthesia is administered as a combination of both techniques. Anesthetic duration associated with the single shot approach used in the spinal technique is limited to the duration of action of the injected medication. The extent of spinal blockade (level) depends on the total dose of local anesthetic mixture, baricity of the injected solution, and patient position after the block. An epidural catheter allows for the continuous infusion of medications prolonging the duration of anesthesia. The spinal anesthesia needle is typically inserted at the level of L2-L3 interspace or below, to avoid trauma to the termination of the conus medullaris. The needle insertion point for epidural anesthesia depends on the extent of the dermatomes required to be anesthetized for the procedure. For orthopedic procedures, it is usually placed in the mid to low lumbar region. The extent of epidural blockade is determined by the volume of local anesthetic injected while density of the block is determined by the concentration of the local anesthetic. Compared to epidural anesthesia, spinal anesthesia produces a denser and more reliable block with lower incidence of block failure.

Peripheral nerve blocks

Peripheral nerve blocks (PNB) entails injecting a local anesthetic (LA) solution in proximity to a specific nerve or nerve bundle to produce a sensory and motor blockade of a specific region of the body. The LA blocks the transmission of painful impulse to the central nervous system. PNB can be used for surgical anesthesia or postoperative analgesia. It is commonly administered as a single shot, but a continuous infusion catheter can be placed to prolong the postoperative analgesic effect. PNB is commonly performed under ultrasound guidance to reduce the risks of intraneural and intravascular injection of LA, avoid peripheral nerve trauma, and to ensure proper delivery of the LA for a successful block. Upper extremity nerve blocks are performed at the level of the brachial plexus. Depending on the surgical site, various nerve blocks can be performed at different levels of the plexus. These blocks include interscalene block, supraclavicular block, infraclavicular block, and axillary block. Lower extremity nerve blocks include femoral nerve block, saphenous nerve block, Sciatic nerve block, iPACK (Infiltration between the Popliteral Artery and Capsule of the Knee) block, ankle block, and lumbar plexus block.

EVALUATING THE ORTHOPEDIC PATIENT FOR REGIONAL ANESTHESIA

Prior to considering a regional anesthetic for a patient, a thorough history and targeted physical examination should be performed to identify risk factors related to the nervous, pulmonary, cardiovascular, and hematologic systems that may affect the safety and efficacy of the nerve block. Certain patient factors may increase the potential for block failure, such as patient obesity[17]. Local skin infection, or systemic infection, may preclude a patient from receiving a regional anesthetic. The decision to proceed with a regional anesthesia block should be collectively agreed upon by the patient, the surgeon, and the anesthesiologist. For patients on anticoagulation / antiplatelet medications receiving superficial peripheral nerve blocks, the decision to proceed is largely dependent on a careful analysis of factors including site compressibility, vascularity, and consequences of bleeding, should it occur. This is often determined on a case-by-case basis.

The nervous system

A comprehensive neurological evaluation should be performed to assess for any pre-existing nervous system condition or nerve injury in the region of the block. Patients with multiple sclerosis may experience a flare up of symptoms with spinal anesthesia. Thus, epidural or general anesthesia may be preferable for these patients. Neuraxial anesthesia in patients with a history of extensive spine surgery with instrumentation may be technically difficult and may result in an inadequate anesthetic level. Scoliosis may increase the difficulty of placing a neuraxial anesthetic. Potential postoperative motor and sensory weakness after a regional anesthetic should be considered. For example, lower extremity motor weakness following a femoral nerve block may limit the patient's ability to participate in therapy post-operatively; as such, an alternative

motor-sparing technique should be considered[18].

The respiratory system

Patients who have a history of severe reactive or obstructive airway disease may benefit from the use of regional anesthesia to avoid airway manipulation and respiratory depression associated with general anesthesia. Pre-operative pulmonary function should be assessed, especially during the performance of upper extremity blocks that may anesthetize the phrenic nerve potentially causing respiratory distress. This may have significant impact on the respiratory function in patients with asthma, chronic obstructive pulmonary disease, or pre-existing diaphragmatic dysfunction [19]. An alternative regional anesthetic approach, such as the axillary block, may be performed in these patients[19].

The cardiovascular system

Patients with a history of severe cardiovascular disease often have an elevated risk of major complications after receiving general anesthesia. Regional anesthesia remains an excellent alternative for these patients and can be associated with lower rates of major cardiac complications[20]. It is important to consider cardiac contraindications for certain regional techniques. Neuraxial anesthesia has widely been contraindicated in the case of severe aortic stenosis and congestive heart failure, due to the sudden decrease in vascular tone and cardiac output. However, a carefully managed neuraxial anesthetic may be appropriate for some of these patients[21,22]. Patients with significant cardiac disease benefit from the gradual onset of epidural anesthesia allowing for careful and slow titration of LA rather than the rapid onset block induced by a single-shot spinal anesthetic.

The hematologic system

Patients who have a history of bleeding disorders or are currently receiving anticoagulants or antiplatelet medications are at an increased risk of bleeding complications after receiving a regional anesthetic. It is important to perform a thorough review of the patient's current medications prior to proceeding with a neuraxial anesthetic or peripheral nerve block. With the advent of novel anticoagulants, perioperative guidelines for regional anesthesia should consistently be adhered to[23].

Laboratory findings consistent with thrombocytopenia or coagulopathy may preclude the administration of regional anesthesia, due to the increased risk of bleeding. Excessive bleeding in neuraxial anesthesia may lead to a spinal hematoma and subsequent adverse neurological consequences. The American Society of Regional Anesthesia (ASRA) has published guidelines for the management of patients receiving antithrombotic or antiplatelet medications[23]. The ASRA guidelines are reviewed in Table 1. Patients who are on certain antiplatelet medications, such as low dose aspirin, may be candidates for peripheral nerve blockade or neuraxial anesthesia[23]. This decision is based on a risk-benefit assessment, taking into account considerations such as site compressibility and underlying bleeding disorders.

BLOCKS FOR UPPER EXTREMITY ORTHOPEDIC PROCEDURES

Understanding upper extremity peripheral nerve blockade requires a detailed knowledge of the brachial plexus anatomy. The muscular and the cutaneous nerve supply of the upper extremity derives mostly from the brachial plexus. The brachial plexus is comprised of ventral nerve roots (rami) of 5 spinal nerve (C5-T1) giving rise to trunks, divisions, cords and terminal branches. The nerve roots merge to form upper, middle and lower trunks. The 3 trunks split to form 6 divisions which merge to form 3 cords; lateral, posterior and medial cords. The nerves supplying most of the upper extremity are the terminal branches of the 3 cords. The cutaneous portion of the shoulder and upper arm is supplemented by nerves that are not part of the brachial plexus[24]. The superior aspect of the shoulder receives sensory innervation by the superficial cervical plexus (C3-C4) *via* the supraclavicular nerve. Seventy percent of the sensory innervation to the shoulder comes from the superior trunk *via* the suprascapular nerve with most of the contributions being from the C5 and C6 nerve roots [25]. The axilla is innervated by the second thoracic nerve root. The brachial plexus is blocked at four different levels: At the level of roots-trunks *via* the interscalene block, at the level of trunks-divisions *via* the supraclavicular block, at the level of cords *via* the infraclavicular block, and at the level of the terminal branches *via* the axillary block. A summary of upper extremity peripheral nerve blocks is included in Table 2.

Table 1 American Society of Regional Anesthesia guidelines for anticoagulant and antiplatelet drugs

Medication	Minimum time between last dose of medication and neuraxial injection or catheter placement	Minimum time after nerve/neuraxial cathether placement and administration of drug	Minimum time between last dose of drug and cathether removal	Minimum time between neuraxial injection or cathether removal and administration of drug
Anticoagulants for venous thromboembolism prophylaxis				
Enoxaparin (Lovenox); prophylaxis, once daily	12 h	≥ 12 h	≥ 12 h	4 h
Enoxaparin (Lovenox); prophylaxis, b.i.d.	12 h	Contraindicated while catheter in place		4 h
Heparin SQ; prophylaxis; low-dose, b.i.d. and t.i.d.	4-6 h	Immediately	4-6 h	Immediately
Heparin SQ; prophylaxis; higher-dose, b.i.d. and t.i.d.	12 h and assessment of coagulation status	Safety of indwelling catheters has not been established for doses > 5000 Units SQ or total daily dose > 15000 Units SQ. Risk/benefit assessment required		Immediately
Dalteparin (Fragmin); prophylaxis, once daily	12 h	≥ 12 h	12 h	4 h
Anticoagulants at therapeutic doses				
Heparin IV; full Dose	4-6 h and normal coagulation status	1 h, with close monitoring	4-6 h and normal coagulation status	1 h
Heparin SQ; therapeutic dose	24 h and assessment of coagulation status	Contraindicated while catheter in place		Immediately
Enoxaparin (Lovenox); therapeutic dose	24 h, consider checking anti-factor Xa level	Contraindicated while catheter in place		4 h
Apixaban (Eliquis)	72 h	Contraindicated while catheter in place		6 h
Rivaroxaban (Xarelto)	72 h	Contraindicated while catheter in place		6 h
Warfarin (Coumadin)	5 d and normal INR	Variable instructions regarding management of catheter		Immediately
Anti-platelet medications				
NSAID's	No restrictions, may increase risk of bleeding			
Aspirin	No restrictions, may increase risk of bleeding			
Plavix	5-7 d	24 h postoperatively; catheter may be maintained for 1-2 d due to delayed antiplatelet effect		Immediately if no loading dose given
Ticlodipine (Ticlid)	10 days	24 h postoperatively; catheter may be maintained for 1-2 d due to delayed antiplatelet effect		Immediately if no loading dose given
Ticagrelor (Brillinta)	5-7 d	Contraindicated while catheter in place		Immediately if no loading dose given

NSAID: Non-steroidal anti-inflammatory drug.

Table 2 Summary of upper extremity peripheral nerve blocks

Block	Clinical application	Nerves blocked	Anatomical landmarks	Advantages	Disadvantages	Complications
Interscalene nerve block	Surgeries involving the shoulder, proximal aspect of humerus and the distal aspect of the clavicle	(1) Brachial plexus:C5 to C7; and (2) Cervical plexus: Supraclavicular nerve (C3 and C4)	LA injected between anterior and middle scalene muscles lateral to carotid artery and internal jugular vein	(1) Easy to perform; and (2) Comfortable for the patient	(1) Hemidiaphragmatic paralysis leading to respiratory compromise in patients with severe COPD; and (2) Not sufficient for elbow, forearm or hand surgeries	(1) Phrenic nerve palsy (100%); (2) Horner syndrome; and (3) Hoarseness
Supraclavicular nerve block	Surgery of the arm, elbow, forearm and hand. Extension into the interscalene area can cover shoulder procedures	C5-T1	LA injected above the clavicle between anterior and middle scalene muscles at the level of the first rib, where the subclavian artery crosses over it	(1) Fast onset; (2) Easier to perform; and (3) Comfortable for the patient	Relatively higher incidence of pneumothorax	(1) Pneumothorax; (2) Phrenic nerve palsy; and (3) Hoarseness
Infraclavicular nerve block	Surgery of the arm, elbow, forearm and hand	C5-T1	LA injected around the axillary artery below the clavicle, medial to coracoid process	Good choice for catheter placement	(1) Deeper block to perform; and (2) Greater discomfort during block placement	Pneumothorax (relatively low incidence)
Axillary nerve block	Surgery of the elbow, forearm and hand	Median nerve, ulnar nerve, radial nerve, and musculocutaneous nerve	LA injected around the axillary artery at the medial aspect of proximal arm	(1) Easy to perform; and (2) Low complication rate	(1) Often spares the musculocutaneous nerve; and (2) Requires arm abduction	(1) Hematoma formation; and (2) Intravascular injection

COPD: Chronic obstructive pulmonary disease.

Interscalene block

The interscalene block is performed at the level of roots-trunks of the brachial plexus. The interscalene block results in anesthesia of C5 through C8, and also blocks the supraclavicular branches of the cervical plexus C3 and C4, which supplies the skin over the acromion and the clavicle. The inferior trunk (C8-T1) is usually spared; an effect referred to as ulnar sparing. Thus, if this block is performed for procedures at or distal to the elbow, an additional ulnar nerve block is required. The coverage of this nerve block makes it effective for procedures involving the shoulder, proximal aspect of humerus and the distal aspect of the clavicle[25].

The interscalene block targets the brachial plexus between the anterior and middle scalene muscle, lateral to the carotid artery and internal jugular vein, directly above the clavicle. Complications associated with the interscalene block include phrenic nerve blockade with an incidence near 100 percent[26,27], sympathetic chain blockade causing Horner's syndrome, inadvertent injection in the vertebral artery, recurrent laryngeal nerve blockade causing hoarseness, and peripheral neuropathy[28]. Rare complications include pneumothorax, epidural injection, intrathecal injection leading to total spinal anesthesia, spinal cord damage, and dorsal scapular or long thoracic nerve injury. Due to the high incidence of phrenic nerve blockade, the interscalene

block is contraindicated in patients with severe pulmonary disease due to elevated risk of respiratory compromise. In an otherwise healthy individual, respiratory compromise is uncommon and the block is well-tolerated.

Supraclavicular block

The supraclavicular block targets the brachial plexus superior to the clavicle at the level of the trunks and divisions. It involves the C5-C7 distribution from the more superficial and lateral branches which supply the shoulder, lateral aspect of arm, and forearm, as well as the deeper and more medial contingent branches of C8 and T1 which supply the hand and medial aspect of forearm. Adequate spread of local anesthetic in both areas is necessary for successful nerve block of the arm and hand [25]. The supraclavicular block involves injection of local anesthetic between anterior and middle scalene muscles at the level of the first rib, where the subclavian artery crosses posterior to the midpoint of the clavicle.

The supraclavicular block results in anesthesia of the upper limb that includes the shoulder because all the trunks and divisions of the brachial plexus are tightly packed and can be anesthetized at this location. Due to the density and extent of the supraclavicular block, it is colloquially known as the "spinal of the arm". Indications of this nerve block include surgery of the hand, forearm, elbow, and arm. The proximal medial side of upper arm is spared since that is supplied by the intercostobrachial nerve (T2), which can be anesthetized separately.

Complications associated with supraclavicular block include pneumothorax (0.6% to 6.1%) as the apical pleural is in close proximity to the nerve block. The prevalence of pneumothorax can reach 0% with proper ultrasound usage[29]. Other complications of the supraclavicular block include phrenic nerve blockade resulting in hemidiaghragmatic paresis (17% to 50%) and recurrent laryngeal nerve blockade leading to hoarseness in (22 %)[30,31].

Infraclavicular block

The infraclavicular block targets the brachial plexus at level of the cords before the branching of the axillary and the musculocutaneous nerves. It results in anesthesia of the upper limb below the shoulder, including the arm, elbow, forearm and hand, sparing the medial proximal upper arm, which is supplied by intercostobrachial nerve (T2)[25].

The infraclavicular block involves the injection of local anesthetic surrounding the axillary artery below the clavicle. Under ultrasound guidance, the local anesthetic is injected surrounding the axillary artery in a U-shaped pattern covering the all three cords of the brachial plexus. The infraclavicular block has a low prevalence of pneumothorax at 0.7%[32].

Axillary block

The axillary block is performed at the level of the branches of the brachial plexus. It anesthetizes the median nerve, the ulnar nerve, the radial nerve, and the musculocutaneous nerve, resulting in anesthesia of the upper limb from mid-arm extending distally to the elbow, forearm, and hand. It is to note that this block does not block the axillary nerve; rather the name of this regional technique is derived from the approach. In order to perform this block, the patient is positioned supine with the arm abducted to 90 degrees. Under ultrasound guidance the median, ulnar and radial nerve are identified surrounding the axillary artery. The nerve bundles are surrounded by three muscles-the biceps is located anterior and superficial, the coracobrachialis is located anterior and deep and the conjoined tendon of the teres major and latissimus dorsi is located medial and posterior. The musculocutaneous nerve is located between the fascial layers of coracobrachialis and biceps muscles. If required, the medial side of upper arm can be blocked separately. The axillary nerve block carries the risk of hematoma formation and intravascular injection, due to its close proximity to the axillary artery and vein. The need to abduct the arm to perform this block may be difficult with certain upper extremity injuries. In such case, other upper extremity blocks such as supraclavicular block can be utilized.

BLOCKS FOR LOWER EXTREMITY ORTHOPEDIC PROCEDURES

Neuraxial blocks for lower extremity procedures

Neruraxial anesthesia results in the blockade of sympathetic, motor, and sensory

nerves, which leads to unopposed parasympathetic tone. Major physiologic effects of neuraxial anesthesia include hypotension, bradycardia, hypothermia, nausea and vomiting, and high neuraxial blockade leading to respiratory depression[33,34]. There are several benefits to using neuraxial anesthesia for lower extremity orthopedic surgery that include reduced incidence of deep venous thrombosis in patients undergoing hip and knee replacement surgery, decreased intraoperative blood loss and transfusion requirements, and improved postoperative cognition[2,3,35,36] .Decreased intraoperative blood loss is likely due to a reduction in venous pressure from the sympathetic blockade. Multiple studies have showed that neuraxial anesthesia reduces the risk of postoperative deep venous thrombosis by at least 50% [36].

Spinal anesthesia

Spinal anesthesia is used for orthopedic procedures including total knee arthroplasty (TKA) and THA. Spinal anesthesia is usually performed with the patient in the sitting position while being continuously monitored. Also, it can be performed in the lateral decubitus position when the patient's condition does not permit sitting.

The complications and adverse effects associated with spinal anesthesia include: high spinal anesthesia, inadequate or failed spinal anesthesia, nerve injury, urinary retention, postdural puncture headache, transient neurologic symptoms, infection, and spinal-epidural hematoma

Epidural anesthesia

Epidural anesthesia and analgesia can be utilized as an effective technique to either supplement general anesthesia or as the primary anesthetic approach for lower extremity orthopedic surgical procedures. Moreover, epidural anesthesia may be supplemented with peripheral nerve blockade to decrease postoperative pain. Common indications for epidural anesthesia in orthopedic surgery include THA, TKA, foot/ankle surgery, and major knee surgery.

Epidural anesthesia is better suited for elderly patients with cardiac comorbidities that limit their ability to tolerate the sudden sympathetic blockade and the resulting hypotension associated with spinal anesthesia[37,38]. An epidural catheter may be incrementally dosed to slowly obtain an adequate surgical anesthetic level, thereby decreasing major rapid fluctuations in blood pressure[39]. Additionally, the epidural catheter can be continuously dosed during the surgery and may remain in place postoperatively for analgesic purposes[39].

With the advent of peripheral nerve blockade, the role of epidural analgesia strictly for postoperative pain has been decreasing in use. When comparing epidural analgesia with peripheral nerve blockade in patients who underwent TKA, a meta-analysis showed equivalent pain scores and morphine consumption between both groups up to 48 h postoperatively (Fowler, SJ 2008)[40]. Additionally, the use of epidural analgesia was associated with a higher incidence of urinary retention and hypotension, suggesting that peripheral nerve blockade provides equivalent postoperative analgesia with a favorable side-effect profile[40,41].

Serious complications of epidural anesthesia are extremely rare (0.03%), but can be potentially devastating[42]. These complications include epidural hematomas, epidural abscesses, nerve damage, infection, and cardiovascular instability[42]. Absolute contraindications to epidural anesthesia include patient refusal, local infection at puncture site, and severe coagulation disorders. Relative contraindications include sepsis, elevated intracranial pressure, anticoagulant use, bleeding disorders, fever, aortic stenosis, pre-existing neurologic injury, prior spine surgery, and placement in anesthetized individuals[43].

COMBINED SPINAL-EPIDURAL

The CSE anesthetic is a technique which combines many of the benefits of epidural and spinal anesthetics in a single approach. It may be utilized in patients undergoing lower extremity orthopedic procedures who require surgical anesthesia with the added ability to add epidural anesthetics for intraoperative or postoperative uses[44]. As with alternative neuraxial techniques, the CSE may be utilized for patients undergoing hip and knee arthroplasty, femur fractures, major knee surgery, and foot/ankle surgery[45].

This technique is performed by injecting an anesthetic solution in the subarachnoid space (coaxial needle placement *via* epidural needle), followed by placing an

indwelling epidural catheter. The CSE technique provides the rapid onset of spinal anesthesia with the prolonged and flexible duration of an epidural catheter[46]. With the CSE technique, surgical anesthesia is achieved rapidly, saving 15-20 min compared to epidural anesthesia[44]. The epidural catheter may be left in place to supplement inadequate spinal anesthesia, prolong surgical anesthesia, and to provide postoperative pain control[44].

The CSE can be used in high-risk patients, in order to facilitate careful titration of epidural anesthetics after surgical anesthesia is initiated with a reduced dose of intrathecal local anesthetic[44]. This can prevent sudden decreases in systemic blood pressure.

Caution should be exercised when intrathecal or epidural long-acting opioids are administered, due to the risk of delayed respiratory depression[47]. The success rate of CSE is higher than has been demonstrated with epidural anesthesia alone[44]. There is a theoretical risk that the epidural catheter may migrate or is non-functioning, which will only be discovered once the spinal blockade begins to diminish, thereby necessitating conversation to general anesthesia[44]. Overall, the CSE remains an excellent anesthetic and analgesic technique in patients undergoing lower extremity orthopedic surgery. While the combined spinal-epidural approach has several benefits over spinal or epidural anesthesia, there is a risk that the epidural may become dislodged during patient positioning. This may not be detected until later in the case, as the spinal anesthetic will provide reliable anesthesia for the first portion of the case, and may mask a poorly-functioning epidural. This may necessitate the administration of sedatives or the conversion to general anesthesia depending on the surgical case. Patients should be considered fall-risks until their neuraxial anesthetic has completely worn off. Moreover, return of motor function often occurs prior to the recovery of functional balance. As such, the first ambulation following neuraxial anesthesia should be performed with caution.

LOWER EXTREMITY PERIPHERAL NERVE BLOCKS

Peripheral nerve blocks may be utilized either as the primary anesthetic modality or as adjuncts to general or neuraxial anesthesia. Due to anatomical limitations in successfully achieving adequate surgical anesthesia through peripheral nerve blockade, lower extremity nerve blocks are typically utilized as an adjunct to general or neuraxial anesthesia. Advances in regional anesthesia have allowed for increased applications of peripheral nerve blocks while minimizing potential side effects such as undesirable motor blockade[16]. A summary of lower extremity peripheral nerve blocks is included in in Table 3.

Femoral nerve block

The femoral nerve block is indicated for lower extremity procedures involving the anterior aspect of the thigh and medial aspect of the leg below the knee. Common uses of the femoral nerve block include providing analgesia for TKA, anterior cruciate ligament reconstruction, quadriceps tendon repair, surgery to the foot, and surgery to the ankle. The femoral nerve block may be combined with other regional anesthetic techniques, such as the sciatic nerve block, to expand the distribution of the anesthetic block, particularly below the knee[16].

The femoral nerve block has been reported to effectively reduce pain and assist with rehabilitation after TKA[48,49]. Patients who received femoral nerve block for knee surgery had fewer unplanned hospital admissions during outpatient surgery [50]. At one major academic center, patients who underwent anterior cruciate ligament (ACL) repair with the assistance of regional anesthesia for postoperative pain control were able to bypass the PACU 82% of the time and were able to avoid hospital admission 96% of the time; both of these values translated into significant hospital cost savings [51].

Absolute contraindications to femoral nerve block include patient refusal and allergy to local anesthetics. Relative contraindications to femoral nerve block include concurrent anticoagulation use, coagulopathy, previous ilioinguinal surgery, local infection, preexisting femoral neuropathy, or large inguinal lymph nodes[16].

Anatomically, the femoral nerve is the largest branch of the lumbar plexus and arises from the ventral rami of the L2-L4 spinal nerve roots[16]. It enters the femoral triangle directly inferior to the inguinal ligament and lies lateral to the femoral artery [52]. The femoral nerve splits distally to the anterior and posterior divisions. The anterior division, gives rise to the medial femoral cutaneous nerve while the posterior

Table 3 Summary of lower extremity peripheral nerve blocks

Block	Clinical application	Nerves blocked	Anatomical landmarks	Advantages	Disadvantages	Complications
Femoral nerve(Femoral nerve block)	Surgeries involving anterior aspect of the thigh and medial aspect of the leg below the knee	Femoral nerve	Inguinal crease; located lateral to femoral artery	(1) Broad coverage; and (2) Easily identifiable landmarks	Causes quadriceps weakness which may lead to falls	(1) LE weakness and falls; (2) Bleeding; (3) Infection; and (4) Nerve damage
Femoral nerve (Fascia Iliaca block)	Surgeries involving anterior aspect of the thigh and medial aspect of the leg below the knee	(1) Femoral nerve; and (2) Lateral femoral cutaneous nerve of the thigh	Inguinal crease, LA injected under fascia iliaca	(1) Easily identifiable landmarks; and (2) Assist in optimal patient positioning for spinal anesthesia	(1) Causes quadriceps weakness which may lead to falls; and (2) Large volume of local anesthetic required	(1) LE weakness and falls; (2) Bleeding; (3) Infection; and (4) Nerve damage
Sciatic nerve (Anterior, transgluteal, and subgluteal approaches)	Surgeries involving foot, ankle, and posterior knee	Sciatic nerve	Variable, based on injection site	(1) Broad lower extremity coverage; and (2) Easilyidentifiable landmarks	Motor blockade	(1) Bleeding; (2) Infection; and (3) Nerve damage, persistent foot drop and heel ulcers
Sciatic nerve (Popliteal Block)	Surgeries involving foot, ankle, posterior knee	Sciatic nerve	Popliteal fossa, located cephalad to the knee near popliteal artery	(1) Broad lower extremity coverage; and (2) Easilyidentifiable landmarks	Motor blockade	(1) Bleeding; (2) Infection; and (3) Nerve damage, persistent foot drop and heel ulcers
Saphenous nerve (Femoral triangle, medial femoral condyle, tibial tuberosity approaches)	Surgeries involving medial aspect of knee, foot, and ankle	Saphenous nerve	Variable, based on injection site	Motor-sparing	Does not provide anesthesia and analgesia to the posterior capsule of knee	(1) Bleeding; (2) Infection; and (3) Nerve damage - Potential lower extremity weakness at high doses
Saphenous nerve (Adductor Canal block)	Surgeries involving medial aspect of knee, foot, and ankle	(1) Saphenous nerve; and (2) Nerve to vastus medialis (branch of femoral nerve)	Medial thigh, located deep to the sartorius muscle, adjacent to the femoral artery and vein.	Motor-sparing	(1) Does not provide anesthesia and analgesia to the posterior capsule of knee; and (2) Compared to femoral nerve block, it is less efficacious for analgesia after ACL reconstruction surgery	(1) Bleeding; (2) Infection; (3) Nerve damage; and (4) Potential lower extremity weakness at high doses
iPACK	Surgeries involving the posterior knee capsule	Articular branches of the tibial, common peroneal, and obturator nerve to the posterior aspect of the knee	Popliteal crease, located cephalad to femoral condyles	Motor-sparing, increased posterior knee coverage	Coverage only to posterior knee; useful as an adjunct to alternative blocks	Inadvertent motor block due to local anesthetic spread to sciatic nerve branches
Ankle	Foot surgery	Saphenous, sural, posterior tibial, superficial peroneal, and deep peroneal nerves	Ankle and foot bony landmarks	Injection based on surface landmarks, no requirement for ultrasound	Limited efficacy for surgery proximal to the foot, potential higher failure rate due to blind technique	(1) Bleeding; (2) Infection; and (3) Nerve damage
Lumbar plexus	Hip surgery	Lumbar plexus, providing blockade to femoral, obturator, and lateral femoral cutaneous nerves	Lateral to lumbar spine, located cephalad to iliac crest	Coverage of multiple nerves with a single block	High potential for complications and block failure, technically challenging block to perform	(1) Bleeding and hematoma; (2) Infection; (3) Nerve damage; (4) Epidural spread resulting in high neuraxial anesthesia; (5) Hypotension, and (6) LAST

ACL: anterior cruciate ligament; LAST: local anesthetic systemic toxicity.

division gives rise to the saphenous nerve.

The femoral nerve provides sensory innervation to the anterior thigh and medial aspects of the calf, foot, and ankle[16]. The femoral nerve additionally provides motor innervation to muscles of the lower extremity, including the quadriceps, sartorius, and pectineus muscles. As such, the femoral nerve block will cause weakness of the quadriceps muscles[53-55]. This may result in decreased patient mobility and may potentially increase the risk of falls. Thus, patients should not be ambulating without assistance after a femoral nerve block[18].

The quadriceps weakness associated with the femoral nerve block has decreased its clinical use for providing post-operative analgesia for patients undergoing TKR. Motor-sparing regional anesthesia techniques are often favored for these patients, such as blocks targeting the saphenous nerve which provides sensory innervation to the anterior and medial aspects of the knee[56,57].Weakness induced by a femoral nerve block may be assessed by manual muscle testing[58]. Recommendations to minimize post-operative falls in patients receiving this block include utilizing ambulation-assistive devices, patient and staff education, and considering post-operative immobilization until muscle strength is regained[16]. Data supports the use of femoral nerve block over adductor canal block for ACL reconstruction, despite the increased risk of quadriceps weakness[59,60].

The femoral nerve block is often well-tolerated by patients, as the needle only traverses through the skin and adipose tissue of the inguinal region. Complications associated with the femoral nerve block are rare, and include nerve injury, intravascular injection, and quadriceps weakness[61]. The femoral nerve block is performed by positioning the patient in a supine position with the targeted limb placed slightly abducted and externally rotated. The femoral nerve is identified lateral to the femoral artery. The femoral nerve is located deep to the fascia lata and fascia iliacia, and superficial to the iliopsoas muscles.

Fascia iliaca block

The fascia iliaca block is a regional anesthetic technique which provides anesthesia to the femoral nerve and lateral femoral cutaneous nerve[62]. It is used in patients who have sustained traumatic hip fractures or for analgesia following hip surgery. This block may be performed pre-operatively while the patient is awaiting their surgery, and has been shown to provide rapid analgesic benefit[63]. Moreover, patients reported improvements with passive hip flexion, which allowed them to sit up in bed pre-operatively[64]. Faster time to fascia iliaca block has been shown to reduce opioid use, pain, and hospital length-of-stay in patients with hip fractures[65]. Pain relief after fascia iliaca block has been shown to be superior to systemic intravenous opioid therapy and this block can be performed upon presentation to the emergency department[66]. The fascia iliaca block may also assist with optimally positioning these patients for spinal anesthetic placement for surgical femur fracture repair[67,68].

The fascia iliaca block is performed by injecting a relatively large volume of local anesthetic (20-30 cc) under the fascia iliaca above the level of the inguinal crease. The goal of this block is to spread local anesthetic laterally to the iliac spine and medially to the femoral nerve, and is typically performed under ultrasound-guidance[62]. The femoral nerve and lateral femoral cutaneous nerve lie deep to the fascia iliaca, and as such, are blocked during this injection[69-71]. The femoral nerve component provides blockade to the anterior and medial thigh, and the lateral femoral cutaneous nerve component provides anesthesia to the anterolateral thigh.

Saphenous nerve block

The saphenous nerve block is indicated for various lower extremity orthopedic procedures involving the knee, foot, or ankle. It may be used as a sole nerve block, or in conjunction with the sciatic nerve block to provide increased anatomical coverage for surgery to the medial aspect of the foot and ankle[16]. The saphenous nerve block results in sensory anesthesia of the medial aspect of the leg down to the foot and ankle.

There are various approaches to performing a block of the saphenous nerve. With the use of ultrasonography, the saphenous nerve block is often performed subsartorially at the adductor canal; hence, this block is referred to as the "adductor canal block". Alternative locations to perform a saphenous nerve block include the femoral triangle, the medial femoral condyle, or the level of the tibial tuberosity.

Adductor canal block

The adductor canal block provides effective analgesia for surgery to the knee and medial aspect of the lower extremity. It may be used as part of a multimodal analgesic

pathway for patients undergoing TKA to facilitate earlier ambulation, improve patient comfort, and enhance patient satisfaction[72]. Over half of the patient's undergoing TKA will likely experience moderate-to-severe post-operative pain which can subsequently result in increased length-of-stay, immobility-related complications, and decreased patient satisfaction[73]. As a result, safe and effective regional anesthetic techniques are of paramount importance to these patients[73,74].

While the femoral nerve block can provide effective analgesia for patients undergoing total knee arthroplasty, it can be associated with quadriceps muscle weakness which may increase the risk of falls[18]. As a result, the adductor canal block is often a favorable alternative used for post-operative analgesia for patients undergoing TKR[56,57]. Compared to the femoral nerve block, the adductor canal block results in significant quadriceps motor sparing and significantly preserved balance while still maintaining a similar degree of postoperative pain relief[53-55]. This allows for effective pain control with the ability to promote early mobilization and ambulation post-operatively[75].

The adductor canal block has been evaluated for its potential analgesic use in patients undergoing ACL reconstruction. The adductor canal block has theoretical advantages for this patient population, including preserved quadriceps strength fulfilling the requirements of short hospital stay and immediate mobilization for outpatient ACL reconstruction. Currently, the data has been inconsistent in supporting the routine use of the adductor canal block over the femoral nerve block for ACL reconstruction with regards to analgesic equivalence; as such, the femoral nerve block for ACL reconstruction remains an appropriate option[60,76-78].

The adductor canal block can be combined with various other regional techniques to increase the overall distribution of analgesia[16]. A limitation of the adductor canal block as a sole nerve block is that it will only produce anesthesia to the anteromedial side of the knee[73]. Patients undergoing knee surgery report improved pain relief by combining the adductor canal block with periarticular injections of local anesthetic by the surgeon[79-81]. The addition of the iPACK block may offer patients improved pain relief and earlier ambulation by providing anesthesia to the posterior capsule of knee [82].

Complications from an adductor canal block are rare and potentially include bleeding, infection, and nerve damage[83]. It is important to note that while the saphenous nerve block is a sensory nerve block, an injection of a large volume of local anesthetic into the adductor canal may result in a partial motor block of the vastus medialis due to a blockade of the femoral nerve's branch to the vastus medialis[84]. As a result, caution must be exercised with patients ambulating without support after receiving an adductor canal block.

The adductor canal block has widely become the standard of care for analgesia for total knee arthroplasty. The downside to the adductor canal block is that often times direct sonographic visualization of the saphenous nerve is not achieved; rather, local anesthetic is deposited within the anatomic region of the adductor canal. It is likely that motor-sparing blocks will increase in their use for a wide array of lower extremity surgical procedures, especially in the ambulatory surgical setting.

iPACK block

The iPACK block has been increasingly utilized in TKA to provide analgesia to the posterior compartment of the knee without compromising lower extremity strength. It targets the medial and lateral superior genicular nerves to provide adequate posterior knee capsule analgesia[85]. The combination of the iPACK block with the ACB provides a larger distribution of anesthetic coverage, by ensuring both anteromedial and posterior joint coverage[73,86].

Recent data indicates the iPACK block, used in conjunction with the adductor canal block and periarticular injection for TKA, substantially decreased pain at rest and on ambulation postoperatively[82,87]. This resulted in earlier hospital discharge, decreased opioid requirements, and earlier ambulation[82].

To perform iPACK block the needle is inserted in the medial thigh under ultrasound guidance. Typically, a total volume of 15-20 cc of a local anesthetic solution is utilized for this block. During the performance of this block, it is important to avoid inadvertent local anesthetic spread to the tibial or common peroneal nerve, which may result in undesirable motor weakness[88].

The IPACK block can be quite uncomfortable for awake patients to undergo, given the needle positioning and needle depth. As such, in certain patients, this block may be performed after the patient has been sedated in order to facilitate proper needle placement. It is likely that in the future the IPACK block will be utilized in combination with the adductor canal block as the standard of care for providing

"circumferential" analgesic coverage for knee surgery. That being said, caution should be exercised to the total volume of local anesthetic utilized in order to avoid inadvertent local anesthetic systemic toxicity.

Sciatic nerve block

The sciatic nerve block is indicated for lower extremity orthopedic procedures involving the foot, ankle, and posterior knee. The sciatic nerve block may be used as a singular block, as in the case of an achilles tendon repair, or in conjunction with the femoral or saphenous nerve block to obtain anesthetic coverage for knee surgery or foot/ankle surgery, respectively[16]. The sciatic nerve is formed from the anterior rami of L4 to S3 and is the largest nerve in the body[89]. The terminal branches of the sciatic nerve are the tibial nerve and common peroneal nerve. The sciatic nerve block provides anesthesia to the posterior aspect of the knee, hamstrings, and the entire limb below the knee (motor and sensory innervation), with the exception of medial lower extremity and foot, which is supplied by the saphenous nerve.

The sciatic nerve may be blocked in several locations, depending upon the region of the limb requiring anesthetic blockade. The anterior approach of the sciatic nerve block is performed on the proximal medial thigh. The transgluteal approach is performed on the posterior buttock, between the ischial tuberosity and greater trochanter. The subgluteal approach is performed posteriorly on the gluteal crease. Commonly, the sciatic nerve block is performed at the level of the popliteal fossa, known as the "popliteal block".

Popliteal block

The popliteal block is performed in conjunction with the saphenous nerve block for surgery involving the foot and ankle[16]. The popliteal fossa is the region where the sciatic nerve divides into its two major terminal branches, the tibial nerve and common peroneal nerve[89]. The popliteal block is often performed proximal to the bifurcation of the tibial and common peroneal nerves; however, a recent study suggests that a popliteal block distal to the sciatic nerve bifurcation may result in 30% faster onset of the blockade while still achieving blockade of the terminal branches[90]. Additionally, injection of local anesthetic distal to the bifurcation of the sciatic nerve provides superior sensory block of the lower extremity[91].

Potential complications from the sciatic nerve block are rare, and include nerve injury, bleeding, and intravascular injection[92]. Nerve injury may be manifested as a persistent foot drop with potential pressure necrosis[16].

The popliteal sciatic nerve block is performed with the patient in the supine position with the affected limb placed in an elevated position with the assistance of blankets or towels for positioning. The knee joint is slightly flexed, and the ultrasound transducer is placed on the posterior aspect of the knee within the popliteal crease. Caution should be exercised to avoid entering the nerve bundle or inadvertently injecting the popliteal artery.

Ankle block

The ankle block can be performed to provide anesthesia to the foot. All types of foot surgery can be performed with the ankle block, including forefoot reconstruction, bunionectomy, osteotomy, and amputation. The ankle block is effective for providing pain relief for foot fractures, soft tissue injuries, and gout. The ankle block has several benefits over alternative regional techniques. It is performed through anatomic landmarks, and does not require ultrasonography to perform; however, data suggests that the addition of ultrasound-guidance may improve the clinical efficacy of the ankle block[93].The ankle block is motor-sparing; however, the ankle block may result in mild impairment to ambulation.

The ankle block is performed by blocking the five peripheral nerves at the level of the ankle. The medial aspect of the foot is innervated by the saphenous nerve, which is a branch of the femoral nerve. The remainder of the foot is innervated by branches of the sciatic nerve—the sural nerve, the posterior tibial nerve, the superficial peroneal nerve, and the deep peroneal nerve[94].

Compared to the ankle block for forefoot surgery, the popliteal block provided improved analgesia and decreased opioid requirements in the immediate post-operative period[95].

Contraindications to the ankle block include local infection, burn, soft tissue injury, scarring, or distorted anatomy in the region of the block. Potential complications of the ankle block are rare, and include bleeding, infection, and nerve damage[96].

The ankle block is often underutilized as a technique to provide analgesia to the midfoot and forefoot. As it does not require ultrasound to perform, it can be reliably performed in settings which may not be equipped with an ultrasound. Moreover, it may be performed upon presentation to the emergency room for providing pain relief for foot fractures or soft tissue injury, as part of a multimodal analgesic plan. The ankle block may also be performed by the surgeon intraoperatively for post-operative analgesia.

Lumbar plexus block

The lumbar plexus block is indicated for lower extremity procedures and has been shown to be useful for hip surgery, including arthroplasty and fracture repair. By performing this regional anesthetic, blockade of the femoral, obturator, and lateral femoral cutaneous nerve can be achieved. Various techniques have been described for this block. The ultrasound-guided shamrock technique, first described in 2013, provides sufficient sonographic visibility of the target plexus[97]. In this technique, an ultrasound-probe is placed in an axial orientation cephalad to the iliac crest approximately along the posterior axillary line. The lumbar plexus block can be combined with the sacral plexus block to provide effective anesthesia for hip surgery; this provides for an alternative to spinal anesthesia which may cause prolonged periods of hypotension[98].

With the advent of alternative regional anesthesia techniques, the lumbar plexus block has seen a decrease in clinical use. These peripheral blocks are often performed with greater ease and reliability by most anesthesiologists, and are better tolerated by patients. Moreover, the potential for serious complications is higher for the lumbar plexus block when compared to alternative peripheral nerve blocks. The fascia iliaca block can be utilized as an alternative for analgesia after hip surgery and has been shown to provide non-inferior pain relief[99,100]. In Addition, the fascia iliaca block is often easier to perform from a technical perspective, which may lead to its increased use[99]. Studies have shown that peripheral nerve blocks for patients who have sustained a traumatic hip fracture can reduce pain on movement and decrease the risk of developing pneumonia[101]. As such, it is important to perform a technique, such as the fascia iliaca block, which can be mastered by most clinicians without advanced specialized regional anesthesia training. However, because of the decreasing utility of the lumbar plexus block, residency training programs often do not emphasize the teaching of this block.

The lumbar plexus block has the potential for causing serious complications, including inadvertent epidural spread resulting in high neuraxial anesthesia, hypotension, local anesthetic toxicity, bleeding, hematoma formation, infection, and nerve damage. In order to minimize these complications, large volumes of local anesthetic should be avoided in patients with multiple comorbidities. During performance of this block, patients should be continuously monitored for unilateral sympathectomy or hypotension due to epidural spread[102]. Deformation or degeneration of spinal anatomy and musculature may result in poor ultrasound image quality, potentially leading to failed blockade[103].

COMPLICATIONS OF REGIONAL ANESTHESIA

Local anesthetic systemic toxicity

Local anesthetic systemic toxicity (LAST), is a potentially life-threatening complication that may result from unintentional intravascular injection of local anesthetic or slow absorption of an inappropriately high dose of local anesthetic injected perineurally. The ASRA publishes practice advisories for the management of patients who experience LAST[104].

The clinical presentation and speed of onset of LAST are extremely variable. Signs and symptoms of toxicity may immediately become apparent; however, they may take as long as 30 min or more to occur[105]. Symptoms typically present as a continuum; neurologic toxicity occurs at lower concentrations followed by cardiac toxicity at higher concentrations.

Early clinical signs of neurotoxicity are subjective, and include dizziness, drowsiness, perioral numbness, and tinnitus[105]. These signs may be missed if the patient is sedated or under general anesthesia. Following this, with increasing plasma concentrations, muscle twitching and tremors are observed. As blood and brain levels of local anesthetic continue to increase, generalized tonic-clonic seizures occur. Finally, generalized central nervous system (CNS) depression occurs leading to a reduced level

of consciousness and coma[106].

Cardiotoxicity follows a two-step pathway[107]. In early cardiotoxicity, activation of the sympathetic nervous system results in hypertension and tachycardia. Following this, myocardial depression occurs leading to ventricular arrhythmias, conduction delays, contractile dysfunction, and eventual cardiovascular collapse. Inhibition of myocardial voltage-dependent sodium channels by local anesthetics may lead to a noticeable increase in the PR interval and QRS duration, as well as the presence of subtle T wave abnormalities[107].

Treatment of LAST begins with the recognition of the early signs and symptoms of toxicity, followed by immediate intervention including early administration of intravenous Intralipid emulsion. Intravenous Intralipid emulsion has been postulated to function by acting as a lipid sink to extract lipophilic local anesthetic from plasma and tissues[108]. It additionally functions directly on myocardial tissue by improving cardiac output[109]. Intralipid should be administered as a weight-dependent bolus followed immediately by an infusion[106]. Boluses may be repeated, and the infusion rate may be doubled if the patient continues to remain unstable[104]. The infusion should be continued for at least 15 min after obtaining hemodynamic stability[104].

CNS instability such as seizures should be appropriately managed with intravenous benzodiazepine administration or low doses of propofol[104]. Cardiovascular collapse should be managed with careful titration of intravenous epinephrine. Individual boluses of less than 1 mcg/kg should be administered to avoid ventricular fibrillation or tachycardia[104]. ACLS dosing of epinephrine (1 mg) may result in poor long-term outcomes due to the increased risk of arrhythmogenicity. A summary of the clinical presentation and treatment of LAST is presented in Table 4.

Risk factors for LAST include extremes of age, low muscle mass, female gender, and patients with cardiac, liver, and metabolic comorbidities[110]. The ASRA recommendations for preventing LAST include the use of ultrasound, use of the lowest effective dose, incremental injections, aspiration before each injection, and the addition of epinephrine when employing potentially toxic doses of local anesthetic[110]. The presence of epinephrine within the local anesthetic solution may cause a transient increase in heart rate if injected intravascularly, thus alerting the clinician of inadvertent intravascular injection. The risk of LAST increases with the administration of large volumes of local anesthetic to perform multiple nerve blocks at the same time. For example, patients who undergo blockade of the saphenous (adductor canal block) and sciatic (popliteal block) nerves may receive a large combined total volume of local anesthetic. As such, extreme caution should be administered to the individual and combined doses of local anesthetic, especially when there are plans to administer further local anesthetic within the surgical field intraoperatively by the surgeon. It is important to utilize the minimum effective dose of local anesthetic required to perform the nerve block.

Prevention of LAST remains a cornerstone of safe administration of regional anesthesia. Checklists and treatment algorithms of LAST should be prominently displayed in any area where regional anesthesia nerve blocks are performed, and resuscitation equipment and medications should be immediately available if required [111,112]. Due to the life-threatening nature of LAST, prompt diagnosis and management of LAST should be frequently reviewed and reinforced with the use of simulation[111]. All personnel, including surgical staff, nursing staff, and anesthesia staff should be trained in recognizing and treating LAST if they work in a perioperative setting where peripheral nerve blocks are performed. Moreover, resuscitative medications should be well-marked and easily accessible by all members of the treatment team.

Block failure

Regional anesthesia is often effectively utilized as the primary anesthetic or as an adjunct for postoperative analgesia; however, despite these benefits, it has an inherent failure risk even in the most experienced hands. Block failure is manifested as inadequate anesthesia or analgesia in the targeted region. This may result in poorly-controlled pain, delayed surgical schedule, subjecting the patients to repeated block attempts, or unanticipated conversion to general anesthesia.

Certain technical variables have been found to be the cause of certain block failures. Injection of anesthetics outside of the neurovascular sheath prevents appropriate spread to the target nerve. Additionally, the utilization of a high threshold for stimulation when using a nerve stimulator technique may lead to an increased rate of failed blocks[17].The experience level of the anesthesiologist performing the block has been reported to impact the performance of a regional anesthetic[113]. It is important to optimize all patient variables for increasing the rate of success. This can be achieved

Table 4 Clinical presentation and management of local anesthetic systemic toxicity

Local anesthetic systemic toxicity (LAST)
Clinical presentation of LAST
1 Dizziness, drowsiness, tinnitus, perioral numbness
2 Muscle twitching and tremors
3 Seizures
4 CNS depression, coma
5 Hypertension, tachycardia
6 Myocardial depression, ventricular arrhythmias, conduction delays
7 EKG changes: Prolonged PR, QRS; T-wave changes
8 Cardiovascular collapse
Management of LAST
1 Call for help
2 Call for LAST rescue kit
3 Consider early lipid emulsion administration
(1) Under 70 kg: Bolus 1.5 mL/kg over 2-3 min, Infuse 0.25 mL/kg/min. Repeat bolus or double the infusion rate if the patient remains unstable
(2) Over 70 kg: Bolus approximately 100 mL over 2-3 min, infuse approximately 250 mL over 15-20 min. Repeat bolus or double the infusion rate if the patient remains unstable
(3) If the patient is stable, continue lipid emulsion ≥ 15 min after hemodynamic stability. Maximum lipid dose: 12 mL/kg
4 Seizure
(1) Airway management
(2) Benzodiazepine
(3) Consider low dose propofol
5 Arrhythmia or cardiovascular Instability
(1) Epinephrine: Administered at lower dose than ACLS dosing, start with ≤ 1 mcg/kg
(2) Avoid local anesthetics, beta-blockers, vasopressin, calcium channel blockers
(3) Consider alerting cardiopulmonary bypass team
6 Close monitoring
Once stable, continue close monitoring: 2 h after seizure, 4-6 h after cardiovascular instability, and as clinically appropriate after cardiac arrest

EKG: Electrocardiogram; CNS: Central nervous system.

by proactively taking measures to optimize patient positioning with towels or pillows, using ultrasonography if available, and to take into account anatomic variation. Current graduating anesthesiology residents are receiving advanced training in peripheral nerve blockade, and are likely to be well-versed in the use of peripheral nerve blockade, which will likely decrease the rate of block failure.

One study noted that regardless of block type, patients with a body mass index (BMI) greater than 25 kg/m^2 are more likely than those with lower BMI to experience non-surgical anesthesia; moreover, the rate of block failure increased incrementally with BMI[17]. This is likely due to the difficulty in identifying anatomical landmarks in these patients. Additionally, patients who were an American Society of Anesthesiologists class IV physical status experienced a higher degree of block failure[17].

Block failure may also occur in patients who undergo placement of continuous peripheral nerve block (CPNB) catheters. One study noted the incidence of failure for continuous peripheral nerve block with the supraclavicular approach to be 26%, the highest among the blocks evaluated[114]. The infraclavicular approach was noted to have a lower failure rate, likely due to anatomical characteristics which allow for a more stable catheter placement with a lower rate of dislodgement[114]. Areas with more stable anatomy, with limited range of motion, may minimize the amount of undue traction placed on catheters resulting in lower rates of catheter dislodgement.

Several mechanisms have been implicated in CPNB failure, including catheter insertion techniques, anatomic variation, and equipment malfunction. The CPNB catheter may have initially been incorrectly placed in relationship to the target nerve, or the catheter can migrate post-placement[115,116]. Other causes of CPNB failure include dislodgement or obstruction of the of the catheter tubing[117]. Leakage of local anesthetic solution after dislodgement may potentially increase the risk of LAST or rarely may even cause myonecrosis[114]. Further upstream, the infusion pump may malfunction or disconnect, causing leakage of local anesthetic solution[118]. Genetic variations in certain patients may result in abnormal metabolism of local anesthetic, which may cause inadequate sensory blockade[119]. Lastly, pain is a subjective multifactorial entity. Thus perception of pain may be affected by psychological factors including anxiety and pain-sensitivity, especially in the perioperative period[114].

The advent and increased clinical use of ultrasound-guidance has been shown to increase success rates and improve the quality of sensory blockade[120]. Also, ultrasound-guidance has been shown to shorten block procedural times by reducing the number of needle passes required to localize the target nerve[121].

The overall success of any regional anesthesia technique relies on the ability to correctly identify the nerves or nerve plexus involved in the surgery and place an adequate dose of local anesthetic surrounding the nerve structures. Advances in the field of regional anesthesiology have led to an increase in the use of regional anesthesia with the addition of novel block techniques, especially with the use of ultrasound-guidance[110]. Given the increasing use of peripheral nerve blockade, anesthesiology training programs have drastically increased their emphasis on mastering regional anesthesia skills, leading to the development of anesthesiologists with a strong skillset of performing safe and effective peripheral nerve blocks[122]. The risk of block failure should be discussed with the patient prior to performing the nerve block, so they are aware of this potential occurrence. As part of this discussion, it is beneficial to review alternative analgesics (*e.g.*, alternative blocks, intravenous, and oral medication) that may be administered if the block provides limited pain relief. It is important to utilize alternative methods of analgesia for patients who experience block failure. Consideration should be given to performing an alternative nerve block, if the first block technique fails while considering the total dose of local anesthetic used.

Nerve injury

Peripheral nerve injury is rare following regional anesthesia. Although the definition of injury varies between studies, the incidence of persistent symptoms of nerve dysfunction may be as high as 8 to 10 percent in the days following the block[123,124]. The majority are transient, lasting days to months. Major complications resulting in permanent (greater than six months) nerve damage ranges between 0.015 and 0.09 percent[125-127]. Incidence of nerve injury associated with continuous catheters is around 0.21 percent[118,128]. Most nerve injuries are believed to occur secondary to intraneural injection. Intrafascicular injections, particularly at high pressure, are felt to result in greater risk of nerve damage[129,130]. To minimize the incidence of intrafascicular injection, injection of anesthetic should be halted if the patient feels a paresthesia (shooting pain), or if the pressure required for injection is greater than usual. Appropriate spread of the anesthetic should be observed when ultrasound-guidance is used. Preexisting nerve pathology (including diabetes) may make a nerve more susceptible to injury. Continuous visualization of the block needle using ultrasound is presumed to decrease the risk of intrafascicular injection, but does not decrease the risk of nerve injury. Also, nerve injury can also occur as a direct effect of certain LA medications[131].

Symptoms of nerve injury are primarily sensory (pain, tingling, or paresthesias), but can include any combination of motor or sensory deficits depending on the nerve involved and severity of the injury. Most symptoms resolve within six months; if symptoms are either severe or persistent, the patient should be referred to a specialist for further evaluation and testing.

Hematoma

Inadvertent puncture of nearby vascular structures can lead to hematoma formation. It is important to avoid performing PNB's in patients with an abnormal coagulation status in anatomic locations in which application of pressure to the puncture site is not possible. The vast majority of hematomas may be controlled with direct pressure to the needle puncture site; rarely, surgical decompression may be required.

Allergic reaction

Most adverse reactions to LAs are non-allergic. However, two different types of allergic reactions to LAs have been described: allergic contact dermatitis and delayed swelling at the site of administration within 72 h, and rarely anaphylaxis.

Infection

Infection risk for single-shot peripheral nerve block is negligible and for peripheral catheters is low (0 to 3.2 percent)[132]. Risk of infection is increased in critically ill patients, admission, trauma patients, immune compromised patients, males, and the absence of antibiotics. The risk of infection may be minimized by removing the catheter within 48 to 72 h of placement.

Fall risk

Certain lower extremity nerve blocks may result in muscle weakness which can secondarily increase the risk of post-operative falls[133].

Local anesthetic-induced central nervous system toxicity (toxic left hemispheric syndrome)

Recently, severe stroke-like symptoms following intrascelene block has been reported after interscalene block. Patients had typical hemispheric symptoms in the absence of cerebral vessel occlusion. Hemispheric syndrome in the reported cases occurred in the ipsilateral side of the interscalene block. The proposed mechanism of injury in these cases was apoptotic cell death due to local anesthetic neurotoxic effects. Patient presented with impaired consciousness, slow-wave EEG activity in the affected hemisphere, epilepsy, global aphasia, dysphagia, dysarthria, facial palsy, hemiparesis, pyramidal tract signs, and complex behavioral manifestations. No abnormal computed tomography or magnetic resonance imaging (MRI) imaging was observed in the immediate postoperative period. MRI imaging abnormalities were appreciated postoperative days 1 through 5 in some patients which included hyperintensity of cortical grey matter and basal ganglia. Hospital stay ranged from 9 to 19 d with patient requiring mechanical ventilation for airway protection. Most patients experienced gradual improvement of the functional outcome after a prolonged course of rehabilitation but still has residual symtpoms[134].

CONCLUSION

Regional anesthesia is one of the cornerstones of successful perioperative orthopedic management. In addition to providing superior anesthesia for orthopedic procedures, regional anesthesia provides superior analgesia with relatively fewer side effects compared to systemic analgesia modalities. Perioperative team awareness of regional anesthesia fundamentals is one essential step towards improving clinical outcomes, lowering health care costs, and sustaining higher patient satisfaction scores.

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REFERENCES

1 **Research and Markets**. Orthopedic Surgery - Global Trends & Opportunities. Region: Global, 2018
2 **Pugely AJ**, Martin CT, Gao Y, Mendoza-Lattes S, Callaghan JJ. Differences in short-term complications between spinal and general anesthesia for primary total knee arthroplasty. *J Bone Joint Surg Am* 2013; **95**: 193-199 [PMID: 23269359 DOI: 10.2106/JBJS.K.01682]
3 **Memtsoudis SG**, Sun X, Chiu YL, Stundner O, Liu SS, Banerjee S, Mazumdar M, Sharrock NE. Perioperative comparative effectiveness of anesthetic technique in orthopedic patients. *Anesthesiology* 2013; **118**: 1046-1058 [PMID: 23612126 DOI: 10.1097/ALN.0b013e318286061d]
4 **Chan EY**, Fransen M, Parker DA, Assam PN, Chua N. Femoral nerve blocks for acute postoperative pain after knee replacement surgery. *Cochrane Database Syst Rev* 2014; CD009941 [PMID:

24825360 DOI: 10.1002/14651858.CD009941.pub2]
5 **Touray ST**, de Leeuw MA, Zuurmond WW, Perez RS. Psoas compartment block for lower extremity surgery: a meta-analysis. *Br J Anaesth* 2008; **101**: 750-760 [PMID: 18945717 DOI: 10.1093/bja/aen298]
6 **Xu J**, Chen XM, Ma CK, Wang XR. Peripheral nerve blocks for postoperative pain after major knee surgery. *Cochrane Database Syst Rev* 2014; CD010937 [PMID: 25501884 DOI: 10.1002/14651858.CD010937.pub2]
7 **Liu Q**, Chelly JE, Williams JP, Gold MS. Impact of peripheral nerve block with low dose local anesthetics on analgesia and functional outcomes following total knee arthroplasty: a retrospective study. *Pain Med* 2015; **16**: 998-1006 [PMID: 25545781 DOI: 10.1111/pme.12652]
8 **Hebl JR**, Dilger JA, Byer DE, Kopp SL, Stevens SR, Pagnano MW, Hanssen AD, Horlocker TT. A pre-emptive multimodal pathway featuring peripheral nerve block improves perioperative outcomes after major orthopedic surgery. *Reg Anesth Pain Med* 2008; **33**: 510-517 [PMID: 19258965]
9 **Ullah H**, Samad K, Khan FA. Continuous interscalene brachial plexus block versus parenteral analgesia for postoperative pain relief after major shoulder surgery. *Cochrane Database Syst Rev* 2014; CD007080 [PMID: 24492959 DOI: 10.1002/14651858.CD007080.pub2]
10 **Fredrickson MJ**, Ball CM, Dalgleish AJ. Analgesic effectiveness of a continuous versus single-injection interscalene block for minor arthroscopic shoulder surgery. *Reg Anesth Pain Med* 2010; **35**: 28-33 [PMID: 20048655 DOI: 10.1097/AAP.0b013e3181c771bd]
11 **Hadzic A**, Williams BA, Karaca PE, Hobeika P, Unis G, Dermksian J, Yufa M, Thys DM, Santos AC. For outpatient rotator cuff surgery, nerve block anesthesia provides superior same-day recovery over general anesthesia. *Anesthesiology* 2005; **102**: 1001-1007 [PMID: 15851888 DOI: 10.1097/00000542-200505000-00020]
12 **Brown AR**, Weiss R, Greenberg C, Flatow EL, Bigliani LU. Interscalene block for shoulder arthroscopy: comparison with general anesthesia. *Arthroscopy* 1993; **9**: 295-300 [PMID: 8323615 DOI: 10.1016/s0749-8063(05)80425-6]
13 **Lenart MJ**, Wong K, Gupta RK, Mercaldo ND, Schildcrout JS, Michaels D, Malchow RJ. The impact of peripheral nerve techniques on hospital stay following major orthopedic surgery. *Pain Med* 2012; **13**: 828-834 [PMID: 22494645 DOI: 10.1111/j.1526-4637.2012.01363.x]
14 **Lovald ST**, Ong KL, Lau EC, Joshi GP, Kurtz SM, Malkani AL. Readmission and Complications for Catheter and Injection Femoral Nerve Block Administration After Total Knee Arthroplasty in the Medicare Population. *J Arthroplasty* 2015; **30**: 2076-2081 [PMID: 26205089 DOI: 10.1016/j.arth.2015.06.035]
15 **Secrist ES**, Freedman KB, Ciccotti MG, Mazur DW, Hammoud S. Pain Management After Outpatient Anterior Cruciate Ligament Reconstruction: A Systematic Review of Randomized Controlled Trials. *Am J Sports Med* 2016; **44**: 2435-2447 [PMID: 26684664 DOI: 10.1177/0363546515617737]
16 **Stein BE**, Srikumaran U, Tan EW, Freehill MT, Wilckens JH. Lower-extremity peripheral nerve blocks in the perioperative pain management of orthopaedic patients: AAOS exhibit selection. *J Bone Joint Surg Am* 2012; **94**: e167 [PMID: 23172334 DOI: 10.2106/JBJS.K.01706]
17 **Cotter JT**, Nielsen KC, Guller U, Steele SM, Klein SM, Greengrass RA, Pietrobon R. Increased body mass index and ASA physical status IV are risk factors for block failure in ambulatory surgery - an analysis of 9,342 blocks. *Can J Anaesth* 2004; **51**: 810-816 [PMID: 15470170 DOI: 10.1007/BF03018454]
18 **Elkassabany NM**, Antosh S, Ahmed M, Nelson C, Israelite C, Badiola I, Cai LF, Williams R, Hughes C, Mariano ER, Liu J. The Risk of Falls After Total Knee Arthroplasty with the Use of a Femoral Nerve Block Versus an Adductor Canal Block: A Double-Blinded Randomized Controlled Study. *Anesth Analg* 2016; **122**: 1696-1703 [PMID: 27007076 DOI: 10.1213/ANE.0000000000001237]
19 **El-Boghdadly K**, Chin KJ, Chan VWS. Phrenic Nerve Palsy and Regional Anesthesia for Shoulder Surgery: Anatomical, Physiologic, and Clinical Considerations. *Anesthesiology* 2017; **127**: 173-191 [PMID: 28514241 DOI: 10.1097/ALN.0000000000001668]
20 **Ahdout J**, Nurok M. Anesthesia Patients with Concomitant Cardiac and Hepatic Dysfunction. *Anesthesiol Clin* 2016; **34**: 731-745 [PMID: 27816131 DOI: 10.1016/j.anclin.2016.06.008]
21 **Johansson S**, Lind MN. Central regional anaesthesia in patients with aortic stenosis - a systematic review. *Dan Med J* 2017; **64** [PMID: 28874243]
22 **McDonald SB**. Is neuraxial blockade contraindicated in the patient with aortic stenosis? *Reg Anesth Pain Med* 2004; **29**: 496-502 [PMID: 15372397 DOI: 10.1016/j.rapm.2004.06.010]
23 **Horlocker TT**, Vandermeuelen E, Kopp SL, Gogarten W, Leffert LR, Benzon HT. Regional Anesthesia in the Patient Receiving Antithrombotic or Thrombolytic Therapy: American Society of Regional Anesthesia and Pain Medicine Evidence-Based Guidelines (Fourth Edition). *Reg Anesth Pain Med* 2018; **43**: 263-309 [PMID: 29561531 DOI: 10.1097/AAP.0000000000000763]
24 **Bruce BG**, Green A, Blaine TA, Wesner LV. Brachial plexus blocks for upper extremity orthopaedic surgery. *J Am Acad Orthop Surg* 2012; **20**: 38-47 [PMID: 22207517 DOI: 10.5435/JAAOS-20-01-038]
25 **Srikumaran U**, Stein BE, Tan EW, Freehill MT, Wilckens JH. Upper-extremity peripheral nerve blocks in the perioperative pain management of orthopaedic patients: AAOS exhibit selection. *J Bone Joint Surg Am* 2013; **95**: e197(1-e1913) [PMID: 24352782 DOI: 10.2106/JBJS.L.01745]
26 **Urmey WF**, Talts KH, Sharrock NE. One hundred percent incidence of hemidiaphragmatic paresis

associated with interscalene brachial plexus anesthesia as diagnosed by ultrasonography. *Anesth Analg* 1991; **72**: 498-503 [PMID: 2006740 DOI: 10.1213/00000539-199104000-00014]

27 **Melton MS**, Monroe HE, Qi W, Lewis SL, Nielsen KC, Klein SM. Effect of Interscalene Brachial Plexus Block on the Pulmonary Function of Obese Patients: A Prospective, Observational Cohort Study. *Anesth Analg* 2017; **125**: 313-319 [PMID: 28609340 DOI: 10.1213/ANE.0000000000002180]

28 **Russon K**, Pickworth T, Harrop-Griffiths W. Upper limb blocks. *Anaesthesia* 2010; **65** Suppl 1: 48-56 [PMID: 20377546 DOI: 10.1111/j.1365-2044.2010.06277.x]

29 **Perlas A**, Lobo G, Lo N, Brull R, Chan VW, Karkhanis R. Ultrasound-guided supraclavicular block: outcome of 510 consecutive cases. *Reg Anesth Pain Med* 2009; **34**: 171-176 [PMID: 19282715 DOI: 10.1097/AAP.0b013e31819a3f81]

30 **Mak PH**, Irwin MG, Ooi CG, Chow BF. Incidence of diaphragmatic paralysis following supraclavicular brachial plexus block and its effect on pulmonary function. *Anaesthesia* 2001; **56**: 352-356 [PMID: 11284823 DOI: 10.1046/j.1365-2044.2001.01708-2.x]

31 **Liu SS**, Gordon MA, Shaw PM, Wilfred S, Shetty T, Yadeau JT. A prospective clinical registry of ultrasound-guided regional anesthesia for ambulatory shoulder surgery. *Anesth Analg* 2010; **111**: 617-623 [PMID: 20686013 DOI: 10.1213/ANE.0b013e3181ea5f5d]

32 **Desroches J**. The infraclavicular brachial plexus block by the coracoid approach is clinically effective: an observational study of 150 patients. *Can J Anaesth* 2003; **50**: 253-257 [PMID: 12620948 DOI: 10.1007/BF03017794]

33 **Carpenter RL**, Caplan RA, Brown DL, Stephenson C, Wu R. Incidence and risk factors for side effects of spinal anesthesia. *Anesthesiology* 1992; **76**: 906-916 [PMID: 1599111 DOI: 10.1097/00000542-199206000-00006]

34 **Tarkkila P**, Isola J. A regression model for identifying patients at high risk of hypotension, bradycardia and nausea during spinal anesthesia. *Acta Anaesthesiol Scand* 1992; **36**: 554-558 [PMID: 1514341 DOI: 10.1111/j.1399-6576.1992.tb03517.x]

35 **Dauphin A**, Raymer KE, Stanton EB, Fuller HD. Comparison of general anesthesia with and without lumbar epidural for total hip arthroplasty: effects of epidural block on hip arthroplasty. *J Clin Anesth* 1997; **9**: 200-203 [PMID: 9172026 DOI: 10.1016/s0952-8180(97)00035-4]

36 **Indelli PF**, Grant SA, Nielsen K, Vail TP. Regional anesthesia in hip surgery. *Clin Orthop Relat Res* 2005; **441**: 250-255 [PMID: 16331011 DOI: 10.1097/01.blo.0000192355.71966.8e]

37 **Imbelloni LE**, Gouveia MA, Cordeiro JA. Continuous spinal anesthesia versus combined spinal epidural block for major orthopedic surgery: prospective randomized study. *Sao Paulo Med J* 2009; **127**: 7-11 [PMID: 19466288 DOI: 10.1590/s1516-31802009000100003]

38 **Rodgers A**, Walker N, Schug S, McKee A, Kehlet H, van Zundert A, Sage D, Futter M, Saville G, Clark T, MacMahon S. Reduction of postoperative mortality and morbidity with epidural or spinal anaesthesia: results from overview of randomised trials. *BMJ* 2000; **321**: 1493 [PMID: 11118174 DOI: 10.1136/bmj.321.7275.1493]

39 **Tummala V**, Rao LN, Vallury MK, Sanapala A. A comparative study-efficacy and safety of combined spinal epidural anesthesia versus spinal anesthesia in high-risk geriatric patients for surgeries around the hip joint. *Anesth Essays Res* 2015; **9**: 185-188 [PMID: 26417125 DOI: 10.4103/0259-1162.153764]

40 **Fowler SJ**, Symons J, Sabato S, Myles PS. Epidural analgesia compared with peripheral nerve blockade after major knee surgery: a systematic review and meta-analysis of randomized trials. *Br J Anaesth* 2008; **100**: 154-164 [PMID: 18211990 DOI: 10.1093/bja/aem373]

41 **Liu Y**, Su M, Li W, Yuan H, Yang C. Comparison of general anesthesia with endotracheal intubation, combined spinal-epidural anesthesia, and general anesthesia with laryngeal mask airway and nerve block for intertrochanteric fracture surgeries in elderly patients: a retrospective cohort study. *BMC Anesthesiol* 2019; **19**: 230 [PMID: 31847846 DOI: 10.1186/s12871-019-0908-2]

42 **Horlocker TT**. Complications of regional anesthesia and acute pain management. *Anesthesiol Clin* 2011; **29**: 257-278 [PMID: 21620342 DOI: 10.1016/j.anclin.2011.04.006]

43 **Picard J**, Meek T. Complications of regional anaesthesia. *Anaesthesia* 2010; **65** Suppl 1: 105-115 [PMID: 20377552 DOI: 10.1111/j.1365-2044.2009.06205.x]

44 **Rawal N**, Van Zundert A, Holmström B, Crowhurst JA. Combined spinal-epidural technique. *Reg Anesth* 1997; **22**: 406-423 [PMID: 9338901 DOI: 10.1016/s1098-7339(97)80026-0]

45 **Holmström B**, Laugaland K, Rawal N, Hallberg S. Combined spinal epidural block versus spinal and epidural block for orthopaedic surgery. *Can J Anaesth* 1993; **40**: 601-606 [PMID: 8104724 DOI: 10.1007/BF03009695]

46 **Albright GA**, Forster RM. The safety and efficacy of combined spinal and epidural analgesia/anesthesia (6,002 blocks) in a community hospital. *Reg Anesth Pain Med* 1999; **24**: 117-125 [PMID: 10204896 DOI: 10.1016/s1098-7339(99)90071-8]

47 **Greenhalgh CA**. Respiratory arrest in a parturient following intrathecal injection of sufentanil and bupivacaine. *Anaesthesia* 1996; **51**: 173-175 [PMID: 8779376 DOI: 10.1111/j.1365-2044.1996.tb07708.x]

48 **Sharma S**, Iorio R, Specht LM, Davies-Lepie S, Healy WL. Complications of femoral nerve block for total knee arthroplasty. *Clin Orthop Relat Res* 2010; **468**: 135-140 [PMID: 19680735 DOI: 10.1007/s11999-009-1025-1]

49 **Paul JE**, Arya A, Hurlburt L, Cheng J, Thabane L, Tidy A, Murthy Y. Femoral nerve block improves analgesia outcomes after total knee arthroplasty: a meta-analysis of randomized controlled

trials. *Anesthesiology* 2010; **113**: 1144-1162 [PMID: 20966667 DOI: 10.1097/ALN.0b013e3181f4b18]

50 **Williams BA**, Kentor ML, Vogt MT, Williams JP, Chelly JE, Valalik S, Harner CD, Fu FH. Femoral-sciatic nerve blocks for complex outpatient knee surgery are associated with less postoperative pain before same-day discharge: a review of 1,200 consecutive cases from the period 1996-1999. *Anesthesiology* 2003; **98**: 1206-1213 [PMID: 12717143 DOI: 10.1097/00000542-200305000-00024]

51 **Williams BA**, Kentor ML, Vogt MT, Vogt WB, Coley KC, Williams JP, Roberts MS, Chelly JE, Harner CD, Fu FH. Economics of nerve block pain management after anterior cruciate ligament reconstruction: potential hospital cost savings *via* associated postanesthesia care unit bypass and same-day discharge. *Anesthesiology* 2004; **100**: 697-706 [PMID: 15108988 DOI: 10.1097/00000542-200403000-00034]

52 **Baker MD**, Gullett JP. Ultrasound-Guided Femoral Nerve Blocks. *Pediatr Emerg Care* 2015; **31**: 864-8; quiz 869 [PMID: 26626896 DOI: 10.1097/PEC.0000000000000634]

53 **Kwofie MK**, Shastri UD, Gadsden JC, Sinha SK, Abrams JH, Xu D, Salviz EA. The effects of ultrasound-guided adductor canal block versus femoral nerve block on quadriceps strength and fall risk: a blinded, randomized trial of volunteers. *Reg Anesth Pain Med* 2013; **38**: 321-325 [PMID: 23788068 DOI: 10.1097/AAP.0b013e318295df80]

54 **Jæger P**, Zaric D, Fomsgaard JS, Hilsted KL, Bjerregaard J, Gyrn J, Mathiesen O, Larsen TK, Dahl JB. Adductor canal block versus femoral nerve block for analgesia after total knee arthroplasty: a randomized, double-blind study. *Reg Anesth Pain Med* 2013; **38**: 526-532 [PMID: 24121608 DOI: 10.1097/AAP.0000000000000015]

55 **Kim DH**, Lin Y, Goytizolo EA, Kahn RL, Maalouf DB, Manohar A, Patt ML, Goon AK, Lee YY, Ma Y, Yadeau JT. Adductor canal block versus femoral nerve block for total knee arthroplasty: a prospective, randomized, controlled trial. *Anesthesiology* 2014; **120**: 540-550 [PMID: 24401769 DOI: 10.1097/ALN.0000000000000119]

56 **Wang D**, Yang Y, Li Q, Tang SL, Zeng WN, Xu J, Xie TH, Pei FX, Yang L, Li LL, Zhou ZK. Adductor canal block versus femoral nerve block for total knee arthroplasty: a meta-analysis of randomized controlled trials. *Sci Rep* 2017; **7**: 40721 [PMID: 28079176 DOI: 10.1038/srep40721]

57 **Lund J**, Jenstrup MT, Jaeger P, Sørensen AM, Dahl JB. Continuous adductor-canal-blockade for adjuvant post-operative analgesia after major knee surgery: preliminary results. *Acta Anaesthesiol Scand* 2011; **55**: 14-19 [PMID: 21039357 DOI: 10.1111/j.1399-6576.2010.02333.x]

58 **Seo SS**, Kim OG, Seo JH, Kim DH, Kim YG, Park BY. Comparison of the Effect of Continuous Femoral Nerve Block and Adductor Canal Block after Primary Total Knee Arthroplasty. *Clin Orthop Surg* 2017; **9**: 303-309 [PMID: 28861197 DOI: 10.4055/cios.2017.9.3.303]

59 **Edwards MD**, Bethea JP, Hunnicutt JL, Slone HS, Woolf SK. Effect of Adductor Canal Block Versus Femoral Nerve Block on Quadriceps Strength, Function, and Postoperative Pain After Anterior Cruciate Ligament Reconstruction: A Systematic Review of Level 1 Studies. *Am J Sports Med* 2020; **48**: 2305-2313 [PMID: 31800300 DOI: 10.1177/0363546519883589]

60 **Espelund M**, Fomsgaard JS, Haraszuk J, Mathiesen O, Dahl JB. Analgesic efficacy of ultrasound-guided adductor canal blockade after arthroscopic anterior cruciate ligament reconstruction: a randomised controlled trial. *Eur J Anaesthesiol* 2013; **30**: 422-428 [PMID: 23549123 DOI: 10.1097/EJA.0b013e328360bdb9]

61 **Ilfeld BM**, Duke KB, Donohue MC. The association between lower extremity continuous peripheral nerve blocks and patient falls after knee and hip arthroplasty. *Anesth Analg* 2010; **111**: 1552-1554 [PMID: 20889937 DOI: 10.1213/ANE.0b013e3181fb9507]

62 **Jones MR**, Novitch MB, Hall OM, Bourgeois AP, Jeha GM, Kaye RJ, Orhurhu V, Orhurhu MS, Eng M, Cornett EM, Kaye AD. Fascia iliaca block, history, technique, and efficacy in clinical practice. *Best Pract Res Clin Anaesthesiol* 2019; **33**: 407-413 [PMID: 31791559 DOI: 10.1016/j.bpa.2019.07.011]

63 **Newman B**, McCarthy L, Thomas PW, May P, Layzell M, Horn K. A comparison of pre-operative nerve stimulator-guided femoral nerve block and fascia iliaca compartment block in patients with a femoral neck fracture. *Anaesthesia* 2013; **68**: 899-903 [PMID: 23789738 DOI: 10.1111/anae.12321]

64 **Candal-Couto JJ**, McVie JL, Haslam N, Innes AR, Rushmer J. Pre-operative analgesia for patients with femoral neck fractures using a modified fascia iliaca block technique. *Injury* 2005; **36**: 505-510 [PMID: 15755432 DOI: 10.1016/j.injury.2004.10.015]

65 **Garlich JM**, Pujari A, Debbi EM, Yalamanchili DR, Moak ZB, Stephenson SK, Stephan SR, Polakof LS, Johnson CR, Noorzad AS, Little MTM, Moon CN, Black JT, Anand KK, Lin CA. Time to Block: Early Regional Anesthesia Improves Pain Control in Geriatric Hip Fractures. *J Bone Joint Surg Am* 2020; **102**: 866-872 [PMID: 32195685 DOI: 10.2106/JBJS.19.01148]

66 **Wathen JE**, Gao D, Merritt G, Georgopoulos G, Battan FK. A randomized controlled trial comparing a fascia iliaca compartment nerve block to a traditional systemic analgesic for femur fractures in a pediatric emergency department. *Ann Emerg Med* 2007; **50**: 162-171, 171.e1 [PMID: 17210208 DOI: 10.1016/j.annemergmed.2006.09.006]

67 **Yun MJ**, Kim YH, Han MK, Kim JH, Hwang JW, Do SH. Analgesia before a spinal block for femoral neck fracture: fascia iliaca compartment block. *Acta Anaesthesiol Scand* 2009; **53**: 1282-1287 [PMID: 19650803 DOI: 10.1111/j.1399-6576.2009.02052.x]

68 **Sia S**, Pelusio F, Barbagli R, Rivituso C. Analgesia before performing a spinal block in the sitting position in patients with femoral shaft fracture: a comparison between femoral nerve block and

intravenous fentanyl. *Anesth Analg* 2004; **99**: 1221-1224 [PMID: 15385380 DOI: 10.1213/01.ANE.0000134812.00471.44]

69 **Hebbard P**, Ivanusic J, Sha S. Ultrasound-guided supra-inguinal fascia iliaca block: a cadaveric evaluation of a novel approach. *Anaesthesia* 2011; **66**: 300-305 [PMID: 21401544 DOI: 10.1111/j.1365-2044.2011.06628.x]

70 **Eastburn E**, Hernandez MA, Boretsky K. Technical success of the ultrasound-guided supra-inguinal fascia iliaca compartment block in older children and adolescents for hip arthroscopy. *Paediatr Anaesth* 2017; **27**: 1120-1124 [PMID: 29030933 DOI: 10.1111/pan.13227]

71 **Swenson JD**, Davis JJ, Stream JO, Crim JR, Burks RT, Greis PE. Local anesthetic injection deep to the fascia iliaca at the level of the inguinal ligament: the pattern of distribution and effects on the obturator nerve. *J Clin Anesth* 2015; **27**: 652-657 [PMID: 26277873 DOI: 10.1016/j.jclinane.2015.07.001]

72 **Kopp SL**, Jacob AK, Hebl JR. Regional Anesthesia in Patients With Preexisting Neurologic Disease. *Reg Anesth Pain Med* 2015; **40**: 467-478 [PMID: 26115188 DOI: 10.1097/AAP.0000000000000179]

73 **Li D**, Alqwbani M, Wang Q, Liao R, Yang J, Kang P. Efficacy of Adductor Canal Block Combined With Additional Analgesic Methods for Postoperative Analgesia in Total Knee Arthroplasty: A Prospective, Double-Blind, Randomized Controlled Study. *J Arthroplasty* 2020; **35**: 3554-3562 [PMID: 32680754 DOI: 10.1016/j.arth.2020.06.060]

74 **Soffin EM**, YaDeau JT. Enhanced recovery after surgery for primary hip and knee arthroplasty: a review of the evidence. *Br J Anaesth* 2016; **117**: iii62-iii72 [PMID: 27940457 DOI: 10.1093/bja/aew362]

75 **Kuang MJ**, Ma JX, Fu L, He WW, Zhao J, Ma XL. Is Adductor Canal Block Better Than Femoral Nerve Block in Primary Total Knee Arthroplasty? *J Arthroplasty* 2017; **32**: 3238-3248.e3 [PMID: 28606458 DOI: 10.1016/j.arth.2017.05.015]

76 **El Ahl MS**. Femoral nerve block versus adductor canal block for postoperative pain control after anterior cruciate ligament reconstruction: A randomized controlled double blind study. *Saudi J Anaesth* 2015; **9**: 279-282 [PMID: 26240546 DOI: 10.4103/1658-354X.154708]

77 **Abdallah FW**, Whelan DB, Chan VW, Prasad GA, Endersby RV, Theodoropolous J, Oldfield S, Oh J, Brull R. Adductor Canal Block Provides Noninferior Analgesia and Superior Quadriceps Strength Compared with Femoral Nerve Block in Anterior Cruciate Ligament Reconstruction. *Anesthesiology* 2016; **124**: 1053-1064 [PMID: 26938989 DOI: 10.1097/ALN.0000000000001045]

78 **Lynch JR**, Okoroha KR, Lizzio V, Yu CC, Jildeh TR, Moutzouros V. Adductor Canal Block Versus Femoral Nerve Block for Pain Control After Anterior Cruciate Ligament Reconstruction: A Prospective Randomized Trial. *Am J Sports Med* 2019; **47**: 355-363 [PMID: 30557034 DOI: 10.1177/0363546518815874]

79 **Goytizolo EA**, Lin Y, Kim DH, Ranawat AS, Westrich GH, Mayman DJ, Su EP, Padgett DE, Alexiades MM, Soeters R, Mac PD, Fields KG, YaDeau JT. Addition of Adductor Canal Block to Periarticular Injection for Total Knee Replacement: A Randomized Trial. *J Bone Joint Surg Am* 2019; **101**: 812-820 [PMID: 31045669 DOI: 10.2106/JBJS.18.00195]

80 **Sawhney M**, Mehdian H, Kashin B, Ip G, Bent M, Choy J, McPherson M, Bowry R. Pain After Unilateral Total Knee Arthroplasty: A Prospective Randomized Controlled Trial Examining the Analgesic Effectiveness of a Combined Adductor Canal Peripheral Nerve Block with Periarticular Infiltration Versus Adductor Canal Nerve Block Alone Versus Periarticular Infiltration Alone. *Anesth Analg* 2016; **122**: 2040-2046 [PMID: 27028771 DOI: 10.1213/ANE.0000000000001210]

81 **Nader A**, Kendall MC, Manning DW, Beal M, Rahangdale R, Dekker R, De Oliveira GS Jr, Kamenetsky E, McCarthy RJ. Single-Dose Adductor Canal Block With Local Infiltrative Analgesia Compared With Local Infiltrate Analgesia After Total Knee Arthroplasty: A Randomized, Double-Blind, Placebo-Controlled Trial. *Reg Anesth Pain Med* 2016; **41**: 678-684 [PMID: 27776098 DOI: 10.1097/AAP.0000000000000494]

82 **Kim DH**, Beathe JC, Lin Y, YaDeau JT, Maalouf DB, Goytizolo E, Garnett C, Ranawat AS, Su EP, Mayman DJ, Memtsoudis SG. Addition of Infiltration Between the Popliteal Artery and the Capsule of the Posterior Knee and Adductor Canal Block to Periarticular Injection Enhances Postoperative Pain Control in Total Knee Arthroplasty: A Randomized Controlled Trial. *Anesth Analg* 2019; **129**: 526-535 [PMID: 30234517 DOI: 10.1213/ANE.0000000000003794]

83 **Greensmith JE**, Murray WB. Complications of regional anesthesia. *Curr Opin Anaesthesiol* 2006; **19**: 531-537 [PMID: 16960487 DOI: 10.1097/01.aco.0000245280.99786.a3]

84 **Kapoor R**, Adhikary SD, Siefring C, McQuillan PM. The saphenous nerve and its relationship to the nerve to the vastus medialis in and around the adductor canal: an anatomical study. *Acta Anaesthesiol Scand* 2012; **56**: 365-367 [PMID: 22335278 DOI: 10.1111/j.1399-6576.2011.02645.x]

85 **Tran J**, Giron Arango L, Peng P, Sinha SK, Agur A, Chan V. Evaluation of the iPACK block injectate spread: a cadaveric study. *Reg Anesth Pain Med* 2019 [PMID: 31061110 DOI: 10.1136/rapm-2018-100355]

86 **Sankineani SR**, Reddy ARC, Eachempati KK, Jangale A, Gurava Reddy AV. Comparison of adductor canal block and IPACK block (interspace between the popliteal artery and the capsule of the posterior knee) with adductor canal block alone after total knee arthroplasty: a prospective control trial on pain and knee function in immediate postoperative period. *Eur J Orthop Surg Traumatol* 2018; **28**: 1391-1395 [PMID: 29721648 DOI: 10.1007/s00590-018-2218-7]

87 **Jinadu S**, Pai P, Lai Y. Ambulatory knee replacements with IPACK block. *J Clin Anesth* 2020; **60**:

55-56 [PMID: 31445181 DOI: 10.1016/j.jclinane.2019.08.021]
88 **Niesen AD**, Harris DJ, Johnson CS, Stoike DE, Smith HM, Jacob AK, Amundson AW, Pawlina W, Martin DP. Interspace between Popliteal Artery and posterior Capsule of the Knee (IPACK) Injectate Spread: A Cadaver Study. *J Ultrasound Med* 2019; **38**: 741-745 [PMID: 30232819 DOI: 10.1002/jum.14761]
89 **Vloka JD**, Hadzić A, April E, Thys DM. The division of the sciatic nerve in the popliteal fossa: anatomical implications for popliteal nerve blockade. *Anesth Analg* 2001; **92**: 215-217 [PMID: 11133630 DOI: 10.1097/00000539-200101000-00041]
90 **Prasad A**, Perlas A, Ramlogan R, Brull R, Chan V. Ultrasound-guided popliteal block distal to sciatic nerve bifurcation shortens onset time: a prospective randomized double-blind study. *Reg Anesth Pain Med* 2010; **35**: 267-271 [PMID: 20921838 DOI: 10.1097/AAP.0b013e3181df2527]
91 **Germain G**, Lévesque S, Dion N, Nadeau MJ, Coté D, Nicole PC, Turgeon AF. Brief reports: a comparison of an injection cephalad or caudad to the division of the sciatic nerve for ultrasound-guided popliteal block: a prospective randomized study. *Anesth Analg* 2012; **114**: 233-235 [PMID: 22003214 DOI: 10.1213/ANE.0b013e3182373887]
92 **Wiegel M**, Gottschaldt U, Hennebach R, Hirschberg T, Reske A. Complications and adverse effects associated with continuous peripheral nerve blocks in orthopedic patients. *Anesth Analg* 2007; **104**: 1578-1582, table of contents [PMID: 17513661 DOI: 10.1213/01.ane.0000261260.69083.f3]
93 **Chin KJ**, Wong NW, Macfarlane AJ, Chan VW. Ultrasound-guided versus anatomic landmark-guided ankle blocks: a 6-year retrospective review. *Reg Anesth Pain Med* 2011; **36**: 611-618 [PMID: 21941219 DOI: 10.1097/AAP.0b013e31822b1291]
94 **Delbos A**, Philippe M, Clément C, Olivier R, Coppens S. Ultrasound-guided ankle block. History revisited. *Best Pract Res Clin Anaesthesiol* 2019; **33**: 79-93 [PMID: 31272656 DOI: 10.1016/j.bpa.2019.05.002]
95 **Schipper ON**, Hunt KJ, Anderson RB, Davis WH, Jones CP, Cohen BE. Ankle Block vs Single-Shot Popliteal Fossa Block as Primary Anesthesia for Forefoot Operative Procedures: Prospective, Randomized Comparison. *Foot Ankle Int* 2017; **38**: 1188-1191 [PMID: 28814096 DOI: 10.1177/1071100717723132]
96 **Kahn RL**, Ellis SJ, Cheng J, Curren J, Fields KG, Roberts MM, YaDeau JT. The Incidence of Complications Is Low Following Foot and Ankle Surgery for Which Peripheral Nerve Blocks Are Used for Postoperative Pain Management. *HSS J* 2018; **14**: 134-142 [PMID: 29983654 DOI: 10.1007/s11420-017-9588-y]
97 **Nielsen MV**, Bendtsen TF, Børglum J. Superiority of ultrasound-guided Shamrock lumbar plexus block. *Minerva Anestesiol* 2018; **84**: 115-121 [PMID: 28749094 DOI: 10.23736/S0375-9393.17.11783-9]
98 **de Visme V**, Picart F, Le Jouan R, Legrand A, Savry C, Morin V. Combined lumbar and sacral plexus block compared with plain bupivacaine spinal anesthesia for hip fractures in the elderly. *Reg Anesth Pain Med* 2000; **25**: 158-162 [PMID: 10746528 DOI: 10.1053/rapm.2000.0250158]
99 **Badiola I**, Liu J, Huang S, Kelly JD 4th, Elkassabany N. A comparison of the fascia iliaca block to the lumbar plexus block in providing analgesia following arthroscopic hip surgery: A randomized controlled clinical trial. *J Clin Anesth* 2018; **49**: 26-29 [PMID: 29860224 DOI: 10.1016/j.jclinane.2018.05.012]
100 **Bravo D**, Layera S, Aliste J, Jara Á, Fernández D, Barrientos C, Wulf R, Muñoz G, Finlayson RJ, Tran Q. Lumbar plexus block versus suprainguinal fascia iliaca block for total hip arthroplasty: A single-blinded, randomized trial. *J Clin Anesth* 2020; **66**: 109907 [PMID: 32502775 DOI: 10.1016/j.jclinane.2020.109907]
101 **Guay J**, Parker MJ, Griffiths R, Kopp S. Peripheral nerve blocks for hip fractures. *Cochrane Database Syst Rev* 2017; **5**: CD001159 [PMID: 28494088 DOI: 10.1002/14651858.CD001159.pub2]
102 **Gadsden JC**, Lindenmuth DM, Hadzic A, Xu D, Somasundarum L, Flisinski KA. Lumbar plexus block using high-pressure injection leads to contralateral and epidural spread. *Anesthesiology* 2008; **109**: 683-688 [PMID: 18813048 DOI: 10.1097/ALN.0b013e31818631a7]
103 **Saranteas T**, Soulioti E, Kostroglou A, Anagnostopoulos D, Koutsomanolis D, Kouki P. Limitations of the ultrasound-assisted Shamrock approach for Lumbar plexus nerve block in elderly patients. *Anaesth Crit Care Pain Med* 2020; **39**: 119-120 [PMID: 31026531 DOI: 10.1016/j.accpm.2019.04.008]
104 **Neal JM**, Neal EJ, Weinberg GL. American Society of Regional Anesthesia and Pain Medicine Local Anesthetic Systemic Toxicity checklist: 2020 version. *Reg Anesth Pain Med* 2021; **46**: 81-82 [PMID: 33148630 DOI: 10.1136/rapm-2020-101986]
105 **Vasques F**, Behr AU, Weinberg G, Ori C, Di Gregorio G. A Review of Local Anesthetic Systemic Toxicity Cases Since Publication of the American Society of Regional Anesthesia Recommendations: To Whom It May Concern. *Reg Anesth Pain Med* 2015; **40**: 698-705 [PMID: 26469367 DOI: 10.1097/AAP.0000000000000320]
106 **Gitman M**, Fettiplace MR, Weinberg GL, Neal JM, Barrington MJ. Local Anesthetic Systemic Toxicity: A Narrative Literature Review and Clinical Update on Prevention, Diagnosis, and Management. *Plast Reconstr Surg* 2019; **144**: 783-795 [PMID: 31461049 DOI: 10.1097/PRS.0000000000005989]
107 **Dickerson DM**, Apfelbaum JL. Local anesthetic systemic toxicity. *Aesthet Surg J* 2014; **34**: 1111-1119 [PMID: 25028740 DOI: 10.1177/1090820X14543102]

108 **Ok SH**, Hong JM, Lee SH, Sohn JT. Lipid Emulsion for Treating Local Anesthetic Systemic Toxicity. *Int J Med Sci* 2018; **15**: 713-722 [PMID: 29910676 DOI: 10.7150/ijms.22643]

109 **Harvey M**, Cave G. Lipid emulsion in local anesthetic toxicity. *Curr Opin Anaesthesiol* 2017; **30**: 632-638 [PMID: 28692439 DOI: 10.1097/ACO.0000000000000498]

110 **Tran DQ**, Salinas FV, Benzon HT, Neal JM. Lower extremity regional anesthesia: essentials of our current understanding. *Reg Anesth Pain Med* 2019 [PMID: 30635506 DOI: 10.1136/rapm-2018-000019]

111 **Neal JM**, Hsiung RL, Mulroy MF, Halpern BB, Dragnich AD, Slee AE. ASRA checklist improves trainee performance during a simulated episode of local anesthetic systemic toxicity. *Reg Anesth Pain Med* 2012; **37**: 8-15 [PMID: 22157743 DOI: 10.1097/AAP.0b013e31823d825a]

112 **Mulroy MF**, Weller RS, Liguori GA. A checklist for performing regional nerve blocks. *Reg Anesth Pain Med* 2014; **39**: 195-199 [PMID: 24718017 DOI: 10.1097/AAP.0000000000000075]

113 **Yeniocak T**, Canbolat N. Retrospective Analysis of Ultrasound-Guided Infraclavicular Block: Effect of Experience of Anesthesiologists on Volume of Local Anesthetic Administered. *Pain Res Manag* 2019; **2019**: 4846956 [PMID: 31198476 DOI: 10.1155/2019/4846956]

114 **Ahsan ZS**, Carvalho B, Yao J. Incidence of failure of continuous peripheral nerve catheters for postoperative analgesia in upper extremity surgery. *J Hand Surg Am* 2014; **39**: 324-329 [PMID: 24480691 DOI: 10.1016/j.jhsa.2013.11.011]

115 **Salinas FV**. Location, location, location: Continuous peripheral nerve blocks and stimulating catheters. *Reg Anesth Pain Med* 2003; **28**: 79-82 [PMID: 12677614 DOI: 10.1053/rapm.2003.50033]

116 **Jenkins CR**, Karmakar MK. An unusual complication of interscalene brachial plexus catheterization: delayed catheter migration. *Br J Anaesth* 2005; **95**: 535-537 [PMID: 16051648 DOI: 10.1093/bja/aei217]

117 **Capdevila X**, Dadure C, Bringuier S, Bernard N, Biboulet P, Gaertner E, Macaire P. Effect of patient-controlled perineural analgesia on rehabilitation and pain after ambulatory orthopedic surgery: a multicenter randomized trial. *Anesthesiology* 2006; **105**: 566-573 [PMID: 16931991 DOI: 10.1097/00000542-200609000-00022]

118 **Capdevila X**, Pirat P, Bringuier S, Gaertner E, Singelyn F, Bernard N, Choquet O, Bouaziz H, Bonnet F; French Study Group on Continuous Peripheral Nerve Blocks. Continuous peripheral nerve blocks in hospital wards after orthopedic surgery: a multicenter prospective analysis of the quality of postoperative analgesia and complications in 1,416 patients. *Anesthesiology* 2005; **103**: 1035-1045 [PMID: 16249678 DOI: 10.1097/00000542-200511000-00018]

119 **Liu J**, Jiang Y, Pang D, Xi H, Liu Y, Li W. Associations between single-nucleotide polymorphisms and epidural ropivacaine consumption in patients undergoing breast cancer surgery. *Genet Test Mol Biomarkers* 2013; **17**: 489-493 [PMID: 23577780 DOI: 10.1089/gtmb.2012.0388]

120 **Grau T**. Ultrasonography in the current practice of regional anaesthesia. *Best Pract Res Clin Anaesthesiol* 2005; **19**: 175-200 [PMID: 15966492 DOI: 10.1016/j.bpa.2004.12.008]

121 **Koscielniak-Nielsen ZJ**. Ultrasound-guided peripheral nerve blocks: what are the benefits? *Acta Anaesthesiol Scand* 2008; **52**: 727-737 [PMID: 18477070 DOI: 10.1111/j.1399-6576.2008.01666.x]

122 **Moon TS**, Lim E, Kinjo S. A survey of education and confidence level among graduating anesthesia residents with regard to selected peripheral nerve blocks. *BMC Anesthesiol* 2013; **13**: 16 [PMID: 23865456 DOI: 10.1186/1471-2253-13-16]

123 **Liu SS**, Zayas VM, Gordon MA, Beathe JC, Maalouf DB, Paroli L, Liguori GA, Ortiz J, Buschiazzo V, Ngeow J, Shetty T, Ya Deau JT. A prospective, randomized, controlled trial comparing ultrasound versus nerve stimulator guidance for interscalene block for ambulatory shoulder surgery for postoperative neurological symptoms. *Anesth Analg* 2009; **109**: 265-271 [PMID: 19535720 DOI: 10.1213/ane.0b013e3181a3272c]

124 **Fredrickson MJ**, Kilfoyle DH. Neurological complication analysis of 1000 ultrasound guided peripheral nerve blocks for elective orthopaedic surgery: a prospective study. *Anaesthesia* 2009; **64**: 836-844 [PMID: 19604186 DOI: 10.1111/j.1365-2044.2009.05938.x]

125 **Sites BD**, Taenzer AH, Herrick MD, Gilloon C, Antonakakis J, Richins J, Beach ML. Incidence of local anesthetic systemic toxicity and postoperative neurologic symptoms associated with 12,668 ultrasound-guided nerve blocks: an analysis from a prospective clinical registry. *Reg Anesth Pain Med* 2012; **37**: 478-482 [PMID: 22705953 DOI: 10.1097/AAP.0b013e31825cb3d6]

126 **Auroy Y**, Benhamou D, Bargues L, Ecoffey C, Falissard B, Mercier FJ, Bouaziz H, Samii K. Major complications of regional anesthesia in France: The SOS Regional Anesthesia Hotline Service. *Anesthesiology* 2002; **97**: 1274-1280 [PMID: 12411815 DOI: 10.1097/00000542-200211000-00034]

127 **Malchow RJ**, Gupta RK, Shi Y, Shotwell MS, Jaeger LM, Bowens C. Comprehensive Analysis of 13,897 Consecutive Regional Anesthetics at an Ambulatory Surgery Center. *Pain Med* 2018; **19**: 368-384 [PMID: 28371877 DOI: 10.1093/pm/pnx045]

128 **Borgeat A**, Blumenthal S, Lambert M, Theodorou P, Vienne P. The feasibility and complications of the continuous popliteal nerve block: a 1001-case survey. *Anesth Analg* 2006; **103**: 229-233, table of contents [PMID: 16790658 DOI: 10.1213/01.ane.0000221462.87951.8d]

129 **Kapur E**, Vuckovic I, Dilberovic F, Zaciragic A, Cosovic E, Divanovic KA, Mornjakovic Z, Babic M, Borgeat A, Thys DM, Hadzic A. Neurologic and histologic outcome after intraneural injections of lidocaine in canine sciatic nerves. *Acta Anaesthesiol Scand* 2007; **51**: 101-107 [PMID: 17081151 DOI: 10.1111/j.1399-6576.2006.01169.x]

130 **Hadzic A**, Dilberovic F, Shah S, Kulenovic A, Kapur E, Zaciragic A, Cosovic E, Vuckovic I, Divanovic KA, Mornjakovic Z, Thys DM, Santos AC. Combination of intraneural injection and high

injection pressure leads to fascicular injury and neurologic deficits in dogs. *Reg Anesth Pain Med* 2004; **29**: 417-423 [PMID: 15372385 DOI: 10.1016/j.rapm.2004.06.002]

131 **Verlinde M**, Hollmann MW, Stevens MF, Hermanns H, Werdehausen R, Lirk P. Local Anesthetic-Induced Neurotoxicity. *Int J Mol Sci* 2016; **17**: 339 [PMID: 26959012 DOI: 10.3390/ijms17030339]

132 **Capdevila X**, Bringuier S, Borgeat A. Infectious risk of continuous peripheral nerve blocks. *Anesthesiology* 2009; **110**: 182-188 [PMID: 19104185 DOI: 10.1097/ALN.0b013e318190bd5b]

133 **Johnson RL**, Kopp SL, Hebl JR, Erwin PJ, Mantilla CB. Falls and major orthopaedic surgery with peripheral nerve blockade: a systematic review and meta-analysis. *Br J Anaesth* 2013; **110**: 518-528 [PMID: 23440367 DOI: 10.1093/bja/aet013]

134 **Spitzer D**, Wenger KJ, Neef V, Divé I, Schaller-Paule MA, Jahnke K, Kell C, Foerch C, Burger MC. Local Anesthetic-Induced Central Nervous System Toxicity during Interscalene Brachial Plexus Block: A Case Series Study of Three Patients. *J Clin Med* 2021; **10** [PMID: 33801401 DOI: 10.3390/jcm10051013]

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REVIEW

Management of proximal biceps tendon pathology

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Abstract

The long head of the biceps tendon is widely recognized as an important pain generator, especially in anterior shoulder pain and dysfunction with athletes and working individuals. The purpose of this review is to provide a current understanding of the long head of the biceps tendon anatomy and its surrounding structures, function, and relevant clinical information such as evaluation, treatment options, and complications in hopes of helping orthopaedic surgeons counsel their patients. An understanding of the long head of the biceps tendon anatomy and its surrounding structures is helpful to determine normal function as well as pathologic injuries that stem proximally. The biceps-labral complex has been identified and broken down into different regions that can further enhance a physician's knowledge of common anterior shoulder pain etiologies. Although various physical examination maneuvers exist meant to localize the anterior shoulder pain, the lack of specificity requires orthopaedic surgeons to rely on patient history, advanced imaging, and diagnostic injections in order to determine the patient's next steps. Nonsurgical treatment options such as anti-inflammatory medications, physical therapy, and ultrasound-guided corticosteroid injections should be utilized before entertaining surgical treatment options. If surgery is needed, the three options include biceps tenotomy, biceps tenodesis, or superior labrum anterior to posterior repair. Specifically for biceps tenodesis, recent studies have analyzed open *vs* arthroscopic techniques, the ideal location of tenodesis with intra-articular, suprapectoral, subpectoral, extra-articular top of groove, and extra-articular bottom of groove approaches, and the best method of fixation using interference screws, suture anchors, or cortical buttons. Orthopaedic surgeons should be aware of the complications of each procedure and respond accordingly for each patient. Once treated, patients often have good to excellent clinical outcomes and low rates of complications.

Grade D (Fair): 0
Grade E (Poor): 0

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Core Tip: Management of proximal pathologies involving the long head of the biceps tendon is evolving. While biceps tenotomy, biceps tenodesis, and superior labrum anterior to posterior repair can be used to treat these pathologic injuries, no consensus exists with regard to which procedure is best. This clinical review provides a current understanding of the long head of the biceps tendon anatomy and its surrounding structures, function, and relevant clinical information such as evaluation, treatment options, and complications in hopes of helping orthopaedic surgeons counsel their patients.

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INTRODUCTION

While the role of the long head of the biceps tendon (LHBT) in shoulder pathology has been studied extensively, the management of such pathology has evolved. Recently, studies have demonstrated that biceps tenodesis can be used to treat individuals with symptomatic superior labrum anterior to posterior (SLAP) lesions[1-3]. As a result, the number of biceps tenodesis procedures performed each year has increased[4]. Despite this rise in volume, there is no consensus on which procedure-biceps tenotomy, biceps tenodesis, or SLAP repair is superior in terms of clinical outcomes. Typically, orthopaedic surgeons use their preference and specific patient factors to determine which procedure is ideal for each patient. Furthermore, in patients who undergo biceps tenodesis, there is controversy as to whether orthopaedic surgeons should utilize open *vs* arthroscopic techniques, the best method of fixation with interference screws, suture anchors, or cortical buttons, and the ideal location of tenodesis with intra-articular, suprapectoral, subpectoral, extra-articular top of groove, or extra-articular bottom of groove approaches. Regardless of this debate, researchers can agree that the LHBT is widely recognized as an important pain generator, especially in anterior shoulder pain and dysfunction[5-8].

The purpose of this review is to provide a current understanding of LHBT anatomy, function, and clinical information such as evaluation, nonsurgical management, surgical management, and complications in hopes of helping orthopaedic surgeons counsel their patients.

ANATOMY AND FUNCTION

An appreciation of the LHBT anatomy and its surrounding structures is helpful to understand normal function as well as proximal pathologic injuries (Figures 1 and 2)[9,10]. The LHBT originates from the supraglenoid tubercle and the superior glenoid labrum and exits the glenohumeral joint through the bicipital groove[11]. The attachment point of the LHBT on the superior labrum is variable amongst patients: equal anterior and posterior attachment is the most common (37%), predominantly anterior is the least common (8%), and other variations such as entirely posterior (22%) or mostly posterior (33%) also exist[12,13]. As it exits the glenohumeral joint and before it enters the bicipital groove, the LHBT is stabilized by a capsule-ligamentous complex referred to as the biceps pulley, which consists of the subscapularis tendon, the supraspinatus tendon, the coracohumeral ligament, the pectoralis major tendon insertion, and the falciform ligament (Figure 1)[14,15]. The LHBT then travels distally into the bicipital groove along the anterior surface of the humerus through the osteoligamentous sheath which is formed by the transverse humeral ligament as well

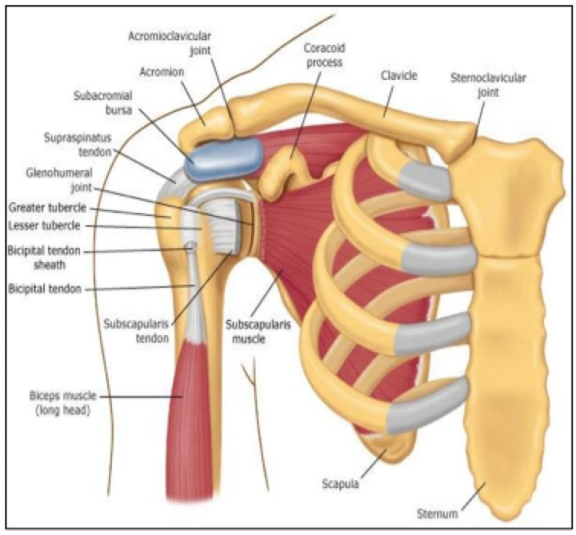


Figure 1 Schematic illustration of anterior shoulder anatomy from Blum *et al*[9]. Citation: Blum K, Chen AL, Chen TJ, Waite RL, Downs BW, Braverman ER, Kerner MM, Savarimuthu SM, DiNubile N. Repetitive H-wave device stimulation and program induces significant increases in the range of motion of post operative rotator cuff reconstruction in a double-blinded randomized placebo controlled human study. BMC Musculoskelet Disord 2009; 10: 132. Copyright© The Authors 2009. Published by BioMed Central Ltd. This is an open access article distributed under the terms of the Creative Commons CC BY license, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

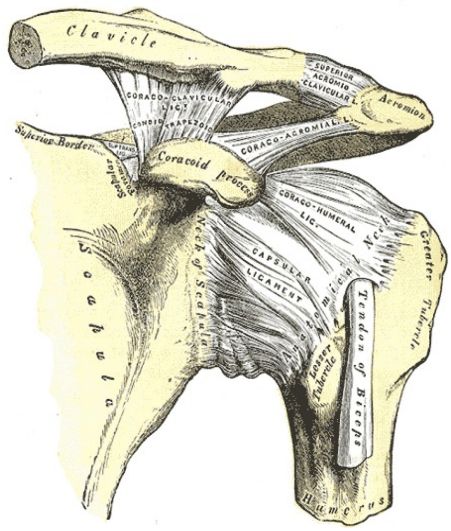


Figure 2 Anterior view of the left shoulder joint depicting tendons and ligaments from Miniato *et al*[10]. Citation: Miniato MA, Anand P, Varacallo M. Anatomy, Shoulder and Upper Limb, Shoulder. [Updated 2020 Jul 31]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing. Available from: https://www.ncbi.nlm.nih.gov/books/NBK536933/. Copyright© The Authors 2021. Published by StatPearls Publishing LLC. This book is distributed under the terms of the Creative Commons Attribution 4.0 International License, which permits use, duplication, adaptation, distribution, and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, a link is provided to the Creative Commons license, and any changes made are indicated.

as the greater and lesser tuberosities (Figures 1 and 2)[16]. The LHBT and the short head of the biceps tendon, which originates from the coracoid process with the coraco-brachialis, give rise to the muscle belly of the biceps brachii which externally rotates 90° before the tendons attach as a single tendinous insertion on the ulnar aspect of the bicipital tuberosity of the radius[6].

Furthermore, the long head of the biceps (LHB) and glenoid labrum have collectively been described as the "biceps-labral complex" (BLC) which can be categorized into three main parts: (1) The inside, which includes the superior labrum and the LHBT anchor at the supraglenoid tubercle; (2) The junction, which includes the intra-articular LHBT and its stabilizing pulley system; and (3) The bicipital tunnel, which includes the LHBT beginning at the articular margin of the humeral head adjacent to the pulley and extending to the subpectoral region (Figure 3)[17-19]. The bicipital tunnel, which houses the extra-articular biceps, is further divided into three

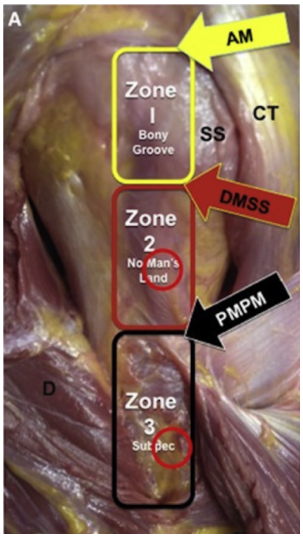


Figure 3 Visual depiction of biceps-labral complex with zone 2 red circle as site for arthroscopic suprapectoral tenodesis and zone 3 red circle as open subpectoral tenodesis location from Forsythe *et al*[120]. Citation: Forsythe B, Zuke WA, Agarwalla A, Puzzitiello RN, Garcia GH, Cvetanovich GL, Yanke AB, Verma NN, Romeo AA. Arthroscopic Suprapectoral and Open Subpectoral Biceps Tenodeses Produce Similar Outcomes: A Randomized Prospective Analysis. Arthroscopy 2020; 36: 23-32. Copyright© The Authors 2020. Published by Elsevier. The authors have obtained the permission for figure (Supplementary material). AM: Articular margin; CT: Conjoined tendon; d: Deltoid; DMSS: Distal margin of subscapularis tendon; PMPM: Proximal margin of pectoralis major; SS: Subscapularis.

clinically relevant zones. Zone 1 stretches from the articular margin to the distal margin of the subscapularis. Zone 2 extends from the distal margin of the subscapularis to the proximal margin of the pectoralis major. Lastly, zone 3 is the subpectoralis region[20].

The function of the LHBT still remains highly debated. Prior cadaveric studies have shown it may serve as a humeral head depressor, a stabilizer of the glenohumeral joint, or a stabilizer of the humeral head particularly in the anterosuperior and anterior directions of shoulder abduction[21-23]. Other authors consider the LHBT to be a vestigial structure that is not active during isolated shoulder movements and may have a larger role in proprioception of the shoulder[24,25]. Anatomically, there is consensus that the LHBT mainly functions as a forearm supinator while the short head of the biceps tendon mostly functions as an elbow flexor[6].

PROXIMAL BICEPS TENDON PATHOLOGY

The pathologic entities involving the LHBT can be classified into three general categories: inflammatory, instability, and traumatic[8]. Inflammation of the biceps tendon is commonly attributed to degenerative tendinopathy and overuse injuries. Additionally, rotator cuff tears and subacromial impingement can also lead to or be associated with bicipital tendinitis[26-30]. Some studies have found a prevalence as high as 93% in the association of LHBT inflammatory injuries and rotator cuff tears [31]. Instability of the tendon can create mechanical symptoms such as popping and clicking with range of motion. If the LHBT is unstable, the physician should highly suspect an associated subscapularis tendon tear or tears of the coracohumeral and/or superior glenohumeral complex[6,8]. Lastly, the LHBT is susceptible to traumatic injury, most commonly a complete rupture of the tendon, where pain resolves over time and function is typically reserved. These injury categories have been associated with other various shoulder conditions such as glenohumeral arthritis, labral lesions, and anterior or anterosuperior rotator cuff tears[1,32-35].

Anatomically, the three main parts of the BLC are associated with specific pathologic entities[17]. Injuries to the inside, which is predominantly associated with SLAP lesions, can be caused by superior migration of the humeral head, biceps tension, or peelback as a result of internal impingement[36]. Injuries to the junction include LHBT tears, LHBT incarceration, biceps chondromalacia, hourglass biceps, and pulley lesions[37-39]. The bicipital tunnel, specifically zones one and two, encompass LHBT tears, loose bodies, and tenosynovitis[18,40].

Evaluation

An in-depth history and physical examination must be done to differentiate biceps pain from other causes of referred shoulder pain[41]. This can be difficult because individuals with biceps pain can also have concomitant pathologies such as rotator cuff tears and may even have similar symptoms to patients with SLAP lesions[42-44]. As a result, physicians should utilize patient history, physical examination results, and imaging modalities to consider multiple differential diagnoses and help determine appropriate management.

A comprehensive history should be acquired when evaluating patients with LHBT injuries. A thorough history that documents the mechanism of injury can help the physician differentiate between various shoulder pathologies[45]. Obtaining information such as hand dominance, history of injury/trauma to the shoulder area, symptom exacerbation with overhead activities, pain at rest and/or pain at night, history or current overhead sport participation, history of current manual labor occupation or employment status, and any relevant surgical history can be incredibly useful in conjunction with the physical examination to determine the etiology of the pain[45].

Physical examination should start with assessment of range of motion as well as neurovascular examination that includes strength testing of all rotator cuff muscles. Common LHBT conditions that should be differentiated with an in depth physical examination include inflammatory injuries, instability, and rupture. LHBT inflammatory changes such as tenosynovitis or tendinitis often presents with pain in the anterior aspect of the shoulder that radiates to the anterior biceps[46]. Symptoms can be exacerbated by overhead activity or elbow flexion. LHBT instability will often present with reproducible clicking or tendon subluxation on physical examination[6]. For this type of injury, the physician should pay special attention to the subscapularis muscle as LHBT instability is associated with rotator cuff tears, especially those of the upper border of the subscapularis[17]. Therefore, physicians should also perform passive external rotation, lift-off, belly-press, and bear hug test for the subscapularis (Figure 4)[8,17,47]. LHBT rupture often occurs with a tearing sensation anteriorly and presents with swelling and ecchymosis. Some patients may have a Popeye deformity or sagging biceps muscle belly which can be exaggerated by having the patient flex his biceps (Figure 5)[6,17,48]. For these patients, muscle belly cramping has also been reported[49]. In patients with symptomatic proximal biceps pathology, pain will often be localized to the bicipital groove. This pain can be elicited on direct palpation of the area 7 cm below the acromion with the arm adducted, internally rotated 10°, and the elbow flexed[50]. To assist in proper palpation and pain elicitation, the shoulder should be internally and externally rotated in this position.

While specific examinations in patients with biceps-related pathology and SLAP tears can be utilized to differentiate etiologies of shoulder pain, these maneuvers often lack specificity[51,52]. For example, the Speed test, which is used to elicit anterior shoulder pain with resisted elbow flexion has overall sensitivity of 57% and specificity of 52% in diagnosing biceps tendon disorders and SLAP lesions (Figure 6)[47,52-55]. Similarly, the Yergason test, which is used to elicit anterior shoulder pain with resisted forearm supination, has been shown to be an unreliable predictor of biceps pathology or SLAP tears with a reported sensitivity of 43% and specificity of 79%[54-56]. Physical examination maneuvers specific for SLAP pathology, such as the O'Brien active compression test and the O'Driscoll dynamic labral shear test, have demonstrated reasonable diagnostic utility, but are still controversial (Figure 7)[57]. While some studies initially reported excellent results for the diagnostic utility of the O'Brien active compression test, recent meta-analyses have suggested that it is not diagnostic of SLAP tears[58,59]. The O'Driscoll dynamic labral shear test was also found to have excellent initial results in terms of diagnostic utility for SLAP tears, but was questioned by further studies[60-62]. Furthermore, examination maneuvers for SLAP pathology are limited by shoulder pathology that is often observed in individuals with SLAP tears, such as Bankart lesions and partial-thickness rotator cuff tears[63-65].

Imaging and diagnostic injections

With the lack of specificity in physical examination maneuvers, imaging studies are often used to differentiate LHBT pathology. Unfortunately, this too has its faults. While radiographs can be useful in assessing bony anomalies and ruling out concomitant osseous disorders, they often appear normal[7,52]. Advanced imaging studies such as MRI demonstrate reasonable sensitivity and specificity for the diagnosis of SLAP tears, LHBT rupture, and other inside lesions of the BLC; however, junctional and bicipital tunnel lesions are poorly identified[66-70]. Additionally,



Figure 4 Special tests for subscapularis from Jain *et al*[47]. Citation: Jain NB, Wilcox RB 3rd, Katz JN, Higgins LD. Clinical examination of the rotator cuff. PM R 2013; 5: 45-56. Copyright© The Authors 2013. Published by John Wiley and Sons. The authors have obtained the permission for figure (Supplementary material). Top left: Lift-off test; Top right: Belly-press test; Bottom: Bear hug test.

ultrasonography is a fast, cost-effective, and radiation-free diagnostic method for shoulder and has been used for LHBT instability, dynamic examination of the tendon, examination of hypoechogenic areas, and increased tendon diameter[71,72]. While ultrasound techniques are useful in detecting LHBT pathology with a sensitivity between 50%-96% and a sensitivity of 98%-100%, it is less helpful in diagnosing partial-thickness tears[71,73,74]. Regardless of its faults, ultrasonography techniques should be used in conjunction with MRI when examining LHBT pathology.

Diagnostic injections could also be utilized in patients with anterior shoulder pain as peritendinous or sheath injections are often used to clinically diagnose and treat biceps tendinopathy[75,76]. Injections into the tendon sheath can be diagnostic and therapeutic by providing the physician information about the patient's pathology based on their pain response post-treatment[77,78]. It is important to note that injections should not be directly inserted into tendons as it can lead to tendon rupture [79]. Improved injection accuracy through ultrasound guidance has proven to be effective compared to blind injection techniques. In a recent study by Hashiuchi *et al* [80], ultrasound-guided injections resulted in 87% accuracy while blind injections were accurate only 27% of the time.

TREATMENT OPTIONS

The treatment of LHBT pathology can be separated into nonsurgical and surgical management. Initially, LHBT injuries should be treated conservatively followed by



Figure 5 Lateral view showing Popeye deformity from José *et al*[48]. Citation: José AG, Luís Felipe HFS, Gabriel RSM, Fernando MI. Treatment of the Distal Biceps Brachii Tendon Rupture Using the Three Mini-Incisions Technique: Evaluation through MEPS and DASH. Ortho Rheum Open Access J. 2019; 14: 555888. Copyright© The Authors 2019. Published by Juniper Publishers INC. This work is licensed under Creative Commons Attribution 4.0 License.



Figure 6 Speed test from Jain *et al*[47]. Citation: Jain NB, Wilcox RB 3rd, Katz JN, Higgins LD. Clinical examination of the rotator cuff. PM R 2013; 5: 45-56. Copyright© The Authors 2013. Published by John Wiley and Sons. The authors have obtained the permission for figure (Supplementary material).

surgery when all conservative treatments fail.

Nonsurgical management

Nonsurgical management of LHBT disorders is largely driven by individual surgeon experience. Typically, management begins with nonsteroidal anti-inflammatory drugs, physical activity, activity modifications, and ultrasound-guided corticosteroid injections into the biceps sheath[56,80,81]. Although physical therapy improves overall shoulder strength, range of motion, and function, limited research has been done that analyzes the outcomes of physical therapy as a nonoperative management option for LHBT pathologies. As mentioned earlier, the corticosteroid injection should be carefully placed as accidentally guiding the injection into the biceps tendon may cause rupture[82]. If correctly placed, ultrasound-guided corticosteroid injections have shown to cause lower patient discomfort as well as superior accuracy compared to palpated and blind injections[83]. Unfortunately, corticosteroid injections were found only to be beneficial in the short term, but may be worse than other treatment options in the intermediate and long terms[84]. Regardless of technique, research on the effectiveness of corticosteroid injections is inconclusive[85].

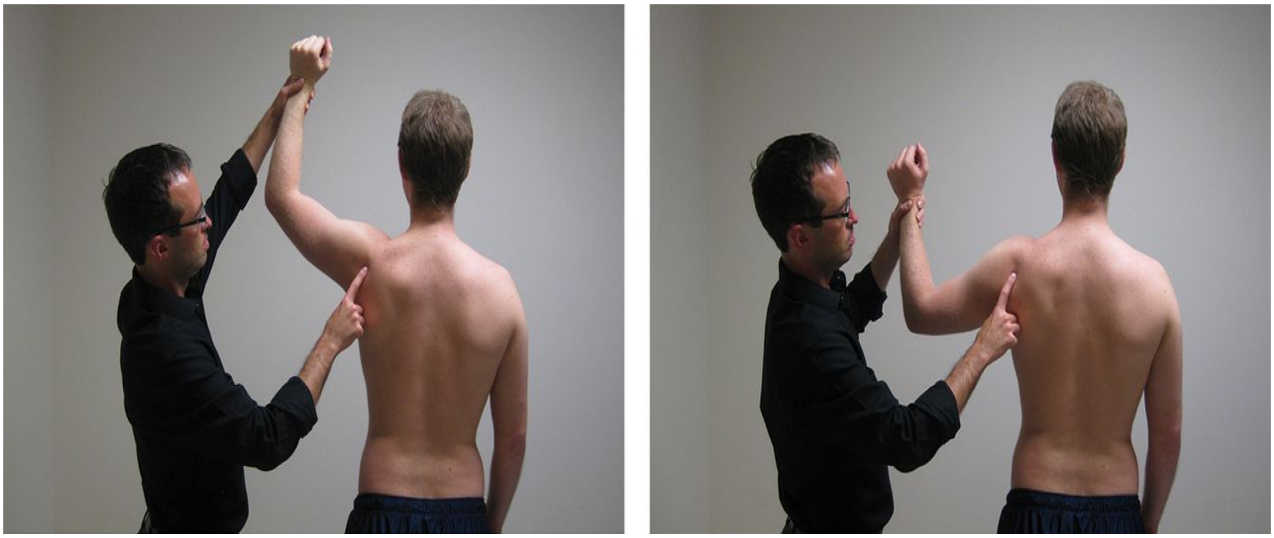


Figure 7 O'Driscoll dynamic labral shear test from Myer *et al*[57]. Citation: Myer CA, Hegedus EJ, Tarara DT, Myer DM. A user's guide to performance of the best shoulder physical examination tests. Br J Sports Med 2013; 47: 903-907. Copyright© The Authors 2013. Published by BMJ Publishing Group Ltd. The authors have obtained the permission for figure (Supplementary material).

Other options for nonsurgical management include iontophoresis, phonophoresis, ultrasonography, extracorporeal shock wave therapy, and laser therapy. Unfortunately, these have shown conflicting results in the literature[86,87]. Furthermore, promising yet inconclusive clinical outcomes have been shown for treatment options such as regenerative injection therapy which includes platelet-rich plasma[88,89]. If all nonsurgical treatment options fail, then patients should consider surgical treatment options.

Surgical management

While surgical management of LHBT pathologies is reserved for individuals who have failed all previously performed nonsurgical treatment options or individuals with acute injuries, the optimal surgical treatment is still up for debate[17]. The three options include biceps tenotomy, biceps tenodesis, and SLAP repair.

Biceps tenotomy: Biceps tenotomy is a viable option to surgically manage LHBT pathology and involves cutting the LHBT at its origin and maintaining the integrity of the labrum (Table 1)[49]. While numerous studies have shown excellent outcomes, pain relief, and improved patient-reported outcomes in individuals who undergo biceps tenotomy, there are a few complications shown in Table 1[46,90-92]. Other cited complications include stiffness, infection, transient nerve injuries, complex regional pain syndrome, and stroke secondary to cerebral hypoperfusion[93]. In recent studies, surgeons have tried to address some of these complications by testing arthroscopic techniques to limit distal migration of the LHB after tenotomy to minimize and even eliminate the occurrence of the Popeye deformity[94-97]. Other studies have reported ways to improve the efficiency of arthroscopic biceps tenotomy by using a biceps squeeze maneuver[98]. This is a simple method that entails manually squeezing the biceps muscle belly while performing the arthroscopic biceps tenotomy in order to shorten and tension the intra-articular portion of the tendon. In doing so, this technique improves the efficiency and safety of the procedure without adding additional cost.

Biceps tenodesis: Biceps tenodesis is increasingly used to treat individuals with LHBT pathology (Table 1). It involves releasing the LHBT from its origin and attaching it at one of four locations: (1) Within the glenohumeral joint to the intact rotator cuff; (2) To the conjoint tendon or the transverse humeral ligament; (3) Proximal to or within the bicipital groove in a suprapectoral fashion; or (4) Distally in a subpectoral fashion (mini-open approach)[6]. Current areas of debate include whether orthopaedic surgeons should perform biceps tenodesis open or arthroscopically, the best method of fixation (interference screw, suture anchor, or cortical button), and the ideal location of tenodesis (intra-articular, suprapectoral, subpectoral, and other positions such as extra-articular top of groove or extra-articular bottom of groove)[99].

Table 1 Comparison of biceps tenotomy *versus* biceps tenodesis

	Biceps tenotomy	Biceps tenodesis
Timing and cost	Quicker, shorter procedure with a lower cost	Technically more challenging with a longer surgical and rehabilitation time as well as a higher cost
Patient population	Symptomatic patients with biceps tenosynovitis > 60 yr of age, individuals with lower demand occupations, those with minimal cosmesis concerns	Symptomatic athletic patients, individuals with higher demand occupations, those with cosmesis concerns
Complications	Postoperative Popeye deformity, muscle belly cramping, discomfort and fatigue	Risk of infection, loss of fixation and recurrence of Popeye deformity, implant failure

Open *vs* arthroscopic: Biceps tenodesis can be performed *via* an open or arthroscopic approach; both methods have excellent clinical outcomes[100,101]. While a comparison between approaches is difficult due to concomitant pathology and different types of fixation, a comparison highlighting timing and cost, functional outcomes, range of motion, and complications can be seen in Table 2[102-105]. With no consensus over which method is superior, surgeons should take into account their own preference and technical experience when deciding on the proper approach for their patients.

A number of studies have analyzed open biceps tenodesis procedures in patients without rotator cuff tears and demonstrated improved patient reported outcome measures as well as pain and functional outcome scores[106-110]. Even though fewer studies have been identified for arthroscopic biceps tenodesis procedures in isolated LHB pathology, the patient reported outcome measures, pain scores, and objective outcomes are satisfactory in 98%-99% of patients with low rates of revision (0.4%) for biceps related problems[111-113].

Some studies have compared open LHB tenodesis to arthroscopic LHB tenodesis in order to determine which is superior. Abraham *et al*[100] and Green *et al*[114] found excellent outcomes with both methods and low complication rates. Gombera *et al*[115] compared forty-six patients who underwent arthroscopic or open biceps tenodesis and found no significant differences in American Shoulder and Elbow Surgeons (ASES) scores, patient satisfaction scores, return to sports activity, pain levels at night, pain levels with heavy activity, or Popeye deformities. In terms of complications, arthroscopic biceps tenodesis mirrors open biceps tenodesis. Complications following arthroscopic biceps tenodesis include residual postoperative groove pain, injury to the surrounding neurovascular structures, and increased risk of early postoperative stiffness[116]. Additionally, complications can be dependent on the fixation strategy. For example, open biceps tenodesis can be associated with fracture when using an interference screw and can also cause neurovascular injury in the subpectoralis region due to association with brachial plexus palsy and musculocutaneous nerve injury[117-119]. From these studies, no difference in outcomes can be found between open and arthroscopic biceps tenodesis.

Tenodesis placement: Biceps tenodesis is mainly done with intra-articular, suprapectoral, or subpectoral placement; other possible positions include extra-articular top of the groove and extra-articular bottom of the groove placement. In the intra-articular approach, the LHBT is cut and reattached within the intertubercular groove. While the clinical outcomes of this approach are excellent, patients may have persistent bicipital groove pain and tendinopathy with a portion of the tendon within the bicipital groove[120,121]. In the suprapectoral approach, the LHBT is cut and reattached distally to the bicipital groove and proximally the pectoralis major tendon. Even though this approach avoids the inflammation from the tendon remaining in the bicipital groove and sheath, it may be a longer and thus more costly approach compared to the subpectoral method and has thinner bone stock for hardware fixation [120,122,123]. Furthermore, in intra-articular and suprapectoral approaches, residual pain has been described[100,124].

In patients with significant inflammation in the biceps groove or patients where the suprapectoral part of the biceps is of poor quality or significantly injured, the subpectoral approach is the preferred method[125]. Subpectoral tenodesis is advantageous because it eliminates the pain created from reattachment within the groove, it is associated with stronger bone for fixation in the humerus, and it can potentially lead to a quicker recovery[126-128]. Like the other approaches, the subpectoral method has its disadvantages. The main disadvantages include scar formation, elongation of the biceps, biceps asymmetry, and partial detaching and reattaching of the pectoralis major to the humerus[126,128,129]. Compared to the suprapectoral approach, the

Table 2 Comparison of open biceps tenodesis *versus* arthroscopic biceps tenodesis

	Open approach	Arthroscopic approach
Timing and cost	Lower cost with slightly longer operation time	Higher cost with slightly lower operation time
Functional outcomes	No significant difference found between ASES, Constant, UCLA, DASH, or SST scores	
Range of motion	Similar in both approaches, forward range of motion slightly higher in arthroscopic approach	
Complications	Higher overall rate of complications such as wound healing issues, hematoma/seroma formation, nerve injury, deep vein thrombosis, and general anesthetic complications	Lower overall rate of complications, but higher incidence of postoperative stiffness and bicipital groove tenderness in early stages of recovery

ASES: American shoulder and elbow surgeons; DASH: Disabilities of the arm, shoulder and hand; SST: Simple shoulder test.

subpectoral approach has more residual tenderness and spasm initially following the procedure[120]. Furthermore, fracture has been described as a complication particularly with the use of interference screws[130,131].

In a study by Godshaw *et al*[121], authors compared forty-three patients who had undergone intra-articular tenodesis to fifty-six patients who had undergone suprapectoral tenodesis. While both groups showed improvement in all outcome measures, there was no difference between the groups in functional outcomes for physical and mental component scores as well as ASES scores. Werner *et al*[128] compared arthroscopic suprapectoral biceps tenodesis in nine cadavers to open subpectoral biceps tenodesis in nine cadavers. They found that the arthroscopic suprapectoral biceps tenodesis group had a significantly decreased load to failure compared to the open subpectoral biceps tenodesis group. Additionally, the arthroscopic suprapectoral technique over-tensioned the biceps tendon. Despite these findings, other individuals did not know if there would be similar results in live patients. To further test this idea, Werner *et al*[132] compared thirty-two patients who underwent arthroscopic suprapectoral biceps tenodesis to fifty patients who underwent open subpectoral biceps tenodesis patients. There was no significant difference reported in Constant, ASES, Single Assessment Numeric Evaluation, Simple Shoulder Test (SST), LHB, and Veterans RAND 36-Item Health Survey scores. Furthermore, there were no range of motion or strength deficits in either group. These studies prove that regardless of associated complications for intra-articular, suprapectoral, and subpectoral biceps tenodesis placement, all three approaches have excellent and similar clinical outcomes.

Fixation strategies: The two types of fixations that can be used in intra-articular, suprapectoral, and subpectoral approaches include inlay and onlay. With inlay fixation, the biceps tendon is inserted perpendicularly into the bicipital groove. This technique is less technically challenging to perform, but can result in tenodesis failure in patients with poor tendon quality or osteoporosis at the screw insertion site[133,134]. For the onlay technique, the biceps tendon lays parallel to the bicipital groove. Onlay fixation with a suture anchor may be technically challenging and require longer operative times, but may have superior clinical and functional outcomes compared to the inlay technique[135,136].

Within inlay and onlay strategies, the different fixation techniques include interference screw and suture anchor, which are the most common, as well as cortical button and all-suture suture anchor constructs. Arthroscopic intra-articular biceps tenodesis has historically utilized an inlay technique in which the tendon is docked into a bone socket perpendicular to the bicipital groove and secured with an interference screw[113,137]. In open subpectoral tenodesis, the onlay technique is used with a suture anchor meant to heal the tendon to the cortical surface of the humerus [138-141].

The various types of interference screws include titanium, polyether ether ketone (PEEK), and bioresorbable screws. Titanium interference screws are infrequently used as they have an increased risk of tendon laceration during screw insertion and can make postoperative assessment challenging due to significant artifact on MRI[142,143]. PEEK interference screws have become more popular for several reasons: (1) They are chemically inert and insoluble; (2) They have a modulus of elasticity similar to human cortical bone; and (3) They are compatible with MRI and have a higher resistance to radiation[144,145]. Suture anchors require a smaller bone socket compared to interference screws and as previously mentioned secure the tendon to the

humeral cortex. Furthermore, all-suture suture anchors allow for even less violation of the cortex.

While all constructs have been studied and proven to be effective, there is no consensus on which fixation strategy provides the most superior fixation[141,146-148]. In a study by Buchholz *et al*[147], researchers compared intramedullary cortical button fixation to interference screw usage and found similar results in regard to stiffness and ultimate failure loads. In Chiang *et al*[149], interference screws and all-suture suture anchors were found to have similar failure loads and stiffness which correlates to an increased likelihood of tenodesis failure. Likewise, Tashjian *et al*[141] found failure loads to be similar when comparing interference screws to dual-anchor all-suture suture anchors. Despite these results, additional studies have concluded contrary findings. In Richards *et al*[148], authors analyzed eleven cadaveric humerus specimens in which biceps tenodesis was performed with interference screw fixation or double suture anchor fixation. Authors reported consistent failure at the anchor or anchor eyelet in the suture anchor cadaver models and concluded that interference screw fixation had superior fixation strength. On the other hand, Golish *et al*[133] found interference screws to have a higher failure load and stiffness compared to all-suture suture anchors. With mixed results from these studies, there is no consensus on which fixation strategy provides the greatest advantage.

Supporters of the interference screw technique argue that it creates more surface area contact between the tendon and cancellous bone and thus results in greater exposure to marrow-derived endogenous stem cells[150-153]. However, this comes at a cost, as securing the tendon within a bone socket can result in local deformations in the tendon[140,154]. In Tan *et al*[150], researchers used a rabbit model of bicep tenodesis and compared tendon healing within the bone socket to healing on the cortical surface. Histologic analysis showed similar healing profiles between the two groups which allowed authors to conclude that the creation of large bone sockets with interference screws, which can lead to increased fracture risk, may be unnecessary. Furthermore, the interference screw technique has been associated with additional complications such as persistent pain and bioabsorbable screw reactions[119,155,156].

In contrast, all-suture suture anchors provide the benefits of conventional interference screws while being less traumatic to the bone and thus having a lower risk of fracture[157,158]. Frank *et al*[157] compared torsional energy in humeri that underwent biceps tenodesis with all-suture suture anchors to humeri that underwent biceps tenodesis with interference screws. They found that humeri in the all-suture suture anchor group required greater torsional energy to fracture suggesting that this construct creates less of a stress riser than the interference screw construct.

Although many studies have compared the biomechanical qualities of these constructs, few have compared differences in clinical outcomes. Park *et al*[140] compared clinical and anatomic outcomes of the interference screw and suture anchor fixation techniques for biceps tenodesis and found that both methods improved functional outcomes. Additionally, there was no difference in patient-reported outcomes measured by the visual analog scale (VAS) for pain, ASES score, SST, Constant score, Korean shoulder score, and LHB score between the two groups. With that said, the authors did find interference screw fixation and more physically demanding work levels to be associated with tenodesis failure. In another study by Millett *et al*[159], no statistically significant differences were reported at thirteen months postoperatively in VAS, ASES, and modified Constant scores between individuals who underwent biceps tenodesis with interference screw fixation and individuals who underwent biceps tenodesis with all-suture suture anchor fixation.

From the various biomechanical studies described above, the decision on which fixation strategy to utilize can be rather nuanced. While some studies have cited no differences in regards to stiffness or ultimate failure load between fixation strategies, other studies have contradicted these findings declaring interference screw fixation as more superior in terms of fixation strength and more inferior in regards to failure load and stiffness[133,141,147-149]. Despite the lack of consensus amongst the ideal fixation technique regarding biomechanical data, there appears to be no difference between fixation techniques in terms of clinical outcomes.

Biceps tenotomy *vs* biceps tenodesis: Several studies have investigated the differences between biceps tenotomy and biceps tenodesis, but mainly for LHB tendinopathy with rotator cuff tears, which makes it difficult to determine the extent to which biceps management influences outcomes[160-162]. A comparison of the techniques can be found in Table 1. In a systematic review by Leroux *et al*[160], authors analyzed patients who underwent rotator cuff repair in combination with either biceps tenotomy or biceps tenodesis. They reported that patients who underwent biceps

tenodesis had better Constant assessment scores (92.8 [tenodesis] *vs* 90.6 [tenotomy], $P < 0.01$) and decreased rates of biceps deformity compared to patients who underwent biceps tenotomy (3.8% [tenodesis] *vs* 15.5% [tenotomy], $P < 0.01$).

Another study compared the clinical results of biceps tenotomy and biceps tenodesis based on technique. In Shank *et al*[163], seventeen patients underwent biceps tenotomy, nineteen patients underwent suprapectoral biceps tenodesis with a double-loaded anchor fixation, and thirty-one control patients did not have any biceps surgery performed. Analysis showed no significant difference in either forearm supination nor elbow flexion strength among patients in all three groups.

One theory that has been challenged recently is the duration of postoperative rehabilitation. Zabrzyński *et al*[164] attempted to test different rehabilitation protocols in tenotomy *vs* tenodesis groups with the tenotomy group undergoing a personalized postoperative rehabilitation protocol. They found that patients who underwent tenotomy with a shortened postoperative rehabilitation protocol were able to achieve better clinical outcomes and ensure faster return to sports activity compared to those who underwent tenodesis[164].

The results described above demonstrate how challenging it can be to make direct comparisons between tenotomy and tenodesis in hopes of determining which is superior. Furthermore, the concern for cosmesis plays a role in determining whether a patient should undergo tenotomy or tenodesis. Typically, tenotomy is indicated in older patients as cosmesis is of minimal concern whereas tenodesis is indicated in younger more active patients where cosmesis tends to play a more significant role. Recent systematic reviews and meta-analyses by MacDonald *et al*[165], Zhou *et al*[166], and Kooistra *et al*[167] confirm the findings that there is no evidence-based difference in LHB tenodesis *vs* tenotomy when evaluating shoulder function, pain, or biceps-related strength.

SLAP lesion: Treatment recommendations for SLAP lesions are based on patient age as well as activity level and include nonsurgical management, arthroscopic debridement, arthroscopic repair, and biceps tenodesis. Over the last five years, orthopaedic literature has documented the growing trend to move away from SLAP repair due to an increased incidence of subsequent revision surgery[168,169]. Instead, literature has shown an increase in the frequency of biceps tenodesis, particularly in patients over the age of forty and athletes as return to activity after biceps tenodesis was significantly higher than the rate after revision SLAP repair[170,171].

SLAP tears are often categorized into Type I through Type X[172]. In a type II SLAP lesion, there is detachment of the superior labrum and the origin of the LHBT insertion from the glenoid[173,174]. Surgical techniques that can be used to repair a standard type II SLAP lesion include the use of a single suture anchor placed posterior to the biceps anchor or the use of two suture anchors with one suture anchor placed anterior and the other placed posterior to the biceps anchor[17]. A few studies have reported on outcomes regarding type II SLAP repair. Sayde *et al* included 506 patients who underwent repair of type II SLAP tear and reported excellent satisfaction in 83% of patients and return to previous level of play in 73% of patients; however, in the 198 patients who were overhead athletes, inferior outcomes were reported with only 63% able to return to previous level of play. Similar studies have assessed the outcomes of overhead athletes who have undergone arthroscopic SLAP lesion repair and report a return to preinjury level of sports activity between 22% and 85%[175-178]. In Frank *et al*[179], sixty-two patients underwent arthroscopic repair of a type II SLAP tear. Authors reported that patients aged twenty years and younger as well as overhead throwers were more likely to require revision surgery than patients greater than twenty years of age and non-overhead throwers. Furthermore, they concluded that patients greater than forty years of age were more likely to have inferior postoperative ASES scores compared to patients aged less than forty years of age.

An increasingly popular alternative to arthroscopic repair of SLAP lesions is biceps tenodesis as it has a significantly higher rate of return to activity following surgery [170,171]. Some studies have performed biceps tenodesis in combination with SLAP repair or performed biceps tenodesis in place of SLAP repair. For example, Boileau *et al*[1] compared ten patients with an isolated type II SLAP lesion who underwent repair with the use of suture anchors to fifteen patients with an isolated type II SLAP lesion who underwent arthroscopic biceps tenodesis with the use of an absorbable interference screw. Patients in the SLAP repair group had inferior outcomes including lower mean Constant assessment scores, lower satisfaction, and lower return to previous level of sports activity. On the other hand, some studies have reported similar outcomes in patients with a type II SLAP tear who undergo biceps tenodesis. In

Denard *et al*[2], thirty-seven patients greater than thirty-five years of age with an isolated type II SLAP tear underwent arthroscopic biceps tenodesis or SLAP repair. Authors demonstrated that patients in the biceps tenodesis group had shorter postoperative recovery, higher satisfaction rates, and higher rates of return to normal activity. Similarly, Ek *et al*[3] compared twenty-five patients with an isolated type II SLAP lesion who underwent biceps tenodesis or SLAP repair and found that both groups had improved clinical outcomes with low failure rates and similar rates of return to sports. These studies demonstrate that patients who undergo biceps tenodesis for SLAP lesions experience a shorter postoperative recovery time, higher Constant assessment scores, higher satisfaction rates, higher rates of return to normal sports activity, and lower failure rates compared to patients who undergo SLAP repair.

While type II SLAP tears have seen an increase in biceps tenodesis as treatment, type III and type IV SLAP tears can be adequately treated with SLAP repair depending on the extent of the injury[172]. In a type III SLAP tear, a bucket-handle tear of the superior labrum occurs with potential displacement of the mobile labral fragment into the glenohumeral joint. In this case, the attachment of LHBT remains intact. Typically, type III SLAP lesions require resection of the unstable bucket-handle fragment with no further stabilization of the biceps anchor[172,180]. Some authors have also recommended refixation of the torn flap analogous to meniscal tears if the lesion is caused by trauma and located within a specific part of the shoulder[181]. For a type IV SLAP tear, there is a bucket-handle tear of the superior labrum that extends to the biceps tendon in a variable degree. Type IV SLAP lesion repair is reliant on biceps tendon stability after resection of the torn flap as at least half of the tendon should be intact to preserve stability of the labro-bicipital complex[172]. In an unstable biceps tendon where more than 50% of the tendon is affected, a tenotomy or tenodesis is preferred over a SLAP repair. With SLAP repairs demonstrating a wide variability in outcomes, specifically in rates of return to play and failure rates for older individuals, biceps tenodesis has shown a significant improvement in ASES scores and VAS scores [182].

The excellent outcomes and low rate of complications of biceps tenodesis for SLAP lesions have led to an increase in frequency of biceps tenodesis[119,183]. In a study by Patterson *et al*[4], trends in the management of SLAP lesions were reviewed and the proportion of SLAP repairs between 2002 and 2011 decreased from 69.3% to 44.8%, whereas the proportion of biceps tenodesis procedures increased from 1.9% to 18.8%. Furthermore, the proportion of SLAP repairs used to manage SLAP lesions in combination with rotator cuff repair decreased from 60.2% to 15.3%, whereas the proportion of biceps tenodesis or tenotomy procedures increased from 6% to 28%. In a more recent study by Cvetanovich *et al*[171], there was a 69.3% decrease in isolated SLAP repair from 2007 to 2016 and an increase of 370% in biceps tenodesis for the diagnosis of an isolated SLAP tear over the same period. With this knowledge, Chalmers *et al*[184] conducted a study with three groups: (1) Forty-five patients with a SLAP tear who underwent isolated SLAP repair; (2) Twenty-three patients with a SLAP tear who underwent isolated biceps tenodesis; and (3) Eighteen patients with a SLAP tear who underwent SLAP repair in combination with biceps tenodesis. Authors reported substantially worse postoperative ASES scores and visual analog scale pain scores in patients who underwent SLAP repair in combination with biceps tenodesis compared to either of the other categories. These studies demonstrate the utility and improved clinical outcomes in patients with SLAP lesions who undergo biceps tenodesis compared to patients with SLAP lesions who undergo arthroscopic repair. Furthermore, improved outcomes seen in biceps tenodesis for SLAP tears is supported by the increase in volume of biceps tenodesis procedures over the last five years or so.

CONCLUSION

LHBT is a common source of disease and shoulder pain with etiologies including inflammation, instability, and trauma. Although the anatomy can be easily digested, the decision to operate is a little more nuanced. Despite various physical examination maneuvers, the lack of specificity requires orthopaedic surgeons to rely on patient history as well as advanced imaging in order to best manage the patient's condition. Nonsurgical treatment typically includes physical therapy, anti-inflammatory medications, and ultrasound-guided corticosteroid injections. If nonsurgical treatment fails, surgical techniques such as biceps tenotomy, biceps tenodesis, or SLAP repair can be used. In biceps tenodesis, differences between arthroscopic and open biceps

tenodesis, type of fixation system, and location of tenodesis should be discussed with patients keeping in mind that no functional differences have been established. Furthermore, SLAP lesions can be treated with SLAP repair or biceps tenodesis depending on the categorization. While debridement has been used as the standard of treatment in the past for SLAP lesions, the increase in volume of biceps tenodesis for SLAP lesions indicates a transition to a treatment option with better functional and clinical outcomes.

REFERENCES

1 **Boileau P**, Parratte S, Chuinard C, Roussanne Y, Shia D, Bicknell R. Arthroscopic treatment of isolated type II SLAP lesions: biceps tenodesis as an alternative to reinsertion. *Am J Sports Med* 2009; **37**: 929-936 [PMID: 19229046 DOI: 10.1177/0363546508330127]

2 **Denard PJ**, Lädermann A, Parsley BK, Burkhart SS. Arthroscopic biceps tenodesis compared with repair of isolated type II SLAP lesions in patients older than 35 years. *Orthopedics* 2014; **37**: e292-e297 [PMID: 24762158 DOI: 10.3928/01477447-20140225-63]

3 **Ek ET**, Shi LL, Tompson JD, Freehill MT, Warner JJ. Surgical treatment of isolated type II superior labrum anterior-posterior (SLAP) lesions: repair *versus* biceps tenodesis. *J Shoulder Elbow Surg* 2014; **23**: 1059-1065 [PMID: 24388713 DOI: 10.1016/j.jse.2013.09.030]

4 **Patterson BM**, Creighton RA, Spang JT, Roberson JR, Kamath GV. Surgical Trends in the Treatment of Superior Labrum Anterior and Posterior Lesions of the Shoulder: Analysis of Data From the American Board of Orthopaedic Surgery Certification Examination Database. *Am J Sports Med* 2014; **42**: 1904-1910 [PMID: 24890780 DOI: 10.1177/0363546514534939]

5 **Krupp RJ**, Kevern MA, Gaines MD, Kotara S, Singleton SB. Long head of the biceps tendon pain: differential diagnosis and treatment. *J Orthop Sports Phys Ther* 2009; **39**: 55-70 [PMID: 19194019 DOI: 10.2519/jospt.2009.2802]

6 **Frank RM**, Cotter EJ, Strauss EJ, Jazrawi LM, Romeo AA. Management of Biceps Tendon Pathology: From the Glenoid to the Radial Tuberosity. *J Am Acad Orthop Surg* 2018; **26**: e77-e89 [PMID: 29337716 DOI: 10.5435/JAAOS-D-17-00085]

7 **Hassan S**, Patel V. Biceps tenodesis *versus* biceps tenotomy for biceps tendinitis without rotator cuff tears. *J Clin Orthop Trauma* 2019; **10**: 248-256 [PMID: 30828187 DOI: 10.1016/j.jcot.2018.12.013]

8 **Patel KV**, Bravman J, Vidal A, Chrisman A, McCarty E. Biceps Tenotomy Versus Tenodesis. *Clin Sports Med* 2016; **35**: 93-111 [PMID: 26614471 DOI: 10.1016/j.csm.2015.08.008]

9 **Blum K**, Chen AL, Chen TJ, Waite RL, Downs BW, Braverman ER, Kerner MM, Savarimuthu SM, DiNubile N. Repetitive H-wave device stimulation and program induces significant increases in the range of motion of post operative rotator cuff reconstruction in a double-blinded randomized placebo controlled human study. *BMC Musculoskelet Disord* 2009; **10**: 132 [PMID: 19874593 DOI: 10.1186/1471-2474-10-132]

10 **Miniato MA**, Anand P, Varacallo M. Anatomy, Shoulder and Upper Limb, Shoulder. [Updated 2020 Jul 31]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing. Available from: https://www.ncbi.nlm.nih.gov/books/NBK536933/

11 **Elser F**, Braun S, Dewing CB, Giphart JE, Millett PJ. Anatomy, function, injuries, and treatment of the long head of the biceps brachii tendon. *Arthroscopy* 2011; **27**: 581-592 [PMID: 21444012 DOI: 10.1016/j.arthro.2010.10.014]

12 **Vangsness CT Jr**, Jorgenson SS, Watson T, Johnson DL. The origin of the long head of the biceps from the scapula and glenoid labrum. An anatomical study of 100 shoulders. *J Bone Joint Surg Br* 1994; **76**: 951-954 [PMID: 7983126]

13 **Habermeyer P**, Magosch P, Lichtenberg S. Chapter 6: Classifications of pathology of long head of the biceps tendon. In: Habermeyer P, Magosch P, Lichtenberg S. Classifications and Scores of the Shoulder. Springer-Verlag Berlin Heidelberg, 2006: 35-47

14 **Walch G**, Nové-Josserand L, Boileau P, Levigne C. Subluxations and dislocations of the tendon of the long head of the biceps. *J Shoulder Elbow Surg* 1998; **7**: 100-108 [PMID: 9593086 DOI: 10.1016/s1058-2746(98)90218-x]

15 **Vap AR**, Katthagen JC, Tahal DS, Horan MP, Fritz EM, Pogorzelski J, Millett PJ. Isolated Biceps Reflection Pulley Tears Treated With Subpectoral Biceps Tenodesis: Minimum 2-Year Outcomes. *Arthroscopy* 2017; **33**: 1788-1794 [PMID: 28888723 DOI: 10.1016/j.arthro.2017.04.021]

16 **Sanders B**, Lavery KP, Pennington S, Warner JJ. Clinical success of biceps tenodesis with and without release of the transverse humeral ligament. *J Shoulder Elbow Surg* 2012; **21**: 66-71 [PMID: 21524923 DOI: 10.1016/j.jse.2011.01.037]

17 **Thorsness RJ**, Romeo AA. Diagnosis and Management of the Biceps-Labral Complex. *Instr Course Lect* 2017; **66**: 65-77 [PMID: 28594489]

18 **Taylor SA**, Khair MM, Gulotta LV, Pearle AD, Baret NJ, Newman AM, Dy CJ, O'Brien SJ. Diagnostic glenohumeral arthroscopy fails to fully evaluate the biceps-labral complex. *Arthroscopy* 2015; **31**: 215-224 [PMID: 25498874 DOI: 10.1016/j.arthro.2014.10.017]

19 **Taylor SA**, Fabricant PD, Bansal M, Khair MM, McLawhorn A, DiCarlo EF, Shorey M, O'Brien SJ. The anatomy and histology of the bicipital tunnel of the shoulder. *J Shoulder Elbow Surg* 2015; **24**:

511-519 [PMID: 25457787 DOI: 10.1016/j.jse.2014.09.026]
20 **Taylor SA**, Newman AM, Dawson C, Gallagher KA, Bowers A, Nguyen J, Fabricant PD, O'Brien SJ. The "3-Pack" Examination Is Critical for Comprehensive Evaluation of the Biceps-Labrum Complex and the Bicipital Tunnel: A Prospective Study. *Arthroscopy* 2017; **33**: 28-38 [PMID: 27450901 DOI: 10.1016/j.arthro.2016.05.015]
21 **Kumar VP**, Satku K, Balasubramaniam P. The role of the long head of biceps brachii in the stabilization of the head of the humerus. *Clin Orthop Relat Res* 1989; 172-175 [PMID: 2743659]
22 **Pagnani MJ**, Deng XH, Warren RF, Torzilli PA, O'Brien SJ. Role of the long head of the biceps brachii in glenohumeral stability: a biomechanical study in cadavera. *J Shoulder Elbow Surg* 1996; **5**: 255-262 [PMID: 8872922 DOI: 10.1016/s1058-2746(96)80051-6]
23 **Warner JJ**, Bowen MK, Deng X, Torzilli PA, Warren RF. Effect of joint compression on inferior stability of the glenohumeral joint. *J Shoulder Elbow Surg* 1999; **8**: 31-36 [PMID: 10077793 DOI: 10.1016/s1058-2746(99)90051-4]
24 **Yamaguchi K**, Riew KD, Galatz LM, Syme JA, Neviaser RJ. Biceps activity during shoulder motion: an electromyographic analysis. *Clin Orthop Relat Res* 1997; 122-129 [PMID: 9060495 DOI: 10.1097/00003086-199703000-00017]
25 **Levy AS**, Kelly BT, Lintner SA, Osbahr DC, Speer KP. Function of the long head of the biceps at the shoulder: electromyographic analysis. *J Shoulder Elbow Surg* 2001; **10**: 250-255 [PMID: 11408907 DOI: 10.1067/mse.2001.113087]
26 **Wittstein J**, Queen R, Abbey A, Moorman CT 3rd. Isokinetic testing of biceps strength and endurance in dominant *versus* nondominant upper extremities. *J Shoulder Elbow Surg* 2010; **19**: 874-877 [PMID: 20381383 DOI: 10.1016/j.jse.2010.01.018]
27 **Edwards TB**, Walch G, Sirveaux F, Molé D, Nové-Josserand L, Boulahia A, Neyton L, Szabo I, Lindgren B. Repair of tears of the subscapularis. *J Bone Joint Surg Am* 2005; **87**: 725-730 [PMID: 15805199 DOI: 10.2106/JBJS.D.02051]
28 **Boileau P**, Baqué F, Valerio L, Ahrens P, Chuinard C, Trojani C. Isolated arthroscopic biceps tenotomy or tenodesis improves symptoms in patients with massive irreparable rotator cuff tears. *J Bone Joint Surg Am* 2007; **89**: 747-757 [PMID: 17403796 DOI: 10.2106/JBJS.E.01097]
29 **Franceschi F**, Longo UG, Ruzzini L, Rizzello G, Maffulli N, Denaro V. No advantages in repairing a type II superior labrum anterior and posterior (SLAP) lesion when associated with rotator cuff repair in patients over age 50: a randomized controlled trial. *Am J Sports Med* 2008; **36**: 247-253 [PMID: 17940144 DOI: 10.1177/0363546507308194]
30 **Osbahr DC**, Diamond AB, Speer KP. The cosmetic appearance of the biceps muscle after long-head tenotomy *versus* tenodesis. *Arthroscopy* 2002; **18**: 483-487 [PMID: 11987057 DOI: 10.1053/jars.2002.32233]
31 **Vestermark GL**, Van Doren BA, Connor PM, Fleischli JE, Piasecki DP, Hamid N. The prevalence of rotator cuff pathology in the setting of acute proximal biceps tendon rupture. *J Shoulder Elbow Surg* 2018; **27**: 1258-1262 [PMID: 29478942 DOI: 10.1016/j.jse.2018.01.006]
32 **Hsu SH**, Miller SL, Curtis AS. Long head of biceps tendon pathology: management alternatives. *Clin Sports Med* 2008; **27**: 747-762 [PMID: 19064154 DOI: 10.1016/j.csm.2008.07.005]
33 **Barber FA**, Field LD, Ryu RK. Biceps tendon and superior labrum injuries: decision making. *Instr Course Lect* 2008; **57**: 527-538 [PMID: 18399607]
34 **Nho SJ**, Frank RM, Reiff SN, Verma NN, Romeo AA. Arthroscopic repair of anterosuperior rotator cuff tears combined with open biceps tenodesis. *Arthroscopy* 2010; **26**: 1667-1674 [PMID: 20729025 DOI: 10.1016/j.arthro.2010.04.008]
35 **Habermeyer P**, Magosch P, Pritsch M, Scheibel MT, Lichtenberg S. Anterosuperior impingement of the shoulder as a result of pulley lesions: a prospective arthroscopic study. *J Shoulder Elbow Surg* 2004; **13**: 5-12 [PMID: 14735066 DOI: 10.1016/j.jse.2003.09.013]
36 **Hwang E**, Carpenter JE, Hughes RE, Palmer ML. Effects of biceps tension and superior humeral head translation on the glenoid labrum. *J Orthop Res* 2014; **32**: 1424-1429 [PMID: 25070392 DOI: 10.1002/jor.22688]
37 **Verma NN**, Drakos M, O'Brien SJ. The arthroscopic active compression test. *Arthroscopy* 2005; **21**: 634 [PMID: 15891739 DOI: 10.1016/j.arthro.2005.02.008]
38 **Byram IR**, Dunn WR, Kuhn JE. Humeral head abrasion: an association with failed superior labrum anterior posterior repairs. *J Shoulder Elbow Surg* 2011; **20**: 92-97 [PMID: 20863719 DOI: 10.1016/j.jse.2010.05.013]
39 **Boileau P**, Ahrens PM, Hatzidakis AM. Entrapment of the long head of the biceps tendon: the hourglass biceps--a cause of pain and locking of the shoulder. *J Shoulder Elbow Surg* 2004; **13**: 249-257 [PMID: 15111893 DOI: 10.1016/j.jse.2004.01.001]
40 **Mazzocca AD**, McCarthy MB, Ledgard FA, Chowaniec DM, McKinnon WJ Jr, Delaronde S, Rubino LJ, Apolostakos J, Romeo AA, Arciero RA, Beitzel K. Histomorphologic changes of the long head of the biceps tendon in common shoulder pathologies. *Arthroscopy* 2013; **29**: 972-981 [PMID: 23571131 DOI: 10.1016/j.arthro.2013.02.002]
41 **Gerber C**, Galantay RV, Hersche O. The pattern of pain produced by irritation of the acromioclavicular joint and the subacromial space. *J Shoulder Elbow Surg* 1998; **7**: 352-355 [PMID: 9752643 DOI: 10.1016/s1058-2746(98)90022-2]
42 **Murthi AM**, Vosburgh CL, Neviaser TJ. The incidence of pathologic changes of the long head of the biceps tendon. *J Shoulder Elbow Surg* 2000; **9**: 382-385 [PMID: 11075320 DOI: 10.1067/mse.2000.108386]

43 **Chen CH**, Hsu KY, Chen WJ, Shih CH. Incidence and severity of biceps long head tendon lesion in patients with complete rotator cuff tears. *J Trauma* 2005; **58**: 1189-1193 [PMID: 15995469 DOI: 10.1097/01.ta.0000170052.84544.34]

44 **Gurnani N**, van Deurzen DF, Janmaat VT, van den Bekerom MP. Tenotomy or tenodesis for pathology of the long head of the biceps brachii: a systematic review and meta-analysis. *Knee Surg Sports Traumatol Arthrosc* 2016; **24**: 3765-3771 [PMID: 25975753 DOI: 10.1007/s00167-015-3640-6]

45 **Varacallo M**, Seaman TJ, Mair SD. Biceps Tendon Dislocation and Instability. [Updated 2021 Jan 7]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2021 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK534102/

46 **Sethi N**, Wright R, Yamaguchi K. Disorders of the long head of the biceps tendon. *J Shoulder Elbow Surg* 1999; **8**: 644-654 [PMID: 10633904 DOI: 10.1016/s1058-2746(99)90105-2]

47 **Jain NB**, Wilcox RB 3rd, Katz JN, Higgins LD. Clinical examination of the rotator cuff. *PM R* 2013; **5**: 45-56 [PMID: 23332909 DOI: 10.1016/j.pmrj.2012.08.019]

48 **José AG**, Luís Felipe HFS, Gabriel RSM, Fernando MI. Treatment of the Distal Biceps Brachii Tendon Rupture Using the Three Mini-Incisions Technique: Evaluation through MEPS and DASH. *Ortho Rheum Open Access J* 2019; **14**: 555888 [DOI: 10.19080/OROAJ.2019.14.555888]

49 **Ding DY**, Garofolo G, Lowe D, Strauss EJ, Jazrawi LM. The biceps tendon: from proximal to distal: AAOS exhibit selection. *J Bone Joint Surg Am* 2014; **96**: e176 [PMID: 25320206 DOI: 10.2106/JBJS.N.00032]

50 **Matsen FA 3rd**, Kirby RM. Office evaluation and management of shoulder pain. *Orthop Clin North Am* 1982; **13**: 453-475 [PMID: 7099584]

51 **Chalmers PN**, Verma NN. Proximal Biceps in Overhead Athletes. *Clin Sports Med* 2016; **35**: 163-179 [PMID: 26614475 DOI: 10.1016/j.csm.2015.08.009]

52 **Gill HS**, El Rassi G, Bahk MS, Castillo RC, McFarland EG. Physical examination for partial tears of the biceps tendon. *Am J Sports Med* 2007; **35**: 1334-1340 [PMID: 17369556 DOI: 10.1177/0363546507300058]

53 **Warner JJ**, McMahon PJ. The role of the long head of the biceps brachii in superior stability of the glenohumeral joint. *J Bone Joint Surg Am* 1995; **77**: 366-372 [PMID: 7890785 DOI: 10.2106/00004623-199503000-00006]

54 **Holtby R**, Razmjou H. Accuracy of the Speed's and Yergason's tests in detecting biceps pathology and SLAP lesions: comparison with arthroscopic findings. *Arthroscopy* 2004; **20**: 231-236 [PMID: 15007311 DOI: 10.1016/j.arthro.2004.01.008]

55 **Parentis MA**, Glousman RE, Mohr KS, Yocum LA. An evaluation of the provocative tests for superior labral anterior posterior lesions. *Am J Sports Med* 2006; **34**: 265-268 [PMID: 16219944 DOI: 10.1177/0363546505279911]

56 **Nho SJ**, Strauss EJ, Lenart BA, Provencher MT, Mazzocca AD, Verma NN, Romeo AA. Long head of the biceps tendinopathy: diagnosis and management. *J Am Acad Orthop Surg* 2010; **18**: 645-656 [PMID: 21041799 DOI: 10.5435/00124635-201011000-00002]

57 **Myer CA**, Hegedus EJ, Tarara DT, Myer DM. A user's guide to performance of the best shoulder physical examination tests. *Br J Sports Med* 2013; **47**: 903-907 [PMID: 23322891 DOI: 10.1136/bjsports-2012-091870]

58 **O'Brien SJ**, Pagnani MJ, Fealy S, McGlynn SR, Wilson JB. The active compression test: a new and effective test for diagnosing labral tears and acromioclavicular joint abnormality. *Am J Sports Med* 1998; **26**: 610-613 [PMID: 9784804 DOI: 10.1177/03635465980260050201]

59 **Hegedus EJ**, Goode AP, Cook CE, Michener L, Myer CA, Myer DM, Wright AA. Which physical examination tests provide clinicians with the most value when examining the shoulder? *Br J Sports Med* 2012; **46**: 964-978 [PMID: 22773322 DOI: 10.1136/bjsports-2012-091066]

60 **Cheung E**, O'Driscoll, SW. The dynamic labral shear test for superior labral anterior to posterior tears of the shoulder. Paper presented at: AAOS annual meeting; February 2007; San Diego, CA.

61 **Ben Kibler W**, Sciascia AD, Hester P, Dome D, Jacobs C. Clinical utility of traditional and new tests in the diagnosis of biceps tendon injuries and superior labrum anterior and posterior lesions in the shoulder. *Am J Sports Med* 2009; **37**: 1840-1847 [PMID: 19509414 DOI: 10.1177/0363546509332505]

62 **Cook C**, Beaty S, Kissenberth MJ, Siffri P, Pill SG, Hawkins RJ. Diagnostic accuracy of five orthopedic clinical tests for diagnosis of superior labrum anterior posterior (SLAP) lesions. *J Shoulder Elbow Surg* 2012; **21**: 13-22 [PMID: 22036538 DOI: 10.1016/j.jse.2011.07.012]

63 **Keener JD**, Brophy RH. Superior labral tears of the shoulder: pathogenesis, evaluation, and treatment. *J Am Acad Orthop Surg* 2009; **17**: 627-637 [PMID: 19794220 DOI: 10.5435/00124635-200910000-00005]

64 **Knesek M**, Skendzel JG, Dines JS, Altchek DW, Allen AA, Bedi A. Diagnosis and management of superior labral anterior posterior tears in throwing athletes. *Am J Sports Med* 2013; **41**: 444-460 [PMID: 23172004 DOI: 10.1177/0363546512466067]

65 **Virk MS**, Arciero RA. Superior labrum anterior to posterior tears and glenohumeral instability. *Instr Course Lect* 2013; **62**: 501-514 [PMID: 23395054]

66 **Taylor SA**, Newman AM, Nguyen J, Fabricant PD, Baret NJ, Shorey M, Ramkumar P, O'Brien SJ. Magnetic Resonance Imaging Currently Fails to Fully Evaluate the Biceps-Labrum Complex and Bicipital Tunnel. *Arthroscopy* 2016; **32**: 238-244 [PMID: 26440371 DOI: 10.1016/j.arthro.2015.08.008]

67 **Mohtadi NG**, Vellet AD, Clark ML, Hollinshead RM, Sasyniuk TM, Fick GH, Burton PJ. A prospective, double-blind comparison of magnetic resonance imaging and arthroscopy in the evaluation of patients presenting with shoulder pain. *J Shoulder Elbow Surg* 2004; **13**: 258-265 [PMID: 15111894 DOI: 10.1016/j.jse.2004.01.003]

68 **Houtz CG**, Schwartzberg RS, Barry JA, Reuss BL, Papa L. Shoulder MRI accuracy in the community setting. *J Shoulder Elbow Surg* 2011; **20**: 537-542 [PMID: 21440460 DOI: 10.1016/j.jse.2011.01.003]

69 **Reuss BL**, Schwartzberg R, Zlatkin MB, Cooperman A, Dixon JR. Magnetic resonance imaging accuracy for the diagnosis of superior labrum anterior-posterior lesions in the community setting: eighty-three arthroscopically confirmed cases. *J Shoulder Elbow Surg* 2006; **15**: 580-585 [PMID: 16979053 DOI: 10.1016/j.jse.2005.10.011]

70 **Dubrow SA**, Streit JJ, Shishani Y, Robbin MR, Gobezie R. Diagnostic accuracy in detecting tears in the proximal biceps tendon using standard nonenhancing shoulder MRI. *Open Access J Sports Med* 2014; **5**: 81-87 [PMID: 24891814 DOI: 10.2147/OAJSM.S58225]

71 **Gagat M**, Zabrzyńska A, Zabrzyńska M, Zielińska W. The advances in diagnostic modalities of disorders of the long head of the biceps tendon-review. *Med Stud Stud Med* 2021; **37**: 83-90 [DOI: 10.5114/ms.2021.105006]

72 **Zabrzyński J**, Paczesny Ł, Zabrzyńska A, Grzanka D, Łapaj Ł. Sonography in the instability of the long head of the biceps tendon confronted with histopathologic and arthroscopic findings. *Folia Morphol (Warsz)* 2018; **77**: 583-590 [PMID: 29399753 DOI: 10.5603/FM.a2018.0012]

73 **Armstrong A**, Teefey SA, Wu T, Clark AM, Middleton WD, Yamaguchi K, Galatz LM. The efficacy of ultrasound in the diagnosis of long head of the biceps tendon pathology. *J Shoulder Elbow Surg* 2006; **15**: 7-11 [PMID: 16414462 DOI: 10.1016/j.jse.2005.04.008]

74 **Skendzel JG**, Jacobson JA, Carpenter JE, Miller BS. Long head of biceps brachii tendon evaluation: accuracy of preoperative ultrasound. *AJR Am J Roentgenol* 2011; **197**: 942-948 [PMID: 21940583 DOI: 10.2214/AJR.10.5012]

75 **Stone TJ**, Adler RS. Ultrasound-Guided Biceps Peritendinous Injections in the Absence of a Distended Tendon Sheath: A Novel Rotator Interval Approach. *J Ultrasound Med* 2015; **34**: 2287-2292 [PMID: 26518277 DOI: 10.7863/ultra.15.02017]

76 **Gofeld M**, Hurdle MF, Agur A. Biceps Tendon Sheath Injection: An Anatomical Conundrum. *Pain Med* 2019; **20**: 138-142 [PMID: 29635324 DOI: 10.1093/pm/pny051]

77 **Lenz R**, Kieb M, Diehl P, Grim C, Vogt S, Tischer T. [Muscle, tendon and joint injections : What is the evidence? *Orthopade* 2016; **45**: 459-468 [PMID: 27147429 DOI: 10.1007/s00132-016-3262-9]

78 **Barile A**, La Marra A, Arrigoni F, Mariani S, Zugaro L, Splendiani A, Di Cesare E, Reginelli A, Zappia M, Brunese L, Duka E, Carrafiello G, Masciocchi C. Anaesthetics, steroids and platelet-rich plasma (PRP) in ultrasound-guided musculoskeletal procedures. *Br J Radiol* 2016; **89**: 20150355 [PMID: 27302491 DOI: 10.1259/bjr.20150355]

79 **Unverferth LJ**, Olix ML. The effect of local steroid injections on tendon. *J Sports Med* 1973; **1**: 31-37 [PMID: 4806601 DOI: 10.1177/036354657300100404]

80 **Hashiuchi T**, Sakurai G, Morimoto M, Komei T, Takakura Y, Tanaka Y. Accuracy of the biceps tendon sheath injection: ultrasound-guided or unguided injection? *J Shoulder Elbow Surg* 2011; **20**: 1069-1073 [PMID: 21782470 DOI: 10.1016/j.jse.2011.04.004]

81 **Schickendantz M**, King D. Nonoperative Management (Including Ultrasound-Guided Injections) of Proximal Biceps Disorders. *Clin Sports Med* 2016; **35**: 57-73 [PMID: 26614469 DOI: 10.1016/j.csm.2015.08.006]

82 **Nichols AW**. Complications associated with the use of corticosteroids in the treatment of athletic injuries. *Clin J Sport Med* 2005; **15**: 370-375 [PMID: 16162982 DOI: 10.1097/01.jsm.0000179233.17885.18]

83 **Yiannakopoulos CK**, Megaloikonomos PD, Foufa K, Gliatis J. Ultrasound-guided *versus* palpation-guided corticosteroid injections for tendinosis of the long head of the biceps: A randomized comparative study. *Skeletal Radiol* 2020; **49**: 585-591 [PMID: 31712838 DOI: 10.1007/s00256-019-03315-9]

84 **Hart L**. Corticosteroid and other injections in the management of tendinopathies: a review. *Clin J Sport Med* 2011; **21**: 540-541 [PMID: 22064721 DOI: 10.1097/01.jsm.0000407929.35973.b9]

85 **Daniels EW**, Cole D, Jacobs B, Phillips SF. Existing Evidence on Ultrasound-Guided Injections in Sports Medicine. *Orthop J Sports Med* 2018; **6**: 2325967118756576 [PMID: 29511701 DOI: 10.1177/2325967118756576]

86 **Childress MA**, Beutler A. Management of chronic tendon injuries. *Am Fam Physician* 2013; **87**: 486-490 [PMID: 23547590]

87 **Andres BM**, Murrell GA. Treatment of tendinopathy: what works, what does not, and what is on the horizon. *Clin Orthop Relat Res* 2008; **466**: 1539-1554 [PMID: 18446422 DOI: 10.1007/s11999-008-0260-1]

88 **Moon JG**. Clinical Application of Radial Head Prosthesis. *Clin Shoulder Elbow* 2011; **14**: 140-145 [DOI: 10.5397/CiSE.2011.14.1.140]

89 **Pogorzelski J**, Fritz EM, Godin JA, Imhoff AB, Millett PJ. Nonoperative treatment of five common shoulder injuries: A critical analysis. *Obere Extrem* 2018; **13**: 89-97 [PMID: 29887915 DOI: 10.1007/s11678-018-0449-1]

90 **Barber FA**, Byrd JW, Wolf EM, Burkhart SS. How would you treat the partially torn biceps tendon? *Arthroscopy* 2001; **17**: 636-639 [PMID: 11447552 DOI: 10.1053/jars.2001.24852]

91 **Gill TJ**, McIrvin E, Mair SD, Hawkins RJ. Results of biceps tenotomy for treatment of pathology of the long head of the biceps brachii. *J Shoulder Elbow Surg* 2001; **10**: 247-249 [PMID: 11408906 DOI: 10.1067/mse.2001.114259]

92 **Kelly AM**, Drakos MC, Fealy S, Taylor SA, O'Brien SJ. Arthroscopic release of the long head of the biceps tendon: functional outcome and clinical results. *Am J Sports Med* 2005; **33**: 208-213 [PMID: 15701606 DOI: 10.1177/0363546504269555]

93 **Farmer KW**, Wright TW. Shoulder arthroscopy: the basics. *J Hand Surg Am* 2015; **40**: 817-821 [PMID: 25726045 DOI: 10.1016/j.jhsa.2015.01.002]

94 **Lemos D**, Esquivel A, Duncan D, Marsh S, Lemos S. Outlet biceps tenodesis: a new technique for treatment of biceps long head tendon injury. *Arthrosc Tech* 2013; **2**: e83-e88 [PMID: 23875155 DOI: 10.1016/j.eats.2012.11.006]

95 **Narvani AA**, Atoun E, Van Tongel A, Sforza G, Levy O. The "anchor shape" technique for long head of the biceps tenotomy to avoid the popeye deformity. *Arthrosc Tech* 2013; **2**: e167-e170 [PMID: 23875145 DOI: 10.1016/j.eats.2013.01.008]

96 **Cho NS**, Cha SW, Rhee YG. Funnel tenotomy *versus* intracuff tenodesis for lesions of the long head of the biceps tendon associated with rotator cuff tears. *Am J Sports Med* 2014; **42**: 1161-1168 [PMID: 24576743 DOI: 10.1177/0363546514523719]

97 **Goubier JN**, Bihel T, Dubois E, Teboul F. Loop biceps tenotomy: an arthroscopic technique for long head of biceps tenotomy. *Arthrosc Tech* 2014; **3**: e427-e430 [PMID: 25264503 DOI: 10.1016/j.eats.2014.04.005]

98 **Zalneraitis BH**, Milam BP, Turner EK, Gasbarro G, Galvin JW. Biceps Squeeze Tenotomy: Technique to Improve Efficiency of Arthroscopic Biceps Tenotomy. *Arthrosc Tech* 2020; **9**: e1851-e1853 [PMID: 33294351 DOI: 10.1016/j.eats.2020.08.009]

99 **Corpus KT**, Garcia GH, Liu JN, Dines DM, O'Brien SJ, Dines JS, Taylor SA. Long Head of Biceps Tendon Management: a Survey of the American Shoulder and Elbow Surgeons. *HSS J* 2018; **14**: 34-40 [PMID: 29398992 DOI: 10.1007/s11420-017-9575-3]

100 **Abraham VT**, Tan BH, Kumar VP. Systematic Review of Biceps Tenodesis: Arthroscopic Versus Open. *Arthroscopy* 2016; **32**: 365-371 [PMID: 26427631 DOI: 10.1016/j.arthro.2015.07.028]

101 **Harris JD**. Editorial Commentary: Open Versus Arthroscopic Biceps Tenodesis--You Choose. *Arthroscopy* 2016; **32**: 372-373 [PMID: 26814399 DOI: 10.1016/j.arthro.2015.12.017]

102 **Hurley DJ**, Hurley ET, Pauzenberger L, Lim Fat D, Mullett H. Open Compared with Arthroscopic Biceps Tenodesis: A Systematic Review. *JBJS Rev* 2019; **7**: e4 [PMID: 31094891 DOI: 10.2106/JBJS.RVW.18.00086]

103 **Yeung M**, Shin JJ, Lesniak BP, Lin A. Complications of Arthroscopic Versus Open Biceps Tenodesis in the Setting of Arthroscopic Rotator Cuff Repairs: An Analysis of the American Board of Orthopaedic Surgery Database. *J Am Acad Orthop Surg* 2020; **28**: 113-120 [PMID: 31977611 DOI: 10.5435/JAAOS-D-19-00252]

104 **DeFroda SF**, Li L, Milner J, Bokshan SL, Owens BD. Cost comparison of arthroscopic rotator cuff repair with arthroscopic vs. open biceps tenodesis. *J Shoulder Elbow Surg* 2021; **30**: 340-345 [PMID: 32562763 DOI: 10.1016/j.jse.2020.05.031]

105 **Tu J**, Xu B, Guo R. Open subpectoral *vs.* arthroscopic proximal biceps tenodesis: A comparison study of clinical outcomes. *Exp Ther Med* 2020; **19**: 428-434 [PMID: 31853318 DOI: 10.3892/etm.2019.8232]

106 **Mazzocca AD**, Cote MP, Arciero CL, Romeo AA, Arciero RA. Clinical outcomes after subpectoral biceps tenodesis with an interference screw. *Am J Sports Med* 2008; **36**: 1922-1929 [PMID: 18697951 DOI: 10.1177/0363546508318192]

107 **Schoch C**, Geyer M, Drews B. Suprapectoral biceps tenodesis using a suture plate: clinical results after 2 years. *Arch Orthop Trauma Surg* 2017; **137**: 829-835 [PMID: 28374091 DOI: 10.1007/s00402-017-2664-4]

108 **Tahal DS**, Katthagen JC, Vap AR, Horan MP, Millett PJ. Subpectoral Biceps Tenodesis for Tenosynovitis of the Long Head of the Biceps in Active Patients Younger Than 45 Years Old. *Arthroscopy* 2017; **33**: 1124-1130 [PMID: 28043748 DOI: 10.1016/j.arthro.2016.10.013]

109 **Ng CY**, Funk L. Symptomatic chronic long head of biceps rupture: Surgical results. *Int J Shoulder Surg* 2012; **6**: 108-111 [PMID: 23493581 DOI: 10.4103/0973-6042.106222]

110 **Euler SA**, Horan MP, Ellman MB, Greenspoon JA, Millett PJ. Chronic rupture of the long head of the biceps tendon: comparison of 2-year results following primary *versus* revision open subpectoral biceps tenodesis. *Arch Orthop Trauma Surg* 2016; **136**: 657-663 [PMID: 26810192 DOI: 10.1007/s00402-015-2393-5]

111 **Tangari M**, Carbone S, Gallo M, Campi A. Long head of the biceps tendon rupture in professional wrestlers: treatment with a mini-open tenodesis. *J Shoulder Elbow Surg* 2011; **20**: 409-413 [PMID: 20888263 DOI: 10.1016/j.jse.2010.08.008]

112 **Vitali M**, Pedretti A, Naim Rodriguez N, Valenti M, Fraschini G. Our Totally Intra-Articular "Needle-Anchor" Tenodesis Technique Applied in Isolated Long Head of the Biceps Tendinopathy: Clinical and Functional Results in 60 Patients. *Tech Hand Up Extrem Surg* 2016; **20**: 26-31 [PMID: 26683115 DOI: 10.1097/BTH.0000000000000110]

113 **Brady PC**, Narbona P, Adams CR, Huberty D, Parten P, Hartzler RU, Arrigoni P, Burkhart SS. Arthroscopic proximal biceps tenodesis at the articular margin: evaluation of outcomes, complications, and revision rate. *Arthroscopy* 2015; **31**: 470-476 [PMID: 25442650 DOI: 10.1016/j.arthro.2014.08.024]

114 **Green JM**, Getelman MH, Snyder SJ, Burns JP. All-Arthroscopic Suprapectoral Versus Open Subpectoral Tenodesis of the Long Head of the Biceps Brachii Without the Use of Interference Screws. *Arthroscopy* 2017; **33**: 19-25 [PMID: 27659242 DOI: 10.1016/j.arthro.2016.07.007]

115 **Gombera MM**, Kahlenberg CA, Nair R, Saltzman MD, Terry MA. All-arthroscopic suprapectoral *versus* open subpectoral tenodesis of the long head of the biceps brachii. *Am J Sports Med* 2015; **43**: 1077-1083 [PMID: 25817189 DOI: 10.1177/0363546515570024]

116 **Werner BC**, Pehlivan HC, Hart JM, Carson EW, Diduch DR, Miller MD, Brockmeier SF. Increased incidence of postoperative stiffness after arthroscopic compared with open biceps tenodesis. *Arthroscopy* 2014; **30**: 1075-1084 [PMID: 24856765 DOI: 10.1016/j.arthro.2014.03.024]

117 **Provencher MT**, LeClere LE, Romeo AA. Subpectoral biceps tenodesis. *Sports Med Arthrosc Rev* 2008; **16**: 170-176 [PMID: 18703977 DOI: 10.1097/JSA.0b013e3181824edf]

118 **Rhee PC**, Spinner RJ, Bishop AT, Shin AY. Iatrogenic brachial plexus injuries associated with open subpectoral biceps tenodesis: a report of 4 cases. *Am J Sports Med* 2013; **41**: 2048-2053 [PMID: 23876520 DOI: 10.1177/0363546513495646]

119 **Nho SJ**, Reiff SN, Verma NN, Slabaugh MA, Mazzocca AD, Romeo AA. Complications associated with subpectoral biceps tenodesis: low rates of incidence following surgery. *J Shoulder Elbow Surg* 2010; **19**: 764-768 [PMID: 20471866 DOI: 10.1016/j.jse.2010.01.024]

120 **Forsythe B**, Zuke WA, Agarwalla A, Puzzitiello RN, Garcia GH, Cvetanovich GL, Yanke AB, Verma NN, Romeo AA. Arthroscopic Suprapectoral and Open Subpectoral Biceps Tenodeses Produce Similar Outcomes: A Randomized Prospective Analysis. *Arthroscopy* 2020; **36**: 23-32 [PMID: 31864581 DOI: 10.1016/j.arthro.2019.07.009]

121 **Godshaw BM**, Kolodychuk N, Browning BB, Williams G, Burdette R, Jones DG. Suprapectoral vs. Intra Articular Biceps Tenodesis: A Comparison of Clinical Outcomes. *Orthop J Sports Med* 2018. [DOI: 10.1177/2325967118S00108]

122 **Lutton DM**, Gruson KI, Harrison AK, Gladstone JN, Flatow EL. Where to tenodese the biceps: proximal or distal? *Clin Orthop Relat Res* 2011; **469**: 1050-1055 [PMID: 21107924 DOI: 10.1007/s11999-010-1691-z]

123 **Johannsen AM**, Macalena JA, Carson EW, Tompkins M. Anatomic and radiographic comparison of arthroscopic suprapectoral and open subpectoral biceps tenodesis sites. *Am J Sports Med* 2013; **41**: 2919-2924 [PMID: 24057029 DOI: 10.1177/0363546513503812]

124 **Denard PJ**, Dai X, Hanypsiak BT, Burkhart SS. Anatomy of the biceps tendon: implications for restoring physiological length-tension relation during biceps tenodesis with interference screw fixation. *Arthroscopy* 2012; **28**: 1352-1358 [PMID: 22925883 DOI: 10.1016/j.arthro.2012.04.143]

125 **Levy DM**, Meyer ZI, Campbell KA, Bach BR Jr. Subpectoral Biceps Tenodesis. *Am J Orthop (Belle Mead NJ)* 2016; **45**: 68-74 [PMID: 26866316]

126 **Gilmer BB**, DeMers AM, Guerrero D, Reid JB 3rd, Lubowitz JH, Guttmann D. Arthroscopic *versus* open comparison of long head of biceps tendon visualization and pathology in patients requiring tenodesis. *Arthroscopy* 2015; **31**: 29-34 [PMID: 25239173 DOI: 10.1016/j.arthro.2014.07.025]

127 **Kolz CW**, Suter T, Henninger HB. Regional mechanical properties of the long head of the biceps tendon. *Clin Biomech (Bristol, Avon)* 2015; **30**: 940-945 [PMID: 26209454 DOI: 10.1016/j.clinbiomech.2015.07.005]

128 **Werner BC**, Lyons ML, Evans CL, Griffin JW, Hart JM, Miller MD, Brockmeier SF. Arthroscopic suprapectoral and open subpectoral biceps tenodesis: a comparison of restoration of length-tension and mechanical strength between techniques. *Arthroscopy* 2015; **31**: 620-627 [PMID: 25498870 DOI: 10.1016/j.arthro.2014.10.012]

129 **Gupta AK**, Chalmers PN, Klosterman EL, Harris JD, Bach BR Jr, Verma NN, Cole BJ, Romeo AA. Subpectoral biceps tenodesis for bicipital tendonitis with SLAP tear. *Orthopedics* 2015; **38**: e48-e53 [PMID: 25611420 DOI: 10.3928/01477447-20150105-60]

130 **Khalid MA**, Morris RP, Black N, Maassen NH. Biomechanical Evaluation of Humerus Fracture After Subpectoral Biceps Tenodesis With Interference Screw Versus Unicortical Button. *Arthroscopy* 2020; **36**: 1253-1260 [PMID: 31973991 DOI: 10.1016/j.arthro.2019.10.034]

131 **Sethi PM**, Vadasdi K, Greene RT, Vitale MA, Duong M, Miller SR. Safety of open suprapectoral and subpectoral biceps tenodesis: an anatomic assessment of risk for neurologic injury. *J Shoulder Elbow Surg* 2015; **24**: 138-142 [PMID: 25193486 DOI: 10.1016/j.jse.2014.06.038]

132 **Werner BC**, Evans CL, Holzgrefe RE, Tuman JM, Hart JM, Carson EW, Diduch DR, Miller MD, Brockmeier SF. Arthroscopic suprapectoral and open subpectoral biceps tenodesis: a comparison of minimum 2-year clinical outcomes. *Am J Sports Med* 2014; **42**: 2583-2590 [PMID: 25201442 DOI: 10.1177/0363546514547226]

133 **Golish SR**, Caldwell PE 3rd, Miller MD, Singanamala N, Ranawat AS, Treme G, Pearson SE, Costic R, Sekiya JK. Interference screw *versus* suture anchor fixation for subpectoral tenodesis of the proximal biceps tendon: a cadaveric study. *Arthroscopy* 2008; **24**: 1103-1108 [PMID: 19028161 DOI: 10.1016/j.arthro.2008.05.005]

134 **Slabaugh MA**, Frank RM, Van Thiel GS, Bell RM, Wang VM, Trenhaile S, Provencher MT, Romeo AA, Verma NN. Biceps tenodesis with interference screw fixation: a biomechanical comparison of screw length and diameter. *Arthroscopy* 2011; **27**: 161-166 [PMID: 21030205 DOI: 10.1016/j.arthro.2010.07.004]

135 **Koh KH**, Ahn JH, Kim SM, Yoo JC. Treatment of biceps tendon lesions in the setting of rotator cuff tears: prospective cohort study of tenotomy *versus* tenodesis. *Am J Sports Med* 2010; **38**: 1584-1590 [PMID: 20551285 DOI: 10.1177/0363546510364053]

136 **Scheibel M**, Schröder RJ, Chen J, Bartsch M. Arthroscopic soft tissue tenodesis *versus* bony fixation anchor tenodesis of the long head of the biceps tendon. *Am J Sports Med* 2011; **39**: 1046-1052 [PMID: 21257843 DOI: 10.1177/0363546510390777]

137 **Boileau P**, Krishnan SG, Coste JS, Walch G. Arthroscopic biceps tenodesis: a new technique using bioabsorbable interference screw fixation. *Arthroscopy* 2002; **18**: 1002-1012 [PMID: 12426544 DOI: 10.1053/jars.2002.36488]

138 **Arora AS**, Singh A, Koonce RC. Biomechanical evaluation of a unicortical button *versus* interference screw for subpectoral biceps tenodesis. *Arthroscopy* 2013; **29**: 638-644 [PMID: 23395466 DOI: 10.1016/j.arthro.2012.11.018]

139 **DeAngelis JP**, Chen A, Wexler M, Hertz B, Grimaldi Bournissaint L, Nazarian A, Ramappa AJ. Biomechanical characterization of unicortical button fixation: a novel technique for proximal subpectoral biceps tenodesis. *Knee Surg Sports Traumatol Arthrosc* 2015; **23**: 1434-1441 [PMID: 24253375 DOI: 10.1007/s00167-013-2775-6]

140 **Park JS**, Kim SH, Jung HJ, Lee YH, Oh JH. A Prospective Randomized Study Comparing the Interference Screw and Suture Anchor Techniques for Biceps Tenodesis. *Am J Sports Med* 2017; **45**: 440-448 [PMID: 28146397 DOI: 10.1177/0363546516667577]

141 **Tashjian RZ**, Henninger HB. Biomechanical evaluation of subpectoral biceps tenodesis: dual suture anchor *versus* interference screw fixation. *J Shoulder Elbow Surg* 2013; **22**: 1408-1412 [PMID: 23415819 DOI: 10.1016/j.jse.2012.12.039]

142 **Sawyer GA**, Anderson BC, Paller D, Heard WM, Fadale PD. Effect of interference screw fixation on ACL graft tensile strength. *J Knee Surg* 2013; **26**: 155-159 [PMID: 23288751 DOI: 10.1055/s-0032-1324808]

143 **Zantop T**, Weimann A, Schmidtko R, Herbort M, Raschke MJ, Petersen W. Graft laceration and pullout strength of soft-tissue anterior cruciate ligament reconstruction: *in vitro* study comparing titanium, poly-d,l-lactide, and poly-d,l-lactide-tricalcium phosphate screws. *Arthroscopy* 2006; **22**: 1204-1210 [PMID: 17084298 DOI: 10.1016/j.arthro.2006.06.015]

144 **Shumborski S**, Heath E, Salmon LJ, Roe JP, Linklater JP, Facek M, Pinczewski LA. A Randomized Controlled Trial of PEEK Versus Titanium Interference Screws for Anterior Cruciate Ligament Reconstruction With 2-Year Follow-up. *Am J Sports Med* 2019; **47**: 2386-2393 [PMID: 31306589 DOI: 10.1177/0363546519861530]

145 **Kurtz SM**, Devine JN. PEEK biomaterials in trauma, orthopedic, and spinal implants. *Biomaterials* 2007; **28**: 4845-4869 [PMID: 17686513 DOI: 10.1016/j.biomaterials.2007.07.013]

146 **Mazzocca AD**, Bicos J, Santangelo S, Romeo AA, Arciero RA. The biomechanical evaluation of four fixation techniques for proximal biceps tenodesis. *Arthroscopy* 2005; **21**: 1296-1306 [PMID: 16325079 DOI: 10.1016/j.arthro.2005.08.008]

147 **Buchholz A**, Martetschläger F, Siebenlist S, Sandmann GH, Hapfelmeier A, Lenich A, Millett PJ, Stöckle U, Elser F. Biomechanical comparison of intramedullary cortical button fixation and interference screw technique for subpectoral biceps tenodesis. *Arthroscopy* 2013; **29**: 845-853 [PMID: 23587927 DOI: 10.1016/j.arthro.2013.01.010]

148 **Richards DP**, Burkhart SS. A biomechanical analysis of two biceps tenodesis fixation techniques. *Arthroscopy* 2005; **21**: 861-866 [PMID: 16012500 DOI: 10.1016/j.arthro.2005.03.020]

149 **Chiang FL**, Hong CK, Chang CH, Lin CL, Jou IM, Su WR. Biomechanical Comparison of All-Suture Anchor Fixation and Interference Screw Technique for Subpectoral Biceps Tenodesis. *Arthroscopy* 2016; **32**: 1247-1252 [PMID: 27039966 DOI: 10.1016/j.arthro.2016.01.016]

150 **Tan H**, Wang D, Lebaschi AH, Hutchinson ID, Ying L, Deng XH, Rodeo SA, Warren RF. Comparison of Bone Tunnel and Cortical Surface Tendon-to-Bone Healing in a Rabbit Model of Biceps Tenodesis. *J Bone Joint Surg Am* 2018; **100**: 479-486 [PMID: 29557864 DOI: 10.2106/JBJS.17.00797]

151 **Dovan TT**, Gelberman RH, Kusano N, Calcaterra M, Silva MJ. Zone I flexor digitorum profundus repair: an *ex vivo* biomechanical analysis of tendon to bone repair in cadavera. *J Hand Surg Am* 2005; **30**: 258-266 [PMID: 15781347 DOI: 10.1016/j.jhsa.2004.11.007]

152 **Lim JK**, Hui J, Li L, Thambyah A, Goh J, Lee EH. Enhancement of tendon graft osteointegration using mesenchymal stem cells in a rabbit model of anterior cruciate ligament reconstruction. *Arthroscopy* 2004; **20**: 899-910 [PMID: 15525922 DOI: 10.1016/j.arthro.2004.06.035]

153 **Soon MY**, Hassan A, Hui JH, Goh JC, Lee EH. An analysis of soft tissue allograft anterior cruciate ligament reconstruction in a rabbit model: a short-term study of the use of mesenchymal stem cells to enhance tendon osteointegration. *Am J Sports Med* 2007; **35**: 962-971 [PMID: 17400750 DOI: 10.1177/0363546507300057]

154 **Silva MJ**, Thomopoulos S, Kusano N, Zaegel MA, Harwood FL, Matsuzaki H, Havlioglu N, Dovan TT, Amiel D, Gelberman RH. Early healing of flexor tendon insertion site injuries: Tunnel repair is mechanically and histologically inferior to surface repair in a canine model. *J Orthop Res* 2006; **24**: 990-1000 [PMID: 16514627 DOI: 10.1002/jor.20084]

155 **Euler SA**, Smith SD, Williams BT, Dornan GJ, Millett PJ, Wijdicks CA. Biomechanical analysis of subpectoral biceps tenodesis: effect of screw malpositioning on proximal humeral strength. *Am J Sports Med* 2015; **43**: 69-74 [PMID: 25371439 DOI: 10.1177/0363546514554563]

156 **Sears BW**, Spencer EE, Getz CL. Humeral fracture following subpectoral biceps tenodesis in 2 active, healthy patients. *J Shoulder Elbow Surg* 2011; **20**: e7-11 [PMID: 21602065 DOI: 10.1016/j.jse.2011.02.020]

157 **Frank RM**, Bernardoni ED, Veera SS, Waterman BR, Griffin JW, Shewman EF, Cole BJ, Romeo

AA, Verma NN. Biomechanical Analysis of All-Suture Suture Anchor Fixation Compared With Conventional Suture Anchors and Interference Screws for Biceps Tenodesis. *Arthroscopy* 2019; **35**: 1760-1768 [PMID: 31072716 DOI: 10.1016/j.arthro.2019.01.026]

158 **Mellano CR**, Frank RM, Shin JJ, Jain A, Zuke WA, Mascarenhas R, Shewman E, Cole BJ, Romeo AA, Verma NN, Forsythe B. Subpectoral Biceps Tenodesis With PEEK Interference Screw: A Biomechanical Analysis of Humeral Fracture Risk. *Arthroscopy* 2018; **34**: 806-813 [PMID: 29287950 DOI: 10.1016/j.arthro.2017.09.012]

159 **Millett PJ**, Sanders B, Gobezie R, Braun S, Warner JJ. Interference screw vs. suture anchor fixation for open subpectoral biceps tenodesis: does it matter? *BMC Musculoskelet Disord* 2008; **9**: 121 [PMID: 18793424 DOI: 10.1186/1471-2474-9-121]

160 **Leroux T**, Chahal J, Wasserstein D, Verma NN, Romeo AA. A Systematic Review and Meta-analysis Comparing Clinical Outcomes After Concurrent Rotator Cuff Repair and Long Head Biceps Tenodesis or Tenotomy. *Sports Health* 2015; **7**: 303-307 [PMID: 26137174 DOI: 10.1177/1941738114539627]

161 **Zhang Q**, Zhou J, Ge H, Cheng B. Tenotomy or tenodesis for long head biceps lesions in shoulders with reparable rotator cuff tears: a prospective randomised trial. *Knee Surg Sports Traumatol Arthrosc* 2015; **23**: 464-469 [PMID: 23828089 DOI: 10.1007/s00167-013-2587-8]

162 **Oh JH**, Lee YH, Kim SH, Park JS, Seo HJ, Kim W, Park HB. Comparison of Treatments for Superior Labrum-Biceps Complex Lesions With Concomitant Rotator Cuff Repair: A Prospective, Randomized, Comparative Analysis of Debridement, Biceps Tenotomy, and Biceps Tenodesis. *Arthroscopy* 2016; **32**: 958-967 [PMID: 26921128 DOI: 10.1016/j.arthro.2015.11.036]

163 **Shank JR**, Singleton SB, Braun S, Kissenberth MJ, Ramappa A, Ellis H, Decker MJ, Hawkins RJ, Torry MR. A comparison of forearm supination and elbow flexion strength in patients with long head of the biceps tenotomy or tenodesis. *Arthroscopy* 2011; **27**: 9-16 [PMID: 21035992 DOI: 10.1016/j.arthro.2010.06.022]

164 **Zabrzyński J**, Huri G, Gryckiewicz S, Çetik RM, Szwedowski D, Łapaj Ł, Gagat M, Paczesny Ł. Biceps Tenodesis *versus* Tenotomy with Fast Rehabilitation Protocol-A Functional Perspective in Chronic Tendinopathy. *J Clin Med* 2020; **9** [PMID: 33291804 DOI: 10.3390/jcm9123938]

165 **MacDonald P**, Verhulst F, McRae S, Old J, Stranges G, Dubberley J, Mascarenhas R, Koenig J, Leiter J, Nassar M, Lapner P. Biceps Tenodesis Versus Tenotomy in the Treatment of Lesions of the Long Head of the Biceps Tendon in Patients Undergoing Arthroscopic Shoulder Surgery: A Prospective Double-Blinded Randomized Controlled Trial. *Am J Sports Med* 2020; **48**: 1439-1449 [PMID: 32223645 DOI: 10.1177/0363546520912212]

166 **Zhou P**, Liu J, Deng X, Li Z. Biceps tenotomy *versus* tenodesis for lesions of the long head of the biceps tendon: A systematic review and meta-analysis of randomized controlled trials. *Medicine (Baltimore)* 2021; **100**: e23993 [PMID: 33545991 DOI: 10.1097/MD.0000000000023993]

167 **Kooistra B**, Gurnani N, Weening A, van Duerzen D, van den Bekerom M. Tenotomy or Tenodesis for Tendinopathy of the Long Head of the Biceps Brachii: An Updated Systematic Review and Meta-analysis. *Arthrosc Sports Med Rehabil* 2021; **3**: e1199-e1209 [PMID: 34430901 DOI: 10.1016/j.asmr.2021.02.010]

168 **Mollon B**, Mahure SA, Ensor KL, Zuckerman JD, Kwon YW, Rokito AS. Subsequent Shoulder Surgery After Isolated Arthroscopic SLAP Repair. *Arthroscopy* 2016; **32**: 1954-1962.e1 [PMID: 27083535 DOI: 10.1016/j.arthro.2016.01.053]

169 **Taylor SA**, Degen RM, White AE, McCarthy MM, Gulotta LV, O'Brien SJ, Werner BC. Risk Factors for Revision Surgery After Superior Labral Anterior-Posterior Repair: A National Perspective. *Am J Sports Med* 2017; **45**: 1640-1644 [PMID: 28282498 DOI: 10.1177/0363546517691950]

170 **Nadeem IM**, Vancolen S, Horner NS, Leroux T, Alolabi B, Khan M. Management of Failed SLAP Repair: A Systematic Review. *HSS J* 2020; **16**: 261-271 [PMID: 33088240 DOI: 10.1007/s11420-019-09700-3]

171 **Cvetanovich GL**, Gowd AK, Agarwalla A, Forsythe B, Romeo AA, Verma NN. Trends in the Management of Isolated SLAP Tears in the United States. *Orthop J Sports Med* 2019; **7**: 2325967119833997 [PMID: 30923727 DOI: 10.1177/2325967119833997]

172 **Popp D**, Schöffl V. Superior labral anterior posterior lesions of the shoulder: Current diagnostic and therapeutic standards. *World J Orthop* 2015; **6**: 660-671 [PMID: 26495243 DOI: 10.5312/wjo.v6.i9.660]

173 **Sullivan S**, Hutchinson ID, Curry EJ, Marinko L, Li X. Surgical management of type II superior labrum anterior posterior (SLAP) lesions: a review of outcomes and prognostic indicators. *Phys Sportsmed* 2019; **47**: 375-386 [PMID: 30977691 DOI: 10.1080/00913847.2019.1607601]

174 **Varacallo M**, Tapscott DC, Mair SD. Superior Labrum Anterior Posterior Lesions. [Updated 2021 Feb 9]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2021 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK538284/

175 **Ide J**, Maeda S, Takagi K. Sports activity after arthroscopic superior labral repair using suture anchors in overhead-throwing athletes. *Am J Sports Med* 2005; **33**: 507-514 [PMID: 15722289 DOI: 10.1177/0363546504269255]

176 **Brockmeier SF**, Voos JE, Williams RJ 3rd, Altchek DW, Cordasco FA, Allen AA; Hospital for Special Surgery Sports Medicine and Shoulder Service. Outcomes after arthroscopic repair of type-II SLAP lesions. *J Bone Joint Surg Am* 2009; **91**: 1595-1603 [PMID: 19571081 DOI: 10.2106/JBJS.H.00205]

177 **Fedoriw WW**, Ramkumar P, McCulloch PC, Lintner DM. Return to play after treatment of superior labral tears in professional baseball players. *Am J Sports Med* 2014; **42**: 1155-1160 [PMID: 24674945 DOI: 10.1177/0363546514528096]

178 **Kim SH**, Ha KI, Kim SH, Choi HJ. Results of arthroscopic treatment of superior labral lesions. *J Bone Joint Surg Am* 2002; **84**: 981-985 [PMID: 12063332 DOI: 10.2106/00004623-200206000-00012]

179 **Frank RM**, Nho SJ, McGill KC, Grumet RC, Cole BJ, Verma NN, Romeo AA. Retrospective analysis of arthroscopic superior labrum anterior to posterior repair: prognostic factors associated with failure. *Adv Orthop* 2013; **2013**: 125960 [PMID: 23585969 DOI: 10.1155/2013/125960]

180 **Higgins LD**, Warner JJ. Superior labral lesions: anatomy, pathology, and treatment. *Clin Orthop Relat Res* 2001; 73-82 [PMID: 11550879]

181 **Lichtenberg S**, Magosch P, Habermeyer P. [Superior labrum-biceps anchor complex]. *Orthopade* 2003; **32**: 616-626 [PMID: 12883761 DOI: 10.1007/s00132-003-0491-5]

182 **Gottschalk MB**, Karas SG, Ghattas TN, Burdette R. Subpectoral biceps tenodesis for the treatment of type II and IV superior labral anterior and posterior lesions. *Am J Sports Med* 2014; **42**: 2128-2135 [PMID: 25053696 DOI: 10.1177/0363546514540273]

183 **Cvetanovich GL**, Gowd AK, Frantz TL, Erickson BJ, Romeo AA. Superior Labral Anterior Posterior Repair and Biceps Tenodesis Surgery: Trends of the American Board of Orthopaedic Surgery Database. *Am J Sports Med* 2020; **48**: 1583-1589 [PMID: 32298133 DOI: 10.1177/0363546520913538]

184 **Chalmers PN**, Monson B, Frank RM, Mascarenhas R, Nicholson GP, Bach BR Jr, Verma NN, Cole BJ, Romeo AA. Combined SLAP repair and biceps tenodesis for superior labral anterior-posterior tears. *Knee Surg Sports Traumatol Arthrosc* 2016; **24**: 3870-3876 [PMID: 26328801 DOI: 10.1007/s00167-015-3774-6]

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ORIGINAL ARTICLE

Retrospective Cohort Study

Should we use similar perioperative protocols in patients undergoing unilateral and bilateral one-stage total knee arthroplasty?

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Author contributions: Laoruengthana A contributed to the conception and design of the study, and performed the operation as the surgeon; Rattanaprichavej P, Samapath P, Chinwatanawongwan B, and Chompoonutprapa P collected the required data; Laoruengthana A and Rattanaprichavej P wrote and completed the manuscript; Laoruengthana A, Rattanaprichavej P, and Pongpirul K were responsible for data interpretation and performed the statistical analysis; all authors have read and approved the manuscript.

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Informed consent statement: All

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Abstract

BACKGROUND

Bilateral one-stage total knee arthroplasty (BTKA) is now in greater use as an alternative option for patients with bilateral end-stage knee arthropathy. However, postoperative pain and disablement during convalescence from BTKA, and procedure-related complications have been concerning issues for patients and surgeons. Although some studies reported that BTKA in selected patients is as safe as the staged procedure, well-defined guidelines for patient screening, and perioperative care and monitoring to avoid procedure-related complications are still controversial.

AIM

To compare the perioperative outcomes including perioperative blood loss (PBL), cardiac biomarkers, pain intensity, functional recovery, and complications between unilateral total knee arthroplasty (UTKA) and BTKA performed with a similar perioperative protocol.

METHODS

We conducted a retrospective study on consecutive patients undergoing UTKA and BTKA that had been performed by a single surgeon with identical perioperative protocols. The exclusion criteria of this study included patients with an American Society of Anesthesiologists score > 3, and known cardiopulmonary comorbidity or high-sensitivity Troponin-T (hs-TnT) > 14 ng/L. Outcome

study participants, or their legal guardian, provided informed written consent prior to study enrollment.

Conflict-of-interest statement: The authors declare that they have no competing interests related to the study design, data collection, and interpretation of results presented in this manuscript.

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measures included visual analogue scale (VAS) score of postoperative pain, morphine consumption, range of knee motion, straight leg raise (SLR), length of stay (LOS), and serum hemoglobin (Hb) and hs-TnT monitored during hospitalization.

RESULTS

Of 210 UTKA and 137 BTKA patients, those in the BTKA group were younger and more predominately female. The PBL of the UTKA *vs* BTKA group was 646.45 ± 272.26 mL *vs* 1012.40 ± 391.95 mL ($P < 0.01$), and blood transfusion rates were 10.48% and 40.88% ($P < 0.01$), respectively. Preoperative Hb and body mass index were predictive factors for blood transfusion in BTKA, whereas preoperative Hb was only a determinant in UTKA patients. The BTKA group had significantly higher VAS scores than the UTKA group at 48, 72, and 96 h after surgery, and also had a significantly lower degree of SLR at 72 h. The BTKA group also had a significantly longer LOS than the UTKA group. Of the patients who had undergone the procedure, 5.71% of the UTKA patients and 12.41% of the BTKA patients ($P = 0.04$) had hs-TnT > 14 ng/L during the first 72 h postoperatively. However, there was no difference in other outcome measures and complications.

CONCLUSION

Following similar perioperative management, the blood transfusion rate in BTKA is 4-fold that required in UTKA. Also, BTKA is associated with higher pain intensity at 48 h postoperatively and prolonged LOS when compared to the UTKA. Hence, BTKA patients may require more extensive perioperative management for blood loss and pain, even if having no higher risk of complications than UTKA.

Key Words: Bilateral one-stage total knee arthroplasty; Unilateral total knee arthroplasty; Blood loss; Postoperative pain; High-sensitivity Troponin-T; Cardiovascular events

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Core Tip: The safety of bilateral one-stage total knee arthroplasty (BTKA) is still debated because of greater blood loss, higher risk of cardiovascular events, increased postoperative pain, and longer disablement period than unilateral total knee arthroplasty (UTKA). After comparing consecutive patients underwent BTKA and UTKA with similar perioperative management, we found that the blood transfusion rate in the BTKA is 4-fold than UTKA. Moreover, BTKA is associated with significantly higher pain intensity at 48 h postoperatively and prolonged hospitalization. Although our study demonstrated that BTKA is a safe procedure in selected patients, extensive perioperative management for blood loss and pain is mandatory for BTKA patients.

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INTRODUCTION

Total knee arthroplasty (TKA) is widely accepted as one of the most effective and safe surgical procedures for treating severe osteoarthritis (OA) of the knee. Currently, advances in anesthesia, surgical techniques, and perioperative care, including multimodal pain management and accelerated rehabilitation, have improved functional recovery and shortened the length of the hospital stay for patients undergoing unilateral total knee arthroplasty (UTKA)[1]. There have also been contemporary blood-conserving methods published that substantially decrease the

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rate of postoperative blood transfusions when kept below 10%[2-4].

Approximately 25% of patients undergoing UTKA have bilateral OA knees[5] and subsequently will undergo contralateral TKA within 1 year[6]. Thus, bilateral one-stage total knee arthroplasty (BTKA) is now in greater use as an alternative option for patients with bilateral OA knees because of the potential advantages that include single anesthesia, reduction in total hospitalization and rehabilitation time, as well as overall costs[7]. However, the safety of BTKA is still debated because of perioperative morbidity that is associated with greater blood loss and a higher risk of cardiovascular adverse events than UTKA[8,9]. Various blood-conserving strategies including regional anesthesia, tourniquet use and deflation after wound closure, femoral canal occlusion, and use of tranexamic acid (TXA) are commonly implemented in patients having BTKA with documented efficacy[10]. However, recently published studies revealed that blood loss after BTKA ranged between 874 and 1067 mL, and blood transfusion rate ranged between 24% and 44% even if TXA was administered[11-13].

The substantial blood loss related to BTKA may subsequently cause occult hypoperfusion of vital organs such as the heart and kidneys. Conversely, requirements for blood transfusions may also increase the risk of complications such as allergic reaction, cardiovascular volume overload, and subsequent heart failure or pulmonary edema [14,15]. The risk of myocardial infarction (MI) has been reported to significantly increase among the TKA group during the immediate postoperative phase when compared to the non-surgical group[16,17]. Taking data from the National Hospital Discharge database, 1.1% of patients were diagnosed with cardiac complications in the 90 d after TKA, and BTKA had a higher rate than UTKA (2.0% *vs* 1.7%)[18]. Therefore, these findings may emphasize the need for extensive perioperative care and monitoring to avoid such complications in BTKA.

Furthermore, significant pain after UTKA has been noted and inadequate pain control has been demonstrated to be associated with inferior functional outcomes at 2 years after TKA[19]. Thus, postoperative pain has been an issue frequently concerning patients as to whether the intensity of pain and disablement during convalescence from BTKA are worse than that following UTKA. Nevertheless, there has been limited evidence comparing postoperative pain and functional recovery after BTKA and UTKA, and the known results are still equivocal[20,21]. Therefore, the objective of the present study was to compare the perioperative outcomes including perioperative blood loss (PBL), cardiac biomarkers, pain intensity and functional recovery, and complications between patients undergoing UTKA and BTKA with a similar perioperative protocol. The authors hypothesized that patients undergoing BTKA may require additional perioperative care and monitoring to improve outcomes.

MATERIALS AND METHODS

The study received institutional review board approval for retrospective analysis of data recorded prior to initiation and has been registered as TCTR20181220001. The authors' criteria for BTKA were painful bilateral end-stage OA knees, and therefore the selection of BTKA or UTKA was based upon patient preference. Consecutive patients who had undergone UTKA and BTKA for primary OA, performed by a single surgeon between January 2016 and December 2019, were enrolled in the study. The exclusion criteria of this study were patients with a history of prior knee surgery or previous knee infection. Participants with an American Society of Anesthesiologists (ASA) score > 3, known cardiopulmonary comorbidity or high-sensitivity Troponin-T (hs-TnT) > 14 ng/L, CKD stage ≥ 3, or significant renal impairment (serum creatinine > 1.5 mg/dL) were also excluded.

All the UTKA and BTKA were performed by a single surgeon with identical pre-, peri-, and postoperative protocols. Regional anesthesia, prophylactic intravenous antibiotics (ATB), and tourniquet control at 250 mmHg were applied for all patients. A medial parapatellar approach was performed through an approximately 10 cm midline skin incision, the cruciate ligaments were excised, and conventional instruments were then used to prepare the proximal tibial and distal femoral bone cuts by using extramedullary and intramedullary reference guides, respectively. A bone plug was applied to occlude the opening hole of the distal femur after finishing all the bone cuts. Soft tissue balancing was performed to achieve appropriate flexion and extension gaps. The patella was selectively resurfaced. Before prosthesis implantation, local infiltration anesthesia (LIA) was induced by injecting Bupivacaine (0.5% Marcaine; AstraZeneca, Sweden), 30 mg of ketorolac tromethamine (ketorolac tromethamine 1 mL; SiuGuan, Taiwan), and sterile normal saline solution into the

anterior and posterior compartment of the knee with the 2:1 ratio technique. All the patients received a fixed bearing, posterior stabilized prosthesis which was implanted with bone cement. A vacuum drain was then applied, and 15 mg/kg of topical tranexamic acid was poured into the knee joint before closure of the arthrotomy. The drain was clamped for 3 h and subsequently removed at 24 h after the surgery.

For postoperative management, intravenous patient-controlled analgesia morphine (100 mL solution containing 50 mg of morphine sulphate) was injected as an on-demand bolus of 1 mL with a 5 min lockout period, 30 mg of ketorolac was given intravenously every 8 h, and 500 mg of oral acetaminophen was administered three times a day. After 48 h, all the catheters were discarded, and 2 mg of morphine were injected every 8 h with an additional 2 mg of morphine used for a breakthrough pain throughout hospitalization. Also, oral medications including 250 mg of naproxen twice a day and 500 mg of acetaminophen three times a day were given. All patients were administered with low molecular weight heparin for the first 48 h and combined with oral warfarin for 10 d. Rehabilitation including active ankle pump was started after the surgery, and a continuous passive motion device was utilized on the day after surgery. Every patient was encouraged to attempt early ambulation with gait aids as able to be tolerated.

Data collected for analysis were patient demography, visual analogue scale (VAS) scores of postoperative pain, morphine consumption, range of knee motion (ROM), straight leg raise (SLR), length of stay (LOS), and laboratory evaluation comprising serum hemoglobin (Hb), blood transfusion rate, creatine phosphokinase (CPK), and hs-TnT preoperatively and at 24, 48, and 72 h after the surgery.

The patient's total blood volume (TBV) was calculated by the equation of Nadler *et al*[22]. The difference between preoperative and lowest postoperative Hb was applied with the Hb balance method to determine PBL[2].

Males: TBV (mL) = [0.0003669 × height^3 (cm)] + [32.19 × body weight (kg)] + 604

Females: TBV (mL) = [0.0003561 × height^3 (cm)] + [33.08 × body weight (kg)] + 183

PBL (mL) = TBV (mL) × (Hb_i – Hb_e)/Hb_i + sum of blood products transfused (mL), where Hb_i (g/dL) is the preoperative Hb, and Hb_e (g/dL) is the postoperative Hb.

Serum Hb level that drops below 9.0 g/dL is indicated for blood transfusion for both the UTKA and BTKA at our institution. A hs-TnT level > 14 ng/L is considered as possible for MI in our laboratory system. Any complications and readmission rates at 90 d after the index surgery were recorded.

Statistical analysis

All demographic data and measured outcomes are summarized with descriptive statistics. Continuous data are presented as the mean and standard deviation, and Student's *t*-test was used to compare between the UTKA and BTKA groups. Categorical data which are presented as counts and percentages were compared by using Chi-square or Fisher's exact test. Repeated-measures analysis of variance was applied to compare the time-dependent variables including VAS, ROM, SLR, Hb, CPK, and hs-TnT between groups. The *post hoc* comparisons of all pairwise points in time were applied to account for multiple testing with Bonferroni adjustments. A multiple logistic regression analysis was performed to determine which of these variables, including age, gender, body mass index (BMI), ASA physical status classification, and preoperative Hb, were the predictive factors for allogeneic blood transfusion. The sample size of the UTKA and BTKA groups had 99.5% power to detect a difference of 200 mL in PBL, which could significantly impact on blood transfusion rate, with standard deviation (SD) of 400 mL, and 95.4% power to ascertain a difference of 1.0 for VAS with SD of 2.5, with type I error of 5%. Stata/MP 15.0 software (StataCorp LP, College Station, TX, United States) was used for all statistical analyses. Statistical significance was defined as $P < 0.05$.

RESULTS

There were 210 UTKA and 137 BTKA included for analysis. The demographic and perioperative characteristics are briefly summarized in Table 1. Patients in the BTKA group were younger and more predominately female, and had a longer total duration of operation (TDO).

Blood loss

The postoperative Hb level of both groups gradually dropped and reached the lowest point at 72 h after the surgery. BTKA was associated with a significantly lower level of

Table 1 Demographic and perioperative characteristics

	UTKA	BTKA	*P* value
Age (yr)	65.00 ± 7.48	63.10 ± 6.83	0.02[a]
Gender (female/male)	178/32	129/8	0.01[a]
BMI (kg/m^2)	26.99 ± 3.49	26.54 ± 3.89	0.20
ASA (1/2/3)	4/134/72	5/101/31	0.05
Preop. VAS pain score	6.89 ± 2.33	6.77 ± 1.89	0.44
Preop. ROM	113.86 ± 13.55	111.16 ± 14.26	0.13
Preop. Hb (g/dL)	12.60 ± 1.19	12.44 ± 1.08	0.21
Preop. CPK (u/L)	125.05 ± 84.64	116.05 ± 65.12	0.41
Preop. TnT (ng/dL)	6.77 ± 3.04	6.46 ± 3.18	0.79
TDO (min)	62.21 ± 9.86	125.12 ± 16.30	< 0.01[a]

[a]$P < 0.05$ indicates statistical significance. All parameters are presented as the mean ± standard deviation, except for gender and American Society of Anesthesiologists score.

BMI: Body mass index; ASA: American Society of Anesthesiologists; Preop.: Preoperative; VAS: Visual analog scale; TDO: Total duration of operation; Hb: Hemoglobin; sCr: Serum creatinine; TnT: Troponin-T; CPK: Creatine Phosphokinase; UTKA: Unilateral total knee arthroplasty; BTKA: Bilateral one-stage total knee arthroplasty.

Hb than UTKA at 24, 48, and 72 h postoperatively (Figure 1). The PBL of the UTKA *vs* BTKA group was 646.45 ± 272.26 mL *vs* 1012.40 ± 391.95 mL ($P < 0.01$), respectively.

Blood transfusion rates in UTKA and BTKA were 10.48% (22/210) and 40.88% (56/137), ($P < 0.01$), respectively. For UTKA, 18 of 69 (26.09%) patients with preoperative anemia (defined as preoperative Hb < 12 g/dL in females and < 13 g/dL in males) received blood transfusion compared to 6 of 141 (4.26%) patients without anemia ($P < 0.01$). Twenty-eight of 43 (65.12%) patients with preoperative anemia in the BTKA group required a transfusion, whereas patients without anemia had a transfusion rate of approximately 1 in 4 (26/94, 27.67%; $P < 0.01$). The multivariate analysis demonstrated that preoperative Hb [odd ratio (OR): 0.33, 95% confidence interval (CI): 0.22-0.50, $P < 0.01$] and BMI (OR: 0.90, 95%CI: 0.81-0.99, $P = 0.03$) were predictive factors for blood transfusion in the BTKA group, whereas preoperative Hb (OR: 0.21, 95%CI: 0.12-0.37, $P < 0.01$) was only a determinant in the UTKA group when using similar perioperative blood management and cut-off values for transfusion.

Postoperative pain and recovery

There was no difference between the UTKA and BTKA groups regarding VAS scores at 6, 12, and 24 h, but the BTKA group had significantly higher VAS scores than the UTKA group at 48, 72, and 96 h after surgery (Figure 2A). The BTKA group had a significantly lower degree of SLR than the UTKA group at 72 h; however, the ROM was comparable between groups throughout the study period (Figure 2B and C). Total morphine consumption in the UTKA *vs* BTKA group was 11.93 ± 9.20 *vs* 13.81 ± 10.81 ($P = 0.16$) at 24 h, and 16.78 ± 13.24 *vs* 19.51 ± 15.47 ($P = 0.15$) at 48 h postoperatively. The incidence of postoperative nausea and vomiting (PONV) during the first 24 h in the UTKA and BTKA groups was 38.79% (90/142) and 46.47% (112/129) ($P = 0.09$), respectively. The UTKA had an LOS of 4.01 ± 0.97 d, which was significantly shorter than that of the BTKA group (5.17 ± 1.32 d; $P < 0.01$).

Cardiac biomarkers

The BTKA group showed significantly higher CPK than the UTKA group at 24 h and 48 h after the surgery (Figure 3A). For the hs-TnT, it was gradually rising during 72 h after the UTKA and it was rising to a peak at 48 h after the BTKA, but the hs-TnT level was not significantly different between groups along the study period (Figure 3B). Nonetheless, there were 12 patients (5.71%) who had hs-TnT > 14 ng/L during the first 72 h after the UTKA compared to 17 patients (12.41%) following the BTKA ($P = 0.04$), but no patient presented cardiovascular symptoms and signs, or abnormal electrocardiogram indicating MI.

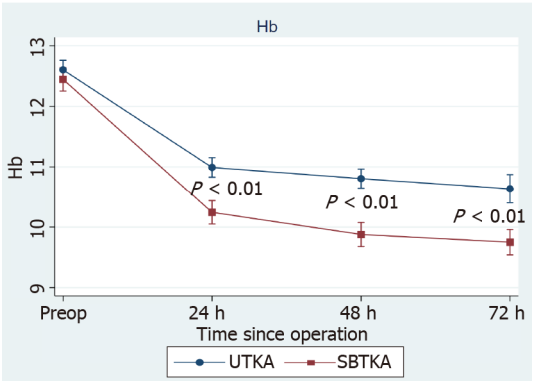


Figure 1 Serum hemoglobin levels preoperatively and at 24 h, 48 h and 72 h after the surgery. UTKA: Unilateral total knee arthroplasty; SBTKA: Safety of bilateral one-stage total knee arthroplasty.

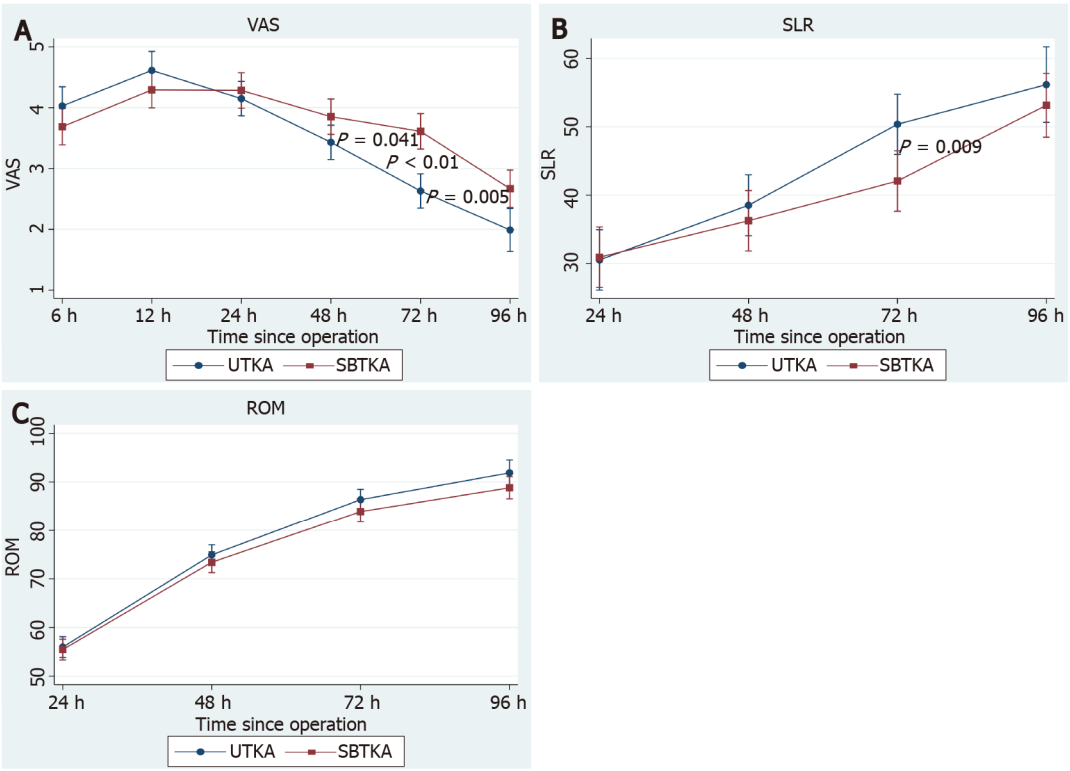


Figure 2 Index changes in different time periods after operation. A: Visual analog scale scores for pain intensity determined at 6 h, 12 h, 24 h, 48 h, and 72 h after the surgery; B: Straight leg raise assessed at 24 h, 48 h, and 72 h postoperatively; C: Range of knee motion measured at 24 h, 48 h, and 72 h after the surgery. VAS: Visual analogue scale; ROM: Range of knee motion; SLR: Straight leg raise; UTKA: Unilateral total knee arthroplasty; SBTKA: Safety of bilateral one-stage total knee arthroplasty.

Complications and readmission at 90 d

During the 90 d after the index surgery, there was one superficial infection, one cerebrovascular event, and two deep vein thromboses (DVT) in the UTKA group. For the BTKA group, one patient experienced peptic ulcer bleeding, one had DVT in the unilateral leg, and one had periprosthetic joint infection (PJI) which was successfully treated by two-stage revision TKA. Additionally, each group had one patient who required readmission due to severe pain at the surgical site.

DISCUSSION

Bilateral one-stage TKA potentially increases the rate of complications which are related to more soft tissue trauma, blood loss, postoperative pain, and cardiovascular

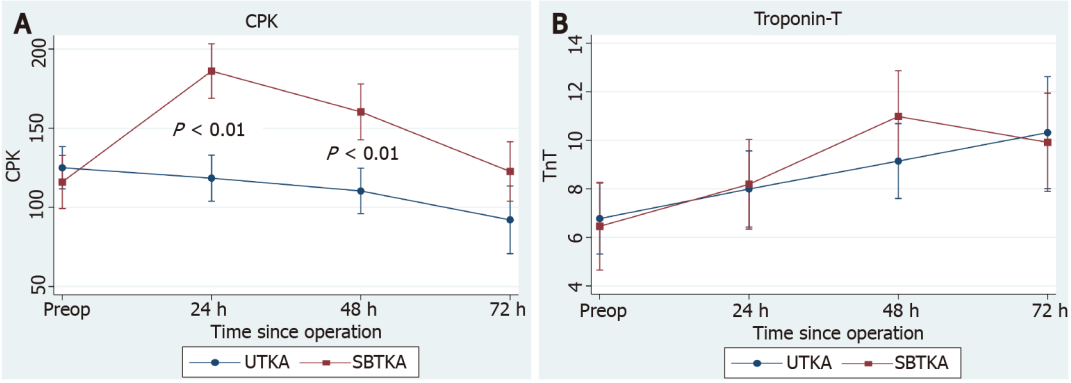


Figure 3 Changes in creatine phosphokinase and high-sensitivity Troponin-T before operation and at 24 h, 48 h, and 72 h after operation.
A: Creatine phosphokinase evaluated preoperatively and at 24 h, 48 h, and 72 h postoperatively; B: High-sensitivity Troponin-T preoperatively and at 24 h, 48 h, and 72 h postoperatively. CPK: Creatine phosphokinase; UTKA: Unilateral total knee arthroplasty; SBTKA: Safety of bilateral one-stage total knee arthroplasty.

adverse events, and therefore this is still a concerning issue for some patients and surgeons[8,9]. However, recent studies reported that BTKA in selected patients is as safe as the staged procedure, but proper patient screening, and perioperative care and monitoring to avoid complications and mortality are still controversial[23,24]. In the current study, BTKA was associated with significantly greater blood loss and higher allogeneic blood transfusion rates, as well as higher CPK levels, when compared to the UTKA group. The BTKA group tended to have higher hs-TnT levels at 48 h despite not reaching statistical significance. After 48 h, the BTKA group had a significantly higher VAS score than the UTKA group, and the SLR at 72 h after the BTKA was also worse than that after the UTKA. The LOS of the BTKA group was also significantly longer than that for the UTKA group. Nevertheless, the total morphine use, ROM, complications, and 90-d readmission rate were not different between the groups.

Generally, BTKA is known for its association with inevitably greater blood loss than UTKA. Advances in surgical techniques, use of TXA, and change in transfusion thresholds have substantially reduced postoperative transfusions following UTKA[3]. Recently, TXA is widely respected as an effective anti-fibrinolytic agent and has been demonstrated as having advantages when used in BTKA[25]. Although TXA is effective for reducing blood loss following BTKA, when it is applied either intravenously (IV) or intra-articularly (IA), the ideal regimen of TXA is still not well defined[13]. Arora *et al*[26] revealed no difference in average drop of Hb and blood transfusion rate between patients undergoing BTKA with IV-TXA or IA-TXA. Also, combined IA and IV TXA administration in BTKA did not show superior efficacy in blood loss reduction[27]. Therefore, the intraoperative IA-TXA use alone, in our study, should be sufficient to control blood loss, while avoiding potential complications related to systemic administration of TXA. However, our transfusion rate in BTKA is still quite high at 40.88%. Chalmers *et al*[28] retrospectively reviewed 475 patients who underwent BTKA and received double doses of TXA and contemporary blood management. They found that BTKA is still associated with a blood transfusion rate of approximately 1 in 5, and 50% of patients with a preoperative Hb < 12.5 required blood transfusion. Accordingly, we identified the preoperative Hb as a predictive factor for allogeneic transfusion in BTKA. Particularly, approximately 1 out of 3 patients in our study had preoperative anemia, and this finding may underline the opportunity for further improvement and for addressing this modifiable risk factor before BTKA. Delasotta *et al*[29] demonstrated that giving three preoperative doses of epoetin-α could significantly increase Hb levels and reduce blood transfusions in BTKA. Intravenous iron supplementation has also been reported for its efficacy in reducing the rate of transfusion in BTKA when combined with IA-TXA administration [30]. Other determinants including female gender, preoperative Hb level, operative time, and drain use have also been identified as risk factors for blood transfusion in BTKA[11,28]. In addition, soft tissue surface and intramedullary canal violation have been revealed as a possible significant source of bleeding[11,31-33]. Nevertheless, the efficacy of fibrin sealant applied to the bleeding soft tissue is unclear for blood loss reduction in BTKA[31], and also outcomes of emerging technologies such as computer-assisted or accelerometer-based navigation are still equivocal[13,34].

Significant pain after UTKA has been noted and this has been an issue frequently concerning patients as to whether the intensity of pain and disablement, during

convalescence from BTKA, is worse than that of UTKA. Shetty *et al*[20] reported that BTKA had significantly higher VAS pain scores than UTKA on the first postoperative day. However, the VAS, ROM, and SLR were equal in both groups at the time of discharge. Other researchers found a 1-point higher VAS in the BTKA group during day 1, with 20% more narcotic use for the first 48 h, and patients in the BTKA group lagged behind the UTKA group in ambulatory milestones by approximately 36 h[21]. In the present study, we found that the UTKA and BTKA group had comparable pain intensity, morphine consumption, and knee function during the first 24 h after the surgery by using the same multimodal pain management. The neuroaxial anesthesia, LIA that was induced by injecting with bupivacaine and ketorolac tromethamine, and opioid-sparing analgesia with a multidrug regimen may be an explanation of the effective pain control during the first 24 h after UTKA and BTKA. Despite that, patients in the BTKA gradually developed higher pain scores afterwards and had worse SLR at 72 h. Higher postoperative CPK levels might reflect the certainty of more muscle injury in the BTKA, and so may indicate the need for intensive pain control extended beyond 48 h after the surgery. Intravenous administration of non-steroidal anti-inflammatory drugs (NSAIDs) is commonly used because of their efficacy in controlling post-TKA pain and may be administered up to 72 h after the surgery. Recently, Parecoxib, which is a selective cyclooxygenase-2 (COX-2) inhibitor, has been demonstrated to be effective in the reduction of post-TKA pain with the additional advantage of having less platelet inhibition and is consequently associated with less blood loss when compared to conventional NSAIDs[2]. Furthermore, intravenous corticosteroid and acetaminophen were also revealed as useful adjuncts for mitigating pain after TKA[35,36].

The safety of BTKA is still debated. Chen *et al*[24] recently demonstrated that patients aged > 80 years with an ASA score ≥ 3 who received careful screening for cardiopulmonary disorder and contemporary perioperative management for BTKA, had significantly decreased incidences of major and minor complications. Gromov *et al*[37] reported a 0% incidence of mortality in 284 selected patients without cardiopulmonary compromise, and they also found that ASA score ≥ 3 was a risk factor for 90-d readmission and prolonged LOS whereas higher BMI was a weak predictive factor for readmission. Lindberg-Larsen *et al*[23] conducted a study to compare outcomes after simultaneous and staged bilateral TKA in propensity-scores matched patients from nine centers. Of 232 matched patients in each group, perioperative complications and re-operation rates were significantly higher after simultaneous bilateral TKA. However, there was no difference in the rate of readmission within 30 d as well as the mortality between groups. In the present study, the hs-TnT level, which is a biomarker for cardiac muscle injury, was not different between UTKA and BTKA when patients had an ASA score ≤ 3 and preoperative hs-TnT within normal values. Although there were 12 and 17 patients after the UTKA and BTKA who had hs-TnT > 14 ng/L, no patients in either group presented symptoms and signs of cardiovascular complications. Hence, serial testing of cardiac biomarkers may be indicated only when patients have suspected clinical presentation[38]. Additionally, Hb evaluation seems to be unnecessary for non-anemic patients who undergo UTKA, due to the very low risk for blood transfusion. However, we suspect that Hb testing at 48 h after BTKA may be appropriate as a reflection of ongoing blood loss that is possibly linked to cardiac stress because the hs-TnT was rising to a peak at 48 h after BTKA when the Hb level was dropping. For other complications, the risk of PJI and DVT was not different between BTKA and UTKA when similar prophylaxis ATB and anticoagulants were applied. Nevertheless, further investigation may be needed to develop well-defined guidelines for perioperative monitoring in patients undergoing BTKA to decrease potential morbidity and mortality.

Nonetheless, we realized some limitations of the present study. First, this investigation is retrospective with some limitations accorded by study design, even if the selection of BTKA or UTKA as patient preference might be better accommodated with our real-life practice. Second, both study groups comprised predominantly female patients. However, previous studies found that gender has no effect on blood loss and functional recovery following TKA[12,39]. Third, variation of thresholds or cut-off values for blood transfusion among individual institutions may result in a different transfused rate. Indeed, the incidence of patients with preoperative anemia in our study seems to be higher than previously reported[3] and thereby may be a reason for higher transfusion rates than those reported in other studies[4,28]. Lastly, our sample size might not be sufficient to assess the exact risk of cardiovascular events and thromboembolism after UTKA and BTKA.

CONCLUSION

Following similar perioperative management, the blood transfusion rate in BTKA is 4-fold that required in UTKA. Also, BTKA is associated with higher pain intensity at 48 h postoperatively and prolonged LOS when compared to UTKA. Hence, patients undergoing BTKA may require more extensive perioperative management for blood loss and pain, even if they have no higher risk of complications and 90-d readmission than those receiving UTKA.

ARTICLE HIGHLIGHTS

Research background

Bilateral one-stage total knee arthroplasty (BTKA) is a notable option for patients with bilateral end-stage knee arthropathy because of the potential advantages that include reduction in total hospitalization and rehabilitation time, as well as overall cost.

Research motivation

Despite previously acknowledged benefits, there is an issue frequently concerning patients as to whether the intensity of pain and disablement during convalescence from BTKA is worse than that following unilateral total knee arthroplasty (UTKA). Also, the risk of cardiovascular morbidity and other complications are subjects that lead some surgeons to refrain from BTKA. Thus, our objective was to identify what perioperative aspects of BTKA need to be improved and handled differently than for UTKA.

Research objectives

To compare the perioperative outcomes including perioperative blood loss (PBL), cardiac biomarkers, pain intensity, functional recovery, and complications between UTKA and BTKA by using an identical perioperative protocol.

Research methods

All patients who had undergone UTKA and BTKA for primary osteoarthritis that had been performed by a single surgeon with identical perioperative protocols between January 2016 and December 2019 were retrospectively reviewed. The exclusion criteria of this study included patients with an American Society of Anesthesiologists score > 3, known cardiopulmonary comorbidity or high-sensitivity Troponin-T (hs-TnT) > 14 ng/L, CKD stage ≥ 3 or significant renal impairment (serum creatinine > 1.5 mg/dL), prior knee surgery, and previous knee infection.

Research results

Patients who received BTKA had significantly higher PBL with a 4-fold greater transfusion rate. As well, the patients in the BTKA group had higher visual analogue scale scores at 48, 72, and 96 h after the surgery and a higher postoperative creatine phosphokinase level. Consequently, a longer length of hospital stays than those who had UTKA was required. However, there was no difference regarding the postoperative hs-TnT level and complications.

Research conclusions

Patients who undergo BTKA may require more extensive perioperative care for blood loss and pain than those patients who undergo UTKA.

Research perspectives

Future prospective studies may be required to develop a particular perioperative protocol in patients undergoing BTKA to decrease potential morbidity and mortality.

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REFERENCES

1 **Fransen BL**, Hoozemans MJM, Argelo KDS, Keijser LCM, Burger BJ. Fast-track total knee arthroplasty improved clinical and functional outcome in the first 7 days after surgery: a randomized controlled pilot study with 5-year follow-up. *Arch Orthop Trauma Surg* 2018; **138**: 1305-1316 [PMID: 30027483 DOI: 10.1007/s00402-018-3001-2]

2 **Laoruengthana A**, Rattanaprichavej P, Reosanguanwong K, Chinwatanawongwan B, Chompoonutprapa P, Pongpirul K. A randomized controlled trial comparing the efficacies of ketorolac and parecoxib for early pain management after total knee arthroplasty. *Knee* 2020; **27**: 1708-1714 [PMID: 33197808 DOI: 10.1016/j.knee.2020.10.005]

3 **Warren JA**, McLaughlin JP, Molloy RM, Higuera CA, Schaffer JL, Piuzzi NS. Blood Management in Total Knee Arthroplasty: A Nationwide Analysis from 2011 to 2018. *J Knee Surg* 2020 [PMID: 33241545 DOI: 10.1055/s-0040-1721414]

4 **Kim TK**, Chang CB, Kang YG, Seo ES, Lee JH, Yun JH, Lee SH. Clinical value of tranexamic acid in unilateral and simultaneous bilateral TKAs under a contemporary blood-saving protocol: a randomized controlled trial. *Knee Surg Sports Traumatol Arthrosc* 2014; **22**: 1870-1878 [PMID: 23592025 DOI: 10.1007/s00167-013-2492-1]

5 **Metcalfe AJ**, Andersson ML, Goodfellow R, Thorstensson CA. Is knee osteoarthritis a symmetrical disease? *BMC Musculoskelet Disord* 2012; **13**: 153 [PMID: 22917179 DOI: 10.1186/1471-2474-13-153]

6 **Walmsley P**, Murray A, Brenkel IJ. The practice of bilateral, simultaneous total knee replacement in Scotland over the last decade. Data from the Scottish Arthroplasty Project. *Knee* 2006; **13**: 102-105 [PMID: 16481171 DOI: 10.1016/j.knee.2006.01.003]

7 **Odum SM**, Troyer JL, Kelly MP, Dedini RD, Bozic KJ. A cost-utility analysis comparing the cost-effectiveness of simultaneous and staged bilateral total knee arthroplasty. *J Bone Joint Surg Am* 2013; **95**: 1441-1449 [PMID: 23965693 DOI: 10.2106/JBJS.L.00373]

8 **Memtsoudis SG**, Besculides MC, Reid S, Gaber-Baylis LK, González Della Valle A. Trends in bilateral total knee arthroplasties: 153,259 discharges between 1990 and 2004. *Clin Orthop Relat Res* 2009; **467**: 1568-1576 [PMID: 19002540 DOI: 10.1007/s11999-008-0610-z]

9 **Bohm ER**, Molodianovitsh K, Dragan A, Zhu N, Webster G, Masri B, Schemitsch E, Dunbar M. Outcomes of unilateral and bilateral total knee arthroplasty in 238,373 patients. *Acta Orthop* 2016; **87** Suppl 1: 24-30 [PMID: 27167849 DOI: 10.1080/17453674.2016.1181817]

10 **Soranoglou V**, Poultsides LA, Triantafyllopoulos GK, De Martino I, Memtsoudis SG, Sculco TP. Optimizing Intraoperative Blood Management for One-Stage Bilateral Total Knee Arthroplasty. *HSS J* 2018; **14**: 202-210 [PMID: 29983664 DOI: 10.1007/s11420-017-9590-4]

11 **Rattanaprichavej P**, Laoruengthana A, Rasamimogkol S, Varakornpipat P, Reosanguanwong K, Pongpirul K. The Effect of Prosthesis Design on Blood Loss in Simultaneous Bilateral Total Knee Arthroplasty: Closed-Box *vs* Open-Box Prosthesis. *Clin Orthop Surg* 2019; **11**: 409-415 [PMID: 31788163 DOI: 10.4055/cios.2019.11.4.409]

12 **Cao G**, Chen G, Huang Q, Huang Z, Alexander PG, Lin H, Xu H, Zhou Z, Pei F. The efficacy and safety of tranexamic acid for reducing blood loss following simultaneous bilateral total knee arthroplasty: a multicenter retrospective study. *BMC Musculoskelet Disord* 2019; **20**: 325 [PMID: 31299945 DOI: 10.1186/s12891-019-2692-z]

13 **Laoruengthana A**, Rattanaprichavej P, Tantimethanon T, Eiamjumras W, Teekaweerakit P, Pongpirul K. Usefulness of an accelerometer-based navigation system in bilateral one-stage total knee arthroplasty. *BMC Musculoskelet Disord* 2021; **22**: 164 [PMID: 33568132 DOI: 10.1186/s12891-021-04027-9]

14 **Friedman R**, Homering M, Holberg G, Berkowitz SD. Allogeneic blood transfusions and postoperative infections after total hip or knee arthroplasty. *J Bone Joint Surg Am* 2014; **96**: 272-278 [PMID: 24553882 DOI: 10.2106/JBJS.L.01268]

15 **Silliman CC**, Fung YL, Ball JB, Khan SY. Transfusion-related acute lung injury (TRALI): current concepts and misconceptions. *Blood Rev* 2009; **23**: 245-255 [PMID: 19699017 DOI: 10.1016/j.blre.2009.07.005]

16 **Lu N**, Misra D, Neogi T, Choi HK, Zhang Y. Total joint arthroplasty and the risk of myocardial infarction: a general population, propensity score-matched cohort study. *Arthritis Rheumatol* 2015; **67**: 2771-2779 [PMID: 26331443 DOI: 10.1002/art.39246]

17 **Lalmohamed A**, Vestergaard P, Klop C, Grove EL, de Boer A, Leufkens HG, van Staa TP, de Vries F. Timing of acute myocardial infarction in patients undergoing total hip or knee replacement: a nationwide cohort study. *Arch Intern Med* 2012; **172**: 1229-1235 [PMID: 22826107 DOI: 10.1001/archinternmed.2012.2713]

18 **Memtsoudis SG**, González Della Valle A, Besculides MC, Gaber L, Sculco TP. In-hospital complications and mortality of unilateral, bilateral, and revision TKA: based on an estimate of 4,159,661 discharges. *Clin Orthop Relat Res* 2008; **466**: 2617-2627 [PMID: 18704616 DOI: 10.1007/s11999-008-0402-5]

19 **Lakra A**, Murtaugh T, Shah RP, Cooper HJ, Geller JA. Early Postoperative Pain Predicts 2-Year

Functional Outcomes following Knee Arthroplasty. *J Knee Surg* 2020; **33**: 1132-1139 [PMID: 31269524 DOI: 10.1055/s-0039-1692650]

20 **Shetty GM**, Mullaji A, Bhayde S, Chandra Vadapalli R, Desai D. Simultaneous bilateral *vs* unilateral computer-assisted total knee arthroplasty: a prospective comparison of early postoperative pain and functional recovery. *Knee* 2010; **17**: 191-195 [PMID: 19786351 DOI: 10.1016/j.knee.2009.08.009]

21 **Powell RS**, Pulido P, Tuason MS, Colwell CW Jr, Ezzet KA. Bilateral *vs* unilateral total knee arthroplasty: a patient-based comparison of pain levels and recovery of ambulatory skills. *J Arthroplasty* 2006; **21**: 642-649 [PMID: 16877148 DOI: 10.1016/j.arth.2005.08.009]

22 **Nadler SB**, Hidalgo JH, Bloch T. Prediction of blood volume in normal human adults. *Surgery* 1962; **51**: 224-232 [PMID: 21936146]

23 **Lindberg-Larsen M**, Pitter FT, Husted H, Kehlet H, Jørgensen CC; Lundbeck Foundation Centre for Fast-Track Hip and Knee Replacement Collaborative Group. Simultaneous *vs* staged bilateral total knee arthroplasty: a propensity-matched case-control study from nine fast-track centres. *Arch Orthop Trauma Surg* 2019; **139**: 709-716 [PMID: 30840128 DOI: 10.1007/s00402-019-03157-z]

24 **Chen SH**, Chen JY, Wong TH, Buechel F Jr, Wu MH. Simultaneous Bilateral Total Knee Arthroplasty Becomes Safer after Institution of Optimal Perioperative Management: A Longitudinal Cohort Study. *J Knee Surg* 2021; **34**: 941-951 [PMID: 31952092 DOI: 10.1055/s-0039-1700979]

25 **Bagsby DT**, Samujh CA, Vissing JL, Empson JA, Pomeroy DL, Malkani AL. Tranexamic Acid Decreases Incidence of Blood Transfusion in Simultaneous Bilateral Total Knee Arthroplasty. *J Arthroplasty* 2015; **30**: 2106-2109 [PMID: 26235522 DOI: 10.1016/j.arth.2015.06.040]

26 **Arora M**, Singh S, Gupta V, Dongre A, Shetty V. Comparing the efficacy of intravenous or intra-articular tranexamic acid in reducing blood loss in simultaneous bilateral knee replacement surgery without the use of tourniquet. *Eur J Orthop Surg Traumatol* 2018; **28**: 1417-1420 [PMID: 29594528 DOI: 10.1007/s00590-018-2194-y]

27 **Meshram P**, Palanisamy JV, Seo JY, Lee JG, Kim TK. Combined Intravenous and Intraarticular Tranexamic Acid Does Not Offer Additional Benefit Compared with Intraarticular Use Alone in Bilateral TKA: A Randomized Controlled Trial. *Clin Orthop Relat Res* 2020; **478**: 45-54 [PMID: 31498264 DOI: 10.1097/CORR.0000000000000942]

28 **Chalmers BP**, Mishu M, Chiu YF, Cushner FD, Sculco PK, Boettner F, Westrich GH. Simultaneous Bilateral Primary Total Knee Arthroplasty With TXA and Restrictive Transfusion Protocols: Still a 1 in 5 Risk of Allogeneic Transfusion. *J Arthroplasty* 2021; **36**: 1318-1321 [PMID: 33190997 DOI: 10.1016/j.arth.2020.10.042]

29 **Delasotta LA**, Orozco F, Jafari SM, Blair JL, Ong A. Should We Use Preoperative Epoetin-α in the Mildly Anemic Patient Undergoing Simultaneous Total Knee Arthroplasty? *Open Orthop J* 2013; **7**: 47-50 [PMID: 23526659 DOI: 10.2174/1874325001307010047]

30 **Suh DW**, Han SB, Park JH, Cheong K, Kyung BS. Intravenous iron supplementation with intra-articular administration of tranexamic acid reduces the rate of allogeneic transfusions after simultaneous bilateral total knee arthroplasty. *Blood Transfus* 2017; **15**: 506-511 [PMID: 27483483 DOI: 10.2450/2016.0051-16]

31 **Skovgaard C**, Holm B, Troelsen A, Lunn TH, Gaarn-Larsen L, Kehlet H, Husted H. No effect of fibrin sealant on drain output or functional recovery following simultaneous bilateral total knee arthroplasty: a randomized, double-blind, placebo-controlled study. *Acta Orthop* 2013; **84**: 153-158 [PMID: 23350579 DOI: 10.3109/17453674.2013.769082]

32 **Aggarwal AK**, Shashikanth VS, Marwaha N. Platelet-rich plasma prevents blood loss and pain and enhances early functional outcome after total knee arthroplasty: a prospective randomised controlled study. *Int Orthop* 2014; **38**: 387-395 [PMID: 24114251 DOI: 10.1007/s00264-013-2136-6]

33 **Kuo SJ**, Wang FS, Wang CJ, Ko JY, Chen SH, Siu KK. Effects of Computer Navigation *vs* Conventional Total Knee Arthroplasty on Endothelial Damage Marker Levels: A Prospective Comparative Study. *PLoS One* 2015; **10**: e0126663 [PMID: 25955252 DOI: 10.1371/journal.pone.0126663]

34 **Jhurani A**, Agarwal P, Aswal M, Jain P, Malepati S, Sharma R. Computer navigation has no beneficial effect on blood loss and transfusion in sequential bilateral total knee Arthroplasty. *J Orthop Surg (Hong Kong)* 2019; **27**: 2309499019832440 [PMID: 30803319 DOI: 10.1177/2309499019832440]

35 **Liang L**, Cai Y, Li A, Ma C. The efficiency of intravenous acetaminophen for pain control following total knee and hip arthroplasty: A systematic review and meta-analysis. *Medicine (Baltimore)* 2017; **96**: e8586 [PMID: 29145272 DOI: 10.1097/MD.0000000000008586]

36 **Zhuo Y**, Yu R, Wu C, Huang Y, Ye J, Zhang Y. The role of perioperative intravenous low-dose dexamethasone in rapid recovery after total knee arthroplasty: a meta-analysis. *J Int Med Res* 2021; **49**: 300060521998220 [PMID: 33685282 DOI: 10.1177/0300060521998220]

37 **Gromov K**, Troelsen A, Stahl Otte K, Ørsnes T, Husted H. Morbidity and mortality after bilateral simultaneous total knee arthroplasty in a fast-track setting. *Acta Orthop* 2016; **87**: 286-290 [PMID: 26823094 DOI: 10.3109/17453674.2016.1141631]

38 **Reichlin T**, Cullen L, Parsonage WA, Greenslade J, Twerenbold R, Moehring B, Wildi K, Mueller S, Zellweger C, Mosimann T, Rubini Gimenez M, Rentsch K, Osswald S, Müller C. Two-hour algorithm for triage toward rule-out and rule-in of acute myocardial infarction using high-sensitivity cardiac troponin T. *Am J Med* 2015; **128**: 369-79.e4 [PMID: 25446294 DOI: 10.1016/j.amjmed.2014.10.032]

39 **Alattas SA**, Smith T, Bhatti M, Wilson-Nunn D, Donell S. Greater pre-operative anxiety, pain and

poorer function predict a worse outcome of a total knee arthroplasty. *Knee Surg Sports Traumatol Arthrosc* 2017; **25**: 3403-3410 [PMID: 27734110 DOI: 10.1007/s00167-016-4314-8]

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Retrospective Study

Epidemiology and incidence of paediatric orthopaedic trauma workload during the COVID-19 pandemic: A multicenter cohort study of 3171 patients

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Informed consent statement: This study was conducted in accordance with the ethical standards of the responsible committee and with the ethical principles of the 1975 Declaration of Helsinki.

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Abstract

BACKGROUND

Coronavirus disease 2019 (COVID-19) has a major influence on all parts of society.

AIM

To examine the consequences of the national lockdown and political initiatives during the first surge of the COVID-19 pandemic expressed by changes in incidences of musculoskeletal paediatric injuries.

METHODS

Study design was a retrospective multicenter cohort study. A 'pandemic' cohort was established from 16 March 2020 to 21 April 2020, where all institutions including day care and schools were closed. A 'pre-pandemic' cohort was established from the same period in 2019 for comparison. Included were all patients admitted at the emergency departments with paediatric musculoskeletal injuries (aged 0-15 years) identified by a relevant musculoskeletal ICD-10 diagnosis (DSxxx), concussions (DZ033D), or burns (DT2xx).

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RESULTS
The 'pre-pandemic' cohort consisted of 2101 patients, and the 'pandemic' cohort consisted of 1070 patients, indicating a decrease of paediatric musculoskeletal injuries of 51%. The incidence of paediatric injury in the 'pre-pandemic' cohort was 10460/100000/year. In the 'pandemic' cohort, the incidence was 5344/100000/year.

CONCLUSION
A resource re-allocation to help serve the COVID-19 patients might be possible without reducing the level of care for injury-related paediatric patients.

Key Words: COVID-19; SARS-CoV-2; Paediatric trauma; Paediatric emergency; Paediatric fracture

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Core Tip: Coronavirus disease 2019 (COVID-19) has had a significant impact on all parts of society and medical services. Here we compare the epidemiology of paediatric trauma at major university hospitals and rural hospitals before and during COVID-19 lockdown in 3171 emergency department contacts.

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INTRODUCTION

From the first reported case of coronavirus disease 2019 (COVID-19) in December 2019 in Wuhan, China, the severe acute respiratory syndrome coronavirus 2 virus spread around the globe at a rapid pace. The World Health Organization declared it a global pandemic on 11 March 2020.

A national lockdown was issued on 11 March 2020 in Denmark, including prolonged closure of schools and the cessation of sporting activities, social activities, and other close-contact situations. The aetiology of paediatric injury is coherent to physical and sporting activities; hence a reduction in paediatric injuries and consultations at the emergency department was to be expected[1-4].

Several epidemiological studies before the COVID-19 pandemic have shown incidence rates of paediatric fracture of 1800-2000/100000/year[3-7]. However, a general overview of musculoskeletal injury treated at emergency departments is poorly reported[8]. To the authors' knowledge, only one former study examined musculoskeletal injuries seen at the emergency department using a population-based incidence rate and reported an incidence of 6300/100000/year[9].

Although current literature investigates the frequencies of paediatric injuries during the COVID-19 pandemic, no overview of the pandemic's consequences of the pandemic on population-based incidences of paediatric injuries and related trauma mechanisms is available[10-15].

The present study aimed to examine the consequences of the national lockdown from 16 March till 21 April 2020 and political initiatives during the first surge of the COVID-19 pandemic expressed by changes in incidences of musculoskeletal paediatric injuries at the emergency departments across multiple hospitals. Furthermore, the aim was to examine changes in the mode of injury and related trauma mechanisms observed.

MATERIALS AND METHODS

The study design was a retrospective cohort study investigating the incidence of paediatric musculoskeletal injuries in patients aged 0–15 years, before and during the national COVID-19 pandemic lockdown in the northern and middle parts of Denmark.

A 'pandemic' cohort was established from 16 March 2020 to 21 April 2020, where all institutions including day care and schools were closed. A 'pre-pandemic' cohort was established from the same period in 2019 for comparison.

Included were five regional hospitals and two university hospitals. The hospitals serve rural and suburban areas with a population of 198138 citizens between 0–15 years of age during the study period in 2019, representing the 'pre-pandemic cohort'. The 'pandemic' cohort includes a population of 197516 citizens during the study period.

In Denmark, a unique possibility of performing population-based studies is present since Danish law requires all patient contact with hospitals and clinics to be registered in the Danish National Patient Register (DNPR)[16]. All Danish residents receive a civil registration number that is registered in the Civil Registration System. Hospital identification, date and time of hospitalization, and municipality are registered. Therefore, a complete registry of all health-related issues, both individual and population-based, is obtainable.

Based on the DNPR, the 'pandemic' and the 'pre-pandemic' cohorts were established for comparison.

Included were all patients admitted at the emergency departments with paediatric musculoskeletal injuries identified by a relevant musculoskeletal ICD-10 diagnosis (DSxxx), concussions (DZ033D), or burns (DT2xx).

Clinical information about diagnosis, age, gender, date, and mode of injury was obtained. Manual chart and X-ray review of 50% of the medical charts (n = 1546) was performed for validating the register data.

This study was conducted in accordance with the ethical standards of the responsible committee and with the ethical principles of the 1975 Declaration of Helsinki. The Danish Data Protection Agency approved the study. The reporting of the study complies with the Strengthening the Reporting of Observational Studies in Epidemiology Statement[17].

RESULTS

In total, 3171 paediatric injuries leading to an emergency department visit at one of the five hospitals were included in the study. The 'pre-pandemic' cohort consisted of 2101 patients, and the 'pandemic' cohort consisted of 1070 patients, indicating a decrease of paediatric musculoskeletal injuries in patients aged 0–15 years of 51% during the COVID-19 pandemic.

Primary outcome

The overall incidence of paediatric injury in the 'pre-pandemic' cohort was 10460/100000/year. In the 'pandemic' cohort, the overall incidence was 5344/100000/year, indicating a twofold decrease in paediatric emergency patients during the COVID19 pandemic.

Secondary outcomes

Gender-divided and age-specific incidence rates are depicted in Figure 1A and B. The incidence rates showed a similar bimodal trend for both genders. Before the pandemic the incidence rates were significantly higher in the age group from 9-15 years compared with the incidence during lockdown of the society (Figure 1A).

No differences were found in the proportion of the various diagnoses, with fractures being the most common in both cohorts. A higher proportion of injuries were found on school days in the 'pre-pandemic' cohort than the 'pandemic' cohort (Supplementary Table 1).

A proportional increase in bicycle (51%), skateboard, scooter, rollerblade (36 %), and trampoline injuries (98%) between the 'pre-pandemic' and the 'pandemic' cohorts was observed. A marked decrease in sports-related injuries and collisions with objects was observed in the 'pandemic period' compared to the pre-pandemic period. (Supplementary Table 2) In the age group 9–15 years of age (Figure 2A and B), a similar distribution was observed, indicating a shift in sporting activities to home-based activities.

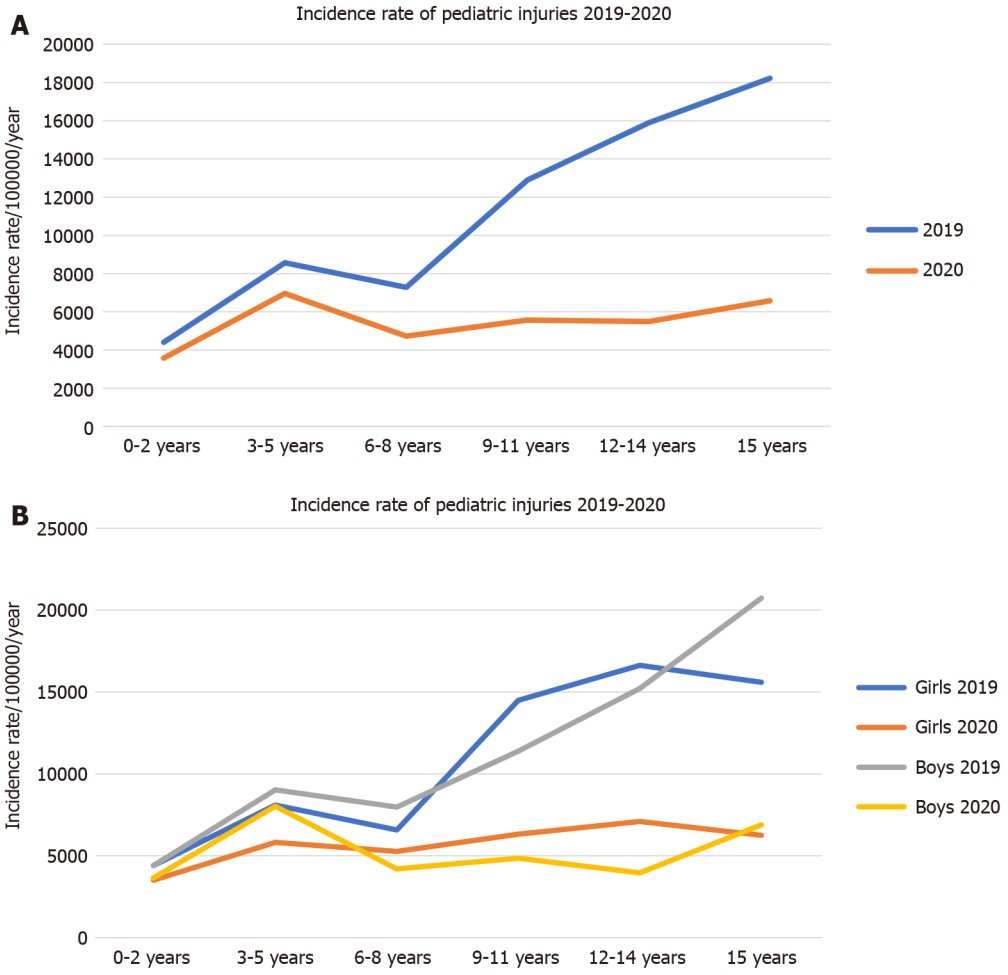


Figure 1 Incidence rates of pediatric injuries 2019 and 2020. A: Divided by year; B: divided by gender.

The manual review of 50% of all contacts showed a high level of accuracy of both diagnosis (< 99%) and trauma mechanism (< 99%), indicating that register data are of very high quality.

DISCUSSION

The overall incidence rate for paediatric injury decreased two-fold during the COVID-19 national lockdown from 16 March 2020 – 21 April 2020 compared with the same weeks in 2019. The overall incidence was 10460/100000/year in 2019 and 5344/100000/year during the lockdown in 2020.

Results from the present study are supported by Sheridan *et al*[18], examining the effect of COVID-19 regulations using the incidence rate for paediatric trauma admissions in Ireland. A reduction of paediatric admissions from 0.146 admissions/person-year to 0.139 admissions/person-year in the pandemic period was reported. Sheridan *et al*[18] reported on relatively small numbers, with only 28 paediatric patients included in the pandemic group. Most other studies evaluating the effect of the COVID-19 pandemic did not report on the incidence, making a further comparison of results from the present study difficult.

Several studies examined the effect of the COVID-19 Lockdown with regards to the prevalence and found a decrease between 33%-68% of paediatric fractures[10-13]. These results align with the present study reporting a decrease of paediatric musculoskeletal injuries in patients aged 0–15 years of 51% during the COVID-19 pandemic.

The age-specific incidence rates showed a bimodal distribution. Children below nine years of age showed similar distributions between the 'pandemic' and the 'pre-pandemic' cohorts. In contrast, children above nine years of age in the 'pandemic' cohort showed a marked decrease in the incidence rates during the COVID-19 Lockdown. This pattern was similar for both genders.

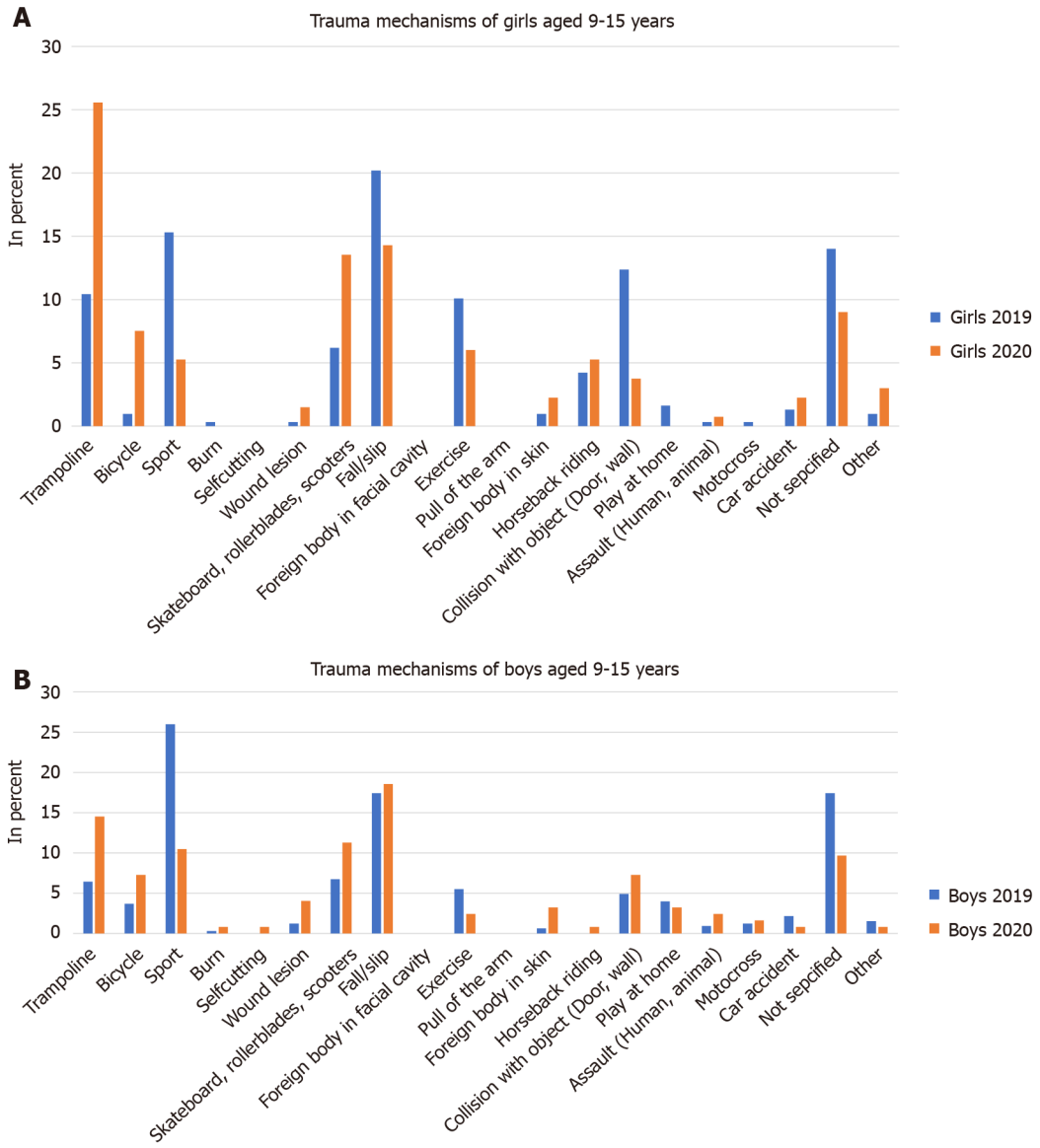


Figure 2 Trauma mechanisms of girls and boys aged 9-15 years. A: Girls; B: Boys.

These findings are corroborated by Bram *et al*[10] and Keays *et al*[14], reporting that the prevalence of paediatric fracture and injury-related emergency department visits decreased the most in children above 12 years of age during the COVID-19 pandemic. The observed decrease in the incidence in the adolescent populations during the COVID-19 pandemic may be due to a reduction in sporting activities and social activities compared to the younger children.

The distribution of paediatric musculoskeletal injuries in patients aged 0–15 years was almost comparable between the 'pre-pandemic' and the 'pandemic' cohorts. The most common diagnose was fracture (2019: 34.0%, 2020: 33.9%) followed by contusion (2019: 19.2%, 2020: 16.2%) and distortion (2019: 18.5%, 2020: 14.3%).

Several studies report change in the distribution of trauma mechanisms during the COVID-19 pandemic[10-12,14]. The present study showed that a higher proportion of injuries in the 'pandemic' cohort was caused by trampoline, bicycling, skateboarding, scooters, and rollerblades compared to the 'pre-pandemic' cohort. Furthermore, a lower proportion of injuries was due to other sporting activities and exercise. Keays *et al*[14] reported a proportional rise in bicycling injuries in the pandemic period, but no change in injuries caused by trampoline, skateboarding, and scootering. Bram *et al*[10] reported an increase in the proportion of injuries during the COVID-19 pandemic occurring at home or on bicycles and a decrease in those related to sports. Other studies reported a reduction of injuries related to sports during the pandemic period [11-12]. These observed small differences between studies may be explained by differences in lockdown procedures in the different countries, influencing the closure

of schools, cessation of sporting activities, social activities, and other close contact situations. Furthermore, regardless of the COVID-19 pandemic, differences in trauma mechanisms between different countries are well-known.

At present, the health care system worldwide is strained due to a large number of patients with COVID-19. A simultaneous reduction in paediatric injuries is observed and well reported. A resource re-allocation to help serve the COVID-19 patients might be possible without reducing the level of care for injury-related paediatric patients. This knowledge could benefit the health care system in a future pandemic. Conversely, when reopening schools and returning to sports, an increase in emergency department visits by paediatric patients is to be expected.

The significant drop in incidence of pediatric injuries during the COVID-19 pandemic may indicates that safety priority issues and the development of prevention strategies may be needed. Guardians may help children to adhere to safety recommendations at play grounds, such as a maximum of one child per trampoline. However, most pediatric musculoskeletal injuries are minor and not complicated. The impact of COVID-19 on children and young people's mental health and well-being has been reported to weigh heavily[19]. The disruption to routines, education, recreation, as well as concern for family income and health, is leaving many young people with significant consequences due to the lock down. Furthermore, the lock down has been reported to significant decrease the level of children's physical activity[20]. Regular physical activity is well-known to improve cardiorespiratory fitness, build strong bones and muscles, control weight, reduce symptoms of depression, and reduce the risk of developing serious health conditions[21].

The present study has several limitations. A limitation may be the use of register data from the DNPR. However, reporting to the DNPR is required by law in Denmark, and allocation of cost to the health providers is partly based on the register. The DNPR is reported with an overall high quality of data, and the positive predictive value of orthopaedic diseases is reported to be 89%–91%[22]. Furthermore, a manual review of 50% of the data for validation showed high data completeness. Another potential limitation is a difference in coding between the different hospitals. However, variation among the various hospitals is of less importance as a difference in coding practice between the 'pandemic' and 'pre-pandemic' cohorts is expected to be comparable. Importantly, the manual check of 50% of the data did not reveal any signs of increase in non-accidental injuries, *i.e.* physical child abuse. However, health care workers should be aware that there may be an increased incidence during the pandemic[23].

CONCLUSION

The overall incidence rate for paediatric injury in the 'pre-pandemic' cohort was 10460/100000 persons/year. The overall incidence rate decreased to 5344/100000 persons/year in the 'pandemic' cohort. The primary decrease in incidence between the 'pandemic' and 'pre-pandemic' cohorts was observed in the adolescents.

ARTICLE HIGHLIGHTS

Research background

Coronavirus disease 2019 (COVID-19) had a major influence on all parts of society. During the total lockdown of the Danish society, we noticed a substantial change in the pediatric and adolescent trauma.

Research motivation

We aimed to quantify the change in workload and estimate the incidence rates.

Research objectives

The aim was to examine the consequences of the national lockdown and political initiatives during the first surge of the COVID-19 pandemic expressed by changes in incidences of musculoskeletal paediatric injuries.

Research methods

We compared the epidemiology of pediatric and adolescent trauma during the lockdown period of approximately one month with the same period of the previous

year.

Research results

The 'pre-pandemic' cohort consisted of 2101 patients, and the 'pandemic' cohort consisted of 1070 patients, indicating a decrease of paediatric musculoskeletal injuries of 51%. The incidence of paediatric injury in the 'pre-pandemic' cohort was 10460/100000/year. In the 'pandemic' cohort, the incidence was 5344/100000/year.

Research conclusions

A resource re-allocation to help serve the COVID-19 patients might be possible without reducing the level of care for injury-related paediatric patients.

Research perspectives

If new lockdowns are enforced, hospitals and emergency and orthopedic departments in particular may be able to redistribute workforce without compromising patient care.

REFERENCES

1 **Joeris A**, Lutz N, Wicki B, Slongo T, Audigé L. An epidemiological evaluation of pediatric long bone fractures - a retrospective cohort study of 2716 patients from two Swiss tertiary pediatric hospitals. *BMC Pediatr* 2014; **14**: 314 [PMID: 25528249 DOI: 10.1186/s12887-014-0314-3]

2 **Schalamon J**, Dampf S, Singer G, Ainoedhofer H, Petnehazy T, Hoellwarth ME, Saxena AK. Evaluation of fractures in children and adolescents in a Level I Trauma Center in Austria. *J Trauma* 2011; **71**: E19-E25 [PMID: 21045737 DOI: 10.1097/TA.0b013e3181f8a903]

3 **Hedström EM**, Svensson O, Bergström U, Michno P. Epidemiology of fractures in children and adolescents. *Acta Orthop* 2010; **81**: 148-153 [PMID: 20175744 DOI: 10.3109/17453671003628780]

4 **Randsborg PH**, Gulbrandsen P, Saltytė Benth J, Sivertsen EA, Hammer OL, Fuglesang HF, Arøen A. Fractures in children: epidemiology and activity-specific fracture rates. *J Bone Joint Surg Am* 2013; **95**: e42 [PMID: 23553305 DOI: 10.2106/JBJS.L.00369]

5 **Ramaesh R**, Clement ND, Rennie L, Court-Brown C, Gaston MS. Social deprivation as a risk factor for fractures in childhood. *Bone Joint J* 2015; **97-B**: 240-245 [PMID: 25628289 DOI: 10.1302/0301-620X.97B2.34057]

6 **Kosuge D**, Barry M. Changing trends in the management of children's fractures. *Bone Joint J* 2015; **97-B**: 442-448 [PMID: 25820880 DOI: 10.1302/0301-620X.97B4.34723]

7 **Cooper C**, Dennison EM, Leufkens HG, Bishop N, van Staa TP. Epidemiology of childhood fractures in Britain: a study using the general practice research database. *J Bone Miner Res* 2004; **19**: 1976-1981 [PMID: 15537440 DOI: 10.1359/JBMR.040902]

8 **de Inocencio J**, Carro MÁ, Flores M, Carpio C, Mesa S, Marín M. Epidemiology of musculoskeletal pain in a pediatric emergency department. *Rheumatol Int* 2016; **36**: 83-89 [PMID: 26259985 DOI: 10.1007/s00296-015-3335-9]

9 **Gunz AC**, Canizares M, Mackay C, Badley EM. Magnitude of impact and healthcare use for musculoskeletal disorders in the paediatric: a population-based study. *BMC Musculoskelet Disord* 2012; **13**: 98 [PMID: 22691633 DOI: 10.1186/1471-2474-13-98]

10 **Bram JT**, Johnson MA, Magee LC, Mehta NN, Fazal FZ, Baldwin KD, Riley J, Shah AS. Where Have All the Fractures Gone? *J Pediatr Orthop* 2020; **40**: 373-379 [PMID: 32433260 DOI: 10.1097/BPO.0000000000001600]

11 **Sugand K**, Park C, Morgan C, Dyke R, Aframian A, Hulme A, Evans S, Sarraf KM, Baker C, Bennett-Brown K, Simon H, Bray E, Li L, Lee N, Pakroo N, Rahman K, Harrison A. Impact of the COVID-19 pandemic on paediatric orthopaedic trauma workload in central London: a multi-centre longitudinal observational study over the "golden weeks". *Acta Orthop* 2020; **91**: 633-638 [PMID: 32835573 DOI: 10.1080/17453674.2020.1807092]

12 **Baxter I**, Hancock G, Clark M, Hampton M, Fishlock A, Widnall J, Flowers M, Evans O. Paediatric orthopaedics in lockdown: A study on the effect of the SARS-Cov-2 pandemic on acute paediatric orthopaedics and trauma. *Bone Jt Open* 2020; **1**: 424-430 [PMID: 33215134 DOI: 10.1302/2633-1462.17.BJO-2020-0086.R1]

13 **Hashmi PM**, Zahid M, Ali A, Naqi H, Pidani AS, Hashmi AP, Noordin S. Change in the spectrum of orthopedic trauma: Effects of COVID-19 pandemic in a developing nation during the upsurge; a cross-sectional study. *Ann Med Surg (Lond)* 2020; **60**: 504-508 [PMID: 33235717 DOI: 10.1016/j.amsu.2020.11.044]

14 **Keays G**, Friedman D, Gagnon I. Injuries in the time of COVID-19. *Health Promot Chronic Dis Prev Can* 2020; **40**: 336-341 [PMID: 32924925 DOI: 10.24095/hpcdp.40.11/12.02]

15 **Memeo A**, Priano D, Caldarini C, Trezza P, Laquidara M, Montanari L, Randelli P. How the pandemic spread of COVID-19 affected children's traumatology in Italy: changes of numbers, anatomical locations, and severity. *Minerva Pediatr* 2020 [PMID: 33016683 DOI: 10.23736/S0026-4946.20.05910-1]

16 **Lynge E**, Sandegaard JL, Rebolj M. The Danish National Patient Register. *Scand J Public Health*

2011; **39**: 30-33 [PMID: 21775347 DOI: 10.1177/1403494811401482]

17 **von Elm E**, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP; STROBE Initiative. Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. *BMJ* 2007; **335**: 806-808 [PMID: 17947786 DOI: 10.1136/bmj.39335.541782.AD]

18 **Sheridan GA**, Nagle M, Russell S, Varghese S, O'Loughlin PF, Boran S, Taylor C, Harty JA. Pediatric Trauma and the COVID-19 Pandemic: A 12-Year Comparison in a Level-1 Trauma Center. *HSS J* 2020; 1-5 [PMID: 33041725 DOI: 10.1007/s11420-020-09807-y]

19 **Patrick SW**, Henkhaus LE, Zickafoose JS, Lovell K, Halvorson A, Loch S, Letterie M, Davis MM. Well-being of Parents and Children During the COVID-19 Pandemic: A National Survey. *Pediatrics* 2020; **146** [PMID: 32709738 DOI: 10.1542/peds.2020-016824]

20 **Xiang M**, Zhang Z, Kuwahara K. Impact of COVID-19 pandemic on children and adolescents' lifestyle behavior larger than expected. *Prog Cardiovasc Dis* 2020; **63**: 531-532 [PMID: 32360513 DOI: 10.1016/j.pcad.2020.04.013]

21 **Sallis JF**, Simons-Morton BG, Stone EJ, Corbin CB, Epstein LH, Faucette N, Iannotti RJ, Killen JD, Klesges RC, Petray CK. Determinants of physical activity and interventions in youth. *Med Sci Sports Exerc* 1992; **24**: S248-S257 [PMID: 1625550]

22 **Andersen JS**, Olivarius Nde F, Krasnik A. The Danish National Health Service Register. *Scand J Public Health* 2011; **39**: 34-37 [PMID: 21775348 DOI: 10.1177/1403494810394718]

23 **Martinkevich P**, Larsen LL, Græsholt-Knudsen T, Hesthaven G, Hellfritzsch MB, Petersen KK, Møller-Madsen B, Rölfing JD. Physical child abuse demands increased awareness during health and socioeconomic crises like COVID-19. *Acta Orthop* 2020; **91**: 527-533 [PMID: 32573297 DOI: 10.1080/17453674.2020.1782012]

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ORIGINAL ARTICLE

Clinical Trials Study

Can bedside needle arthroscopy of the ankle be an accurate option for intra-articular delivery of injectable agents?

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Clinical trial registration statement: Prior to the first inclusion, the study was registered at ToetsingOnline.nl with reference NL71185.018.19.

Informed consent statement: All patients provided written consent for their participation in the study prior to enrollment.

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Abstract

BACKGROUND

Bedside needle arthroscopy of the ankle under local anesthesia has been proposed for intra-articular delivery of injectable agents. Accuracy and tolerability of this approach in the clinical setting–including patients with end-stage ankle pathology and/or a history of prior surgery–is not known.

AIM

To assess clinical accuracy and tolerability of bedside needle arthroscopy as a delivery system for injectable agents into the tibiotalar joint.

METHODS

This was a prospective study that included adult patients who were scheduled for an injection with hyaluronic acid to the tibiotalar joint. In our center, these injections are used as a last resort prior to extensive surgery. The primary outcome was injection accuracy, which was defined as injecting through the arthroscopic cannula with intra-articular positioning confirmed by a clear arthroscopic view of the joint space. Secondary outcome measures included a patient-reported numeric rating scale (NRS, 0-10) of pain during the procedure and willingness of patients to return for the same procedure. NRS of ankle pain at rest

Conflict-of-interest statement: Dr. Kennedy reports consultancy fees from Arthrex, outside the submitted work.

Data sharing statement: The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

CONSORT 2010 statement: The authors have read the CONSORT 2010 Statement, and the manuscript was prepared and revised according to the CONSORT 2010 Statement.

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Grade C (Good): 0
Grade D (Fair): 0
Grade E (Poor): 0

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and during walking was collected at baseline and at 2-wk follow-up. Complications were monitored from inclusion up to a 2-wk control visit.

RESULTS
We performed 24 inspection-injections. Eleven (46%) participants were male, and mean age was 46.8 ± 14.5 years. Osteoarthritis was the indication for injection in 20 (83%) cases, of which 8 (33%) patients suffered from osteoarthritis Kellgren-Lawrence grade IV, and 10 (42%) patients from Kellgren-Lawrence grade III. An osteochondral defect was the indication for injection in 4 (17%) cases. A history of ankle surgery was present in 14 (58%) participants and a history of multiple ankle surgeries in 11 (46%) participants. It was possible to confirm accuracy in 21 (88%) procedures. The 3 (12%) participants where needle arthroscopy did not reach a clear view of the joint space all suffered from Kellgren-Lawrence grade IV osteoarthritis. Pain during the procedure was reported with a median of 1 [interquartile ranges (IQR): 0–2]. Willingness to return was 100%. Pain in rest decreased from a median NRS of 4 (IQR: 2–7) at baseline to a median of 3 (IQR: 1–5) at follow-up ($P < 0.01$). Pain during walking decreased from a median NRS of 8 (IQR: 6–9) to a median of 7 (IQR: 4–8) ($P < 0.01$). Infections or other complications were not encountered.

CONCLUSION
Clinical accuracy and tolerability of bedside needle arthroscopy of the ankle as a delivery system for injectable agents are excellent. Accuracy was 100% in patients without total ventral joint obliteration.

Key Words: Ankle arthroscopy; NanoScope; Needle arthroscopy; Injections; Proof of concept; Patient experience

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Core Tip: Needle arthroscopy is rapidly attracting the interest of the orthopedic field, as recent technical innovation has increased image quality and improved surgical handling. Bedside needle arthroscopy under local anesthesia has been proposed as a possible use. In this study, we performed needle arthroscopic inspection-injections of the tibiotalar joint in the procedure room and using only local anesthesia. We found high accuracy of these guided injections, and excellent patient tolerability of the procedure. The results of this study may form the groundwork for further expansion of indications that merit needle arthroscopy of the ankle under local anesthesia, including operative procedures.

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INTRODUCTION

Intra-articular injections play an important role in orthopedic surgery[1], and innovative injectable agents promise to further increase their importance as minimally invasive treatment[2,3]. Yet, accuracy of articular injections is often limited, which lowers the chance of a positive treatment effect[4]. In the tibiotalar joint, accuracy of injections ranges between a mere 67% and 77% when guided by palpation[4]. The effect of ultrasound guidance is highly variable, and often does not improve injection accuracy at all[5]. Inaccurate injections may be especially unacceptable in case of expensive biologic augments, slowly releasing delivery systems, or for injections that have a detrimental effect on soft tissue.

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Needle arthroscopy was first introduced in the 1990s, yet was never adopted as standard modality due to low image quality and inconvenient machinery. However, recent innovation has led to a substantial increase in image quality and has reduced the size of supportive devices to the likes of a tablet computer[6]. In a cadaveric study, this improved version of needle arthroscopy provided easy and safe access to the ankle[6].

Based on cadaveric experience, it has been suggested to use needle arthroscopy under local anesthesia as a means to inspect the ankle joint and to simultaneously deliver an injectable in a minimally invasive yet highly accurate manner[6]. Yet, feasibility of this approach has not been tested in a patient setting so far. The cadaveric setting may differ from clinical practice, as for example patient discomfort, time pressure, scar tissue and joint stiffness may hamper a successful procedure. Therefore, the aim of this study was to assess the accuracy and patient tolerability of bedside needle arthroscopy to deliver injectable agents to the ankle joint in a clinical setting, which may include participants with advanced pathology and a history of previous ankle surgery. We hypothesized that even in such a difficult patient group, we would be able to deliver injections with high accuracy, and that procedures would be well tolerated by patients.

MATERIALS AND METHODS

A prospective pilot study of consecutive patients was conducted in our academic hospital between December 2019 and December 2020. The study was approved by our institutional ethical review board with reference 2019_203 and conducted in agreement with the 1964 Helsinki Declaration and its later amendments. All patients provided written consent for their participation. The study was monitored by our institution's monitoring board. Prior to the first inclusion, the study was registered at ToetsingOnline.nl with reference NL71185.018.19.

Patients

All patients between 18 years and 80 years of age that were planned for an injection with hyaluronic acid in the tibiotalar joint were potentially eligible for inclusion. In our center, these injections are used as a last resort of conservative management. Patients were excluded from the study who had concern for active local or systemic infection, known history of bleeding disorders, were unable to communicate informed consent, or were logistically unavailable at the time of planned needle arthroscopy.

Arthroscopic procedure

We used a 1.9-millimeter arthroscope (NanoScope, Arthrex, Naples, FL, United States) for procedures. Procedures were performed by two fellowship trained foot and ankle surgeons with extensive experience in ankle arthroscopy (SAS and GK) in an outpatient treatment room, suitable for small interventions. The patient was positioned in supine semi-sitting position on a standard operating chair. The ankle was disinfected with a chlorohexidine solution and standard surgical draping was applied. A standard anteromedial portal was utilized and located by palpation. The portal was locally anesthetized with lidocaine 2%, injected along the entire tract including the joint capsule. Once the anesthetic had taken effect, a 2-mm stab incision of the skin was made at the desired portal location. A 2.3-mm diameter cannula was positioned intra-articular, with help of a blunt obturator and slight non-invasive distraction. The obturator was removed and the arthroscope was inserted. Syringes with sterile saline could be connected to the cannula for improving visibility. If needed, the cannula was repositioned (with a maximum of three attempts) until a clear view of the intra-capsular joint space was obtained. No power tools were used and the joint capsule was not resected or debrided. Once the intra-articular view was confirmed, any injected saline was aspirated, after which the pre-packed syringe with hyaluronic acid was connected to the cannula, and the hyaluronic acid was delivered to the joint space through the cannula. The cannula was then flushed with 1cc of saline in order to deliver all the remaining hyaluronic acid. The arthroscope and cannula were removed and the 2-mm portal was closed with sterile wound closure strips. Standard post-treatment care–including 48 h of partial weightbearing–was advised. In the cases where a clear view of the joint space could not be obtained after three attempts, we converted to an intra-articular injection through a standard 21G (green) needle.

Outcome measures

The primary outcome measure was injection accuracy. An accurate injection was defined as injecting through the arthroscopic cannula with intra-articular positioning confirmed by a clear arthroscopic view of the intra-capsular joint space. As secondary outcome measures we collected intra-operative complications, need for conversion to a conventional injection, reason for conversion and procedure time (from patient entrance to patient departure from the procedure room). In addition, patient-reported outcome measures (PROMS) were collected at discharge and during a control visit 2 wk after the procedure. PROMS included numeric rating scales (NRS, 0–10) of pain at rest and during walking as experienced in the 2 wk prior to answering the questionnaire (*i.e.* in the 2 wk prior to either the intervention or the follow-up visit). At discharge, PROMS additionally included NRS of pain during the procedure, and a dichotomous promotor score, asking patients whether they would undergo the procedure again if needed. Complications (infection, neurovascular damage, pain or other complaints prompting contact with a physician) were monitored from inclusion up to study end upon completing the control visit. Follow-up and collection of PROMS was not performed by the orthopedic surgeon but by an independent PhD-fellow (TS) instead.

Analysis

We determined to include 24 patients which, applying the sample size calculation for pilot studies by Viechtbauer *et al*[7] (2015), gives 95% certainty to detect problems that arise with a probability of at least 12%. Descriptive statistics of primary and secondary outcome parameters were provided. Each variable was tested for normality with the Shapiro-Wilk test. Medians and interquartile ranges (IQR) were calculated in case of non-normally distributed data. Otherwise, means and standard deviations (SD) were provided. The Wilcoxon signed-rank test was used to compare preoperative and postoperative outcome scores. In case of a statistically significant difference in PROMS between discharge and follow-up, the number of patients that met the threshold for a minimal clinically important difference (MCID) was calculated[8]. For the NRS of pain, this MCID was set a minimal difference of three points on the 0–10 scale[9]. Data was collected using CASTOR EDC[10]. Analyses were conducted using Stata 12 (StataCorp, College Station, TX, United States).

RESULTS

Twenty-four patients were screened for eligibility and included in the study and received a needle arthroscopic injection. Eleven (46%) patients were male (Table 1). Mean age was 46.8 ± 14.5 years (range: 20–71 years). Twenty (83%) injections were performed as a temporizing biotribologic therapeutic for advanced osteoarthritis with near obliteration of the joint space. Kellgren-Lawrence grading was grade IV in 8 (33%) patients and grade III in 10 (42%) patients. Four (17%) injections were performed as a treatment modality for a talar osteochondral defect. Fourteen (58%) patients had a history of prior surgery–either open or arthroscopic–to the applicable ankle, and 11 (46%) had a history of multiple prior surgeries.

Procedure

It was possible to perform an injection with arthroscopic confirmation of accuracy in 21 (88%) patients (Table 2 and Figure 1). Conversion to a conventional injection needle was needed in 3 (12%) patients, all on account of technical inability to achieve intra-articular positioning of the needle arthroscope within three attempts. All failures occurred in patients suffering from end-stage osteoarthritis with Kellgren-Lawrence grade IV. Two of the failed cases occurred in a patient with a history of prior ankle surgery, of which 1 patient had had multiple prior surgeries. There were no intra-operative complications. Mean intra-OR time was 17 ± 5 min. Sterile wound closure strips were sufficient for wound closure in all cases and sutures were never required.

Follow-up

All (100%) patients completed the follow-up visit and questionnaire (Table 2). The follow-up visit was performed at a median of 14 d (IQR: 14–16) after the intervention. Due to restrictions in the first wave of the COVID-19 pandemic, 2 follow-up visits were conducted by phone. All other visits were conducted in person. No infectious or neurovascular complications were found. No patient contacted a physician in the

Table 1 Patient demographics at the time of the intervention (mean ± SD)

Parameter	Value
Age in yr (range)	46.8 ± 14.5 (20–71)
Sex	
Male, *n* (%)	11 (46%)
Female, *n* (%)	13 (54%)
Indication for injection	
Osteoarthritis, *n* (%)	20 (83%)
Kellgren-Lawrence Grade I (*n*)	0
Kellgren-Lawrence Grade II (*n*)	2
Kellgren-Lawrence Grade III (*n*)	10
Kellgren-Lawrence Grade IV (*n*)	8
(Osteo)chondral defect, *n* (%)	4 (17%)
Prior ankle surgery	
None, *n* (%)	10 (42%)
Any, *n* (%)	14 (58%)
Multiple, *n* (%)	11 (46%)

Table 2 Procedure and follow-up (mean ± SD)

Parameter	Value
Accurate injections, *n* (%)	21 (88%)
Accuracy by indication	
Kellgren-Lawrence Grade I [*n* accurate (% of subset)]	NA
Kellgren-Lawrence Grade II [*n* accurate (% of subset)]	2 (100%)
Kellgren-Lawrence Grade III [*n* accurate (% of subset)]	10 (100%)
Kellgren-Lawrence Grade IV [*n* accurate (% of subset)]	5 (62.5%)
(Osteo)chondral defect [*n* accurate (% of subset)]	4 (100%)
Accuracy by prior ankle surgery	
None [*n* accurate (% of subset)]	9 (90.0%)
Any [*n* accurate (% of subset)]	12 (85.7%)
Multiple [*n* accurate (% of subset)]	10 (90.1%)
Procedure time (min)	17 ± 5
Completed follow-up, *n* (%)	24 (100%)
Follow-up time (median days, IQR)	14 (IQR, 14–16)
Complications, *n* (%)	0 (0%)

NA: Not applicable; IQR: Interquartile ranges.

period between intervention and follow-up.

PROMS

The median NRS of pain during the arthroscopic procedure was 1 (IQR: 0–2) (Table 3). All (100%) patients were willing to return for another bedside needle arthroscopic injection if needed. Median NRS of pain in rest decreased from 4 (IQR: 2–7) in the 2 wk prior to the intervention, to 3 (IQR: 1–5) in the 2 wk prior to the follow-up visit (P < 0.01). In 6 patients, pain in rest decreased with at least 3 points (MCID) on the NRS

Table 3 Patient reported outcome

Activity	Intervention	Follow-up	Difference (*P* value)
Willing to return, *n* (%)	24 (100%)	NA	NA
NRS of pain (0–10)			
During procedure (median, IQR)	1 (0–2)	NA	NA
In rest (past 2 wk) (median, IQR)	4 (2–7)	3 (1–5)	< 0.01
Walking (past 2 wk) (median, IQR)	8 (6–9)	7 (4–8)	< 0.01

NA: Not applicable; NRS: Numeric rating scale; IQR: Interquartile ranges.

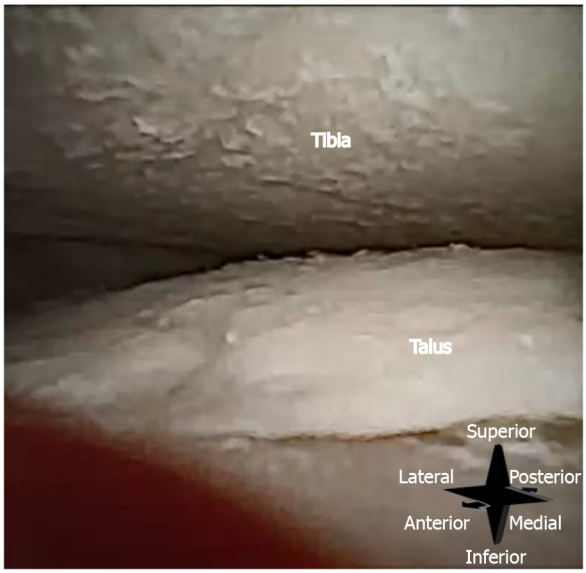


Figure 1 Intra-articular image of a right tibiotalar joint, taken with the 0° arthroscope inserted through the anteromedial portal. Substantial chondral wear can be seen on talus and tibia, with uncovered bone clearly visible.

scale. Pain during walking decreased from a median NRS of 8 (IQR: 6–9) to a median NRS of 7 (IQR: 4–8) ($P < 0.01$). In 7 patients, pain during walking decreased with at least 3 points (MCID) on the NRS scale.

DISCUSSION

Can bedside needle arthroscopy of the ankle be an accurate option for intra-articular delivery of injectable agents? Yes, but be aware that a difficult patient population with extensive scar tissue due to prior surgeries and severe joint space narrowing due to advanced osteoarthritic joint obliteration will not provide a 100% success rate. The main finding of this study was that 2-mm diameter needle arthroscopy of the ankle was able to achieve clear intra-articular positioning in 88% (21 out of 24) of cases. It was then possible to deliver hyaluronic acid in the joint space with absolute certainty in these 21 cases. The success rate was 100% in patients with less advanced osteoarthritis (Kellgren-Lawrence grade III) or lower and the success rate was 90% in patients without a history prior ankle surgery. Therefore, patient selection and counseling is important before considering inspection-injection through needle arthroscopy of the ankle. Procedures were well tolerated and there were no complications in this cohort, including a follow-up visit at 14 d.

A recent literature review by Hall[4] (2013) found that in a clinical setting, ankle injections are delivered with an accuracy ranging between 67% and 77%, if guided by palpation[4]. Although not statistically tested, the 88% accuracy this study found for needle arthroscopic injections is higher. This could be explained by the visual confirmation of the position of the arthroscope. In case of extra-articular positioning,

the arthroscope was repositioned until correctly located in the joint. Repositioning of the needle in conventional procedures still could result in an extra-articular injection.

Intra-articular positioning of the arthroscope and cannula was not achieved in 3 patients (12%). All 3 patients suffered from Kellgren-Lawrence grade IV osteoarthritis, with complete obliteration of the ventral joint space. The joint space between their talus and tibia was less than 2 mm–too narrow for a safe introduction of the arthroscope, despite the use of non-invasive distraction. In addition, osteophytes narrowed the angle in which it was possible to navigate the arthroscope. As the needle arthroscope that was used has a 0° direction of view, changing the direction of view cannot be achieved by rotating the camera, as it can with for example conventional 30° arthroscopes. Instead, the direction of view can only be changed by tilting the entire arthroscope. Osteophytes limit the possibility for this tilting of the arthroscope, which may hamper visualization of the joint. Furthermore, the flexibility of the small diameter needle scope prevents using the barrel of the scope as a lever to gain access to the joint. We therefore recommend to carefully examine the patient's radiological studies, which may constitute simple X-ray's–in case of severe osteoarthritis, before considering needle arthroscopic injections. The amount of joint distraction that can be achieved with non-invasive distraction in patients with end-stage joint destruction under local anesthesia is a subject for further study.

Fourteen patients (58%) had a history of prior surgery. We noted difficulty with arthroscope introduction in 5 of them. In conventional arthroscopy, partial synovectomy is performed to obtain a clear view in these patients[11]. Needle arthroscopic synovectomy has been performed in the knee[12], and cadaveric studies have shown the feasibility of operative needle arthroscopy in the ankle[6]. In the knee, synovectomy under local anesthesia is well tolerated by most patients[13]. For the ankle, clinical feasibility of needle arthroscopic (partial) synovectomy under local anesthesia has yet to be established. Nevertheless, whether it is acceptable to perform a synovectomy may depend on the indication for needle arthroscopy, and may be excessively invasive for a simple injection. Extensive prior surgery may hence be a contraindication for bedside needle arthroscopy in these cases.

Procedures were well tolerated by patients and there were no complications up to a 2-wk follow-up. Although this is the first study to evaluate bedside needle arthroscopy of the ankle, needle arthroscopic procedures have been performed under local anesthesia in the knee and shoulder, and were well tolerated by patients in these joints as well[14]. That the procedure is well tolerated is further substantiated by 100% of participants being willing to return for another needle arthroscopic injection if needed. A recent cadaveric study showed that needle arthroscopy of the ankle does not pose a risk of damaging major neurovascular structures when using the anteromedial portal [6], which substantiates that our current study did not find any signs of neurovascular complications at 2-wk follow-up. Although this study cannot exclude that complications with a low prevalence (such as infection) may arise, a review of 1419 patients that underwent diagnostic needle arthroscopy of the knee or shoulder found no major complications[15], providing further assurance of the safety of the procedure.

This study is limited by its design as a pilot study. It does not offer a comparison with conventional injections, nor with conventional arthroscopy or more invasive forms of anesthesia. It should rather be interpreted as a proof of feasibility of bedside needle arthroscopy of the ankle and delivery of injectable agents under local anesthesia. Arthroscopy is difficult to perform in the ankle, especially with a 0° direction of view. In that sense, it is important to note that the study may have been underpowered to detect problems or events such as rare complications that occur with a frequency of less than 12%.

The basic procedure as reviewed in this study may be further augmented in order to increase benefit to patient and physician. A recent systematic review showed that compared to MRI, needle arthroscopy has higher accuracy in diagnosing knee osteoarthritis, anterior cruciate ligament insufficiency, meniscal tears, and osteochondral defects[14]. Needle arthroscopic diagnosis and delivery of an injectable treatment would be a beneficial combination. In general, the results of this study may form the groundwork for further expansion of indications that merit needle arthroscopy of the ankle under local anesthesia, including operative procedures.

CONCLUSION

In conclusion, in this clinical pilot study, needle arthroscopy of the ankle showed to be a procedure that is well tolerated by patients under local anesthesia. It is able to

confirm intra-articular delivery of injectable agents with high accuracy. Accuracy may approach 100% by excluding patients with total ventral joint obliteration and patients with a history of extensive prior ankle surgery.

ARTICLE HIGHLIGHTS

Research background

Needle arthroscopy is rapidly attracting the interest of the orthopedic field, as recent technical innovation has increased image quality and improved surgical handling. Bedside needle arthroscopy of the ankle under local anesthesia has been proposed for intra-articular delivery of injectable agents.

Research motivation

Clinical accuracy and tolerability of this approach is not known.

Research objectives

To assess clinical accuracy and tolerability of bedside needle arthroscopy as a delivery system for injectable agents into the tibiotalar joint.

Research methods

A prospective clinical study was conducted. Adult patients who were scheduled for an injection to the ankle joint were included. The primary outcome was accuracy of bedside needle arthroscopic injections under local anesthesia. Additionally, a patient reported numeric rating scale (NRS, 0-10) of pain during the procedure and willingness of patients to return for a similar procedure if needed were recorded. Occurrence of complications was monitored from inclusion up to a 2-wk control visit.

Research results

Of 24 inspection-injections were performed. Osteoarthritis was the indication for injection in 20 (83%) cases–of which 8 cases (33%) were Kellgren-Lawrence grade IV, and 10 cases (42%) were Kellgren-Lawrence grade III. The indication was an osteochondral defect in 4 (17%) participants. Fourteen (58%) participants had a history of ankle surgery and 11 (46%) patients a history of multiple ankle surgeries. It was possible to confirm accuracy in 21 (88%) procedures. The 3 (12%) participants where this confirmation failed all suffered from Kellgren-Lawrence grade IV osteoarthritis. Participants reported a NRS of pain during the procedure with a median of 1 (interquartile ranges: 0–2), and a willingness to return of 100%. We did not encounter infections or other complications.

Research conclusions

Clinical accuracy and tolerability of bedside needle arthroscopy of the ankle as a delivery system for injectable agents are excellent. Accuracy was 100% in patients without total ventral joint obliteration.

Research perspectives

The results of this study may form the groundwork for further expansion of indications that merit needle arthroscopy of the ankle under local anesthesia, including operative procedures.

REFERENCES

1 **Vereniging FMS-NO**. Conservatieve behandeling van artrose in heup of knie. 2018. [cited 10 May 2021]. Available from: https://richtlijnendatabase.nl/richtlijn/artrose_in_heup_of_knie/startpagina_-_heup-_of_knieartrose.html

2 **Repetto I**, Biti B, Cerruti P, Trentini R, Felli L. Conservative Treatment of Ankle Osteoarthritis: Can Platelet-Rich Plasma Effectively Postpone Surgery? *J Foot Ankle Surg* 2017; **56**: 362-365 [PMID: 28231968 DOI: 10.1053/j.jfas.2016.11.015]

3 **Sandker MJ**, Duque LF, Redout EM, Chan A, Que I, Löwik CWGM, Klijnstra EC, Kops N, Steendam R, van Weeren R, Hennink WE, Weinans H. Degradation, intra-articular retention and biocompatibility of monospheres composed of [PDLLA-PEG-PDLLA]-b-PLLA multi-block copolymers. *Acta Biomater* 2017; **48**: 401-414 [PMID: 27816621 DOI: 10.1016/j.actbio.2016.11.003]

4 **Hall MM**. The accuracy and efficacy of palpation *vs* image-guided peripheral injections in sports medicine. *Curr Sports Med Rep* 2013; **12**: 296-303 [PMID: 24030302 DOI: 10.1097/01.CSMR.0000434103.32478.36]

5 **Gilliland CA**, Salazar LD, Borchers JR. Ultrasound *vs* anatomic guidance for intra-articular and periarticular injection: a systematic review. *Phys Sportsmed* 2011; **39**: 121-131 [PMID: 22030948 DOI: 10.3810/psm.2011.09.1928]

6 **Stornebrink T**, Altink JN, Appelt D, Wijdicks CA, Stufkens SAS, Kerkhoffs GMMJ. Two-millimetre diameter operative arthroscopy of the ankle is safe and effective. *Knee Surg Sports Traumatol Arthrosc* 2020; **28**: 3080-3086 [PMID: 32065244 DOI: 10.1007/s00167-020-05889-7]

7 **Viechtbauer W**, Smits L, Kotz D, Budé L, Spigt M, Serroyen J, Crutzen R. A simple formula for the calculation of sample size in pilot studies. *J Clin Epidemiol* 2015; **68**: 1375-1379 [PMID: 26146089 DOI: 10.1016/j.jclinepi.2015.04.014]

8 **Harris JD**, Brand JC, Cote MP, Faucett SC, Dhawan A. Research Pearls: The Significance of Statistics and Perils of Pooling. Part 1: Clinical Versus Statistical Significance. *Arthroscopy* 2017; **33**: 1102-1112 [PMID: 28454999 DOI: 10.1016/j.arthro.2017.01.053]

9 **Lee JS**, Hobden E, Stiell IG, Wells GA. Clinically important change in the visual analog scale after adequate pain control. *Acad Emerg Med* 2003; **10**: 1128-1130 [PMID: 14525749 DOI: 10.1111/j.1553-2712.2003.tb00586.x]

10 **Castor EDC**. Castor Electronic Data Capture. 2019. [cited 10 May 2021]. Available from: https://link.springer.com/referenceworkentry/10.1007/978-0-387-39940-9_2541

11 **Guhl JF**. New concepts (distraction) in ankle arthroscopy. *Arthroscopy* 1988; **4**: 160-167 [PMID: 3166653 DOI: 10.1016/s0749-8063(88)80020-3]

12 **Lavender C**, Patel T, Adil S, Blickenstaff B, Oliashirazi A. Incisionless Knee Synovectomy and Biopsy With Needle Arthroscope and Autologous Tissue Collector. *Arthrosc Tech* 2020; **9**: e1259-e1262 [PMID: 33024664 DOI: 10.1016/j.eats.2020.05.002]

13 **Takahashi T**, Tanaka M, Ikeuchi M, Sadahiro T, Tani T. Pain in arthroscopic knee surgery under local anesthesia. *Acta Orthop Scand* 2004; **75**: 580-583 [PMID: 15513490 DOI: 10.1080/00016470410001457]

14 **Zhang K**, Crum RJ, Samuelsson K, Cadet E, Ayeni OR, de Sa D. In-Office Needle Arthroscopy: A Systematic Review of Indications and Clinical Utility. *Arthroscopy* 2019; **35**: 2709-2721 [PMID: 31416656 DOI: 10.1016/j.arthro.2019.03.045]

15 **McMillan S**, Chhabra A, Hassebrock JD, Ford E, Amin NH. Risks and Complications Associated With Intra-articular Arthroscopy of the Knee and Shoulder in an Office Setting. *Orthop J Sports Med* 2019; **7**: 2325967119869846 [PMID: 31632993 DOI: 10.1177/2325967119869846]

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ORIGINAL ARTICLE

Observational Study

High-resolution, three-dimensional magnetic resonance imaging axial load dynamic study improves diagnostics of the lumbar spine in clinical practice

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Institutional review board statement: The study was conducted according to the guidelines of the Declaration of Helsinki and approved by the Institutional Bioethical Review Board at Medical University of Warsaw (AKBE/100/13—obtained on December 10, 2013).

Informed consent statement: Informed consent was obtained from all subjects involved in the study.

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Abstract

BACKGROUND

The response to axial physiological pressure due to load transfer to the lumbar spine structures is among the various back pain mechanisms. Understanding the spine adaptation to cumulative compressive forces can influence the choice of personalized treatment strategies.

AIM

To analyze the impact of axial load on the spinal canal's size, intervertebral foramina, ligamenta flava and lumbosacral alignment.

METHODS

We assessed 90 patients using three-dimensional isotropic magnetic resonance imaging acquisition in a supine position with or without applying an axial compression load. Anatomical structures were measured in the lumbosacral region from L1 to S1 in lying and axially-loaded magnetic resonance images. A paired *t* test at $\alpha = 0.05$ was used to calculate the observed differences.

RESULTS

After axial loading, the dural sac area decreased significantly, by 5.2% on average (4.1%, 6.2%, $P < 0.001$). The intervertebral foramina decreased by 3.4% (2.7%, 4.1%, $P < 0.001$), except for L5-S1. Ligamenta flava increased by 3.8% (2.5%, 5.2%,

Data sharing statement: The dataset analyzed are not publicly available but are available from the corresponding author upon reasonable request.

STROBE statement: The guidelines of the STROBE Statement-checklist of items have been adopted.

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Grade B (Very good): B, B
Grade C (Good): 0
Grade D (Fair): 0
Grade E (Poor): 0

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$P < 0.001$), and the lumbosacral angle increased.

CONCLUSION
Axial load exacerbates the narrowing of the spinal canal and intervertebral foramina from L1-L2 to L4-L5. Cumulative compressive forces thicken ligamenta flava and exaggerate lumbar lordosis.

Key Words: Lumbar spine; Low back pain; Musculoskeletal disorder; Diagnosis; Axial loading; Magnetic resonance imaging; Spine biomechanics

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Core Tip: In this study, a statistically proven correlation was made between the axial loading and lumbar spinal stenosis, thickening of the ligamenta flava, narrowing of the intervertebral foramina from L1-L2 to L4-L5 and lumbar lordosis exaggeration. A novel aspect of this study was a simultaneous comparison of the dural sac size, ligamenta flava thickness, foraminal dimensions and lumbar sagittal alignment between axial loaded and recumbent three-dimensional high-resolution magnetic resonance imaging in an extensive group of lower back pain patients. This was done to conduct a detailed evaluation for better spinal surgery decision-making and spinal injections.

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INTRODUCTION

Lower back pain (LBP) remains a major worldwide public health problem that has increased substantially over several decades[1]. The problem of LBP affects epidemiology[2-5], health economics[6,7] and social aspects (disability, inability to work, limited daily activity)[8]. LBP is a common problem affecting most adults at some point during their lifetime[3,4,9]. More than half of the population may experience a pain relapse within a year, and 8% of people will have chronic pain[10]. In their systematic review, Meucci *et al*[11] revealed that chronic LBP prevalence was 4.2% in individuals aged between 24 and 39 years. The LBP prevalence equals 19.6% between 20 and 59 years of age and increases linearly from the third decade of life until 60. Chronic LBP is a significant contributor to the global disability burden[12]. Disability besides pain due to LBP is reported frequently and continues to be the leading cause of years lived with disability[13].

The vertically-oriented human spine acts as a dynamic and static column connecting the skeletal system. Substantial forces act on the longitudinal axis of the spine in the human's upright position. Spinal compression is traditionally considered the primary biomechanical mechanism associated with work-related LBP[14,15]. Human erect position can lead to increased axial compression in the lumbar spine and several side effects, including back pain. The lifting of objects raises the axial compression in the lumbar spine and increases LBP risk[16-19].

The classic works of Nachemson *et al*[20,21] from the early 1960s showed that the highest degree of intradiscal pressure in the lumbar spine occurs in standing and sitting positions, mainly when a person leans forward. The intradiscal pressure is lower when an individual is in the lying position than in the sitting and standing positions[22]. These observations were confirmed by Rohlmann *et al*[23,24] using wireless measurement. Schonstrom *et al*[25] showed that the intradiscal force difference measured at rest and axial loading acting on the spine reaches 500 N on human spine segments. The difference in intradiscal pressure observed in the spine segments is comparable to the values found in volunteers subjected to different loads and different body positions[21].

Correct, quick and precise determination of the underlying causes of back pain symptoms is crucial for many patients. Imaging for LBP is considered appropriate when clinical suspicion of severe pathology or surgery addresses a specific pathology [26,27]. Imaging may also be used to diagnose chronic LBP; however, particular indicators for appropriate imaging use are less well defined, with pain lasting longer than 6 weeks being an indicator for imaging in some guidelines but not in others[26]. Axial compression imaging may improve the diagnostics in clinical management of LBP and improve appropriate treatment decisions[28-30].

Even though the highest spinal loading occurs in the upright and sitting positions, a typical magnetic resonance imaging (MRI) examination is performed with the patient lying supine when no loads are exerted on the spine. As a result, the lying position of the examined patient poses a limitation on magnetic resonance tomography. An attempt at overcoming MRI limitations caused by the patient being in a lying position led to the introduction in clinical practice of an examination performed in the supine position with axial loading, simulating physiological loading. The load distribution among lumbar spinal structures, in general, is still an unanswered question and should be the focus of biomechanical testing. Previous studies showed that axial-loaded MRI could simulate the standing position and reveal additional valuable pathological findings not detected by conventional recumbent MRI[31,32]. Compressive loads on the vertebral discs are not the only ones occurring in the spine; load indicators other than disc compression are at least equally relevant, so attention should be paid to them. Few studies simultaneously investigated several anatomical structures in the lumbar spine using upright, open and low-field MRI[33] or axial loaded MRI[16]. However, these studies did not use dynamic three-dimensional (3D) high-resolution images and failed to measure the ligamentum flavum area, foraminal area and lumbar lordosis.

Moreover, previous studies were performed in a young, small group of asymptomatic volunteers[33], or simultaneous measurements were not correlated between the sets of variables[16]. No study has simultaneously compared dural sac size, ligamenta flava thickness, foraminal dimensions and lumbar sagittal alignment between axial-loaded and recumbent MRI in a large group of LBP patients to identify dynamic changes and associations between morphology and demography. Therefore, this study's objective was to evaluate and measure the changes presented by MRI of selected lumbar spine structures upon axial-loading compared with recumbent MRI and correlate them to morphologic changes and demographic data. Additionally, the study aimed to assess the value and potential use of axial loading in lumbar spine examinations. The detailed evaluation seems crucial for spinal surgery decision-making. The spinal injections or transforaminal[34,35] or interlaminar spinal endoscopy[36,37] can be used to relieve symptoms due to the intervertebral foramen narrowing or spinal canal stenosis caused by the thickening of the ligamentum flavum.

MATERIALS AND METHODS

We enrolled 90 patients diagnosed at the Magnetic Resonance Laboratory with LBP inclusion criteria as an indication. Exclusion criteria included significant spinal injury, osteoporosis, previous spine surgery, lack of good patient cooperation, a body mass below 40 kg and a lack of written consent from the patient. General contraindications for MRI examinations (*e.g.*, pacemakers, ferromagnetic implants, foreign bodies and claustrophobia) were also considered. A total of 46 (51%) men and 44 (49%) women were included in the study with an age and body mass index (mean ± standard deviation) of 49 ± 16 years and 26.0 ± 4.2 kg/m^2, respectively. The study was conducted according to the Declaration of Helsinki guidelines and approved by the Institutional Bioethical Review Board at Medical University of Warsaw (AK-BE/100/13 — obtained on December 10, 2013). Informed consent was obtained from all subjects involved in the study.

Lumbar spine MRI examination protocol without and after axial loading

The examination was performed using a 1.5 T MRI (Ingenia; Philips Healthcare, Eindhoven, The Netherlands). After performing recumbent MRI examinations, axial loading was applied using an external commercially available nonmagnetic DynaWell (DynaWell L-Spine; DynaWell Diagnostics, Las Vegas, NV, United States) compression device. The phase without axial loading was identical to a standard lumbar spine examination. Both the axial-loaded and unloaded MRI examinations were performed with a 3D T2-weighted Volume ISotropic Turbo spin-echo

Acquisition sequence (Table 1). According to previous disc pressure measurements[21] the chosen load was equal to 40%-50% of the patient's body weight, with equal load distribution on both legs (20%-25% of patient body mass per leg). The patient was subjected to this load in the lying position for at least 5 min before the examination.

Image analysis

Images were assessed on a dedicated workstation (IntelliSpace Portal; Philips Healthcare, Eindhoven, The Netherlands) at a single center. Based on recumbent and axial-loaded MRIs, the lumbosacral angles between the superior vertebral endplate of L1 and superior vertebral endplate of S1 were measured, enabling the observation of spine adaptations at a whole lumbar level (Figure 1). The dural sac cross-sectional area was calculated for each level from L1-L2 to L5-S1 for examination with and without axial loading. Measurements were performed by encircling the dural sac transverse area, capturing T2-weighted MRI at the same levels for phases without and with axial loading with the plane precisely positioned parallel to the midplane of the intervertebral disc (Figure 1). The vertebral foramina sagittal cross-section area was determined for each level, from L1-L2 to L5-S1, on both sides. Measurements were performed by encircling the vertebral foramina area in sagittal cross-sections on the same levels for the phase with and without axial loading (Figure 1). The cross-sectional area of the ligamentum flavum was determined for levels from L1-L2 to L5-S1 on both sides. The measurements were captured by encircling the area of the ligamentum flavum in cross-sections at facet joint levels with and without axial loading (Figure 1). The degree of disc and facet joint degeneration, the degree of spinal canal stenosis, the degree of foraminal stenosis and the degree of disc herniation were assessed on recumbent images on all disc levels according to the classifications of Pfirrmann *et al* [38], Weishaupt *et al*[39], Schizas *et al*[40], Lee *et al*[41] and the Michigan State University classification of lumbar disc herniation[42].

Statistical analysis

The assessment criterion used was the percentage difference of measured parameters with a 95% confidence interval (CI). A paired *t* test was applied at an $\alpha = 0.05$ level to verify the hypothesis regarding the statistical significance of changes observed. The Pearson correlation test was used to explore the mutual relations of the spine structural parameters. A paired *t* test was applied to determine the relationship between age and sex for each measured parameter. The statistical methods of this study were reviewed by Wojciech Michalski from the Department of Mathematical Oncology, Maria Skłodowska-Curie National Research Institute of Oncology, Warsaw, Poland. The IBM SPSS Statistics (IBM Corp., Armonk, NY, United States) version 20 for Linux OS was used for statistical analysis.

RESULTS

Ligamentum flavum

Upon axial loading, the area of the ligamenta flava was statistically significantly increased on average by 3.8% (95%CI: 2.5%, 5.2%, $P < 0.001$; Table 2).

Dural sac

Upon axial loading, the dural sac area significantly decreased on average by 5.2% (95%CI: 4.1%, 6.2%, $P < 0.001$; Table 3).

Intervertebral foramen

The area of the intervertebral foramina decreased on average by 3.4% (95%CI: 2.7%, 4.1%, $P < 0.001$) except for the L5-S1 section of the spine, which increased by 2.0% on average (95%CI: 0.5%, 3.9%, $P = 0.045$; Table 4).

Lumbosacral angle

The lumbosacral angles increased, on average, by 7.7% (95%CI: 5.7%, 9.6%, $P < 0.001$; Table 5).

Correlation analysis

A statistically significant correlation between exaggerated lumbosacral angle and age was found (Pearson correlation coefficient (r) = -0.253, $P < 0.05$). The negative correlation indicated that axial force on increasing lumbar lordosis in older patients is

Table 1 Three-dimensional Volume ISotropic Turbo spin-echo Acquisition magnetic resonance pulse parameters

Parameters	3D VISTA T2
Repetition time/Echo time (ms)	2000/90
Number of signal averaging	1
Field of View (mm)	300 × 200 × 75
Acquisition matrix	300 × 196
Acquisition voxel (mm)	1 × 1 × 0.5
Reconstruction matrix	640
Reconstruction voxel (mm)	0.47 × 0.47 × 0.5
Turbo factor	61
Sensitivity encoding factor	1.3
Scan time	06:46

3D: Three-dimensional; VISTA: Volume ISotropic Turbo spin-echo Acquisition.

Table 2 Cross-sectional area of the ligamentum flavum on the same levels with and without axial loading on both sides

Ligamenta flava(right + left) / section of the spine	Mean difference of area between unloaded and axial loading (%)	95%CI		*P* value
		Lower	Upper	
L1-L2	4.1	1.8	6.4	0.001
L2-L3	4.8	2.0	7.6	0.001
L3-L4	4.0	0.5	4.7	0.024
L4-L5	2.1	-0.5	6.3	0.116
L5-S1	4.1	2.5	5.2	< 0.001
All from L1-L2 to L5-S1	3.8	2.5	5.2	< 0.001

Negative value corresponds to a decrease. CI: Confidence interval.

less than in younger patients. Neither the area of the intervertebral foramina nor the area of the dural sac was correlated with age. Additionally, a percentage difference of the sagittal cross-section area of vertebral foramina, the cross-section area of the dural sac and ligamenta flava and the percentage difference of the lumbosacral angles did not significantly correlate with sex. The relationship testing between spine structure parameters did not deliver any significant association between any variables.

Degenerative changes

Degenerative changes of the lumbar spine are listed in Table 6.

DISCUSSION

Compression devices can be applied to high-field units. Therefore, high-resolution, 3D MRI might be obtained. This advantage of recumbent axially loaded MRI creates possibilities in determining the precise measurements and making an accurate diagnosis. The upright MRI would be a theoretically ideal diagnostic tool to simulate the spinal column under physiological conditions, but those systems are low-field MRI, which provides low image quality. Other studies have simultaneously analyzed several anatomical structures in the lumbar spine using upright, open and low-field (0.5T *vs* 1.5T in our study) MRI[33].

Table 3 Percentage difference of the cross-sectional area of the dural sac on transverse, T2-dependent magnetic resonance imaging at the same levels for phases both with and without axial loading

Dural sac/section of the spine	Mean difference of area between unloaded and axial loading (%)	95%CI		*P* value
		Lower	Upper	
L1-L2	-2.6	-3.6	-1.6	< 0.001
L2-L3	-5.5	-6.8	-4.2	< 0.001
L3-L4	-6.7	-8.9	-4.4	< 0.001
L4-L5	-8.1	-10.5	-5.7	< 0.001
L5-S1	-3.0	-4.9	-1.0	0.004
All from L1-L2 to L5-S1	-5.2	-6.2	-4.1	< 0.001

Negative values correspond to a decrease. CI: Confidence interval.

Table 4 Percentage difference of the sagittal cross-sectional area of vertebral foramina on the same levels both with and without axial loading on both sides

Intervertebral foramina (right + left)/section of the spine	Mean difference of area between unloaded and axial loading (%)	95%CI		*P* value
		Lower	Upper	
L1-L2	-4.0	-5.1	-2.9	< 0.001
L2-L3	-6.7	-8.0	-5.5	< 0.001
L3-L4	-5.1	-6.2	-4.0	< 0.001
L4-L5	-3.3	-4.8	-1.7	< 0.001
L5-S1	2.0	0.5	3.9	0.045
All from L1-L2 to L5-S1	-3.4	-4.1	-2.7	< 0.001

Negative values correspond to a decrease. CI: Confidence interval.

Table 5 Percentage difference of the lumbosacral angles between L1 and S1 measured based on recumbent and axial-loaded magnetic resonance images

Lumbosacral angle	Mean difference of angle between unloaded and axial loading (%)	95%CI		*P* value
		Lower	Upper	
From L1 to S1	7.7	5.7	9.6	< 0.001

CI: Confidence interval.

Contrary to our study, the previous study group was limited to young (*vs* any age in our study), less populated (12 *vs* 90 in our study) asymptomatic volunteers. No 3D high-resolution images and failure to measure several anatomical structures were reported. The proposed idea of applying axial-loaded MRI aimed to mimic as close as possible the load conditions occurring in the upright position. That position is currently impossible to apply in conventional recumbent high-field MRI. Devices intended for axial loading are commercially available and approved by the United States Food and Drug Administration. They also meet the New Approach Directive requirements of the European Union; yet, according to many authors, they are still in their experimental stage[43]. As a result, biomechanical testing has focused on many spinal structures simultaneously. The load distribution among the dural sac, ligamenta flava, intervertebral foramina and lumbar sagittal alignment was considered in this

Table 6 Degenerative pathologies of the lumbar spine

Analyzed factors	Grade	*n*	%
Intervertebral disc degeneration according to Pfirrmann *et al*[38] classification	1	0	0
	2	72	16
	3	196	44
	4	159	35
	5	23	5
Facet joint degeneration, according to Weishaupt *et al*[39] classification	0	300	33
	1	405	45
	2	149	17
	3	46	5
Grade of lumbar spinal canal stenosis according to Schizas *et al*[40] classification	A1	349	78
	A2	22	5
	A3	47	10
	A4	3	1
	B	20	4
	C	7	2
	D	2	0
Disc herniation according to the Michigan State University[42] classification of lumbar disc herniation	0	342	76
	1a, 1b, 1ab, 1c	88	20
	2a, 2b, 2ab, 2c	18	4
	3a, 3b, 3ab, 3c	2	0
Foraminal stenosis, according to Lee *et al*[41] classification	0	664	74
	1	168	19
	2	56	6
	3	12	1

spinal biomechanical assessment.

Dural sac

The dural sac occupies the most significant part of the spinal canal. Therefore, spinal stenosis mainly affects the dural sac, narrowed in the highest grade from all structures filling the spinal canal (Figure 2). The cross-sectional dural sac area measurement provides the most precise assessment of the spinal canal, but its time consumption is the main disadvantage of this method[44]. The results in this study showed that the mean dural sac cross-sectional area was significantly lower when loaded than relaxed at all lumbar spine levels from L1-L2 to L5-S1 (Figure 2). The rates of dynamic change were the highest at L4-L5 (mean of 8.1%; range of 5.7%-10.5%) and the lowest at L1-L2 (mean of 2.6%; range of 1.6%-3.6%).

The high sensitivity and specificity of axial-loaded MRI for detecting severe constriction were demonstrated by Kanno *et al*[32]. MRI examinations under axial loading are highly relevant in detecting central stenosis of the spinal canal, as to be confirmed by results reported by other authors[45]. Axial-loaded MRI demonstrated a significant reduction in the dural sac size and significant correlations of dural sac diameters with the upright myelogram. Therefore, axial-loaded MRI can be used to represent positional changes in dural sac size detected by upright myelography in patients with lumbar spinal canal stenosis[32]. Numerous *in vitro* experiments showed that axial loading results in spinal canal stenosis.

Schonstrom *et al*[25] specified that axial loading results in a spinal canal volume reduction in a spine segment, measured at an intervertebral disc level by about 40-50 mm^2. In their previous studies, the authors discovered that a pressure increase in the

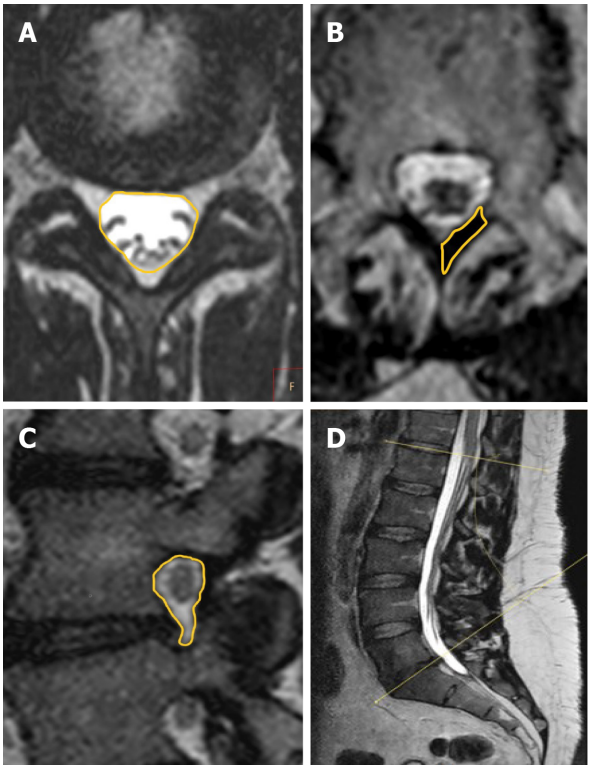


Figure 1 Specific measurements of (A) the cross-section area of the dural sac on transverse magnetic resonance imaging, (B) the cross-section area of the ligamentum flavum, (C) the sagittal cross-section area of vertebral foramina and (D) the lumbosacral angles between L1 and S1.

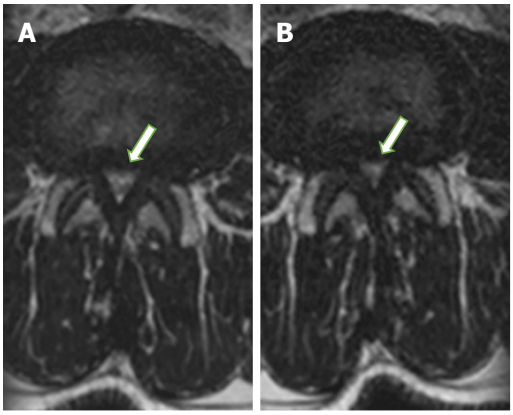


Figure 2 Transverse magnetic resonance imaging. A: Recumbent T2-weighted images. The rootlets occupy the whole of the dural sac (arrow), but they can still be individualized; B: Spinal stenosis with a reduction in the dural sac size after axial loading. No rootlets can be recognized, but some cerebrospinal fluid is still present, giving a grainy appearance to the sac (arrow).

dural sac of spinal segments reduces the spinal canal area down to approximately 79 mm^2[46]. Based on this discovery, contemporary authors assumed that 75 mm^2 is the borderline value of the dural sac cross-sectional area. Below this value, the authors suggested a diagnosis of absolute stenosis, and the range of 75-100 mm^2 indicates a diagnosis of relative spinal canal stenosis. Kim *et al*[47] arbitrarily defined a 10% reduction in the dural sac cross-sectional area as a significant reduction. They found a significant reduction in the cross-sectional area of the dural sac in 42% of patients, of which severe stenosis with a cross-sectional area lower than 75 mm^2 was found in 25% of patients.

Danielson and Willen[31] described an additional significant decrease in the cross-sectional area of the dural sac with axial-loading MRI as an area change more than 15 mm^2. They concluded that axial-loading MRI provided "additional, significant information" in 50 of 172 patients (29%). They also observed additional significant

findings in 69% of patients with neurogenic claudication, 14% of patients with sciatica and 0% of patients with LBP[31]. Of patients studied by Manenti *et al*[48], who were subjected to axial-loading MRI, 18 (45%) displayed cases of spinal canal stenosis emergence, 8 (20%) displayed cases of hernia enlargement, and 6 (15%) showed profound spondylolisthesis.

Ligamentum flavum

The ligamenta flava fills the space between the vertebral arches. They run just behind the facet joint and act as an extra reinforcement of the joint capsule. The ligamenta flava thickens with age. The ligamenta flava thickening is connected to fibrous tissue hypertrophy, which is a result of cyclooxygenase-2 and transforming growth factor-beta expression[49,50]. The changes are prominent in the dorsal part of the ligamenta flava, where the most potent axial load forces are observed[49]. This study showed that the mean cross-sectional area of the ligamenta flava was significantly higher when loaded than relaxed at all lumbar spine levels from L1-L2 to L5-S1. The rates of dynamic changes were the highest at L2-L3 (mean of 4.8%; range of 2.0%-7.6%) and the lowest at L4-L5.

According to the study of Hansson *et al*[45], it is not intervertebral discs but the ligamenta flava that have the most significant impact on spinal stenosis, being responsible for 50%-80% of spinal stenosis induced by axial loading. The case report of dynamic lumbar spinal stenosis with neurogenic claudication caused by the thickening of the ligamentum flavum, with MRI in decumbency, revealed no definite pathologic condition associated with symptoms[51]. According to some authors, the pathogenesis of thickening of the ligamentum flavum is unclear, and whether ligamentum flavum thickening is due to tissue hypertrophy or buckling remains controversial. Some studies claimed that canal narrowing, in part, results from the hypertrophy of the ligamentum flavum. In contrast, others argued that the ligamentum flavum bulges inside the spinal canal and compresses nerve tissues[49,50,52]. This information is relevant clinically because spinal stenosis may be underdiagnosed with regular MRI, and surgical intervention without adequate decompression may lead to poor outcomes.

Intervertebral foramen

Intervertebral foramina are triangular or oval at the lumbar level and broader in the coronal than the sagittal plane. Measurements recorded by encircling the intervertebral foramina sagittal cross-sections were proposed as the most accurate[53]. Our analysis of lumbar neural foramina showed that variation in the cross-sectional area of the neural foramen in the lumbar spine was significantly axially-loaded-dependent. We identified a statistically significant decrease in average percent foraminal area from recumbent to axially loaded at all levels except at L5-S1. Surprisingly, intervertebral foramina at L5-S1 widened after axial loading by 2%, on average (Figure 3).

Iwata *et al*[54] reported similar findings in computed tomography examinations using DynaWell equipment. They observed an enlargement of the intervertebral foramina area at the L5-S1 level and a simultaneous reduction in the intervertebral foramina area at L1-L2 levels to L4-L5 after axial loading. Conversely, MRI studies demonstrated a decrease in the foraminal area at all levels during weight-bearing in neutral, flexion and extension positions compared to unloaded supine imaging. The magnitude of change in the foraminal area increased as an angular motion at the segment increased. The most significant average percent decrease in the foraminal area occurs at L2-L3 and the smallest change at L5-S1, but a reduction at this level was still observed[53]. Therefore, changes caused by a compression device in foraminal dimensions at L5-S1 do not simulate physiological standing conditions.

Suppose the different types of loading simulated by DynaWell equipment and those occurring in the standing position responsible for differences in foraminal stenosis observed in those methods have not yet been determined. The axial load may be transmitted to the feet and the buttocks in the supine position. A reaction force acts on the buttocks causing the posterior rotation of the pelvis. That results in a significant decrease in the pelvic angle during axial loading[55]. According to Hioki *et al*[56], the disc wedge angles at the L5-S1 level with axial loading using DynaWell equipment differed from those in the standing posture. The magnitudes of changes were significantly smaller than in the standing position. They suggested that axial loading of the lumbar spine in the supine position decreases the angle between the L5 and S1 [56]. However, the L5-S1 angle did not significantly change in the standing posture than the controls in the supine position at rest. These observations of different lumbar-pelvic angular behavior could correspond with an enlargement of the area of intervertebral foramina at the L5-S1 level observed in our study. An awareness of these

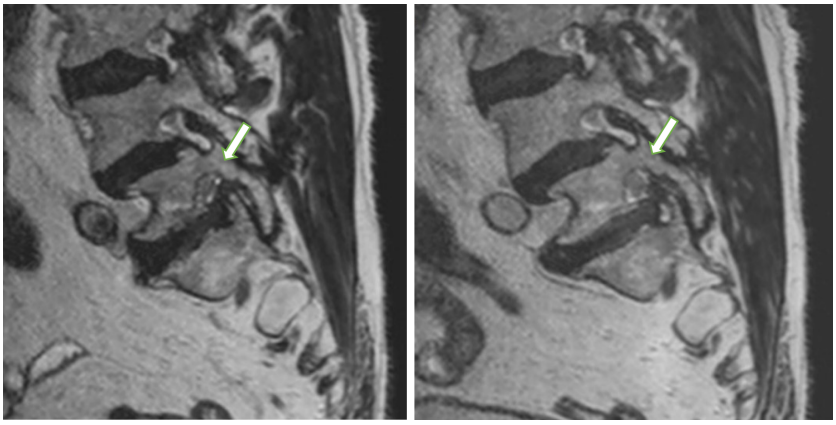


Figure 3 Sagittal magnetic resonance imaging. Morphologic changes in a foraminal zone at L5-S1 (arrow) with nerve root collapse and perineural fat obliteration were seen with and without axial loading.

phenomena is essential to allow clinicians to evaluate imaging results accurately.

The results in this study showed that the most significant foraminal constriction was by 6.7% (range of 5.5%-8.0%) under loading occurred at the L2-L3 level. Diagnostic benefits with a high grade of foraminal spinal detection could be achieved if inclusion criteria were limited to the suspicion of single spinal nerve involvement, as described by Splendiani *et al*[57]. They detected foraminal spinal stenosis at 61 of 230 levels and called it "hidden" stenosis, as it was not revealed on conventional recumbent MR examinations; it was only detected on examinations performed with the patient in the orthostatic position. The authors also discovered that stenosis of the intervertebral foramen was never found either in the presence of normal intervertebral discs or in the absence of facet disease in either the clinostatic or orthostatic position[57].

Lumbosacral angle

The spine is highly resistant to axial pressure. That resistance depends on the size and shape of the spine as well as spine curvatures. The human spine, at an early stage, consists of only one curvature: spine kyphosis. The following curvatures occur when the human develops the erected position: (1) At the cervical level: lordosis (cervical lordosis); (2) At the thoracic level: kyphosis (thoracic kyphosis); (3) At the lumbar level: lordosis (lumbar lordosis); and (4) At a sacral level: kyphosis (sacral kyphosis).

Curvatures in the sagittal plane make the spine more durable compared to the straight column. Therein one function of the lumbar lordosis is to provide a higher bearing resistance. Lumbar lordosis in the sagittal plane of the spine is unique only in the human population. It is not observed in any other animal. The changes in lordosis markedly affect the stabilizing sagittal moments.

Our results indicated that lordosis of the spine varies from the initial sagittal curvature by +7.7° after axial loading, responsible for more lordotic posture. Older patients show lower increases in lumbar lordosis when exposed to an axial force. As we observed a decreased elasticity of the spine in the older population, it is worth proposing axial-loading MRI as elasticity imaging: an innovative "elastography" method designed for the lumbar spine to explore the age of the spine, the percentile grids of degenerative changes.

Huang *et al*[58] reported that the mean lumbosacral angle was 37° in unloaded MRI examinations and increased to 39° after axial loading. Our lumbar spine biomechanics analysis also showed that axial loading increases lumbar lordosis. According to Hioki *et al*[56], lumbar axial loading with DynaWell in the supine position can simulate the lumbar spine position in the standing position. This loading device alters lumbar sagittal alignment differently from an upright standing position at the L5-S1 level.

Conversely, lumbar lordosis was more extensive after the axial load in the supine position compared to the standing position, according to Madsen *et al*[59]. This intriguing observation that the lumbosacral angle was 6° larger in the supine position than in the standing position, as explained by the author, was due to patients leaning against MRI walls to maintain a safe position and immobility when standing. Meakin *et al*[60] suggested that patients in the standing position are exposed to additional bearing forces. Patients with a lumbosacral angle smaller than the mean in an unloaded examination tend to straighten the spine after additional bearing forces. Patients with a lumbosacral angle greater than the mean in an unloaded examination

were observed to increase lumbar lordosis after additional bearing forces.

Correlation analysis

Simultaneous measurements of the percentage difference of the sagittal cross-section area of vertebral foramina, the cross-section areas of the dural sac and ligamenta flava as well as the percentage difference of the lumbosacral angles offered new information. According to our data, a statistically significant correlation exists between exaggerated lumbosacral angle and age (r = -0.253, P < 0.05). A negative correlation was found and showed that older patients have a lower increase in lumbar lordosis when exposed to axial force, similar to that found in the spine in the standing position. The percentage difference of the sagittal cross-section area of vertebral foramina, the cross-section areas of the dural sac and ligamenta flava, as well as the percentage difference of the lumbosacral angles, did not significantly correlate with each other and sex.

Limitations

This study has significant limitations. The research's main limitation is that all patients in the study were referred for MRI examinations for LBP, and there was no asymptomatic healthy control group. These results may not apply to asymptomatic, dynamic foraminal or spinal stenosis in the healthy population. Another potential limitation is that the inter-rater assessment has not been calculated. The force equal to half the body weight may not necessarily represent the lumbar spine load while standing. There may be a bias of data in the comparison between axial loading and standing conditions. Further comparative analyses between standing and axially-loaded MRI findings in the supine position would provide more clinically relevant information.

Another source of weakness in this study was the lack of computational approach in automatic image recognition based on machine learning and deep learning to ease radiological measurements of the lumbar spine. However, it is within the scope of our scientific interests, and we hope to expand artificial intelligence in image recognition and segmentation to automate lumbar spine assessment and to obtain a good level of clinical prediction. In our opinion, high resolution 3D imaging will make automatic image recognition more accurate. We showed in this study, that high resolution 3D MRI is feasible under axial compression. Volume ISotropic Turbo spin-echo Acquisition techniques have been used to acquire high-resolution, contiguous, thin-section isotropic images for complex spine anatomy and replace several two-dimensional acquisitions. The voxels generated by the 3D acquisition are submillimeter and measure the same in each direction, allowing the images to be reformatted with equal resolution in any direction.

CONCLUSION

The lumbar spine MRI is one of the most frequently performed examinations of all MRIs, but the MRI does not correlate significantly with back pain causes. The current study may help clinical practice understand spine physiology exposed to external forces, better-clarifying indications for axial load, and help identify the relationship between imaging examination results and perceived symptoms. A comparative evaluation of images obtained before and after axial loading of the spine showed changes in lumbosacral angles between L1 and S1, the dural sac cross-sectional area, the sagittal cross-sectional area of the intervertebral foramina and the cross-sectional area of the ligamentum flavum. Consistency in detecting central stenosis and ligamenta flava thickening between studies supports using an axial load of 50% body weight to simulate relaxed standing in the supine position. Changes in foraminal dimensions at L5-S1 do not affect physiological standing conditions. Axial loading intensifies the narrowing of the intervertebral foramina. Applying an axial compressive load increases lumbar lordosis, whereas the smallest changes were observed in older patients.

ARTICLE HIGHLIGHTS

Research background

Biomechanics of the individual lumbar spine structures are important since the overall spinal adaptation to compressive forces is comprised of the cumulative changes of respective elements.

Research motivation

There is a lack of works simultaneously comparing dural sac size, ligamenta flava thickness, foraminal dimensions and lumbar sagittal alignment between axial loaded and recumbent magnetic resonance imaging (MRI) in an extensive group of lower back pain patients.

Research objectives

To help the surgeons in the choice of the spinal endoscopy and spinal injections. The objective of the study was to evaluate the changes depicted by MRI of chosen lumbar spine structures upon axial-loading in comparison with recumbent MRI.

Research methods

The study covered 90 individuals assessed with three-dimensional volume isotropic acquisition MRI, first imaged in the supine position with no axial load and then again following application of an axial compressive load. Based on recumbent MRI as well as axial-loaded ones, the following were measured: the dural sac area, the ligamenta flava, the intervertebral foramina from L1-L2 to L5-S1 and the lumbosacral angle.

Research results

We found out that axial loading intensifies the narrowing of the spinal canal, thickens the ligamenta flava, narrows the intervertebral foramina from L1-L2 to L4-L5 and exaggerates lumbar lordosis.

Research conclusions

Our study reveals that there is a correlation between force compression and intensification of the lumbar spinal stenosis, intervertebral foramina narrowing, ligamenta flava thickening as well as increasing lumbar lordosis due to axial loading.

Research perspectives

There is a need to introduce computational approaches in automatic image recognition based on machine learning and deep learning to ease radiological measurements of the lumbar spine and obtain a good level of clinical prediction. Moreover, it is worth proposing axial-loading MRI as an elasticity imaging: an innovative "elastography" method designed for the lumbar spine to explore the age of the spine and the percentile grids of degenerative changes.

REFERENCES

1 **Clark S**, Horton R. Low back pain: a major global challenge. *Lancet* 2018; **391**: 2302 [PMID: 29573869 DOI: 10.1016/S0140-6736(18)30725-6]

2 **Croft PR**, Dunn KM, Raspe H. Course and prognosis of back pain in primary care: the epidemiological perspective. *Pain* 2006; **122**: 1-3 [PMID: 16530969 DOI: 10.1016/j.pain.2006.01.023]

3 **Dunn KM**, Croft PR. Epidemiology and natural history of low back pain. *Eura Medicophys* 2004; **40**: 9-13 [PMID: 16030488]

4 **Dunn KM**, Hestbaek L, Cassidy JD. Low back pain across the life course. *Best Pract Res Clin Rheumatol* 2013; **27**: 591-600 [PMID: 24315141 DOI: 10.1016/j.berh.2013.09.007]

5 **van der Windt DA**, Dunn KM. Low back pain research--future directions. *Best Pract Res Clin Rheumatol* 2013; **27**: 699-708 [PMID: 24315150 DOI: 10.1016/j.berh.2013.11.001]

6 **Gore M**, Sadosky A, Stacey BR, Tai KS, Leslie D. The burden of chronic low back pain: clinical comorbidities, treatment patterns, and health care costs in usual care settings. *Spine* 2012; **37**: E668-E677 [PMID: 22146287 DOI: 10.1097/BRS.0b013e318241e5de]

7 **Balagué F**, Mannion AF, Pellisé F, Cedraschi C. Non-specific low back pain. *Lancet* 2012; **379**: 482-491 [PMID: 21982256 DOI: 10.1016/S0140-6736(11)60610-7]

8 **Stewart WF**, Ricci JA, Chee E, Morganstein D, Lipton R. Lost productive time and cost due to common pain conditions in the US workforce. *JAMA* 2003; **290**: 2443-2454 [PMID: 14612481 DOI:

10.1001/jama.290.18.2443]
9 **Freburger JK**, Holmes GM, Agans RP, Jackman AM, Darter JD, Wallace AS, Castel LD, Kalsbeek WD, Carey TS. The rising prevalence of chronic low back pain. *Arch Intern Med* 2009; **169**: 251-258 [PMID: 19204216 DOI: 10.1001/archinternmed.2008.543]
10 **Burton AK**, Balagué F, Cardon G, Eriksen HR, Henrotin Y, Lahad A, Leclerc A, Müller G, van der Beek AJ; COST B13 Working Group on Guidelines for Prevention in Low Back Pain. Chapter 2. European guidelines for prevention in low back pain : November 2004. *Eur Spine J* 2006; **15** Suppl 2: S136-S168 [PMID: 16550446 DOI: 10.1007/s00586-006-1070-3]
11 **Meucci RD**, Fassa AG, Faria NM. Prevalence of chronic low back pain: systematic review. *Rev Saude Publica* 2015; **49** [PMID: 26487293 DOI: 10.1590/S0034-8910.2015049005874]
12 **GBD 2017 Disease and Injury Incidence and Prevalence Collaborators**. Global, regional, and national incidence, prevalence, and years lived with disability for 354 diseases and injuries for 195 countries and territories, 1990-2017: a systematic analysis for the Global Burden of Disease Study 2017. *Lancet* 2018; **392**: 1789-1858 [PMID: 30496104 DOI: 10.1016/S0140-6736(18)32279-7]
13 **Hurwitz EL**, Randhawa K, Yu H, Côté P, Haldeman S. The Global Spine Care Initiative: a summary of the global burden of low back and neck pain studies. *Eur Spine J* 2018; **27**: 796-801 [PMID: 29480409 DOI: 10.1007/s00586-017-5432-9]
14 **Bogduk N**. Functional anatomy of the spine. *Handb Clin Neurol* 2016; **136**: 675-688 [PMID: 27430435 DOI: 10.1016/B978-0-444-53486-6.00032-6]
15 **Izzo R**, Popolizio T, D'Aprile P, Muto M. Spinal pain. *Eur J Radiol* 2015; **84**: 746-756 [PMID: 25824642 DOI: 10.1016/j.ejrad.2015.01.018]
16 **Kinder A**, Filho FP, Ribeiro E, Domingues RC, Marchiori E, Gasparetto E. Magnetic resonance imaging of the lumbar spine with axial loading: a review of 120 cases. *Eur J Radiol* 2012; **81**: e561-e564 [PMID: 21741192 DOI: 10.1016/j.ejrad.2011.06.027]
17 **Lorme KJ**, Naqvi SA. Comparative analysis of low-back loading on chiropractors using various workstation table heights and performing various tasks. *J Manipulative Physiol Ther* 2003; **26**: 25-33 [PMID: 12532135 DOI: 10.1067/mmt.2003.43]
18 **Granata KP**, Marras WS. Relation between spinal load factors and the high-risk probability of occupational low-back disorder. *Ergonomics* 1999; **42**: 1187-1199 [PMID: 10503053 DOI: 10.1080/001401399185072]
19 **Han JS**, Goel VK, Ahn JY, Winterbottom J, McGowan D, Weinstein J, Cook T. Loads in the spinal structures during lifting: development of a three-dimensional comprehensive biomechanical model. *Eur Spine J* 1995; **4**: 153-168 [PMID: 7552650 DOI: 10.1007/BF00298240]
20 **Nachemson A**. The load on lumbar disks in different positions of the body. *Clin Orthop Relat Res* 1966; **45**: 107-122 [PMID: 5937361]
21 **Nachemson A**, Elfström G. Intravital dynamic pressure measurements in lumbar discs. A study of common movements, maneuvers and exercises. *Scand J Rehabil Med Suppl* 1970; **1**: 1-40 [PMID: 4257209]
22 **Nachemson AL**. Disc pressure measurements. *Spine* 1981; **6**: 93-97 [PMID: 7209680 DOI: 10.1097/00007632-198101000-00020]
23 **Rohlmann A**, Graichen F, Bender A, Kayser R, Bergmann G. Loads on a telemeterized vertebral body replacement measured in three patients within the first postoperative month. *Clin Biomech (Bristol, Avon)* 2008; **23**: 147-158 [PMID: 17983694 DOI: 10.1016/j.clinbiomech.2007.09.011]
24 **Rohlmann A**, Petersen R, Schwachmeyer V, Graichen F, Bergmann G. Spinal loads during position changes. *Clin Biomech (Bristol, Avon)* 2012; **27**: 754-758 [PMID: 22571842 DOI: 10.1016/j.clinbiomech.2012.04.006]
25 **Schönström N**, Lindahl S, Willén J, Hansson T. Dynamic changes in the dimensions of the lumbar spinal canal: an experimental study in vitro. *J Orthop Res* 1989; **7**: 115-121 [PMID: 2908901 DOI: 10.1002/jor.1100070116]
26 **Koes BW**, van Tulder M, Lin CW, Macedo LG, McAuley J, Maher C. An updated overview of clinical guidelines for the management of non-specific low back pain in primary care. *Eur Spine J* 2010; **19**: 2075-2094 [PMID: 20602122 DOI: 10.1007/s00586-010-1502-y]
27 **Maher C**, Underwood M, Buchbinder R. Non-specific low back pain. *Lancet* 2017; **389**: 736-747 [PMID: 27745712 DOI: 10.1016/S0140-6736(16)30970-9]
28 **Sasani H**, Solmaz B, Sasani M, Vural M, Ozer AF. Diagnostic Importance of Axial Loaded Magnetic Resonance Imaging in Patients with Suspected Lumbar Spinal Canal Stenosis. *World Neurosurg* 2019; **127**: e69-e75 [PMID: 30857995 DOI: 10.1016/j.wneu.2019.02.091]
29 **Lorenc T**, Palczewski P, Wójcik D, Glinkowski W, Gołębiowski M. Diagnostic Benefits of Axial-Loaded Magnetic Resonance Imaging Over Recumbent Magnetic Resonance Imaging in Obese Lower Back Pain Patients. *Spine* 2018; **43**: 1146-1153 [PMID: 30059481 DOI: 10.1097/BRS.0000000000002532]
30 **Maquer G**, Brandejsky V, Benneker LM, Watanabe A, Vermathen P, Zysset PK. Human intervertebral disc stiffness correlates better with the Otsu threshold computed from axial T2 map of its posterior annulus fibrosus than with clinical classifications. *Med Eng Phys* 2014; **36**: 219-225 [PMID: 24309128 DOI: 10.1016/j.medengphy.2013.11.008]
31 **Danielson BI**, Willén J, Gaulitz A, Niklason T, Hansson TH. Axial loading of the spine during CT and MR in patients with suspected lumbar spinal stenosis. *Acta Radiol* 1998; **39**: 604-611 [PMID: 9817029 DOI: 10.3109/02841859809175484]
32 **Kanno H**, Endo T, Ozawa H, Koizumi Y, Morozumi N, Itoi E, Ishii Y. Axial loading during

magnetic resonance imaging in patients with lumbar spinal canal stenosis: does it reproduce the positional change of the dural sac detected by upright myelography? *Spine* 2012; **37**: E985-E992 [PMID: 21258271 DOI: 10.1097/BRS.0b013e31821038f2]

33 **Schmid M**, Stucki G. , Duewell S. Changes in cross-sectional measurements of the spinal canal and intervertebral foramina as a function of body position: in vivo studies on an open-configuration MR system. *AJR Am J Roentgenol* 1999; **172**: 1095-1102 [PMID: 10587155 DOI: 10.2214/ajr.172.4.10587155]

34 **Lewandrowski KU**. Retrospective analysis of accuracy and positive predictive value of preoperative lumbar MRI grading after successful outcome following outpatient endoscopic decompression for lumbar foraminal and lateral recess stenosis. *Clin Neurol Neurosurg* 2019; **179**: 74-80 [PMID: 30870712 DOI: 10.1016/j.clineuro.2019.02.019]

35 **Sairyo K**, Chikawa T, Nagamachi A. State-of-the-art transforaminal percutaneous endoscopic lumbar surgery under local anesthesia: Discectomy, foraminoplasty, and ventral facetectomy. *J Orthop Sci* 2018; **23**: 229-236 [PMID: 29248305 DOI: 10.1016/j.jos.2017.10.015]

36 **Wagner R**, Haefner M. Indications and Contraindications of Full-Endoscopic Interlaminar Lumbar Decompression. *World Neurosurg* 2021; **145**: 657-662 [PMID: 32810629 DOI: 10.1016/j.wneu.2020.08.042]

37 **Park CH**, Lee SH. Endoscope-Assisted Minimally Invasive Interlaminar Lumbar Decompression for Spinal Stenosis. *Pain Physician* 2019; **22**: E573-E578 [PMID: 31775410]

38 **Pfirrmann CW**, Metzdorf A, Zanetti M, Hodler J, Boos N. Magnetic resonance classification of lumbar intervertebral disc degeneration. *Spine* 2001; **26**: 1873-1878 [PMID: 11568697 DOI: 10.1097/00007632-200109010-00011]

39 **Weishaupt D**, Zanetti M, Boos N, Hodler J. MR imaging and CT in osteoarthritis of the lumbar facet joints. *Skeletal Radiol* 1999; **28**: 215-219 [PMID: 10384992 DOI: 10.1007/s002560050503]

40 **Schizas C**, Theumann N, Burn A, Tansey R, Wardlaw D, Smith FW, Kulik G. Qualitative grading of severity of lumbar spinal stenosis based on the morphology of the dural sac on magnetic resonance images. *Spine* 2010; **35**: 1919-1924 [PMID: 20671589 DOI: 10.1097/BRS.0b013e3181d359bd]

41 **Lee S**, Lee JW, Yeom JS, Kim KJ, Kim HJ, Chung SK, Kang HS. A practical MRI grading system for lumbar foraminal stenosis. *AJR Am J Roentgenol* 2010; **194**: 1095-1098 [PMID: 20308517 DOI: 10.2214/AJR.09.2772]

42 **Mysliwiec LW**, Cholewicki J, Winkelpleck MD, Eis GP. MSU classification for herniated lumbar discs on MRI: toward developing objective criteria for surgical selection. *Eur Spine J* 2010; **19**: 1087-1093 [PMID: 20084410 DOI: 10.1007/s00586-009-1274-4]

43 **Dahabreh IJ**, Hadar N, Chung M. Emerging magnetic resonance imaging technologies for musculoskeletal imaging under loading stress: scope of the literature. *Ann Intern Med* 2011; **155**: 616-624 [PMID: 22041950 DOI: 10.7326/0003-4819-155-9-201111010-00009]

44 **Schonstrom NS**, Bolender NF, Spengler DM. The pathomorphology of spinal stenosis as seen on CT scans of the lumbar spine. *Spine* 1985; **10**: 806-811 [PMID: 4089655 DOI: 10.1097/00007632-198511000-00005]

45 **Hansson T**, Suzuki N, Hebelka H, Gaulitz A. The narrowing of the lumbar spinal canal during loaded MRI: the effects of the disc and ligamentum flavum. *Eur Spine J* 2009; **18**: 679-686 [PMID: 19277726 DOI: 10.1007/s00586-009-0919-7]

46 **Schönström N**, Bolender NF, Spengler DM, Hansson TH. Pressure changes within the cauda equina following constriction of the dural sac. An in vitro experimental study. *Spine* 1984; **9**: 604-607 [PMID: 6495030 DOI: 10.1097/00007632-198409000-00011]

47 **Kim YK**, Lee JW, Kim HJ, Yeom JS, Kang HS. Diagnostic advancement of axial loaded lumbar spine MRI in patients with clinically suspected central spinal canal stenosis. *Spine* 2013; **38**: E1342-E1347 [PMID: 23797506 DOI: 10.1097/BRS.0b013e3182a0dfa5]

48 **Manenti G**, Liccardo G, Sergiacomi G, Ferrante L, D'Andrea G, Konda D, Fraioli B, Schillaci O, Simonetti G, Masala S. Axial loading MRI of the lumbar spine. *In Vivo* 2003; **17**: 413-420 [PMID: 14598603]

49 **Sairyo K**, Biyani A, Goel V, Leaman D, Booth R Jr, Thomas J, Gehling D, Vishnubhotla L, Long R, Ebraheim N. Pathomechanism of ligamentum flavum hypertrophy: a multidisciplinary investigation based on clinical, biomechanical, histologic, and biologic assessments. *Spine* 2005; **30**: 2649-2656 [DOI: 10.1097/01.brs.0000188117.77657.ee]

50 **Sairyo K**, Biyani A, Goel VK, Leaman DW, Booth R, Jr. , Thomas J, Ebraheim NA, Cowgill IA, Mohan SE. Lumbar ligamentum flavum hypertrophy is due to accumulation of inflammation-related scar tissue. *Spine* 2007; **32**: E340-347 [DOI: 10.1097/01.brs.0000263407.25009.6e]

51 **Choi KC**, Kim JS, Jung B, Lee SH. Dynamic lumbar spinal stenosis : the usefulness of axial loaded MRI in preoperative evaluation. *J Korean Neurosurg Soc* 2009; **46**: 265-268 [PMID: 19844630 DOI: 10.3340/jkns.2009.46.3.265]

52 **Altinkaya N**, Yildirim T, Demir S, Alkan O, Sarica FB. Factors associated with the thickness of the ligamentum flavum: is ligamentum flavum thickening due to hypertrophy or buckling? *Spine* 2011; **36**: E1093-E1097 [PMID: 21343862 DOI: 10.1097/BRS.0b013e318203e2b5]

53 **Singh V**, Montgomery SR, Aghdasi B, Inoue H, Wang JC, Daubs MD. Factors affecting dynamic foraminal stenosis in the lumbar spine. *Spine J* 2013; **13**: 1080-1087 [PMID: 23669126 DOI: 10.1016/j.spinee.2013.03.041]

54 **Iwata T**, Miyamoto K, Hioki A, Ohashi M, Inoue N, Shimizu K. In vivo measurement of lumbar foramen during axial loading using a compression device and computed tomography. *J Spinal Disord*

Tech 2013; **26**: E177-E182 [PMID: 23381186 DOI: 10.1097/BSD.0b013e318286f635]

55 **Hioki A**, Miyamoto K, Shimizu K, Inoue N. Test-retest repeatability of lumbar sagittal alignment and disc height measurements with or without axial loading: a computed tomography study. *J Spinal Disord Tech* 2011; **24**: 93-98 [PMID: 21430497 DOI: 10.1097/BSD.0b013e3181dd611f]

56 **Hioki A**, Miyamoto K, Sakai H, Shimizu K. Lumbar axial loading device alters lumbar sagittal alignment differently from upright standing position: a computed tomography study. *Spine* 2010; **35**: 995-1001 [PMID: 20139804 DOI: 10.1097/BRS.0b013e3181bb8188]

57 **Splendiani A**, Ferrari F, Barile A, Masciocchi C, Gallucci M. Occult neural foraminal stenosis caused by association between disc degeneration and facet joint osteoarthritis: demonstration with dedicated upright MRI system. *Radiol Med* 2014; **119**: 164-174 [PMID: 24337755 DOI: 10.1007/s11547-013-0330-7]

58 **Huang KY**, Lin RM, Lee YL, Li JD. Factors affecting disability and physical function in degenerative lumbar spondylolisthesis of L4-5: evaluation with axially loaded MRI. *Eur Spine J* 2009; **18**: 1851-1857 [PMID: 19526378 DOI: 10.1007/s00586-009-1059-9]

59 **Madsen R**, Jensen TS, Pope M, Sørensen JS, Bendix T. The effect of body position and axial load on spinal canal morphology: an MRI study of central spinal stenosis. *Spine* 2008; **33**: 61-67 [PMID: 18165750 DOI: 10.1097/BRS.0b013e31815e395f]

60 **Meakin JR**, Smith FW, Gilbert FJ, Aspden RM. The effect of axial load on the sagittal plane curvature of the upright human spine in vivo. *J Biomech* 2008; **41**: 2850-2854 [PMID: 18715567 DOI: 10.1016/j.jbiomech.2008.06.035]

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ORIGINAL ARTICLE

Prospective Study

Comparing shoulder maneuvers to magnetic resonance imaging and arthroscopic findings in patients with supraspinatus tears

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Abstract

BACKGROUND

Shoulder maneuvers and magnetic resonance imaging (MRI) are performed to diagnose supraspinatus tendon tears regardless of arthroscopy exam. Although there are many studies on this subject, there is a lack of studies comparing the sensitivity (Se) and specificity (Sp) of shoulder maneuvers and MRI to arthroscopic findings (intact, partial, or full thickness supraspinatus tendon tear).

AIM

To compare the diagnostic values of shoulder maneuvers with MRI for supraspinatus tendon tears in patients undergoing shoulder arthroscopy.

METHODS

A total of 199 consecutive patients from four orthopedic centers met the eligibility criteria of shoulder pain persisting for at least four weeks. They were prospectively enrolled in this study from April 2017 to April 2019. Seven clinical tests (full can, empty can, drop arm, Hawkins', painful arc, Neer's sign and resisted external rotation) and MRI were performed, and all were compared with surgical findings. Full can, empty can and resisted external rotation tests were interpreted as positive in the case of pain and/or weakness. We assessed the Se, Sp, accuracy, positive predictive value (PPV) and negative predictive value (NPV), positive and negative likelihood ratio and diagnostic odds ratio for overall, partial and full-thickness supraspinatus tears.

guardian, provided written consent prior to study enrollment.

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RESULTS

MRI had the highest Se for overall (0.97), partial (0.91) and full-thickness (0.99) tears; moreover, MRI had the highest NPV: 0.90, 0.88 and 0.98 for overall, partial and full-thickness tears, respectively. For overall supraspinatus tears, the Se and PPV were: Painful arc (Se = 0.85/PPV = 0.91), empty can (pain) (Se = 0.80/PPV = 0.89), full can (pain) (Se = 0.78/PPV = 0.90), resisted external rotation (pain) (Se = 0.48/PPV = 0.87), drop arm (Se = 0.19/PPV = 0.97), Neer's sign (Se = 0.78/PPV = 0.93) and Hawkins' (Se = 0.80/PPV = 0.88). MRI had the highest PPV (0.99). The Hawkin's test had the highest false positive rate in patients with intact tendons (0.36). The Sp of the empty can and full can (both tests positive for pain and weakness), drop arm and MRI were: 0.93, 0.91, 0.98 and 0.96, respectively. For partial and full-thickness tears, the empty can test (positive for pain and weakness) had a Sp of 0.93, and the drop arm and MRI had the same Sp (0.98).

CONCLUSION

Physical examination demonstrated good diagnostic value, the drop arm test had a Sp as good as MRI for supraspinatus tears; however, MRI was more accurate in ruling out tears. The Hawkins' test had high false-positive findings in patients with intact tendons.

Key Words: Rotator cuff injuries; Physical examination; Magnetic resonance imaging; Arthroscopy

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Core Tip: Shoulder maneuvers and magnetic resonance imaging (MRI) are performed to diagnose supraspinatus tendon tears regardless of arthroscopy exam. The shoulder maneuvers are useful for diagnosing supraspinatus tears in patients for whom surgery is being considered; however, they showed limited values in ruling out tears compared with MRI. Moreover, some shoulder maneuvers had high false-positive findings in patients with intact tendons.

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INTRODUCTION

Several shoulder maneuvers have been described and performed on patients undergoing shoulder arthroscopy; however, previous studies have shown that only the empty can and full can tests accurately diagnose supraspinatus tears[1]. Moreover, other studies demonstrated that the drop arm test has the highest specificity (Sp) for supraspinatus tears[2].

For diagnostic confirmation of clinical findings, magnetic resonance imaging (MRI) has been used to evaluate rotator cuff tears (RCTs). MRI showed high sensitivity (Se) and Sp for full thickness tears; however, poor Se for detecting partial tears[3]. Moreover, MRI is valuable in surgical planning of RCTs, allowing a detailed assessment of the tear size and muscle atrophy[4-7].

Systematic reviews point out limitations in the accuracy studies of clinical tests and imaging exams for diagnosing RCTs, and these reviews suggested new research with improved methodological standards[3,8-10]. The main weakness identified was the lack of standardization of the clinical tests, small sample size, absence of blinded evaluators, long time interval between the index tests and arthroscopy, retrospective method evaluation and the use of MRI as a reference standard instead of arthroscopy [3,9].

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Although the literature is extensive on this subject, there is a lack of studies that compared the Se and Sp of shoulder maneuvers and MRI for supraspinatus tears. Therefore, the aim of this study was to evaluate the diagnostic values of seven clinical tests and MRI for supraspinatus tears in patients undergoing shoulder arthroscopy. We hypothesized that clinical tests will be as specific as MRI in diagnosing supraspinatus tendon tears.

MATERIALS AND METHODS

Study design

We carried out a prospective multicenter accuracy study at four orthopedic centers (Sao Paulo Hospital, Christóvão da Gama Hospital and Maternity, Wladimir Arruda Hospital and the Japanese-Brazilian Beneficent Hospital of São Paulo) from April 2017 to April 2019. The study was approved by an institutional review board under registration number 1662/2016 and registered on the ISRCTN registry platform (ID: ISRCTN13083925 – https://doi.org/10.1186/ISRCTN13083925)[11,12].

The inclusion criteria were patients who had an indication of arthroscopy for RCTs with symptoms of shoulder pain for at least 4 wk. The patients included in this study underwent shoulder maneuvers, MRI and arthroscopy; some of these patients were treated with physiotherapy for RCTs between the physical examination and arthroscopy. Patients excluded were those with adhesive capsulitis, glenohumeral osteoarthritis, or shoulder instability, three months after the physical examination, MRI and arthroscopy.

The following demographic information was obtained: Gender, age, symptoms duration (months), side involved, dominance of the affected limb, and history of previous shoulder trauma. Moreover, the time between the index tests (shoulder maneuvers and MRI) and the reference standard (arthroscopy) was evaluated.

Physical examination

Seven clinical tests (full can, empty can, drop arm, resisted external rotation, Hawkins', painful arc, and Neer's sign) were independently performed by four experienced orthopedic shoulder surgeons, in all patients sequentially, following a random order according to the choice of each evaluator and were not always performed in the same order. These tests were chosen based on previously published studies that evaluated the diagnostic values of the shoulder maneuvers for RCTs. The empty can, full can, Hawkin's painful arc and Neer's sign were standardized according to their original description; the drop arm and resisted external rotation tests, according to the description in the study by Hanchard *et al*[9]. Before the start of the study, all four evaluators underwent training to standardize the technique and the positivity criteria of the shoulder maneuvers, in a sample of patients who were not included in this study. Clinical tests were conducted following an average interval of two minutes between each maneuver and a goniometer was used to measure the angles in the limb assessed. The evaluators were blinded to any previous clinical examination and imaging exams but had access to the history and demographic data of the patients. Only one shoulder surgeon assessed each patient.

The seven clinical tests were performed as described below:

Empty can test: With the arm at a position of 90° of abduction in the scapula plane and internal rotation (thumb pointing down), the patient was asked to isometrically resist a downward pressure applied by the examiner[13].

Full can test: With the arm at 90° of abduction in the plane of the scapula and external rotation (thumb pointing up), the patient was asked to resist a downward pressure applied by the examiner isometrically[14].

Drop arm test: The patient elevated the arm above 90° of abduction, using a goniometer, passively by the examiner; the support was removed, and the patient attempted to lower the arm actively in the plane of abduction. This maneuver was considered positive if the patient did not hold the position or if the arm dropped abruptly when lowering the arm in the coronal plane[9,15].

Resisted external rotation test: The patient stands, elbow at side and flexed at 90°, shoulder in neutral rotation, and then asked to externally rotate the shoulder maximally against the tester's isometric resistance, applied at the wrist[9].

Hawkins' test: The upright patient's arm was passively positioned at 90° of shoulder and 90° of elbow flexion. The examiner then forced an internal rotation of the patient's shoulder. The test was considered positive if pain was reported[16].

Neer's sign: The tester passively elevated the patient's arm in the plane of the scapula, preventing scapular movement by holding with the other hand. The test was considered positive if pain occurred during the elevation[17].

Painful arc: The patient actively elevates the shoulder to full elevation, and then lowers it in the scapula plane. The test was interpreted positively if pain was reported during elevation, lowering, or both, between 60˚ and 120˚[18].

The muscle strength of empty can, full can and resisted external rotation was manually measured and interpreted positively if the patient was unable to overcome the resistance imposed by the examiner or if the strength decreased in relation to the contralateral side[1]. If weakness was observed, the test was interpreted as positive. The pain was not graduated, and any level of pain when performing the maneuver was considered positive. The empty can, full can and resisted external rotation tests were interpreted as positive in the case of pain and/or weakness.

MRI

MRI results were evaluated by two blinded musculoskeletal radiologists, who had no prior information on the patient's physical examination. The radiologists evaluated each MRI together and there was a consensus on diagnosis of the lesions. MRI was performed using 3.0 Tesla devices, and the shoulder was placed in a dedicated receive-only shoulder coil. The supraspinatus was evaluated in the axial, oblique coronal, and oblique sagittal planes, at 4 to 5-mm section thickness. The sequences performed were two T1-weighted planes centered on the rotator cuff muscles: The axial plane, covering from the greater tubercle of the humerus to the spinal edge of the scapula, and the oblique sagittal plane, covering the tuberosity to the medial third of the scapula. In T2-weighted imaging, three acquisition planes were chosen: The axial plane, from the top of the acromioclavicular joint to the lower recess of the glenohumeral joint; oblique coronal plane, parallel to the supraspinatus and covering the entire scapular-humeral joint; and the oblique sagittal plane, perpendicular to the supraspinatus, from the distal end of the tendon to the middle part of the rotator cuff muscle belly. The supraspinatus was classified as intact tendon, partial or full-thickness tears according to the fluid signal intensity in T2-weighted coronal and sagittal scans.

Arthroscopy

Arthroscopy was the reference standard and was performed by two experienced orthopedic shoulder surgeons. The principal surgeon was involved in the clinical history and the preoperative physical examination; the assistant was blinded to all the clinical tests and MRI. All patients were placed in the lateral decubitus position with an anterior pad and another in the back, under general anesthesia, and a brachial plexus block. Eleven pounds of balanced suspension was used with the arm in 30˚ to 45˚ of abduction and 30˚ to 45˚ of forward flexion, and posterior inclination of the back to leave the glenoid parallel with the horizontal. The standard posterior portal was used to evaluate the supraspinatus tendon from the articular side. Through the lateral portal, the tendon was assessed from the subacromial space with a 30˚ arthroscope. A probe was used to identify tears, and the supraspinatus tendon was classified as intact, partial or full-thickness tears.

Sample size

The sample size was calculated assuming that the Se was 0.90, the prevalence of RCTs in the general population was 22%, a confidence interval (CI) of 95% with a marginal error of 0.10, resulting in a sample size of at least 157 patients[19-21].

Statistical analysis

The clinical tests and MRI results were compared with the surgical findings of arthroscopy to analyze the diagnostic values. Statistical analysis included the Se, Sp, positive predictive value (PPV), negative predictive value (NPV), accuracy, diagnostic odds ratio (DOR), and likelihood ratio[22]. These ratios were used to predict overall, partial and full-thickness tears. The Se and Sp are presented with the 95%CI. Tests were performed using SPSS software (ver. 25 for Mac; IBM Corp., New York, United States).

RESULTS

A total of 720 patients were consecutively seen at four orthopedic centers, 213 had an indication for shoulder arthroscopy and were included. Fourteen patients were

excluded because the period between the performance of the index tests (shoulder maneuvers and MRI) and arthroscopy was greater than three months, and 199 patients met enrollment criteria for the final analysis. Demographic data were collected and are shown in Table 1.

A total of 47 intact tendons, 62 partial tears (32 bursal-side and 30 articular-side tears) and 90 full-thickness tears (70 supraspinatus, 20 supraspinatus and infraspinatus tears) were found during arthroscopy. The arthroscopy was performed within a mean of 37 d (range, 1 to 83 d) after the physical examination and within 55 d (range, 4 to 89 d) after MRI.

MRI had the highest Se for overall tears (Table 2) (Se = 0.97). Among the clinical tests, the painful arc had the highest Se (Se = 0.85) and the empty can (positive for pain and weakness) had the best performance (DOR = 40). The drop arm test had the highest Sp (0.98), whereas the Sp for MRI for diagnosis of supraspinatus tears was 0.96. The shoulder maneuvers presented low values to rule out tears and the empty can test had the highest NPV between the physical examinations (0.70). The drop arm test and MRI had the highest PPV (0.97 and 0.99, respectively).

The false positive results for overall tears were: Painful arc (0.28), empty can (pain = 0.19/pain and weakness = 0.08), full can (pain = 0.19/pain and weakness = 0.11), resisted external rotation (pain = 0.20/pain and weakness = 0.06), drop arm (0.04), Neer's sign (0.19), Hawkin's (0.36), and MRI (0.02).

For partial tears (Table 3), MRI had the highest Se (0.91); however, MRI had the same Sp (0.98) as the drop arm test. For full thickness tears (Table 4), the empty can test (positive for pain and weakness) had a Se = 0.84; Sp of the drop arm was 0.98, and the MRI had a Se = 0.99 and Sp = 0.98.

DISCUSSION

This study demonstrated the significance of clinical tests for the diagnosis of supraspinatus tears in patients with an indication for shoulder arthroscopy. The Sp of the drop arm test for supraspinatus tears was similar to that of MRI. On the other hand, the physical examination demonstrated limited diagnostic value in ruling out tears when compared to MRI.

The strengths of this study were the inclusion of a consecutive and representative sample of patients; experienced shoulder surgeons performed the physical examination; the technique was standardized, and the positivity criterion for each clinical test was fulfilled. Therefore, we demonstrated that trained orthopedists could perform clinical tests with high Sp for the diagnosis of supraspinatus tears[3,23-27]. Moreover, arthroscopy was utilized as a reference standard, a minimally invasive surgical procedure that is the gold standard for diagnosis and is widely used to treat RCTs[1]. Through arthroscopy, the evaluator can inspect and probe the partial articular and bursal-side tears, assess the rotator cuff footprint accurately and perform a general examination of the shoulder joint in order to identify and treat associated rotator cuff lesions[3].

To standardize shoulder maneuvers is challenging due to the high variability in performance and interpretation. The empty can test, for example, adopts the interpretative criteria of pain, muscle weakness, or both, affecting Se and Sp, as demonstrated in this study[8,9]. Muscle weakness was previously demonstrated in other studies as a reliable criterion, and in our study, the pain associated with weakness obtained the highest Sp[1,28]. We observed that many patients with supraspinatus tears had pain associated with weakness, demonstrating that pain can be a cause for functional disability when performing the test[1,28], as described by Jobe *et al*[13,29].

The empty can, full can and resisted external rotation tests showed improved results when positive for pain and weakness. Positivity only for pain in these tests had better Se, but less Sp; the positivity only for muscle weakness occurred in just a few cases and it was not possible to perform statistical analysis for this specific positivity criterion. The diagnostic values of these three clinical tests were calculated according to positivity only for pain and pain associated with weakness.

Another methodological criterion adopted here was establishing a time limit between physical examination, MRI and arthroscopy, a criterion little used in other accuracy studies and cited as one of the weaknesses in systematic reviews[3,9]. In this study, we choose a three-month interval between the index tests and arthroscopy, to reduce the interpretation bias, different to that in other studies[5,30-33]. The ideal would be to carry out the index tests and arthroscopy in the same day or week;

Table 1 Demographic data of the patients studied, median and standard deviation are shown

Patient variables (*n* = 213)	Statistic *n* (%)
Median age (yr)	47.4; SD = 13.2; range 19 to 76
Symptoms duration (mo)	21.2; range 1 to 144
Gender	
Male	123 (57.7)
Female	90 (42.3)
Laterality	
Right	131 (61.5)
Left	82 (38.5)
Dominant arm	
Dominant	129 (60.5)
Non-dominant	84 (39.4)
History of previous trauma	
Yes	73 (34.3)
No	140 (65.7)

Table 2 Diagnostic values for overall tears

Test	Se	95%CI	Sp	95%CI	Ac	PPV	NPV	LR +	LR -	DOR
Painful arc	0.85	0.79-0.90	0.73	0.60-0.84	0.83	0.91	0.60	3.22	0.20	16.27
Empty can										
P	0.80	0.71-0.87	0.82	0.69-0.90	0.81	0.89	0.68	4.35	0.24	17.78
P and W	0.75	0.63-0.84	0.93	0.81-0.98	0.82	0.94	0.70	10.75	0.27	40.00
Full can										
P	0.78	0.69-0.85	0.81	0.68-0.90	0.79	0.90	0.63	4.15	0.27	15.26
P and W	0.63	0.50-0.74	0.91	0.78-0.96	0.74	0.91	0.63	6.76	0.41	16.53
Resisted external rotation										
P	0.48	0.39-0.57	0.84	0.71-0.92	0.59	0.87	0.43	3.01	0.62	4.87
P and W	0.40	0.31-0.50	0.95	0.85-0.99	0.58	0.95	0.43	8.89	0.62	14.25
Drop arm	0.19	0.13-0.25	0.98	0.89-1.00	0.37	0.97	0.26	9.21	0.83	11.10
Neer's sign	0.78	0.71-0.84	0.82	0.69-0.90	0.79	0.93	0.53	4.26	0.27	15.92
Hawkins'	0.80	0.73-0.85	0.65	0.51-0.77	0.77	0.88	0.49	2.30	0.31	7.53
MRI	0.97	0.93-0.99	0.96	0.86-0.99	0.97	0.99	0.90	23.76	0.03	752

Se: Sensitivity; Sp: Specificity; Ac: Accuracy; PPV: Positive predictive value; NPV: Negative predictive value; LR +: Positive likelihood ratio; LR -: Negative likelihood ratio; DOR: Diagnostic odds ratio; CI: Confidence interval; P: Positive for pain; W: Positive for weakness; MRI: Magnetic resonance imaging.

however, we chose the limit of three months, mainly due to the logistics of the orthopedic centers included in the study, as there is a waiting list for these procedures [34].

We demonstrated high Sp and PPV of the drop arm test, unlike Somerville *et al*[33], who mentioned that no clinical test in isolation is sufficient to diagnose RCTs. Our results showed that the drop arm test is valuable for confirming overall supraspinatus tears (PPV = 0.97). The drop arm test had a similar Sp to MRI for supraspinatus tears; however, one factor contributing to the high Sp of these clinical tests was the possible association of supraspinatus and infraspinatus tears in patients included in this study.

Table 3 Diagnostic values for partial tears

Test	Se	95%CI	Sp	95%CI	Ac	PPV	NPV	LR +	LR -	DOR
Painful arc	0.78	0.66-0.86	0.75	0.61-0.85	0.76	0.81	0.70	3.10	0.30	10.40
Empty can										
P	0.74	0.61-0.84	0.82	0.69-0.90	0.78	0.81	0.75	4.06	0.31	12.99
P and W	0.70	0.55-0.81	0.93	0.81-0.98	0.81	0.91	0.75	10.00	0.32	30.77
Full can										
P	0.72	0.59-0.82	0.81	0.68-0.90	0.76	0.82	0.71	3.84	0.34	11.10
P and W	0.57	0.41-0.71	0.91	0.79-0.96	0.75	0.84	0.71	6.12	0.48	12.80
Resisted external rotation										
P	0.43	0.32-0.55	0.84	0.71-0.92	0.61	0.78	0.52	2.70	0.67	4.01
P and W	0.25	0.15-0.39	0.95	0.85-0.99	0.58	0.87	0.52	5.61	0.78	7.18
Drop arm	0.09	0.04-0.18	0.98	0.89-1.00	0.46	0.86	0.43	4.30	0.93	4.62
Neer's sign	0.72	0.60-0.81	0.83	0.70-0.91	0.76	0.86	0.68	4.30	0.34	12.63
Hawkins'	0.73	0.61-0.82	0.67	0.52-0.78	0.70	0.75	0.64	2.19	0.40	5.44
MRI	0.91	0.81-0.96	0.98	0.89-1.00	0.94	0.98	0.88	42.59	0.09	444.67

Se: Sensitivity; Sp: Specificity; Ac: Accuracy; PPV: Positive predictive value; NPV: Negative predictive value; LR +: Positive likelihood ratio; LR -: Negative likelihood ratio; DOR: Diagnostic odds ratio; CI: Confidence interval; P: Positive for pain; W: Positive for weakness; MRI: Magnetic resonance imaging.

Table 4 Diagnostic values for full-thickness tears

Test	Se	95%CI	Sp	95%CI	Ac	PPV	NPV	LR +	LR -	DOR
Painful arc	0.91	0.84-0.95	0.75	0.61-0.85	0.86	0.91	0.75	3.64	0.12	30.00
Empty can										
P	0.86	0.73-0.94	0.82	0.69-0.90	0.84	0.81	0.87	4.70	0.17	28.15
P and W	0.84	0.65-0.94	0.93	0.81-0.98	0.90	0.87	0.91	12.04	0.17	70
Full can										
P	0.85	0.72-0.92	0.81	0.68-0.90	0.83	0.82	0.85	4.54	0.18	24.76
P and W	0.72	0.52-0.86	0.91	0.78-0.96	0.84	0.82	0.85	7.74	0.31	25.07
Resisted external rotation										
P	0.56	0.41-0.70	0.84	0.71-0.92	0.71	0.74	0.70	3.51	0.52	6.71
P and W	0.58	0.43-0.72	0.95	0.85-0.99	0.77	0.92	0.70	12.79	0.44	29.17
Drop arm	0.25	0.18-0.35	0.98	0.89-1.00	0.49	0.96	0.39	12.12	0.76	15.88
Neer's sign	0.83	0.74-0.89	0.83	0.70-0.91	0.83	0.91	0.70	4.97	0.21	24.12
Hawkins'	0.85	0.76-0.91	0.67	0.52-0.78	0.79	0.84	0.68	2.54	0.23	11.20
MRI	0.99	0.95-1.00	0.98	0.89-1.00	0.98	0.99	0.98	46.35	0.01	3266

Se: Sensitivity; Sp: Specificity; Ac: Accuracy; PPV: Positive predictive value; NPV: Negative predictive value; LR +: Positive likelihood ratio; LR -: Negative likelihood ratio; DOR: Diagnostic odds ratio; CI: Confidence interval; P: Positive for pain; W: Positive for weakness; MRI: Magnetic resonance imaging.

Physical examination has already been demonstrated in previous studies as limited in ruling out RCTs[1,33]. The limitations of the shoulder maneuvers for excluding supraspinatus tears were also shown in our study; moreover, the painful arc and Hawkins' tests had the highest false-positive rates in patients with intact tendons.

Physical examination alone cannot quantify the size and extension of the supraspinatus tear, muscle atrophy, and associated rotator cuff lesions (biceps tendon pathologies and acromioclavicular joint osteoarthritis). Therefore, imaging exams,

such as radiography, ultrasonography, or MRI, are essential to determine surgical indication[33].

Limitations

First, the reliability of the clinical tests, MRI and arthroscopy was not evaluated. Previous studies demonstrated a moderate to substantial agreement of the empty can, painful arc and external rotation resistance tests, but a fair agreement for the Hawkins' and the Neer's sign[35]. We suggest that future studies should evaluate mainly the reliability and analysis of Se and Sp of the physical examination.

Second, muscle weakness was evaluated manually using subjective criteria according to each tester. We did not use a dynamometer for objective data collection, as some studies considered a 20% decrease in strength in relation to the contralateral side, a positivity criterion for weakness[36]. Moreover, we did not quantify pain when performing each maneuver, with a visual analogue scale, for example, and any shoulder pain during the test was considered positive.

Third, the principal surgeon performing the arthroscopy was not blinded to the shoulder maneuvers and MRI; however, to reduce this bias, we included a second surgeon's evaluation, blinded to physical examination and MRI.

CONCLUSION

Physical examination demonstrated good diagnostic value, showing that the drop arm test had a similar Sp to MRI for supraspinatus tears. However, MRI had higher Se compared with the shoulder maneuvers and was more accurate in ruling out supraspinatus tears.

ARTICLE HIGHLIGHTS

Research background

Shoulder maneuvers and magnetic resonance imaging (MRI) are performed in current practice in patients with rotator cuff tears (RCTs); however, there is insufficient evidence as to which clinical test is efficient for diagnosing supraspinatus tears.

Research motivation

The motivation for this study was the exponential increase in MRI requests and little appreciation of physical examination in patients with RCTs.

Research objectives

The objective of this study was to compare the accuracy of clinical tests with MRI for diagnosing supraspinatus tears.

Research methods

A prospective multicenter accuracy study of seven shoulder maneuvers and MRI for supraspinatus tears in patients undergoing arthroscopy was performed.

Research results

MRI and the drop arm test had the highest specificity (0.99 and 0.97, respectively) for overall supraspinatus tears; the Hawkin's test had the highest rate of false-positive findings (0.36) in patients with intact tendons.

Research conclusions

Shoulder maneuvers had good diagnostic value for supraspinatus tears; however, MRI had the highest diagnostic value for ruling out tears.

Research perspectives

Futures studies are necessary to analyze the accuracy of clinical tests and MRI for infraspinatus and subscapularis tears.

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REFERENCES

1 **Sgroi M**, Loitsch T, Reichel H, Kappe T. Diagnostic Value of Clinical Tests for Supraspinatus Tendon Tears. *Arthroscopy* 2018; **34**: 2326-2333 [PMID: 29802066 DOI: 10.1016/j.arthro.2018.03.030]

2 **Jain NB**, Luz J, Higgins LD, Dong Y, Warner JJ, Matzkin E, Katz JN. The Diagnostic Accuracy of Special Tests for Rotator Cuff Tear: The ROW Cohort Study. *Am J Phys Med Rehabil* 2017; **96**: 176-183 [PMID: 27386812 DOI: 10.1097/PHM.0000000000000566]

3 **Lenza M**, Buchbinder R, Takwoingi Y, Johnston RV, Hanchard NC, Faloppa F. Magnetic resonance imaging, magnetic resonance arthrography and ultrasonography for assessing rotator cuff tears in people with shoulder pain for whom surgery is being considered. *Cochrane Database Syst Rev* 2013; CD009020 [PMID: 24065456 DOI: 10.1002/14651858.CD009020.pub2]

4 **Magee T**, Williams D. 3.0-T MRI of the supraspinatus tendon. *AJR Am J Roentgenol* 2006; **187**: 881-886 [PMID: 16985129 DOI: 10.2214/AJR.05.1047]

5 **Sharma G**, Bhandary S, Khandige G, Kabra U. MR Imaging of Rotator Cuff Tears: Correlation with Arthroscopy. *J Clin Diagn Res* 2017; **11**: TC24-TC27 [PMID: 28658874 DOI: 10.7860/JCDR/2017/27714.9911]

6 **Parker L**, Nazarian LN, Carrino JA, Morrison WB, Grimaldi G, Frangos AJ, Levin DC, Rao VM. Musculoskeletal imaging: medicare use, costs, and potential for cost substitution. *J Am Coll Radiol* 2008; **5**: 182-188 [PMID: 18312965 DOI: 10.1016/j.jacr.2007.07.016]

7 **Tawfik AM**, El-Morsy A, Badran MA. Rotator cuff disorders: How to write a surgically relevant magnetic resonance imaging report? *World J Radiol* 2014; **6**: 274-283 [PMID: 24976930 DOI: 10.4329/wjr.v6.i6.274]

8 **Gismervik SØ**, Drogset JO, Granviken F, Rø M, Leivseth G. Physical examination tests of the shoulder: a systematic review and meta-analysis of diagnostic test performance. *BMC Musculoskelet Disord* 2017; **18**: 41 [PMID: 28122541 DOI: 10.1186/s12891-017-1400-0]

9 **Hanchard NC**, Lenza M, Handoll HH, Takwoingi Y. Physical tests for shoulder impingements and local lesions of bursa, tendon or labrum that may accompany impingement. *Cochrane Database Syst Rev* 2013; CD007427 [PMID: 23633343 DOI: 10.1002/14651858.CD007427.pub2]

10 **Hegedus EJ**, Goode A, Campbell S, Morin A, Tamaddoni M, Moorman CT 3rd, Cook C. Physical examination tests of the shoulder: a systematic review with meta-analysis of individual tests. *Br J Sports Med* 2008; **42**: 80-92; discussion 92 [PMID: 17720798 DOI: 10.1136/bjsm.2007.038406]

11 **Cohen JF**, Korevaar DA, Altman DG, Bruns DE, Gatsonis CA, Hooft L, Irwig L, Levine D, Reitsma JB, de Vet HC, Bossuyt PM. STARD 2015 guidelines for reporting diagnostic accuracy studies: explanation and elaboration. *BMJ Open* 2016; **6**: e012799 [PMID: 28137831 DOI: 10.1136/bmjopen-2016-012799]

12 **Korevaar DA**, Cohen JF, Reitsma JB, Bruns DE, Gatsonis CA, Glasziou PP, Irwig L, Moher D, de Vet HCW, Altman DG, Hooft L, Bossuyt PMM. Updating standards for reporting diagnostic accuracy: the development of STARD 2015. *Res Integr Peer Rev* 2016; **1**: 7 [PMID: 29451535 DOI: 10.1186/s41073-016-0014-7]

13 **Jobe FW**, Moynes DR. Delineation of diagnostic criteria and a rehabilitation program for rotator cuff injuries. *Am J Sports Med* 1982; **10**: 336-339 [PMID: 7180952 DOI: 10.1177/036354658201000602]

14 **Kelly BT**, Kadrmas WR, Speer KP. The manual muscle examination for rotator cuff strength. An electromyographic investigation. *Am J Sports Med* 1996; **24**: 581-588 [PMID: 8883676 DOI: 10.1177/036354659602400504]

15 **Codman E**. The shoulder: Ruptures of the supraspinatus tendon and other lesions in or about the subacromial bursa. 1934: 1869-1940

16 **Naredo E**, Aguado P, De Miguel E, Uson J, Mayordomo L, Gijon-Baños J, Martin-Mola E. Painful shoulder: comparison of physical examination and ultrasonographic findings. *Ann Rheum Dis* 2002; **61**: 132-136 [PMID: 11796399 DOI: 10.1136/ard.61.2.132]

17 **Neer CS 2nd**. Impingement lesions. *Clin Orthop Relat Res* 1983; 70-77 [PMID: 6825348]

18 **Kessel L**, Watson M. The painful arc syndrome. Clinical classification as a guide to management. *J Bone Joint Surg Br* 1977; **59**: 166-172 [PMID: 873977 DOI: 10.1302/0301-620X.59B2.873977]

19 **Liu F**, Cheng X, Dong J, Zhou D, Han S, Yang Y. Comparison of MRI and MRA for the diagnosis of rotator cuff tears: A meta-analysis. *Medicine (Baltimore)* 2020; **99** (12): e19579 [DOI: 10.1097/md.0000000000019579]

20 **Hajian-Tilaki K**. Sample size estimation in diagnostic test studies of biomedical informatics. *J Biomed Inform* 2014; **48**: 193-204 [PMID: 24582925 DOI: 10.1016/j.jbi.2014.02.013]

21 **Minagawa H**, Yamamoto N, Abe H, Fukuda M, Seki N, Kikuchi K, Kijima H, Itoi E. Prevalence of symptomatic and asymptomatic rotator cuff tears in the general population: From mass-screening in

one village. *J Orthop* 2013; **10**: 8-12 [PMID: 24403741 DOI: 10.1016/j.jor.2013.01.008]
22 **Glas AS**, Lijmer JG, Prins MH, Bonsel GJ, Bossuyt PM. The diagnostic odds ratio: a single indicator of test performance. *J Clin Epidemiol* 2003; **56**: 1129-1135 [PMID: 14615004 DOI: 10.1016/s0895-4356(03)00177-x]
23 **Bhatnagar A**, Bhonsle S, Mehta S. Correlation between MRI and Arthroscopy in Diagnosis of Shoulder Pathology. *J Clin Diagn Res* 2016; **10**: RC18-RC21 [PMID: 27042543 DOI: 10.7860/JCDR/2016/14867.7309]
24 **Iannotti JP**, Ciccone J, Buss DD, Visotsky JL, Mascha E, Cotman K, Rawool NM. Accuracy of office-based ultrasonography of the shoulder for the diagnosis of rotator cuff tears. *J Bone Joint Surg Am* 2005; **87** (6): 1305-1311 [DOI: 10.2106/00004623-200506000-00017]
25 **Saqib R**, Harris J, Funk L. Comparison of magnetic resonance arthrography with arthroscopy for imaging of shoulder injuries: retrospective study. *Ann R Coll Surg Engl* 2017; **99**: 271-274 [PMID: 27652790 DOI: 10.1308/rcsann.2016.0249]
26 **Nanda R**, Gupta S, Kanapathipillai P, Liow RYL, Rangan A. An assessment of the inter examiner reliability of clinical tests for subacromial impingement and rotator cuff integrity. *Eur J Orthop Surg Traumatol* 2008; **18**: 495-500 [DOI: 10.1007/s00590-008-0341-6]
27 **Schünemann HJ**, Oxman AD, Brozek J, Glasziou P, Jaeschke R, Vist GE, Williams JW Jr, Kunz R, Craig J, Montori VM, Bossuyt P, Guyatt GH; GRADE Working Group. Grading quality of evidence and strength of recommendations for diagnostic tests and strategies. *BMJ* 2008; **336**: 1106-1110 [PMID: 18483053 DOI: 10.1136/bmj.39500.677199.AE]
28 **Kim E**, Jeong HJ, Lee KW, Song JS. Interpreting positive signs of the supraspinatus test in screening for torn rotator cuff. *Acta Med Okayama* 2006; **60**: 223-228 [PMID: 16943859 DOI: 10.18926/AMO/30715]
29 **Jobe FW**, Jobe CM. Painful athletic injuries of the shoulder. *Clin Orthop Relat Res* 1983; 117-124 [PMID: 6825323]
30 **Park HB**, Yokota A, Gill HS, El Rassi G, McFarland EG. Diagnostic accuracy of clinical tests for the different degrees of subacromial impingement syndrome. *J Bone Joint Surg Am* 2005; **87**: 1446-1455 [PMID: 15995110 DOI: 10.2106/JBJS.D.02335]
31 **Cardoso A**, Amaro P, Barbosa L, Coelho AM, Alonso R, Pires L. Diagnostic accuracy of clinical tests directed to the long head of biceps tendon in a surgical population: a combination of old and new tests. *J Shoulder Elbow Surg* 2019; **28**: 2272-2278 [PMID: 31500987 DOI: 10.1016/j.jse.2019.07.007]
32 **Bak K**, Sørensen AK, Jørgensen U, Nygaard M, Krarup AL, Thune C, Sloth C, Pedersen ST. The value of clinical tests in acute full-thickness tears of the supraspinatus tendon: does a subacromial lidocaine injection help in the clinical diagnosis? *Arthroscopy* 2010; **26**: 734-742 [PMID: 20511030 DOI: 10.1016/j.arthro.2009.11.005]
33 **Somerville LE**, Willits K, Johnson AM, Litchfield R, LeBel ME, Moro J, Bryant D. Clinical Assessment of Physical Examination Maneuvers for Rotator Cuff Lesions. *Am J Sports Med* 2014; **42**: 1911-1919 [PMID: 24936584 DOI: 10.1177/0363546514538390]
34 **Moosmayer S**, Lund G, Seljom US, Haldorsen B, Svege IC, Hennig T, Pripp AH, Smith HJ. Tendon repair compared with physiotherapy in the treatment of rotator cuff tears: a randomized controlled study in 103 cases with a five-year follow-up. *J Bone Joint Surg Am* 2014; **96**: 1504-1514 [PMID: 25232074 DOI: 10.2106/JBJS.M.01393]
35 **Michener LA**, Walsworth MK, Doukas WC, Murphy KP. Reliability and diagnostic accuracy of 5 physical examination tests and combination of tests for subacromial impingement. *Arch Phys Med Rehabil* 2009; **90**: 1898-1903 [PMID: 19887215 DOI: 10.1016/j.apmr.2009.05.015]
36 **Barth JR**, Burkhart SS, De Beer JF. The bear-hug test: a new and sensitive test for diagnosing a subscapularis tear. *Arthroscopy* 2006; **22**: 1076-1084 [PMID: 17027405 DOI: 10.1016/j.arthro.2006.05.005]

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SYSTEMATIC REVIEWS

Long-term outcomes of the four-corner fusion of the wrist: A systematic review

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Author contributions: Andronic O designed the research methodology and the research question; Jud L managed the research team and wrote the first draft of the manuscript; Burkhard MD, Casari FA, Kriechling P and Karczewski D performed the systematic research and the risk of bias assessment analysis; Nagy L and Schweizer A critically appraised the scientific approach and the final draft of the manuscript; All authors read, edited and approved the final manuscript.

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Abstract

BACKGROUND

Four-corner fusion (4CF) is a motion sparing salvage procedure that is used to treat osteoarthritis secondary to advanced scapholunate collapse or longstanding scaphoid nonunion advanced collapse. Little is known about the long-term survivorship and outcomes of 4CF.

AIM

To report on clinical and functional long-term outcomes as well as conversion rates to total wrist fusion or arthroplasty.

METHODS

The systematic review protocol was registered in the international prospective register of systematic reviews (PROSPERO) and followed the PRISMA guidelines. Original articles were screened using four different databases. Studies with a minimum Level IV of evidence that reported on long-term outcome after 4CF with a minimum follow-up of 5 years were included. Quality assessment was performed using the Methodological Index for Non-Randomized Studies criteria.

RESULTS

A total of 11 studies including 436 wrists with a mean follow-up of 11 ± 4 years (range: 6-18 years) was included. Quality assessment according to Methodological Index for Non-Randomized Studies criteria tool averaged 69% ± 11% (range: 50%-87%). Fusion rate could be extracted from 9/11 studies and averaged 91%. Patient-reported outcomes were extracted at last follow-up from 8 studies with an average visual analog scale of 1 ± 1 (range: 0-2) and across 9 studies with an average Disabilities of the Arm, Shoulder and Hand score of 21 ± 8 (range: 8-37).

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Grade B (Very good): 0
Grade C (Good): C
Grade D (Fair): 0
Grade E (Poor): 0

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At last follow-up, the cumulative conversion rate to total wrist fusion averaged 6%. There were no conversions to total wrist arthroplasty.

CONCLUSION
The 4CF of the wrist is a reliable surgical technique, capable of achieving a good long-term patient satisfaction and survivorship with low rates of conversion to total wrist fusion.

Key Words: Four-corner fusion; Partial wrist arthrodesis; Midcarpal arthrodesis; Scapholunate collapse wrist; Scaphoid nonunion advanced collapse; Scaphoid nonunion

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Core Tip: Four-corner fusion is a motion sparing salvage procedure that is used to treat osteoarthritis secondary to scaphoid advanced collapse or longstanding scaphoid nonunion advanced collapse. Our systematic review evaluated long-term clinical and radiographic outcomes of the four-corner fusion and critically appraised the methodology of studies. The results showed that four-corner fusion is capable of achieving a good long-term patient satisfaction and survivorship with low rates of conversion to total wrist fusion. Recommendations for future research are provided.

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INTRODUCTION

Four-corner fusion (4CF) is a motion sparing salvage procedure that is used to treat osteoarthritis secondary to advanced scapholunate collapse or longstanding scaphoid nonunion advanced collapse. Proximal row carpectomy (PRC) and 4CF are the two mainly used surgical techniques in such cases[1]. The decision to choose one technique over the other is primarily based on the surgeon's preference and experience, as long-term results are not clearly elucidated in the current literature so far[2]. 4CF seems to show longer survivorship, where PRC seems to provide better wrist motion[1,3-5]. Since the introduction of the 4CF by Watson and Ballet in 1984[6], various fixation techniques have been described, including Kirschner wires, headless compression screws, staples and plates[6-9]. However, using these techniques, different potential complications have been observed, in particular: nonunion, progressive osteoarthritis (OA) or hardware impingement/irritation[1,10-12].

The long-term survivorship and ultimate conversion rate of 4CF to wrist arthrodesis remains an unelucidated aspect. Although different studies are emerging that report on long-term outcomes of 4CF, it remains difficult to draw conclusions based on individual studies due to heterogeneity of outcome measures and surgical techniques. Hence, it was the aim of the current study to provide a systematic approach on evaluating evidence reporting on the long-term outcomes of 4CF with appropriate tools for critical appraisal.

MATERIALS AND METHODS

Search strategy

A systematic computer-based database search was conducted using CENTRAL (Cochrane Central Register of Controlled Trials), MEDLINE (Pubmed), EMBASE and Web of Science Core Collection. A total of fifteen combinations for each database using the following key-words were used: "four corner," "4 corner," "midcarpal," "scapholunate advanced collapse" and "scaphoid nonunion advanced collapse" with

the terms "surgery," "fusion" and "arthrodesis." All published studies from January 1, 1978 until January 1, 2020 were included in the systematic search. First, a blinded and independent process of selection was carried out by two authors (D.K., P.K.) based on title and abstract. Next, a thorough analysis of eligible studies was performed by evaluating full texts. Any excluded study together with the reason of exclusion was noted and compared between readers. Studies reporting clinical or radiographic outcomes of 4CF for the treatment of degenerative wrist conditions were selected based on predefined eligibility criteria. The protocol of a parallel ongoing systematic review used by the same group regarding the 4CF has been published and registered in the international prospective register of systematic reviews (PROSPERO) under the registration number: CRD42020164301. Inclusion and exclusion criteria are emphasized in Table 1.

Data extraction and quality assessment

Data collection included fusion rates, revision rates and conversion rates to total wrist arthrodesis. Wrist range of motion (ROM), including wrist flexion and extension, total flexion-extension arc as well as radial-ulnar deviation, was extracted. Grip strength was noted as percentage of the opposite hand. Patient-reported outcome measures were included as the Disabilities of the Arm, Shoulder and Hand questionnaire (DASH) and the visual analog scale (VAS) scores. Where available, data regarding incidence of radiolunate arthritis was included. The quality of all the studies was then assessed using the Methodological Index for Non-Randomized Studies criteria[13]. Methodological Index for Non-Randomized Studies criteria assess eight critical aspects of the study design for non-comparative clinical studies and an additional four aspects of study design for comparative clinical studies. Each item is given a score of zero if information is not reported, one if information is reported but inadequate, and two if information is reported and adequate. Therefore, the maximum possible score is 16 for non-comparative studies and 24 for comparative studies. Each score was then converted into a percentage to harmonize the scoring system.

Statistical analysis

The statistical analysis was performed using Review Manager (RevMan Cochrane) and Comprehensive Meta-Analysis Software. For quantification of methodological inconsistency and heterogeneity across studies, an I^2 test was performed, with a P value of $P = 0.10$. A level of more than 75% was considered as considerable. This has assessed whether observed differences in results are compatible with chance alone.

RESULTS

Systematic database search

The initial database search yielded 4726 studies. After removal of duplicates, 2323 studies remained. Next, screening based on title and abstract was performed, and 126 studies remained for further assessment. These were then screened for eligibility against the inclusion and exclusion criteria based on abstract and full-text review. Finally, 11 studies could be included in the final analysis (Figure 1) with the reasons for exclusion separately emphasized in the flow-chart.

Quality assessment

A quality assessment was performed in all included studies (Table 2). There were seven retrospective case series[3,5,14-18], three retrospective cohort studies[19-21] and one prospective cohort study[22]. The calculated average from scores according to the Methodological Index for Non-Randomized Studies criteria tool was 69.0% ± 11.1% (range: 50%-87%).

Demographics, indications and surgical fixation techniques

A total of 463 wrists was included for further analysis (Table 2). The mean age at time of surgery over all included studies was 49 ± 7 years (range: 34-63 years). The most frequent indications were degenerative wrist conditions such as scapholunate collapse (10/11 studies)[3,5,14-19,21,22] or scaphoid nonunion advanced collapse (8/11 studies)[3,5,15-19,21]. Other less frequent indications were scaphoid chondrocalcinosis advanced collapse[16], an unclassified OA[5,20] and perilunate OA[21]. The following fixation techniques were used: Kirschner wires[3,5,14,15,18,19,21], locking or non-locking plates[3,16,17,21], staples[3,22] and screws[3,21].

Table 1 Criteria for study selection

Inclusion criteria	Exclusion criteria
Human studies in English or German language	Oral presentations, cadaveric or review articles, animal studies
Minimum Level IV case series studies using Oxford Centre for Evidence-Based Medicine 2011 Levels of Evidence	Language not in English or German
Four corner fusion surgery using any technique	Minimum follow-up less than 5 yr
A minimum follow-up of 5 yr	Inflammatory arthropathy as etiology
Clinical and radiographic data including patient-reported outcomes, grip/pinch strength, range of motion, fusion rates, revisions or complications have been reported	Insufficient outcome data reported

Table 2 Demographics, surgical techniques and patient-reported outcomes

Author	Year	Study design	Number of wrists	Indication	Mean age (yr)	Fixation Technique	VAS		DASH		MINORS (%)
							Preop	Postop	Preop	Postop	
Cha SM	2013	Retrospective case series	40	SLAC	47	K-wires	6.3	2.0	44	17	75
Luegmair M	2012	Retrospective case series	24	SLAC, SNAC, SCAC	53	Plates	-	-	-	19	75
Bain GI	2010	Prospective cohort study	31	SLAC	47	Staples	6.0	1.0	-	-	87
Berkhout MJL	2015	Retrospective cohort study	8	SLAC, SNAC	45	K-wires	-	0.3	-	-	62
Kitzinger HB	2003	Retrospective case series	37	SLAC, SNAC	46	K-wires	2.7	1.7	-	24	62
Trail I	2015	Retrospective case series	116	SLAC, SNAC	47	K-wires, Plates, Staples, Screws	-	1.9	-	37	62
Neubrech F	2012	Retrospective case series	60	SLAC, SNAC, unclassified OA	63	K-Wires	-	1.4	-	20	87
Odella S	2018	Retrospective case series	20	SLAC, SNAC	53	Plates	-	2.0	-	17	62
Traverso P	2017	Retrospective case series	15	SLAC, SNAC	49	K-wires	-	-	-	8	62
Wagner ER	2017	Retrospective cohort study	51	Unclassified OA	34	Plates	-	-	-	19	75
Williams J	2018	Retrospective cohort study	61	SLAC, SNAC, perilunate OA	52	K-wires, Plates, Screws	-	1.0	-	27	50
Total/Averages			463		49			1.4		21	69
SD					± 7			± 0.6		± 8	± 11

SD: Standard deviation; VAS: Visual analog scale; DASH: Disabilities of the Arm, Shoulder and Hand questionnaire; SLAC: Scapholunate advanced collapse; SNAC: Scaphoid nonunion advanced collapse; SCAC: Scaphoid chondrocalcinosis advanced collapse; MINORS: Methodological items for non-randomized studies; OA: Osteoarthritis; K-wires: Kirschner wires.

Patient-reported outcomes

Preoperative VAS and DASH scores were only reported in a minority of studies (3 for VAS[14,15,22] and 1 for DASH[14]), which did not allow direct pre- to postoperative comparison (Table 2). Eight studies reported on postoperative VAS score and averaged 1 ± 1 (range: 0-2) at the latest follow-up. Postoperative data on DASH scores were pooled from 9 studies[3,5,14-18,20,21], which averaged 21 ± 8 (range: 8-37).

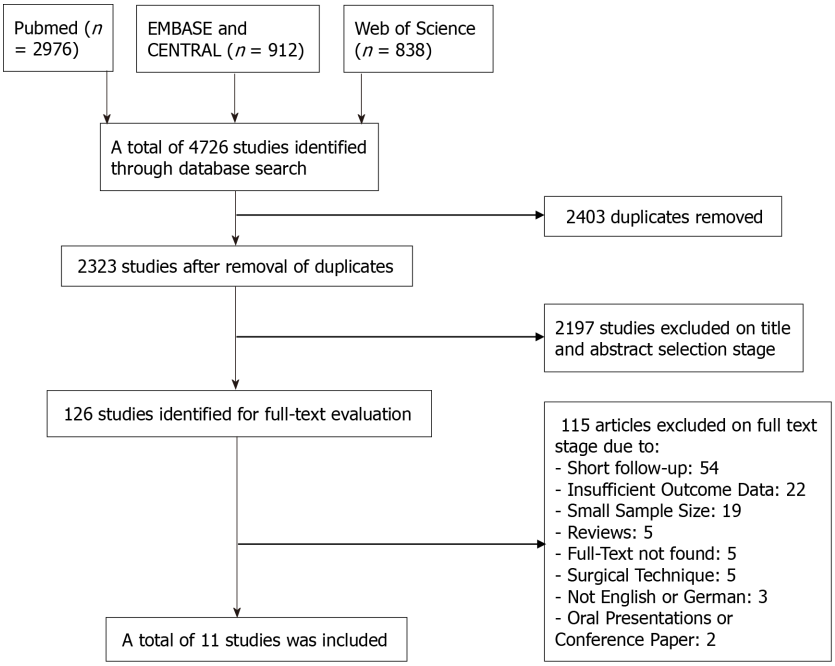


Figure 1 Flowchart of the systematic search.

Fusion rates, revisions and survivorship

The mean follow-up was 11 ± 4 years (range: 6-18 years) (Table 3). Revision rates were reported in 8 studies[3,14,16-18,20-22] and had an overall average of 13% (range: 5%-34%). Nine studies (82%)[3,14,16-22] included data on the total number of nonunions, averaging 9% (range: 0%-24%) at last follow-up, resulting in a fusion rate of 91% (range: 76%-100%). Eight studies[3,14,16-18,20-22] reported on conversion rates to a total wrist fusion (TWF). A conversion to a TWF was needed on average in 6% of cases (range: 0%-20%). There were no cases reported of conversion to total wrist arthroplasty.

Development of radiocarpal osteoarthritis

None of the included studies reported on preoperative signs of radiocarpal OA (Table 3). Five studies[5,14,15,18,20] reported on postoperative signs of radiocarpal OA of grade 2 or higher with an average incidence of 42% ± 26% (range: 5%-73%) at an average follow-up of 13 ± 3 years (range: 8-18 years). This was determined radiographically on conventional radiographs.

Grip strength and range of motion

Preoperative grip strength was only available in 5 studies and preoperative data on ROM in only 4 studies (Table 4), which did not allow meaningful comparison to the postoperative results. The postoperative grip strength was noted in 8 studies[3,5,14-17,20,22] and averaged 68% ± 18% of the contralateral side (range: 30%-85%). Total postoperative flexion-extension arc, noted in 10 studies[3,5,14-20,22], was on average 66 ± 9 (range: 54-87). Postoperative ROM for radial-ulnar deviation, available in 9 studies[3,5,14-16,18-20,22], averaged 34 ± 6 (range: 26-49).

Statistical analysis

The level of evidence of studies that were included lacked randomized controlled trials and did not allow performance of meta-analysis.

DISCUSSION

This is the first systematic review to investigate outcomes of the 4CF procedure at the long-term follow-up. The most important finding of the study is that 4CF can achieve good long-term patient satisfaction as well as good functional results. This can be observed out of the pooled data with low VAS values and positive DASH scores on

Table 3 Fusion rates, survivorship including rates of conversion to total wrist fusion and complications

Author	Number of wrists	Fixation technique	Nonunion (*n*)	Fusion (%)	Revisions (%)	Conversion to TWF (%)	Complications
Cha SM	40	K-wires	0	100	2 (5)	1 (3)	1 x impingement
Luegmair M	24	Plates	2	92	2 (8)	0	-
Bain GI	31	Staples	3	90	5 (16)	2 (7)	1 x delayed union
Berkhout MJL	8	K-wires	1	88	-	-	1 x CRPS, 1 x delayed union
Kitzinger HB	37	K-wires	-	-	-	-	-
Trail I	116	K-wires, plates, staples, screws	28	76	14 (12)	6 (5)	3 x impingement
Neubrech F	60	K-wires	-	-	-	-	-
Odella S	20	Plates	0	100	1 (5)	0	1 x implant loosening
Traverso P	15	K-wires	0	100	2 (13)	1 (7)	-
Wagner ER	51	Plates	6	88	15 (29)	6 (12)	1 x infection, 8 x impingement
Williams J	61	K-wires, plates, screws	3	95	21 (34)	12 (20)	4 x impingement, 1 x ulnar impaction, 1 x infection
Totals/Averages	463		43 (9%)	91 ± 7	62 (13%)	28 (6%)	

TWF: Total wrist fusion; CRPS: Complex regional pain syndrome; K-wires: Kirschner wires.

Table 4 Range of motion and grip strength

Author	Grip strength (%)		ROM Flexion-extension		ROM radial-ulnar (%)	
	Preop	Postop	Preop	Postop	Preop	Postop
Cha SM	71	85	84	66	45	39
Luegmair M	38	70	57	64	24	30
Bain GI	27	30	78	57	35	30
Berkhout MJL	-	-	-	87	-	49
Kitzinger HB	69	80	68	62	35	34
Trail I	-	53	-	60	-	26
Neubrech F	-	85	-	63	-	30
Odella S	-	75	-	79	-	-
Traverso P	-	-	-	69	-	33
Wagner ER	60	65	-	54	-	32
Williams J	-	-	-	-	-	-
Averages	53	68	72	66	35	34
SD	± 17	± 18	± 10	± 10	± 8	± 6

ROM: Range of motion; SD: Standard deviation; Preop: Preoperative; Postop: Postoperative.

last follow-up. An average fusion rate over 90% could be achieved, however with large variations across studies. Trail *et al*[3] reported a high nonunion percentage with only 76% fusion, further indicating the future need of 4CF for technique improvements and advancements in implant choice. Surprisingly, in the case of a successful 4CF, only an average of 6% of ultimate conversion to TWF was observed. This was in the context of lacking data on the preoperative state of the radiolunate joint, where a substantial amount could have been present at the time of surgery.

Nevertheless, the quality assessment provided important data on the evidence level of the studies, where relevant issues were elucidated. First, there were no double-blinded randomized controlled trials. Second, the single prospective cohort study, as declared by authors, had a questionable design whereas only the data collection might have been prospective[22]. The lack of preoperative data for almost all functional outcomes (ROM, grip strength) in the majority of studies precludes the quantification of the clinical gain from surgery[5,17-21]. Another important limitation was the fact that the outcomes were mostly reported in a cumulative fashion and not longitudinally over time. As such, a subgroup analysis of outcomes based on etiology (degenerative or post-traumatic) or the creation of a Kaplan-Meier survivorship curve to observe the time points of conversions could not be performed.

Although many treatments are available for scapholunate collapse and scaphoid nonunion advanced collapse wrist[23], the main debatable alternative to 4CF is the PRC[24,25]. A systematic review of long-term outcomes of PRC studies reported a reoperation rate of 14.3%[26].Of particular value is to mention that these failures were not only represented by conversions to TWF but also contained cases where revision arthroplasty was undertaken[4]. As such, the reoperation rates and conversion rates to TWF were not equal in this systematic review[26]. Generally, it was thought that PRC might yield better ROM[27]. However, this cannot be stated consistently, as recent systematic reviews and meta-analysis question the clinical relevance of differences that were observed between these techniques[2]. These relevant differences were limited to ROM, grip strength and patient-reported outcomes. In contrast, another systematic review reported a benefit in 4CF in terms of grip strength[28].

A further subject that was recently explored is the cost-effectiveness of PRC, where findings yielded either superior[29,30] or similar results[31] when compared to 4CF. Revision rates, especially during early follow-up, are higher in 4CF among some reports[21], highlighting impingement of hardware and nonunion as main reasons of revision[32]. This is attributed by authors to technical challenges and aspects, such as incomplete removal of the cartilage and subchondral bone, which is a key step of the procedure[11], quality and location of bone graft[33] as well as compression and carpal height achieved[34]. Optimal placement has yet to be defined to avoid revisions in 4CF due to impingement[32].

As such, in the context of continuous debate, an analysis of the long-term results, especially of the ultimate conversion rate to TWF or wrist arthroplasty, is crucial in determining the long-term benefit when choosing the surgical treatment option. The current systematic review is a substantial contribution to the understanding and knowledge of 4CF long-term outcomes as well as an analytical exploration of the limitations of studies (sources of heterogeneity and bias) that provide recommendations for future work.

CONCLUSION

The 4CF of the wrist is a reliable surgical technique, capable of achieving a good long-term patient satisfaction and survivorship with low rates of conversion to total wrist fusion.

ARTICLE HIGHLIGHTS

Research background

Four-corner fusion (4CF) is a motion sparing salvage procedure that is used to treat osteoarthritis secondary to advanced collapse or longstanding scaphoid nonunion advanced collapse. Proximal row carpectomy and 4CF are the two mainly used surgical techniques in such cases. The decision to choose one technique over the other is primarily based on the surgeon's preference and experience, as long-term results are not clearly elucidated in the current literature so far.

Research motivation

The long-term survivorship and ultimate conversion rate of 4CF to wrist arthrodesis remains poorly described. As various fixation techniques have been employed (Kirschner wires, headless compression screws, staples, plates), different potential complications have been observed, in particular, nonunion, progressive osteoarthritis or hardware impingement/irritation. There is no consensus on the best surgical

implant and no synthesis on the long-term outcomes.

Research objectives

To provide a systematic approach on evaluating evidence reporting on the long-term outcomes of 4CF with appropriate tools for critical appraisal. We aimed to compare patient-reported outcomes, fusion rates, grip strength, range of motion and rates of development of radiocarpal osteoarthritis and revision to total wrist fusion.

Research methods

A study protocol for the systematic search was registered prospectively in the international prospective register (PROSPERO) and performed according to the PRISMA guidelines. Data collection included fusion rates, revision rates and conversion rates to total wrist arthrodesis. Wrist range of motion, including wrist flexion and extension, total flexion-extension arc, as well as radial-ulnar deviation, was extracted. Grip strength was noted as percentage of the opposite hand. Patient-reported outcome measures were included as the Disabilities of the Arm, Shoulder, and Hand questionnaire and the visual analog scale scores (Table 4). Where available, data regarding incidence of radiolunate arthritis was included. The quality of all the studies were then assessed using the Methodological Index for Non-Randomized Studies criteria.

Research results

A total of 11 studies including 436 wrists with a mean follow-up of 11 ± 4 years (range: 6-18 years) was included. Quality assessment according to Methodological Index for Non-Randomized Studies criteria tool averaged 69% ± 11% (range: 50%-87%). Fusion rate could be extracted from 9/11 studies and averaged 91%. Patient-reported outcomes were extracted at last follow-up from 8 studies with an average visual analog score of 1 ± 1 (range: 0-2) and across 9 studies with an average Disabilities of the Arm, Shoulder, and Hand score of 21 ± 8 (range: 8-37). The postoperative grip strength was noted in 8 studies and averaged 68% ± 18% of the contralateral side. Total postoperative flexion-extension arc was on average 66 ± 9. At last follow-up, the cumulative conversion rate to total wrist fusion averaged 6%.

Research conclusions

The 4CF of the wrist is a reliable surgical technique, capable of achieving a good long-term patient satisfaction and survivorship with low rates of conversion to total wrist fusion.

Research perspectives

Future studies should define their study populations and protocols a priori before analysis. More in-depth details regarding patient selection (mostly preoperative data on range of motion, grip strength and radiolunate osteoarthritis) should be provided that would allow objective comparison.

REFERENCES

1 **Mulford JS**, Ceulemans LJ, Nam D, Axelrod TS. Proximal row carpectomy vs four corner fusion for scapholunate (SLAC) or scaphoid nonunion advanced collapse (SNAC) wrists: A systematic review of outcomes. *Hand Surg Eur Vol* 2009 [DOI: 10.1177/1753193409347481]

2 **Amer KM**, Thomson JE, Vosbikian MM, Ahmed I. Four-Corner Arthrodesis Versus Proximal Row Carpectomy for Scapholunate Advanced Collapse: A Systematic Literature Review and Meta-analysis. *Ann Plast Surg* 2020; **85**: 699-703 [PMID: 32384352 DOI: 10.1097/SAP.0000000000002398]

3 **Trail I**, Murali R, Stanley J, Hayton M, Talwalkar S, Sreekumar R, Birch A. The Long-Term Outcome of Four-Corner Fusion. *J Wrist Surg* 2015 [DOI: 10.1055/s-0035-1549277]

4 **Ali MH**, Rizzo M, Shin AY, Moran SL. Long-term outcomes of proximal row carpectomy: a minimum of 15-year follow-up. *Hand (N Y)* 2012; **7**: 72-78 [PMID: 23449142 DOI: 10.1007/s11552-011-9368-y]

5 **Neubrech F**, Mühldorfer-Fodor M, Pillukat T, Schoonhoven Jv, Prommersberger KJ. Long-term results after midcarpal arthrodesis. *J Wrist Surg* 2012; **1**: 123-128 [PMID: 24179715 DOI: 10.1055/s-0032-1329616]

6 **Watson HK**, Ballet FL. The SLAC wrist: scapholunate advanced collapse pattern of degenerative arthritis. *J Hand Surg Am* 1984; **9**: 358-365 [PMID: 6725894 DOI: 10.1016/S0363-5023(84)80223-3]

7 **Krakauer JD**, Bishop AT, Cooney WP. Surgical treatment of scapholunate advanced collapse. *J Hand Surg Am* 1994; **19**: 751-759 [PMID: 7806795 DOI: 10.1016/0363-5023(94)90178-3]

8 **Espinoza DP**, Schertenleib P. Four-corner bone arthrodesis with dorsal rectangular plate: series and personal technique. *J Hand Surg Eur Vol* 2009; **34**: 609-613 [PMID: 19587076 DOI: 10.1177/1753193409105684]

9 **Ozyurekoglu T**, Turker T. Results of a method of 4-corner arthrodesis using headless compression screws. *J Hand Surg Am* 2012; **37**: 486-492 [PMID: 22305735 DOI: 10.1016/j.jhsa.2011.12.022]

10 **Wyrick JD**, Stern PJ, Kiefhaber TR. Motion-preserving procedures in the treatment of scapholunate advanced collapse wrist: proximal row carpectomy versus four-corner arthrodesis. *J Hand Surg Am* 1995; **20**: 965-970 [PMID: 8583069 DOI: 10.1016/S0363-5023(05)80144-3]

11 **Vance MC**, Hernandez JD, Didonna ML, Stern PJ. Complications and outcome of four-corner arthrodesis: circular plate fixation versus traditional techniques. *J Hand Surg Am* 2005; **30**: 1122-1127 [PMID: 16344166 DOI: 10.1016/j.jhsa.2005.08.007]

12 **Bedford B**, Yang SS. High fusion rates with circular plate fixation for four-corner arthrodesis of the wrist. *Clin Orthop Relat Res* 2010; **468**: 163-168 [PMID: 19838645 DOI: 10.1007/s11999-009-1139-5]

13 **Slim K**, Nini E, Forestier D, Kwiatkowski F, Panis Y, Chipponi J. Methodological index for non-randomized studies (minors): development and validation of a new instrument. *ANZ J Surg* 2003; **73**: 712-716 [PMID: 12956787 DOI: 10.1046/j.1445-2197.2003.02748.x]

14 **Cha SM**, Shin HD, Kim KC. Clinical and radiological outcomes of scaphoidectomy and 4-corner fusion in scapholunate advanced collapse at 5 and 10 years. *Ann Plast Surg* 2013; **71**: 166-169 [PMID: 23277107 DOI: 10.1097/SAP.0b013e31824b3e1e]

15 **Kitzinger HB**, Löw S, Karle B, Lanz U, Krimmer H. Der posttraumatische karpale Kollaps-Längerfristiger Verlauf nach mediokarpaler Teilarthrodese. *Handchirurgie Mikrochirurgie Plast Chir* 2003 [DOI: 10.1055/s-2003-43116]

16 **Luegmair M**, Houvet P. Effectiveness of four-corner arthrodesis with use of a locked dorsal circular plate hand. *Clin Orthop Relat Res* 2012 [DOI: 10.1007/s11999-012-2312-9]

17 **Odella S**, Querenghi AM, Locatelli FM, Dacatra U, Creta E, Tos P. Locking Dorsal Plate in Four-Bone Arthrodesis in SLAC and SNAC 3 Wrist. *Joints* 2018; **6**: 37-41 [PMID: 29675505 DOI: 10.1055/s-0038-1626738]

18 **Traverso P**, Wong A, Wollstein R, Carlson L, Ashmead D, Watson HK. Ten-Year Minimum Follow-Up of 4-Corner Fusion for SLAC and SNAC Wrist. *Hand (N Y)* 2017; **12**: 568-572 [PMID: 29091493 DOI: 10.1177/1558944716681949]

19 **Berkhout MJ**, Bachour Y, Zheng KH, Mullender MG, Strackee SD, Ritt MJ. Four-Corner Arthrodesis Versus Proximal Row Carpectomy: A Retrospective Study With a Mean Follow-Up of 17 Years. *J Hand Surg Am* 2015; **40**: 1349-1354 [PMID: 25701487 DOI: 10.1016/j.jhsa.2014.12.035]

20 **Wagner ER**, Werthel JD, Elhassan BT, Moran SL. Proximal Row Carpectomy and 4-Corner Arthrodesis in Patients Younger Than Age 45 Years. *J Hand Surg Am* 2017; **42**: 428-435 [PMID: 28410937 DOI: 10.1016/j.jhsa.2017.03.015]

21 **Williams J**, Weiner H, Tyser A. Long-Term Outcome and Secondary Operations after Proximal Row Carpectomy or Four-Corner Arthrodesis. *J Wrist Surg* 2018 [DOI: 10.1055/s-0037-1604395]

22 **Bain GI**, Watts AC. The outcome of scaphoid excision and four-corner arthrodesis for advanced carpal collapse at a minimum of ten years. *J Hand Surg Am* 2010; **35**: 719-725 [PMID: 20381980 DOI: 10.1016/j.jhsa.2010.01.025]

23 **Abdelaziz AM**, Aldahshan W, Elsherief FAH, Wahd YESH, Soliman HAG, El Behairy HF, Ismail MA. Scaphoid excision with lunatocapitate fusion for the treatment of scaphoid nonunion with advanced collapsed wrist. *Int Orthop* 2020; **44**: 1153-1157 [PMID: 32303792 DOI: 10.1007/s00264-020-04570-5]

24 **Streich NA**, Martini AK, Daecke W. Proximal row carpectomy: an adequate procedure in carpal collapse. *Int Orthop* 2008; **32**: 85-89 [PMID: 17089124 DOI: 10.1007/s00264-006-0281-x]

25 **Zhang Y**, Gillis JA, Moran SL. Management of scapholunate advanced collapse and scaphoid nonunion advanced collapse without proximal row carpectomy or four corner fusion. *J Hand Surg Eur Vol* 2021; **46**: 50-57 [PMID: 33202162 DOI: 10.1177/1753193420973322]

26 **Chim H**, Moran SL. Long-term outcomes of proximal row carpectomy: a systematic review of the literature. *J Wrist Surg* 2012; **1**: 141-148 [PMID: 24179718 DOI: 10.1055/s-0032-1329547]

27 **Van Nuffel M**, Vanhees M, Maeckelbergh L, Degreef I, De Smet L. Four-corner fusion versus proximal row carpectomy : a retrospective review with a minimal follow-up of 9 years. *Acta Orthop Belg* 2020; **86**: 146-150 [PMID: 32490786]

28 **Saltzman BM**, Frank JM, Slikker W, Fernandez JJ, Cohen MS, Wysocki RW. Clinical outcomes of proximal row carpectomy versus four-corner arthrodesis for post-traumatic wrist arthropathy: a systematic review. *J Hand Surg Eur Vol* 2015; **40**: 450-457 [PMID: 25294736 DOI: 10.1177/1753193414554359]

29 **Yoo M**, Nelson RE, Illing DA, Martin BI, Tyser AR, Kazmers NH. Cost-Effectiveness Analysis Comparing Proximal Row Carpectomy and Four-Corner Arthrodesis. *JB JS Open Access* 2020; **5**: e0080 [PMID: 33123669 DOI: 10.2106/JBJS.OA.19.00080]

30 **Retrouvey H**, Sander B, von Schroeder HP, Binhammer P, Baltzer HL. Cost-Effectiveness Analysis of Motion-Preserving Operations for Wrist Arthritis. *Plast Reconstr Surg* 2020; **146**: 588e-598e [PMID: 33141535 DOI: 10.1097/PRS.0000000000007260]

31 **Daar DA**, Shah A, Mirrer JT, Thanik V, Hacquebord J. Proximal Row Carpectomy versus Four-

Corner Arthrodesis for the Treatment of Scapholunate Advanced Collapse/Scaphoid Nonunion Advanced Collapse Wrist: A Cost-Utility Analysis. *Plast Reconstr Surg* 2019; **143**: 1432-1445 [PMID: 31033826 DOI: 10.1097/PRS.0000000000005558]

32 **Shindle MK**, Burton KJ, Weiland AJ, Domb BG, Wolfe SW. Complications of circular plate fixation for four-corner arthrodesis. *J Hand Surg Eur Vol* 2007; **32**: 50-53 [PMID: 17049699 DOI: 10.1016/j.jhsb.2006.08.016]

33 **Athlani L**, Sabau S, Pauchard N, Dap F, Dautel G. Four-corner arthrodesis with a dorsal locking plate: 4-9-year follow-up. *J Hand Surg Eur Vol* 2020; **45**: 673-678 [PMID: 32536296 DOI: 10.1177/1753193420930587]

34 **Laronde P**, Christiaens N, Aumar A, Chantelot C, Fontaine C. Carpal height and postoperative strength after proximal row carpectomy or four-corner arthrodesis: Clinical, anatomical and biomechanical study. *Hand Surg Rehabil* 2016; **35**: 100-106 [PMID: 27117123 DOI: 10.1016/j.hansur.2016.01.003]



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MINIREVIEWS

Developments in diagnosis and treatment of paediatric septic arthritis

Cornelia M Donders, Anne J Spaans, Herbert van Wering, Christiaan JA van Bergen

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Abstract

Acute septic arthritis in children is an orthopaedic emergency. A delay in diagnosis and inappropriate treatment can result in devastating damage to the joint with lifelong disability as a consequence. The clinical presentation can be a diagnostic challenge, especially in young children. A recent systematic review showed that joint tenderness and fever are important signals of septic arthritis. Ultrasound is helpful in detecting the presence of a joint effusion. Plain radiographs may show bone changes but magnetic resonance imaging is the most reliable imaging study for detecting concomitant osteomyelitis. The diagnosis of acute septic arthritis is highly suggestive when pus is aspirated from the joint, in case of a positive culture or a positive gram stain of the joint fluid, or if there is a white blood-cell count in the joint fluid of more than 50000/mm^3. *Staphylococcus aureus* is the most commonly cultured organism. Recent systematic reviews have identified the most effective drainage techniques, including needle aspiration, arthroscopy and arthrotomy, depending on the affected joint. After the drainage procedure it is important to monitor the clinical and laboratory outcomes. Additional drainage procedures may be necessary in select cases.

Key Words: Septic arthritis; Paediatric; Children; Analysis; Treatment; Drainage

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Core Tip: This article provides an up-to-date evidence-based review on the diagnosis and treatment of paediatric septic arthritis. Acute septic arthritis in children is an orthopaedic emergency. It can be a diagnostic challenge, especially in young children. Accurate history, physical exam, laboratory findings and imaging can contribute to the diagnosis of septic arthritis. The following step of joint aspiration with an appropriate treatment must be made in a short time period. Clinical predicting tools and optimal drainage techniques for paediatric septic arthritis were evaluated in recent systematic reviews. After the drainage procedure it is important to monitor the clinical and laboratory outcomes.

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INTRODUCTION

Acute septic arthritis in children is an orthopaedic emergency. Since the clinical presentation can be similar to other joint pathologies, acute septic arthritis is a diagnostic challenge. This is especially true for infants and neonates, in whom refusal to feed, crying and discomfort with limitations of joint movement can be the presenting symptoms. A delay in diagnosis and inappropriate treatment can result in a devastating damage to the joint with lifelong disability as a consequence[1]. According to laboratory evidence, the loss of glycosaminoglycan in cartilage begins within eight hours after the onset of an infection in a joint[2]. An increase in intracapsular pressure in the hip joint, when not promptly decompressed, may lead to compressive ischemia and avascular necrosis of the femoral head[3]. Therefore, it is important to perform an appropriate diagnostic workup and an optimal treatment of this challenging disease. In 2020, a systematic review was published that stated the test characteristics of history, physical examination and laboratory and image investigations in the evaluation for septic arthritis in children presenting with an acute nontraumatic limp[4]. Recently, we published two systematic reviews with a clear overview of the literature on drainage techniques for septic knee and hip arthritis in children[5,6]. In this evidence-based current concept review we therefore provide an update on the diagnostic workup and treatment of paediatric septic arthritis.

BACKGROUND

Epidemiology

The incidence of septic arthritis is two to seven per 100000 children in Europe and three to four per 100000 in the United States of America[7-9]. The highest incident rates are seen among the group of children aged between zero and four years old[9]. Septic arthritis is typically monoarticulair. The most commonly affected joints are the hip (32%-39%) and knee (26%-47%). Other affected joints are ankle (9%-18%), shoulder (2%-12%), elbow (4%-13%) and wrist (1%-2%)[9-14]. Septic arthritis is 1.4 to 1.7 times more common in males than in females[9,10,12].

Bacteriology

Staphylococcus aureus is the most commonly cultured organism. Other common pathogens are *Kingella kingae*, *Streptococcus pyogenes* and *Streptococcus pneumoniae*[10,15,16]. High prevalence of *Salmonella* infection is seen in patients with septic arthritis from Africa[17,18]. The causative pathogens overall can vary depending on the child's age, immunodeficiency, socio-economic factors and vaccination status[9]. *Kingella kingae* is more frequently isolated among children under 36 mo of age in comparison to older children[15]. Before an effective vaccine, *Haemophilus influenzae* type B was a very common cause of septic hip arthritis. This pathogen is now rarely reported in well-immunized populations[19-21]. Some causative organisms are less common, but are seen in specific groups. *Salmonella typhi* can be suspected outside Africa in children with sickle cell disease and has been found in immunoincompetent children [22,23]. *Pseudomonas aeruginosa* is often found after a wound nearby the joint and *Pasteurella canis* is found most often after animal bites[23,24]. *Neisseria gonorrhoeae* should be suspected in sexually active adolescents or in cases of sexual abuse[25].

In 2010, Pääkkönen *et al*[20], showed in septic hip arthritis in children with culture-positive cases that bacteria grew from the synovial fluid only in 34 percent cases, from blood in only 27 percent cases, and from both joint and blood in 39 percent cases.

DIAGNOSIS

Clinical presentation

The classical presentation of septic arthritis in children is a combination of a painful joint with limited range of movement, the inability to bear weight on the involved limb, fever and malaise[3,26-28]. The symptoms can rapidly progress in hours. At physical examination, effusion, erythema, heat, tenderness to palpation and, in the lower extremities, inability to bear weight can be seen. The affected joint is irritable and is most often held in a position of comfort, one that maximizes intracapsular volume. For example, the hip is flexed, abducted, and externally rotated. A characteristic sign is micromotion tenderness[28]. A recent systematic review showed that the presence of joint tenderness and fever increases the risk of septic arthritis[4]. The presence of fever (≥ 38.5°C) has a positive likelihood ratio (LR) of 2.1 to 18.2. The absence of fever had a negative LR of 0.2 to 0.6. Joint tenderness had a positive LR of 11.4 and a negative LR of 0.3[4].

During infancy, the clinical presentation differs from the presentation in older children. Sepsis is often the first notable presentation of septic arthritis in neonates and infants. The symptoms are comprehensive and include irritability, failure to feed or gain weight and muscular spasm. Also, fever, tachycardia, anaemia and the presence of associated infection are occasionally seen. Involvement of the hip joint must be suspected in any infant with sepsis. The following characteristics at physical examination can be present: pain on palpation or passive movement of the hip, lack of active movement of the leg, asymmetrical buttock creases, unilateral oedema or swelling of an extremity, a buttock or the genitalia[29].

Paediatric septic arthritis can occur several weeks after an upper respiratory infection. In infants and neonates, underlying diseases have been recognized as risk factors for septic arthritis, including respiratory distress syndrome, congenital anomalies and extremely low birth weight[30].

Laboratory studies

The initial laboratory testing for a patient with suspected osteoarticular infection should consist of serum samples with complete blood count, Erythrocyte sedimentation rate (ESR), C-reactive protein (CRP) and two blood cultures[31,32]. In 1999, Kocher *et al*[33] identified four predictors that, by combining, had excellent diagnostic performance in differentiating between septic hip arthritis and transient synovitis of the hip in children. These four predictors were a history of fever, non-weight-bearing, an ESR of at least 40 mm/h, and a serum white blood-cell (WBC) count of more than 12000 cells/mm^3. Kocher *et al*[34] concluded that patients with a very high probability of septic arthritis of the hip have three or four positive predictors. They advised that these patients may be good candidates for aspiration in the operating room, given the likelihood that subsequent arthrotomy and drainage will be needed. Patients who have an intermediate probability (two positive predictors) of septic arthritis of the hip may be good candidates for aspiration under ultrasound. Patients who have an extremely low probability (zero or one positive predictors) of septic arthritis of the hip may be appropriate candidates for careful observation without aspiration. After five years, this clinical prediction algorithm was validated in a prospective study[34]. In 2006, Caird *et al*[35] in a prospective study added an elevated CRP level to the Kocher criteria. They stated that a CRP level of more than 2.0 mg/dL (> 20 mg/L) is a strong independent predictor. A recent systematic review showed that the performances of both clinical risk prediction tools are somewhat lower than originally reported. The predicted probability of septic arthritis for the Kocher criteria ranges from 59.1% to 99.6%; this probability remains similar (60% to 98%) when CRP is added[4].

Imaging

Plain radiographs are the next step in the diagnostic workup of paediatric septic arthritis, mainly to rule out bone changes. Additionally, an increased joint space of the affected septic joint may be visualized on radiographs. In case of suspected hip arthritis, an anteroposterior pelvic radiograph allows assessment of the joint space compared to the contralateral hip.

Both ultrasound and magnetic resonance imaging (MRI) are good non-invasive diagnostic tools without radiation exposure in the evaluation of septic arthritis. Ultrasound is an easily implicated diagnostic tool for detecting the presence of a joint effusion[3]. Joint effusion on ultrasound is seen in 91 percent of patients with septic arthritis[36]. However, it cannot distinguish between sterile, purulent, and hemo-rrhagic fluid accumulations[37]. The data from a negative ultrasound in children with less than 24 h of symptoms should be used with caution and must be interpreted along with a careful history and physical examination[38]. An advantage of ultrasound is that no sedation is required in young children. Furthermore, ultrasound is more sensitive in detecting joint effusion and synovial swelling in children with septic arthritis compared to radiography and MRI[4,36]. One drawback of ultrasound is that it can be user-dependent. In addition, it does not necessarily rule out osteomyelitis or nearby intramuscular abscesses.

Although costly, MRI is the most reliable imaging study for detecting bone and periosteal changes in patients with concomitant osteomyelitis[36,39]. Also, MRI can be used to distinguish septic arthritis of the hip from a psoas abscess and help identify adjacent infection sites. However, in young children

sedation in often needed. Although, after the MRI there is a possibility to go straight to the operation room under continuous sedation for a drainage procedure. Recently, an algorithm has been proposed to help identify patients at risk for adjacent infections who would benefit from MRI to identify additional sites of infection. This algorithm contains five variables: older than 3.6 years, CRP > 13.8 mg/L, duration of symptoms > 3 d, platelets < 314 × 10 cells per μL (microliter), and absolute neutrophil count > 8.6 × 10 cells per μL. Patients with three or more risk factors are classified as high risk for having an adjacent infection and would benefit from MRI[40].

Microbiology testing

Synovial fluid analysis by aspiration is an important part of the diagnostic workup when septic arthritis is suspected. Synovial fluid should be sent for white blood cell count, gram stain, culture and antibiotic sensitivity. The diagnosis of acute septic arthritis is highly suggestive when pus is aspirated from the joint, when there is a positive culture of the joint fluid, a positive gram stain of the joint fluid or a WBC count in the joint fluid of > 50000/mm^3. Despite appropriate cultures, a notable proportion remains culture negative. Polymerase chain reaction testing of synovial fluid for *Kingella kingae* (generally seen in children younger than 36 mo of age) and other fastidious pathogens increases detection, particularly in patients who received antibiotics before synovial fluid sampling[41,42].

DIFFERENTIAL DIAGNOSIS

It is important to consider several diseases in the differential diagnosis of septic arthritis[43].

The differentiation between septic hip arthritis and transient synovitis, also known as coxitis fugax, can be difficult because both conditions often present with similarities. Transient synovitis presents as an atraumatic, acutely irritable hip in a child who has progressive symptoms, often sub febrile temperature and refuses to bear weight. Transient synovitis is a self-limiting disorder that is managed nonoperatively and without antibiotics. It typically occurs in children between the ages of three to eight years, with a mean age at presentation of five to six years[44,45]. Most children have symptoms for less than a week at the time of presentation. However, in a retrospective review in 1986, 12 percent of patients had discomfort dating back at least one month[45]. The Kocher criteria can help differentiate between septic arthritis and transient synovitis[33,34]. A transient synovitis is plausible when zero predictors are found.

Juvenile idiopathic arthritis is usually polyarticular and often has gradual onset of symptoms. The first peak is between two to five years of age and the second is between 10 to 14 years of age. Joints are warm and markedly swollen, but not especially painful. The symptoms tend to be worst upon rising in the morning. Joint involvement is generally symmetric and most frequently affected locations are the knees, wrists and ankles. The hip is rarely the initial joint. Children with systematic onset of juvenile idiopathic arthritis and intermittent fever, often have a skin rash[46].

Lyme arthritis needs to be considered in lyme disease endemic areas. About 90 percent of children with Lyme disease present with erythema migrans, which is an early stage of the disease[47]. In six percent an arthritis can present, but arthritis is the most common manifestation of late Lyme disease. Monoarthritis of the knee is most common, but Lyme arthritis may also cause an asymmetric oligoarthritis. The affected joint is usually swollen and may be tender, but the pain is less intense and the range of motion greater as compared to bacterial arthritis. Besides, fever is uncommon[48,49].

In addition to clinical presentation and laboratory studies, plain radiographs should eliminate fracture and other structural diagnoses. For example, in children with pain in the hip or knee joint, plain radiographs are used to exclude slipped capital femoral epiphysis and Legg-Calvé-Perthes disease. Legg-Calvé-Perthes is a syndrome of idiopathic osteonecrosis (avascular necrosis) of the hip. It typically presents as hip pain and/or limp of acute or insidious onset in children between the ages of 3 to 12 years of age, with a peak incidence between five to seven years of age[50]. Stress fractures are rarely seen in children, but they can occur in athletes engaged in endurance sports. Sometimes the radiographs of Legg-Calvé-Perthes and stress fractures are negative and MRI is needed to confirm the diagnosis.

An MRI can also be used when osteomyelitis, pyomyositis, subperiosteal abscess, cellulitis, intramuscular abscess, or tumour are still in the differential diagnosis. MRI is the gold standard imaging technique for osteomyelitis[51]. The tibia and femur are the most commonly affected bones in children with osteomyelitis. A systematic review showed that the clinical features of osteomyelitis include fever (60%), localized pain (70%), reduced range of movement (50%) and reduced weight-bearing (50%)[51]. In contrast to isolated septic arthritis, the child with osteomyelitis usually allows some joint movement and pain-free range of motion with gentle examination. Osteomyelitis can occur next to septic arthritis (Figure 1).

Pyomyositis is a purulent infection of skeletal muscle that arises from haematogenous spread[52]. It commonly manifests as a local abscess but may also present as a diffuse inflammatory or a rapidly progressing myonecrotic process. The quadriceps, gluteal, and iliopsoas muscles are the most commonly affected anatomic sites[53]. It is classically an infection of the tropics (Africa and the South Pacific), although it has been recognized in temperate climates. Trauma has been postulated as a predis-

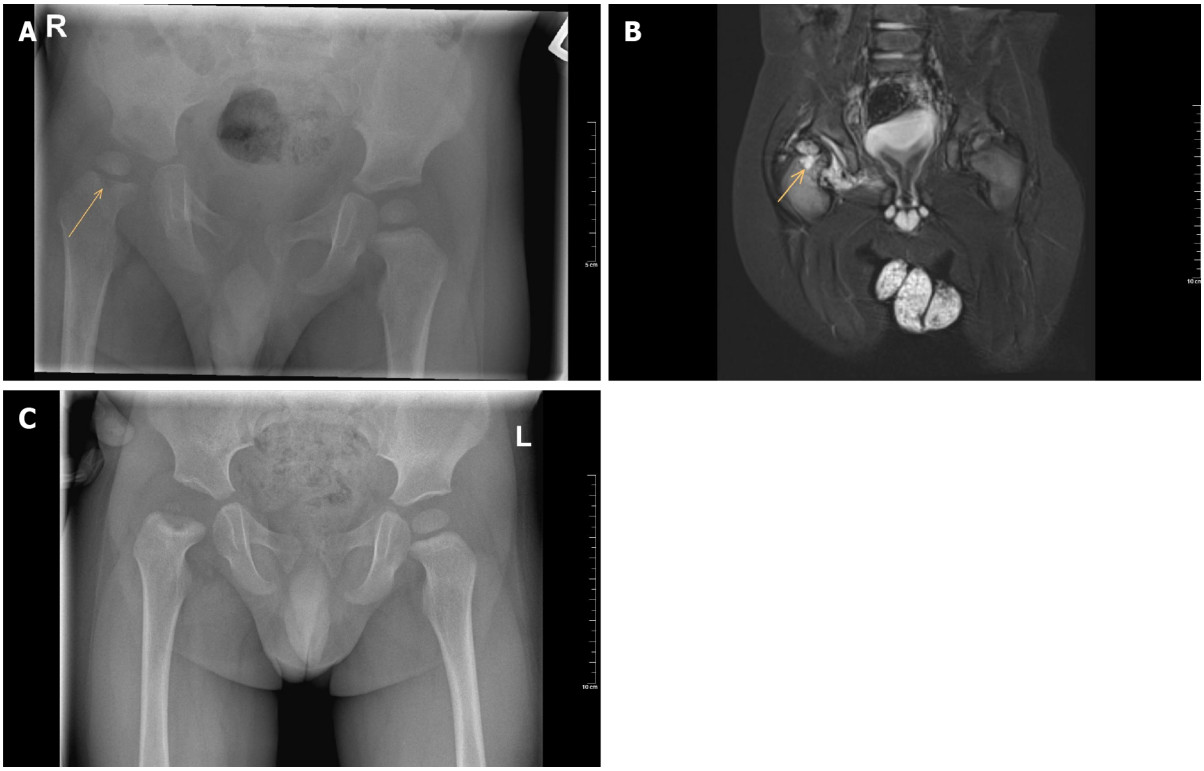


Figure 1 Radiograph images. A: Plain anteroposterior pelvic radiograph of a one-year-old boy with septic hip arthritis showing concomitant osteomyelitis of the proximal femur at the right side (arrow); B: T2 magnetic resonance imaging coronal view confirms joint effusion, suggestive of hip arthritis, and increased signal of the metaphysis, suggestive of osteomyelitis (arrow); C: Plain anteroposterior radiograph of the same boy after six months follow-up, which shows avascular necrosis of the femoral head.

posing factor for pyomyositis. Pyomyositis presents with fever and pain with cramping localized to a single muscle group. On physical examination, exquisite muscle tenderness, oedema, and/or fluctuance of the involved muscle group may be present. MRI is the optimal imaging technique, because it is highly sensitive for muscle inflammation (Figure 2)[53].

TREATMENT AND FOLLOW-UP

Drainage procedures

Paediatric septic arthritis can be treated by arthrocentesis (articular needle aspiration) with or without irrigation, arthroscopy or arthrotomy. All procedures are followed by antibiotics. Each of the drainage techniques have advantages and disadvantages within the different joints. Arthrocentesis, usually ultrasound-guided, has the advantage of a minimally invasive and short procedure. Generally, this can be used as a first procedure in different joints. However, in the very young, arthrocentesis requires an anaesthetic. Arthrocentesis without anaesthesia or sedation can be an anxiety-producing and painful experience. Advantages of arthroscopy include direct visualization of the joint, the ability to perform a complete debridement of the necrotic synovium and a thorough irrigation of the joint with minimal operative morbidity[54,55]. An arthrotomy gives a good overview of the joint and allows a thorough irrigation, but a disadvantage is a larger incision with more scar tissue. The anterior approach is the most mentioned approach for arthrotomy in paediatric septic hip arthritis[6].

Recent systematic reviews showed a clear overview of the literature on drainage techniques for septic knee and hip arthritis in children[5,6]. It was concluded that knee arthroscopy might have a lower risk of additional drainage procedures as compared to arthrocentesis and arthrotomy in paediatric septic knee arthritis[5]. In septic hip arthritis, arthrocentesis and arthroscopic procedures may have a higher risk of additional drainage procedures in comparison with arthrotomy. Nonetheless, arthrotomy in septic hip arthritis might be associated with inferior outcomes on the long term[6]. However, the studies about the optimal drainage procedure of the several joints were diverse and the scientific quality was generally low[5,6].

Antibiotics

Antibiotic coverage should start in suspected cases as soon as cultures and synovial fluid samples are collected and the joint has been drained, unless the patient is septic[26,27]. Most surgeons agree that

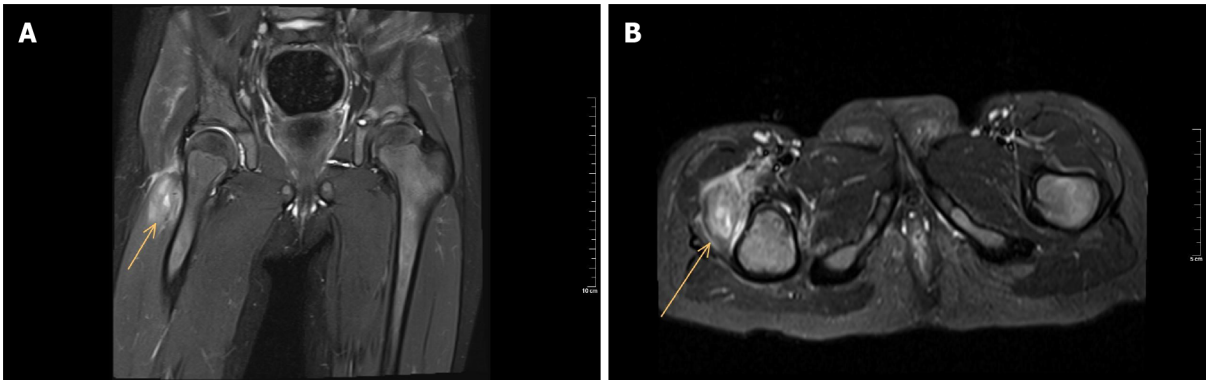


Figure 2 T2 magnetic resonance imaging of a three-year-old girl with pyomyositis of the vastus lateralis at the right side (arrow). There is no excessive fluid in the hip joint space. A: Coronal view; B: Sagittal view.

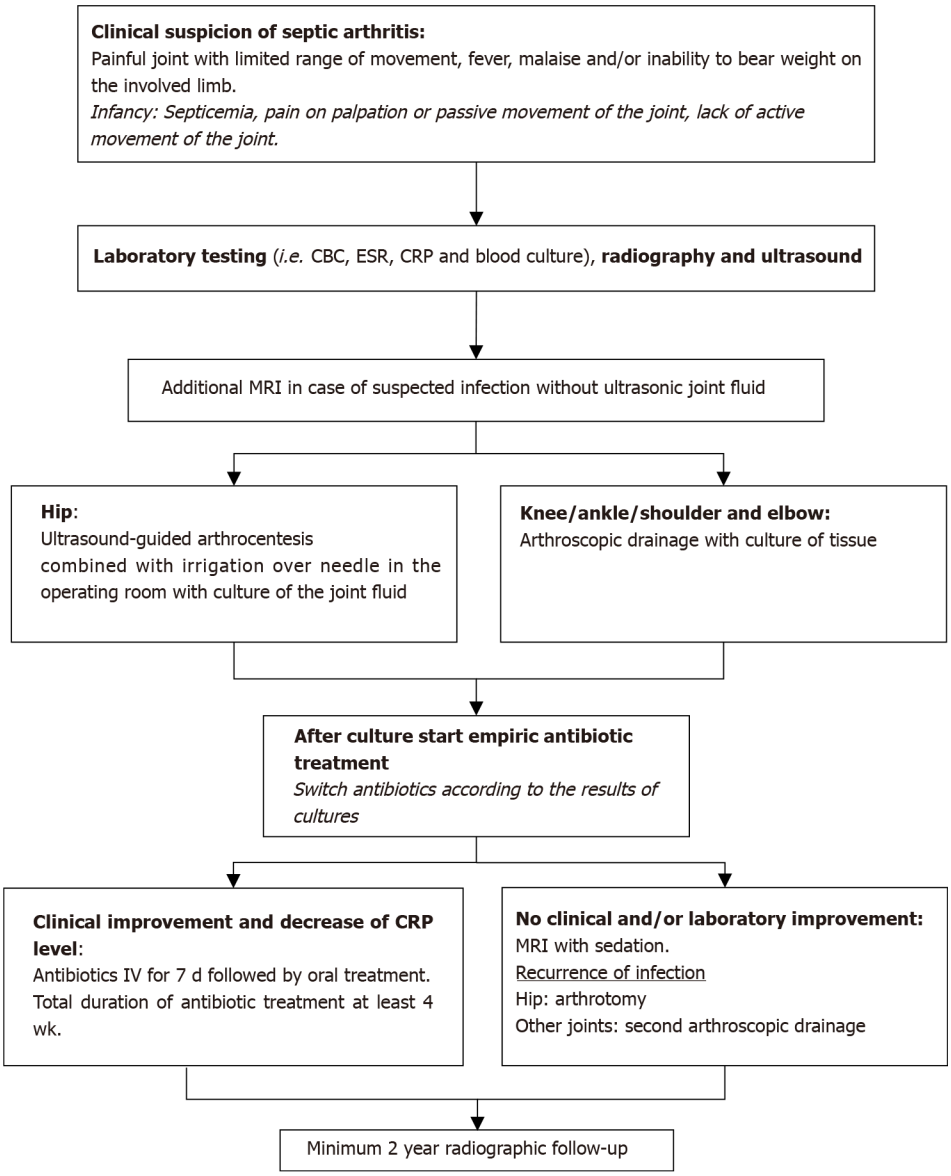


Figure 3 Diagnostic and treatment algorithm for paediatric septic arthritis. CBC: Complete blood count; ESR: Erythrocyte sedimentation rate; CRP: C-reactive protein; WBC: White blood cell; MRI: Magnetic resonance imaging; IV: Intravenous.

preoperative antibiotics should be avoided in the management of paediatric septic arthritis, because MacLean *et al*[56] showed that it leads to additional washouts and complications.

In consultation with the infectious disease team, the patient is transitioned to oral antibiotics after clinical and laboratory improvement, see Figure 3. It has been reported that the treatment with large doses of well-absorbed antimicrobials for 10 d (started intravenously for a few days only) is as effective as a 30 d treatment in children with septic arthritis, provided that the clinical response is good and the CRP level normalizes quickly[10]. However, the ideal duration of treatment has not yet been determined.

Follow-up

After the drainage procedure it is important to monitor the clinical and laboratory outcomes. Peltola *et al* [10] showed in a prospective trial that the CRP level and ESR can increase the first few days after starting the therapy. The highest scores were found on day two and three. A second or third drainage procedure is not exceptional[5,6].

The duration of symptoms between onset and the procedure is negatively associated with the prognosis, especially in infants and neonates with septic hip arthritis[30]. Septic hip arthritis can lead to serious musculoskeletal sequelae, which include: leg length discrepancy, pathologic hip dislocation, a hip joint surface irregularity, coxa magna or avascular necrosis (Figure 1C)[30]. Close follow-up with radiographic observation of at least two years is recommended.

RECOMMENDATIONS FOR FUTURE RESEARCH

There is a need for clinical risk prediction tools of paediatric septic arthritis to be prospectively validated [4]. Furthermore, the current literature about drainage techniques of paediatric septic arthritis is diverse and the quality is generally low[5,6]. Future prospective studies should ideally endeavour larger numbers of patients, define an established diagnosis of acute septic arthritis, report the delay between the first symptoms and the diagnosis, randomize treatment, and provide adequate follow-up time.

CONCLUSION

Paediatric septic arthritis can be a diagnostic challenge, especially in young children. A delay in diagnosis and inappropriate treatment can result in devastating damage to the joint with lifelong disability as a consequence. An accurate history, physical exam, laboratory findings and appropriate imaging can contribute to the diagnosis of septic arthritis. Prompt initiation of appropriate treatment is of paramount importance. After the drainage procedure it is important to monitor the clinical and laboratory outcomes. Based on the available scientific evidence, a diagnostic and treatment algorithm for paediatric septic arthritis is proposed (Figure 3).

FOOTNOTES

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REFERENCES

1 **Peters W**, Irving J, Letts M. Long-term effects of neonatal bone and joint infection on adjacent growth plates. *J Pediatr Orthop* 1992; **12**: 806-810 [PMID: 1452755 DOI: 10.1097/01241398-199211000-00020]
2 **Smith RL**, Schurman DJ, Kajiyama G, Mell M, Gilkerson E. The effect of antibiotics on the destruction of cartilage in experimental infectious arthritis. *J Bone Joint Surg Am* 1987; **69**: 1063-1068 [PMID: 3654698]
3 **Montgomery NI**, Epps HR. Pediatric Septic Arthritis. *Orthop Clin North Am* 2017; **48**: 209-216 [PMID: 28336043 DOI: 10.1016/j.ocl.2016.12.008]
4 **Tu J**, Gowdie P, Cassar J, Craig S. Test characteristics of history, examination and investigations in the evaluation for septic arthritis in the child presenting with acute non-traumatic limp. A systematic review. *BMJ Open* 2020; **10**: e038088 [PMID: 33380476 DOI: 10.1136/bmjopen-2020-038088]
5 **Donders CM**, Spaans AJ, Bessems JHJM, van Bergen CJA. Arthrocentesis, arthroscopy or arthrotomy for septic knee arthritis in children: a systematic review. *J Child Orthop* 2021; **15**: 48-54 [PMID: 33643458 DOI: 10.1302/1863-2548.15.200129]
6 **Donders CM**, Spaans AJ, Bessems JHJM, van Bergen CJA. A systematic review of the optimal drainage technique for septic hip arthritis in children. *Hip Int* 2021; 1120700021989666 [PMID: 33566696 DOI: 10.1177/1120700021989666]
7 **Faust SN**, Clark J, Pallett A, Clarke NM. Managing bone and joint infection in children. *Arch Dis Child* 2012; **97**: 545-553 [PMID: 22440930 DOI: 10.1136/archdischild-2011-301089]
8 **Peltola H**, Vahvanen V. A comparative study of osteomyelitis and purulent arthritis with special reference to aetiology and recovery. *Infection* 1984; **12**: 75-79 [PMID: 6610642 DOI: 10.1007/BF01641675]
9 **Okubo Y**, Nochioka K, Marcia T. Nationwide survey of pediatric septic arthritis in the United States. *J Orthop* 2017; **14**: 342-346 [PMID: 28706377 DOI: 10.1016/j.jor.2017.06.004]
10 **Peltola H**, Pääkkönen M, Kallio P, Kallio MJ; Osteomyelitis-Septic Arthritis (OM-SA) Study Group. Prospective, randomized trial of 10 days versus 30 days of antimicrobial treatment, including a short-term course of parenteral therapy, for childhood septic arthritis. *Clin Infect Dis* 2009; **48**: 1201-1210 [PMID: 19323633 DOI: 10.1086/597582]
11 **Speiser JC**, Moore TL, Osborn TG, Weiss TD, Zuckner J. Changing trends in pediatric septic arthritis. *Semin Arthritis Rheum* 1985; **15**: 132-138 [PMID: 4071065 DOI: 10.1016/0049-0172(85)90031-9]
12 **Cole WG**, Elliott BG, Jensen F. The management of septic arthritis in childhood. *Aust N Z J Surg* 1975; **45**: 178-182 [PMID: 1081390 DOI: 10.1111/j.1445-2197.1975.tb05756.x]
13 **Griffet J**, Oborocianu I, Rubio A, Leroux J, Lauron J, Hayek T. Percutaneous aspiration irrigation drainage technique in the management of septic arthritis in children. *J Trauma* 2011; **70**: 377-383 [PMID: 21307737 DOI: 10.1097/TA.0b013e31820318f0]
14 **Wiley JJ**, Fraser GA. Septic arthritis in childhood. *Can J Surg* 1979; **22**: 326-330 [PMID: 313236]
15 **Moumile K**, Merckx J, Glorion C, Pouliquen JC, Berche P, Ferroni A. Bacterial aetiology of acute osteoarticular infections in children. *Acta Paediatr* 2005; **94**: 419-422 [PMID: 16092454 DOI: 10.1111/j.1651-2227.2005.tb01911.x]
16 **Calvo C**, Núñez E, Camacho M, Clemente D, Fernández-Cooke E, Alcobendas R, Mayol L, Soler-Palacin P, Oscoz M, Saavedra-Lozano J; Collaborative Group. Epidemiology and Management of Acute, Uncomplicated Septic Arthritis and Osteomyelitis: Spanish Multicenter Study. *Pediatr Infect Dis J* 2016; **35**: 1288-1293 [PMID: 27455444 DOI: 10.1097/INF.0000000000001309]
17 **Smith SP**, Thyoka M, Lavy CB, Pitani A. Septic arthritis of the shoulder in children in Malawi. A randomised, prospective study of aspiration versus arthrotomy and washout. *J Bone Joint Surg Br* 2002; **84**: 1167-1172 [PMID: 12463664 DOI: 10.1302/0301-620x.84b8.13080]
18 **Lavy CB**. Septic arthritis in Western and sub-Saharan African children - a review. *Int Orthop* 2007; **31**: 137-144 [PMID: 16741731 DOI: 10.1007/s00264-006-0169-9]
19 **Biyani A**, Sharma JC. Continuous suction and intermittent irrigation for septic coxitis. *Acta Orthop Scand* 1988; **59**: 664-666 [PMID: 3264986 DOI: 10.3109/17453678809149420]
20 **Pääkkönen M**, Kallio MJ, Peltola H, Kallio PE. Pediatric septic hip with or without arthrotomy: retrospective analysis of 62 consecutive nonneonatal culture-positive cases. *J Pediatr Orthop B* 2010; **19**: 264-269 [PMID: 20220532 DOI: 10.1097/BPB.0b013e32833822be]
21 **Bennett OM**, Namnyak SS. Acute septic arthritis of the hip joint in infancy and childhood. *Clin Orthop Relat Res* 1992; 123-132 [PMID: 1499198]
22 **Balakumar B**, Gangadharan S, Ponmudi N, Kumar S, Prakash JJ, Palocaren T. Atypical osteomyelitis and concurrent septic arthritis due to Salmonella in immunocompetent children. *J Clin Orthop Trauma* 2017; **8**: 293-297 [PMID: 28951650 DOI: 10.1016/j.jcot.2017.05.008]
23 **Kaziz H**, Triki MA, Mouelhi T, Bouattour K, Naouar N, Ben Ayeche ML. Septic elbow arthritis in children: Epidemiology and outcome. *Arch Pediatr* 2019; **26**: 38-43 [PMID: 30554847 DOI: 10.1016/j.arcped.2018.11.001]
24 **Hazelton BJ**, Axt MW, Jones CA. Pasteurella canis osteoarticular infections in childhood: review of bone and joint infections due to pasteurella species over 10 years at a tertiary pediatric hospital and in the literature. *J Pediatr Orthop* 2013; **33**: e34-e38 [PMID: 23482278 DOI: 10.1097/BPO.0b013e318287ffe6]
25 **Jackson MA**, Nelson JD. Etiology and medical management of acute suppurative bone and joint infections in pediatric patients. *J Pediatr Orthop* 1982; **2**: 313-323 [PMID: 6752200]
26 **Quick RD**, Williams J, Fernandez M, Gottschalk H, Cosgrove P, Kahlden K, Merkel K, Thoreson L, Boswell P, Hauger SB. Improved Diagnosis and Treatment of Bone and Joint Infections Using an Evidence-based Treatment Guideline. *J Pediatr Orthop* 2018; **38**: e354-e359 [PMID: 29727410 DOI: 10.1097/BPO.0000000000001187]
27 **Kocher MS**, Mandiga R, Murphy JM, Goldmann D, Harper M, Sundel R, Ecklund K, Kasser JR. A clinical practice guideline for treatment of septic arthritis in children: efficacy in improving process of care and effect on outcome of septic arthritis of the hip. *J Bone Joint Surg Am* 2003; **85**: 994-999 [PMID: 12783993]
28 **Baldwin KD**, Brusalis CM, Nduaguba AM, Sankar WN. Predictive Factors for Differentiating Between Septic Arthritis and Lyme Disease of the Knee in Children. *J Bone Joint Surg Am* 2016; **98**: 721-728 [PMID: 27147684 DOI:

10.2106/JBJS.14.01331]
29 **Nade S**. Acute septic arthritis in infancy and childhood. *J Bone Joint Surg Br* 1983; **65**: 234-241 [PMID: 6841388 DOI: 10.1302/0301-620X.65B3.6841388]
30 **Lee SC**, Shim JS, Seo SW, Lee SS. Prognostic factors of septic arthritis of hip in infants and neonates: minimum 5-year follow-up. *Clin Orthop Surg* 2015; **7**: 110-119 [PMID: 25729527 DOI: 10.4055/cios.2015.7.1.110]
31 **Arnold JC**, Bradley JS. Osteoarticular Infections in Children. *Infect Dis Clin North Am* 2015; **29**: 557-574 [PMID: 26311358 DOI: 10.1016/j.idc.2015.05.012]
32 **Pääkkönen M**, Kallio MJ, Kallio PE, Peltola H. Sensitivity of erythrocyte sedimentation rate and C-reactive protein in childhood bone and joint infections. *Clin Orthop Relat Res* 2010; **468**: 861-866 [PMID: 19533263 DOI: 10.1007/s11999-009-0936-1]
33 **Kocher MS**, Zurakowski D, Kasser JR. Differentiating between septic arthritis and transient synovitis of the hip in children: an evidence-based clinical prediction algorithm. *J Bone Joint Surg Am* 1999; **81**: 1662-1670 [PMID: 10608376 DOI: 10.2106/00004623-199912000-00002]
34 **Kocher MS**, Mandiga R, Zurakowski D, Barnewolt C, Kasser JR. Validation of a clinical prediction rule for the differentiation between septic arthritis and transient synovitis of the hip in children. *J Bone Joint Surg Am* 2004; **86**: 1629-1635 [PMID: 15292409 DOI: 10.2106/00004623-200408000-00005]
35 **Caird MS**, Flynn JM, Leung YL, Millman JE, D'Italia JG, Dormans JP. Factors distinguishing septic arthritis from transient synovitis of the hip in children. A prospective study. *J Bone Joint Surg Am* 2006; **88**: 1251-1257 [PMID: 16757758 DOI: 10.2106/JBJS.E.00216]
36 **Manz N**, Krieg AH, Heininger U, Ritz N. Evaluation of the current use of imaging modalities and pathogen detection in children with acute osteomyelitis and septic arthritis. *Eur J Pediatr* 2018; **177**: 1071-1080 [PMID: 29728840 DOI: 10.1007/s00431-018-3157-3]
37 **Milla SS**, Coley BD, Karmazyn B, Dempsey-Robertson ME, Dillman JR, Dory CE, Garber M, Hayes LL, Keller MS, Meyer JS, Paidas C, Raske ME, Rigsby CK, Spottswood S, Strouse PJ, Widmann RF, Wootton-Gorges SL. ACR Appropriateness Criteria® limping child--ages 0 to 5 years. *J Am Coll Radiol* 2012; **9**: 545-553 [PMID: 22863462 DOI: 10.1016/j.jacr.2012.04.017]
38 **Gordon JE**, Huang M, Dobbs M, Luhmann SJ, Szymanski DA, Schoenecker PL. Causes of false-negative ultrasound scans in the diagnosis of septic arthritis of the hip in children. *J Pediatr Orthop* 2002; **22**: 312-316 [PMID: 11961445]
39 **Saavedra-Lozano J**, Falup-Pecurariu O, Faust SN, Girschick H, Hartwig N, Kaplan S, Lorrot M, Mantadakis E, Peltola H, Rojo P, Zaoutis T, LeMair A. Bone and Joint Infections. *Pediatr Infect Dis J* 2017; **36**: 788-799 [PMID: 28708801 DOI: 10.1097/INF.0000000000001635]
40 **Rosenfeld S**, Bernstein DT, Daram S, Dawson J, Zhang W. Predicting the Presence of Adjacent Infections in Septic Arthritis in Children. *J Pediatr Orthop* 2016; **36**: 70-74 [PMID: 25575359 DOI: 10.1097/BPO.0000000000000389]
41 **Carter K**, Doern C, Jo CH, Copley LA. The Clinical Usefulness of Polymerase Chain Reaction as a Supplemental Diagnostic Tool in the Evaluation and the Treatment of Children With Septic Arthritis. *J Pediatr Orthop* 2016; **36**: 167-172 [PMID: 25887824 DOI: 10.1097/BPO.0000000000000411]
42 **Hashavya S**, Gross I, Michael-Gayego A, Simanovsky N, Lamdan R. The efficacy of 16S ribosomal DNA sequencing in the diagnosis of bacteria from blood, bone and synovial fluid samples of children with musculoskeletal infections. *J Child Orthop* 2018; **12**: 204-208 [PMID: 29707061 DOI: 10.1302/1863-2548.12.170049]
43 **Schoolmeesters BJA**, van den Hout JAAM, Joosten AJP, Terra MP, Elmans-Reuvers MJCM, van Bergen CJA. [The limping child: a red flag for every physician]. *Ned Tijdschr Geneeskd* 2019; **163** [PMID: 31682088]
44 **Harrison WD**, Vooght AK, Singhal R, Bruce CE, Perry DC. The epidemiology of transient synovitis in Liverpool, UK. *J Child Orthop* 2014; **8**: 23-28 [PMID: 24488848 DOI: 10.1007/s11832-014-0556-5]
45 **Haueisen DC**, Weiner DS, Weiner SD. The characterization of "transient synovitis of the hip" in children. *J Pediatr Orthop* 1986; **6**: 11-17 [PMID: 3941171 DOI: 10.1097/01241398-198601000-00003]
46 **Cassidy JT**, Levinson JE, Bass JC, Baum J, Brewer EJ Jr, Fink CW, Hanson V, Jacobs JC, Masi AT, Schaller JG. A study of classification criteria for a diagnosis of juvenile rheumatoid arthritis. *Arthritis Rheum* 1986; **29**: 274-281 [PMID: 3485433 DOI: 10.1002/art.1780290216]
47 **Gerber MA**, Shapiro ED, Burke GS, Parcells VJ, Bell GL. Lyme disease in children in southeastern Connecticut. Pediatric Lyme Disease Study Group. *N Engl J Med* 1996; **335**: 1270-1274 [PMID: 8857006 DOI: 10.1056/NEJM199610243351703]
48 **Thompson A**, Mannix R, Bachur R. Acute pediatric monoarticular arthritis: distinguishing lyme arthritis from other etiologies. *Pediatrics* 2009; **123**: 959-965 [PMID: 19255026 DOI: 10.1542/peds.2008-1511]
49 **Deanehan JK**, Kimia AA, Tan Tanny SP, Milewski MD, Talusan PG, Smith BG, Nigrovic LE. Distinguishing Lyme from septic knee monoarthritis in Lyme disease-endemic areas. *Pediatrics* 2013; **131**: e695-e701 [PMID: 23420916 DOI: 10.1542/peds.2012-2531]
50 **Perry DC**, Skellorn PJ, Bruce CE. The lognormal age of onset distribution in Perthes' disease: an analysis from a large well-defined cohort. *Bone Joint J* 2016; **98-B**: 710-714 [PMID: 27143746 DOI: 10.1302/0301-620X.98B5.36453]
51 **Dartnell J**, Ramachandran M, Katchburian M. Haematogenous acute and subacute paediatric osteomyelitis: a systematic review of the literature. *J Bone Joint Surg Br* 2012; **94**: 584-595 [PMID: 22529075 DOI: 10.1302/0301-620X.94B5.28523]
52 **Elzohairy MM**. Primary pyomyositis in children. *Orthop Traumatol Surg Res* 2018; **104**: 397-403 [PMID: 29274860]
53 **Bickels J**, Ben-Sira L, Kessler A, Wientroub S. Primary pyomyositis. *J Bone Joint Surg Am* 2002; **84**: 2277-2286 [PMID: 12473721 DOI: 10.2106/00004623-200212000-00024]
54 **Sanchez AA**, Hennrikus WL. Arthroscopically assisted treatment of acute septic knees in infants using the Micro-Joint Arthroscope. *Arthroscopy* 1997; **13**: 350-354 [PMID: 9195033 DOI: 10.1016/s0749-8063(97)90033-5]
55 **Agout C**, Lakhal W, Fournier J, de Bodman C, Bonnard C. Arthroscopic treatment of septic arthritis of the knee in children. *Orthop Traumatol Surg Res* 2015; **101**: S333-S336 [PMID: 26421608 DOI: 10.1016/j.otsr.2015.09.007]
56 **MacLean SB**, Timmis C, Evans S, Lawniczak D, Nijran A, Bache E. Preoperative antibiotics for septic arthritis in children: delay in diagnosis. *J Orthop Surg (Hong Kong)* 2015; **23**: 80-83 [PMID: 25920651 DOI: 10.1177/230949901502300119]

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ORIGINAL ARTICLE

Retrospective Cohort Study

All-epiphyseal versus trans-epiphyseal screw fixation for tillaux fractures: Does it matter?

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Abstract

BACKGROUND

Tillaux fractures occur primarily in adolescents due to the pattern of physeal closure and are classified as Salter-Harris type III physeal fractures. Operative management with screw fixation is recommended for more than 2 mm of displacement or more than 1 mm of translation. However, the efficacy and complications of trans-physeal *vs* all-physeal screw fixation have not been investigated extensively.

AIM

To compare the clinical and functional outcomes of trans-physeal (oblique) and all-epiphyseal (parallel) screw fixation in management of Tillaux fractures among pediatric patients.

METHODS

This was an ethics board approved retrospective review of pediatric patients who presented to our tertiary children's care facility with Tillaux fractures. We included patients who had surgical fixation of a Tillaux fracture over a 10 year period. Data analysis included demographics, mode of injury, management protocols, and functional outcomes. The patients were divided into group 1 (oblique fixation) and group 2 (parallel fixation). Baseline patient characteristics and functional outcomes were compared between groups. Statistical tests to evaluate differences included Fisher's Exact or Chi-squared and independent samples t or Mann Whitney tests for categorical and continuous variables, respectively.

RESULTS

A total of 42 patients (28 females and 14 males) were included. There were no

significant differences in body mass index, sex, age, or time to surgery between the groups [IK2]. Sports injuries accounted for 61.9% of the cases, particularly non-contact (57.1%) and skating (28.6%) injuries. Computed Tomography (CT) scan was ordered for 28 patients (66.7%), leading to diagnosis confirmation in 17 patients and change in management plan in 11 patients. [GRC3] Groups 1 and 2 consisted of 17 and 25 patients, respectively. For mid to long-term functional outcomes, there were 14 and 10 patients in groups 1 and 2, respectively. Statistical analysis revealed no significant differences in the functional outcomes, pain scores, or satisfaction between groups. No infections, non-unions, physeal arrest, or post-operative ankle deformities were reported. Two (4.8%) patients had difficulty returning to sports post-surgery due to pain. One was a dancer, and the other patient had pain while running, which led to hardware removal. Both patients had parallel fixation. Hardware removal for groups 1 and 2 were 4 (23.5%) and 5 (20.0%) patients, respectively. The reasons for removal was pain in 2 patients, and parental preference in the remaining.

CONCLUSION

This is the largest reported series of pediatric patients with Tillaux fractures comparing functional outcomes of different methods of screw fixation orientation to the physis, which showed no difference regarding functional outcomes.

Key Words: Tillaux fracture; Orthopedic surgery; Fixation technique; Functional outcomes

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Core Tip: Tillaux fractures that require surgery can undergo screw fixation by all-epiphyseal or trans-epiphyseal techniques. This study shows that there were no statistically significant differences between the functional outcomes or complications between the two techniques. Therefore, we suggest using the trans-epiphyseal techniques because it has an easier screw trajectory in surgery, all-epiphyseal screws have been shown to increase pressure in the tibiotalar joint, and the trajectory is trigonometrically a better angle to compress the fracture.

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INTRODUCTION

Tillaux fracture is an avulsion fracture of the anterolateral distal tibial epiphysis that occurs primarily in adolescents due to the pattern of physeal closure, and is classified as a Salter-Harris type III physeal fracture[1]. They occur most commonly in children near skeletal maturity at around ages 12-14 years old during the period of distal tibial physis closure, with supination-external rotation being the typical mechanism of injury. In children, the cartilaginous physes are more susceptible to injury than the surrounding tissues, leading to bone failure prior to the failure of ligamentous attachments. The physis initially closes centrally, then medially, and finally laterally, giving rise to the anterolateral location of the Tillaux fracture[2]. In the Tillaux fracture pattern, this manifests as an avulsion of the distal lateral tibial epiphysis at the site of attachment of the anterior inferior tibiofibular ligament where the physis is still cartilaginous and weaker than the ligament[3].

Ankle fractures account for approximately 5% of all pediatric fractures and 15% of all injuries involving a physis[4]. Tillaux fractures specifically account for 3%-5% of all pediatric ankle fractures[5, 6], and the amount of data in the literature on these fractures is limited. Operative management with screw fixation is recommended for fractures with more than 2 mm of displacement or more than 1 mm of translation[2]. Fixation can be performed by an all-epiphyseal (parallel) or trans-physeal (oblique) screw orientation. Traditional treatment of this injury involved all–epiphyseal screw fixation (parallel to the ankle joint line) because it avoids the open physis, theoretically preventing growth arrest. However, a previous cadaveric study showed that parallel screw fixation can lead to increased joint pressures[7], potentially altering ankle joint biomechanics and increasing the risk of arthritis and complications in the long term[8]. Oblique screws may have an easier to achieve intra-operative trajectory, serve as a better fixation construct as they are relatively more perpendicular to the fracture line, and would not lead to increased pressure in the ankle joint articular cartilage.

To our knowledge, the efficacy (including functional outcomes) and complications of oblique *vs* parallel screw fixation for Tillaux fractures have not yet been investigated in the literature. This study aims to compare the healing and functional outcomes of both fixation techniques. We hypothesized that oblique fixation would result in no differences in bone healing, complications, or functional outcomes compared to parallel fixation.

MATERIALS AND METHODS

This cohort study was conducted at a single-center following institution review board approval. All patients under 18 years old who underwent surgical fixation of Tillaux fractures between January 2010 and March 2020 were included in the study. Patients were excluded if they had underlying conditions interfering with either bone physiology, anatomy, or healing, such as cerebral palsy, osteogenesis imperfecta, *etc.* Patients were stratified into two groups based on the screw fixation technique: Group 1 consisted of patients with oblique (trans-physeal) fixation (Figure 1), and group 2 consisted of patients with parallel to the ankle (all-epiphyseal) fixation (Figure 2). Screw fixation technique was determined by a review of operative notes and post-operative radiographs.

Patients' charts were reviewed for the following data: Age, sex, body mass index (BMI), mechanisms of injury (Sports Contact, Sports Non-Contact, Motor Vehicle Collision [MVC], Non-Sports related Fall, and Other), radiographs and advanced imaging, and time to surgery. Complications such as physeal/growth arrest, deformity of the ankle at follow-up, revisions/hardware removal, and infections were analyzed. Functional outcomes were obtained at a minimum of 1 year post-operatively and included the Oxford Ankle Foot Questionnaire for Children (OxAFQ-C) score, Single Assessment Numeric Evaluation (SANE) score, Visual Analog Scale (VAS) pain scores, and patient satisfaction. Satisfaction was set as a binary variable, with answers categorized as satisfied or dissatisfied.

Statistical analysis

Baseline patient characteristics, complications and functional outcomes were compared between groups. Statistical tests to evaluate differences included Fisher's Exact or Chi-squared and independent samples t or Mann Whitney tests for categorical and continuous variables, respectively. Normality assessments were conducted using the Kolmogorov-Smirnov test for all continuous variables. All statistical analyses were performed and reviewed by BH and IAI trained in these techniques using IBM SPSS Statistics V.27.0 (IBM Corp, Armonk, NY). The *P* value was set at < 0.05 for statistical significance. Results are reported as counts with corresponding percentages or means with standard deviation.

RESULTS

A total of 42 patients (28 females and 14 males) were included in the analysis. There were no significant differences in BMI, sex, age, or time-to-surgery between the groups (Table 1). Sports injuries accounted for 61.9% of all injuries, particularly non-contact (57.1%) and skating (28.6%) (Table 2). However, there were no significant differences between groups. A CT scan was ordered for 28 patients (66.7%), which led to 11 patients (26.2%) changing treatment plan from non-operative treatment to surgery, and the remaining led to the confirmation of surgical management.

Groups 1 and 2 consisted of 17 and 25 patients, respectively. Functional outcomes were available for 14 (82.4%) and 10 (40.0%) patients in groups 1 and 2, respectively. The average follow-up for the long-term outcomes was 3.5 (± 2.8) years. Statistical analysis revealed no statistically significant differences in functional outcomes between groups (Table 3). No infections, non-unions, physeal arrest, or post-operative ankle deformities were reported. Two patients had difficulty returning to sports post-surgery due to pain (1 from each group). One was a dancer, and the other patient had pain while running, which resulted in hardware removal. Hardware removal occurred for 4 and 5 patients in groups 1 and 2, respectively. The reason for removal was the persistence of pain in 2 patients (1 from each group), and parental preference in the remaining.

DISCUSSION

Our study assessed the functional outcomes of Tillaux fracture patients, and compared them based on screw fixation technique (oblique *vs* parallel). The results suggest no differences in the SANE, VAS and Oxford scores, or patient satisfaction. These findings support our hypothesis that there would not be any differences between the two groups.

The radiographic cutoffs for surgical or non-surgical management of Tillaux fractures is generally recognized as more than 2 mm of displacement or greater than 1 mm of translation[9]. Liporace *et al*[10] questioned the efficacy of CT scans in this patient population because the addition of CT scans did not

Table 1 Demographics

Variable	Total Sample (*n* = 42)	Oblique (*n* = 17)	Parallel (*n* = 25)	*P* value
Sex				
Female	28 (66.7)	13 (76.5)	15 (60.0)	0.27
Male	14 (33.3)	4 (23.5)	10 (40.0)	
Age (yr.)	13.5 ± 1.4	13.4 ± 1.7	13.6 ± 1.2	0.43
Body mass index (lbs/m^2)	26.3 ± 6.4	26.2 ± 4.5	26.4 ± 7.3	0.93
Time-to-surgery (d)	7.6 ± 9.6	6.9 ± 4.7	8.0 ± 11.8	0.38

Table 2 Mechanism of injury

Factor	Total sample (*n* = 42)	Oblique (*n* = 17)	Parallel (*n* = 25)	*P* value
Sports	26 (61.9)	11 (64.7)	15 (60.0)	1.00
Skating	12 (28.6)	7 (41.2)	5 (20.0)	0.17
Contact	3 (7.1)	1 (5.9)	2 (8.0)	1.00
Non-contact	24 (57.1)	10 (58.8)	14 (56.6)	0.86
Motor vehicle collision	0	0	0	-
Fall	10 (23.8)	3 (17.6)	7 (28.0)	0.49

Table 3 Functional outcomes

Variable	Oblique (*n* = 14)	Parallel (*n* = 10)	*P* value
SANE score (0-100)	90 ± 18.58	88.5 ± 16.3	0.86
Pain score (0-10)	1.8 ± 1.7	1.7 ± 1.9	0.61
Oxford score (0-100)			
Physical scale score	76.2 ± 20.6	82.5 ± 20.95	0.70
School and play scale score	91.5 ± 14.6	93.8 ± 13.5	0.67
Emotional scale score	91.5 ± 14.6	96.9 ± 7.9	0.36
Satisfaction			
Satisfied	13 (92.9)	10 (100)	1.00
Dissatisfied	1 (7.1)	0	

significantly change the impression of the amount of displacement per case. However, it did influence the decision to operate as seen in our cohort, as 40% of the patients who underwent CT scans were changed to surgical management.

During surgery, the fracture can be fixed with a screw in oblique or parallel orientation relative to the tibiotalar joint. The oblique fixation technique involves placing a screw directly through the Tillaux fragment and ending in the metaphysis, which violates the physis[6,11,12]. Lintecum *et al*[13] described a parallel fixation technique that involves placing a screw parallel to the tibiotalar joint, through the Tillaux fragment, and into the distal epiphysis. The rationale of this technique was to avoid interrupting the physis and subsequently, growth potential. However, Crawford *et al*[14] found that growth interruption rarely occurred in patients who underwent surgical fixation. Another case series has found that obliquely oriented screws did not lead to leg length discrepancy[15]. This is most likely due to imminent physeal closure and the fact that there is little remaining linear growth potential. Further, parallel screws are not ideal because they lead to increased pressure in the joint, fixation is not perpendicular to the physeal fracture line, and the all-epiphyseal trajectory is more challenging to achieve with fear of penetrating the articular cartilage due to proximity.

Charlton *et al*[7] showed in cadavers that parallel screw fixation led to a statistically significant increase of forces in the tibiotalar joint following fixation and that the increase in force disappeared following removal of the screw. Theoretically, increased joint pressures can lead to altered joint

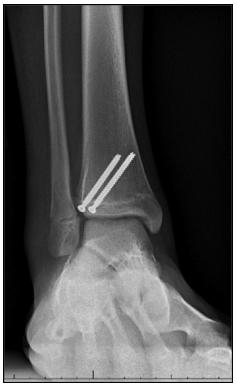


Figure 1 Oblique fixation of tillaux fracture.



Figure 2 Parallel fixation of tillaux fracture.

biomechanics and associated complications such as arthritis over time. However, there are no long-term studies following surgical fixation of Tillaux fractures to prove this.

In normal ankle fractures, hardware removal is a controversial topic and generally left up to surgeon preference[16]. Some studies have shown negative outcomes with leaving in the screws[17], and Jung *et al* showed that functional outcomes and pain improve with removal[18]. The negative outcomes of parallel screw fixation could be avoided if an oblique screw trajectory led to less post-operative pain, decreased joint pressures and associated complications, and similar functional outcomes compared to parallel screw fixation. As the Tillaux fragment is avulsed from the anterolateral corner of the distal tibia, a parallel screw does not sit perpendicular to the fracture (Figure 1), which could lead to worse fixation compared to an oblique screw which could instead be placed perpendicular to the fracture line.

Multiple small studies have examined the functional outcomes of surgically treated Tillaux fractures and have found excellent outcomes[2,19-23]. These studies often consisted of a mixture of fixation techniques and did not compare between them. In a study of 7 patients treated with screw fixation (1 patient and 6 patients *via* open and closed reduction internal fixation, respectively), 6 had full and immediate recovery without complication with a mean Foot and Ankle score of 96.71 out of 100. One patient had pain and joint stiffness in the post-operative period with resolution following conservative management[21]. A study of 23 children with 2-5 mm of displacement following Tillaux fracture reported a mean Foot and Ankle Ability Measure of 91.2% following both open and closed reduction with no difference in outcomes between the two types of management[20]. Another study of 13 adolescent patients with Tillaux fractures treated with a 4 mm partially threaded cancellous screw directed horizontally into the epiphysis *via* anterolateral approach found radiographical evidence of fracture union in all cases (100%) and a mean Foot and Ankle Score of 97[6]. Another study of 6 children treated with screw fixation found that patients regained complete and painless ankle mobility after a follow-up of 5-7 months[19]. These studies show excellent outcomes but do not compare the two fixation techniques. The fact that most patients have excellent outcomes regardless of the fixation type was the basis of our hypothesis that the oblique screw is most likely an equivalent, if not better, option.

Pilla *et al*[15] demonstrated that oblique compression screw fixation in 10 patients with an average final follow-up of 15 months resulted in equal leg lengths and no angulation, joint stiffness, or limitations of activities. This study serves to disprove the notion that placing the screw across the physis will have adverse functional and leg length outcomes. Combined with our results of equal functional outcomes, it is evident that patients would only benefit from oblique screws due to previously mentioned reasons as opposed to negative outcomes. However, there is still no data on whether oblique

screws lead to increased joint pressures as do parallel screws. There is additionally no data on long-term complications, such as post-operative pain or arthritis, between groups. Our findings of equivalent functional outcomes between screw placement groups validates the need to obtain more information on long-term complications of oblique screw fixation in order to properly evaluate whether this method is equivalent or superior to parallel screw fixation.

Approximately 62% of the Tillaux fracture patients in our cohort were related to sports injuries, with 46% of these sports injuries resulting from skating accidents. We speculate that high and hard booted skates (hockey and roller) may provide a fulcrum at the level of the ankle that leads to increased risk of supination-external rotation type injuries, which is the most common mechanism leading to Tillaux fractures. One study that analyzed injuries sustained while rollerblading found that the ankle was involved in 10% (3rd most) of injuries[24]. All ankle injuries sustained involved a rotational mechanism, and supination-external rotation injuries were associated with high top skates. Thus, an activity that leads to extreme rotation about the ankle and/or a supination-external rotation moment increases the risk of a Tillaux fracture, especially in the appropriate age group[24]. Participation in skating sports and activities (street or ice hockey, roller-blading, roller-skating, *etc*.) is likely associated with an increased risk of Tillaux fracture compared to other sports.

Limitations of the study

The limitations of this study are that the patient numbers are relatively small which could lead to the study being underpowered. However, due to the rarity of the injury, our numbers are the largest reported in the literature for this type of comparison. The assignment of patients and perioperative complications were all based on a retrospective review of patient records, which leaves the opportunity for error and misinterpretation. While the type of surgical fixation performed was determined by individual surgeon preference, there was no standardized criteria for assigning patients to undergo either parallel or oblique fixation. [GRC1] In addition, we were only able to contact 57% of the patients for functional outcomes, but these limitations are shared among similar studies on this topic. Despite these limitations, this study is one of the largest studies on Tillaux fractures with mid to long-term outcomes. To our knowledge, it is the only study that has compared functional outcomes based on screw orientation techniques.

CONCLUSION

In comparing functional outcomes of different methods of screw fixation orientation to the physis, we concluded that there were no differences with a mean follow-up of 3.5 years. This suggests that the oblique fixation is equivalent to parallel fixation; however, more rigorous longitudinal[GRC1] studies are needed to assess long-term complications of oblique screw fixation to further prove superiority.

ARTICLE HIGHLIGHTS

Research background

Operative management of Tillaux fractures in adolescent patients is recommended for more than 2 mm of displacement or more than 1 mm of translation with screw fixation.

Research motivation

The efficacy, superiority and complications of trans-physeal *vs* all-physeal screw fixation have not been investigated in literature yet.

Research objectives

To compare outcomes of trans-physeal and all-epiphyseal screw fixation in management of Tillaux fractures in young patients.

Research methods

The patients were divided into group 1 (oblique screw fixation) and group 2 (parallel screw fixation). Patient characteristics and functional outcomes were compared between groups.

Research results

A total of 42 patients (28 females and 14 males) were divided into Groups 1 and 2, which consisted of 17 and 25 patients, respectively. Statistical analysis revealed no significant differences in the functional outcomes, pain scores, or satisfaction between groups.

Research conclusions

In young patients with Tillaux fractures, comparing functional outcomes of different methods of screw fixation orientation to the physis, showed no difference regarding functional outcomes.

Research perspectives

Based on our findings, oblique screws, which provide better compression of the Tillaux fracture, are recommended over parallel screws, which create more joint forces and require a more difficult screw trajectory.

FOOTNOTES

Author contributions: All the authors contributed appropriately and equally in the execution of the study and drafting of manuscript.

Institutional review board statement: This study was approved by IRB for retrospective review of pediatric patients with Tillaux fracture.

Conflict-of-interest statement: The authors report no conflict of interest.

Data sharing statement: Technical appendix, statistical code, and dataset available from the corresponding author at ikushare@texaschildrens.org.

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REFERENCES

1 **Duchesneau S**, Fallat LM. The Tillaux fracture. *J Foot Ankle Surg* 1996; **35**: 127-33; discussion 189 [PMID: 8722880 DOI: 10.1016/s1067-2516(96)80029-9]
2 **Ali Al-Ashhab ME**, Mahmoud Mohamed AA. Treatment for displaced Tillaux fractures in adolescent age group. *Foot Ankle Surg* 2020; **26**: 295-298 [PMID: 31031149 DOI: 10.1016/j.fas.2019.04.001]
3 **Wuerz TH**, Gurd DP. Pediatric physeal ankle fracture. *J Am Acad Orthop Surg* 2013; **21**: 234-244 [PMID: 23545729 DOI: 10.5435/JAAOS-21-04-234]
4 **Kay RM**, Matthys GA. Pediatric ankle fractures: evaluation and treatment. *J Am Acad Orthop Surg* 2001; **9**: 268-278 [PMID: 11476537 DOI: 10.5435/00124635-200107000-00007]
5 **Spiegel PG**, Cooperman DR, Laros GS. Epiphyseal fractures of the distal ends of the tibia and fibula. A retrospective study of two hundred and thirty-seven cases in children. *J Bone Joint Surg Am* 1978; **60**: 1046-1050 [PMID: 721852 DOI: 10.2106/00004623-197860080-00004]
6 **Dias LS**, Giegerich CR. Fractures of the distal tibial epiphysis in adolescence. *J Bone Joint Surg Am* 1983; **65**: 438-444 [PMID: 6833316]
7 **Charlton M**, Costello R, Mooney JF 3rd, Podeszwa DA. Ankle joint biomechanics following transepiphyseal screw fixation of the distal tibia. *J Pediatr Orthop* 2005; **25**: 635-640 [PMID: 16199946 DOI: 10.1097/01.bpo.0000161834.65032.c5]
8 **Ewalefo SO**, Dombrowski M, Hirase T, Rocha JL, Weaver M, Kline A, Carney D, Hogan MV. Management of Posttraumatic Ankle Arthritis: Literature Review. *Curr Rev Musculoskelet Med* 2018; **11**: 546-557 [PMID: 30327933 DOI: 10.1007/s12178-018-9525-9]
9 **Gourineni P**, Gupta A. Medial joint space widening of the ankle in displaced Tillaux and Triplane fractures in children. *J Orthop Trauma* 2011; **25**: 608-611 [PMID: 21670707 DOI: 10.1097/BOT.0b013e318206f8bc]
10 **Liporace FA**, Yoon RS, Kubiak EN, Parisi DM, Koval KJ, Feldman DS, Egol KA. Does adding computed tomography change the diagnosis and treatment of Tillaux and triplane pediatric ankle fractures? *Orthopedics* 2012; **35**: e208-e212 [PMID: 22310408 DOI: 10.3928/01477447-20120123-11]

11 **Gordon JE**, Schoenecker PL, Klein SE. Juvenile Tillaux Fractures: A Comparison of Direct and Indirect Fixation. *Integr J Orthop Traumatol* 2019; **2**: 1-6 [DOI: 10.31038/ijot.2019234]

12 **Kling TF Jr**, Bright RW, Hensinger RN. Distal tibial physeal fractures in children that may require open reduction. *J Bone Joint Surg Am* 1984; **66**: 647-657 [PMID: 6725313 DOI: 10.2106/00004623-198466050-00002]

13 **Lintecum N**, Blasier RD. Direct reduction with indirect fixation of distal tibial physeal fractures: a report of a technique. *J Pediatr Orthop* 1996; **16**: 107-112 [PMID: 8747366 DOI: 10.1097/00004694-199601000-00022]

14 **Crawford AH**. Triplane and Tillaux fractures: is a 2 mm residual gap acceptable? *J Pediatr Orthop* 2012; **32** Suppl 1: S69-S73 [PMID: 22588107 DOI: 10.1097/BPO.0b013e31824b25a1]

15 **Pilla NI**, Borusiewicz M, Smith E, Hennrikus WL. Oblique Compression Screw Fixation across the Physis for Tillaux Fractures in Adolescent. *J Orthop Sports Med* 2020; **2**: 150-156 [DOI: 10.26502/josm.511500030]

16 **Hanson B**, van der Werken C, Stengel D. Surgeons' beliefs and perceptions about removal of orthopaedic implants. *BMC Musculoskelet Disord* 2008; **9**: 73 [PMID: 18501014 DOI: 10.1186/1471-2474-9-73]

17 **Böstman O**, Pihlajamäki H. Routine implant removal after fracture surgery: a potentially reducible consumer of hospital resources in trauma units. *J Trauma* 1996; **41**: 846-849 [PMID: 8913214 DOI: 10.1097/00005373-199611000-00013]

18 **Jung HG**, Kim JI, Park JY, Park JT, Eom JS, Lee DO. Is Hardware Removal Recommended after Ankle Fracture Repair? *Biomed Res Int* 2016; **2016**: 5250672 [PMID: 27819005 DOI: 10.1155/2016/5250672]

19 **Aguilar Ezquerra A**, Monge Vazquez ME, Torralba LG, Angulo Tabernero M. Tillaux fractures: functional results after surgical treatment. *Rev Fac Cien Med Univ Nac Cordoba* 2017; **74**: 7-9 [PMID: 28379125]

20 **Lurie B**, Van Rysselberghe N, Pennock AT, Upasani VV. Functional Outcomes of Tillaux and Triplane Fractures with 2 to 5 Millimeters of Intra-Articular Gap. *J Bone Joint Surg Am* 2020; **102**: 679-686 [PMID: 32079882 DOI: 10.2106/JBJS.19.01170]

21 **Tiefenboeck TM**, Binder H, Joestl J, Tiefenboeck MM, Boesmueller S, Krestan C, Schurz M. Displaced juvenile Tillaux fractures : Surgical treatment and outcome. *Wien Klin Wochenschr* 2017; **129**: 169-175 [PMID: 27534865 DOI: 10.1007/s00508-016-1059-9]

22 **Feng SM**, Sun QQ, Wang AG, Li CK. "All-Inside" Arthroscopic Treatment of Tillaux-Chaput Fractures: Clinical Experience and Outcomes Analysis. *J Foot Ankle Surg* 2018; **57**: 56-59 [PMID: 29037924 DOI: 10.1053/j.jfas.2017.07.020]

23 **Choudhry IK**, Wall EJ, Eismann EA, Crawford AH, Wilson L. Functional outcome analysis of triplane and tillaux fractures after closed reduction and percutaneous fixation. *J Pediatr Orthop* 2014; **34**: 139-143 [PMID: 24172672 DOI: 10.1097/BPO.0000000000000085]

24 **Ferkel RD**, Mai LL, Ullis KC, Finerman GA. An analysis of roller skating injuries. *Am J Sports Med* 1982; **10**: 24-30 [PMID: 6797309 DOI: 10.1177/036354658201000107]

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ORIGINAL ARTICLE

Retrospective Study

Femoroacetabular offset restoration in total hip arthroplasty; Digital templating a short stem *vs* a conventional stem

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Abstract

BACKGROUND

Failure in restoring individual anatomy could be a reason for persistent functional limitations post total hip arthroplasty. Femoroacetabular offset (FAO) plays an important role in anatomic restoration, as loss of offset ≥ 5 mm is associated with altered gait and decreased functional outcome. Preoperative assessment by use of digital templating has shown to be a reliable method for sizing the components in total hip arthroplasty, and can show if anatomic restoration is achieved. In recent years, short stems are growing in popularity as it could allow better restoration due to more variety in placement.

AIM

To assess whether restoration of the FAO differs between a short or a conventional stem by use of digital templating. Additionally, association of the preoperative offset and caput-colllum-diaphyseal angle (CCD-angle) within restoration of both stems was investigated, and the reliability of measurements was assessed.

METHODS

A total of 100 standardized hip radiographs were used for digital templating. Restoration of FAO was classified into "restored" or "not restored", when a < 5 mm or ≥ 5 mm difference from baseline value presented, respectively. Differences between the two stems concerning proportions of correct restoration of the FAO were analyzed by use of McNemar tests. To assess association between CCD-angle and preoperative FAO with absolute FAO restoration, multi-level analysis was performed by use of a linear mixed model to account for paired measurements. Through determination of the optimal point under the curve in operating curve-analysis, bootstrapping of thousand sets was performed to determine the optimal cutoff point of the preoperative FAO for restoration within

the limits of 5 mm. Three observers participated for inter-observer reliability, with two observers measuring the radiographs twice for intra-observer reliability.

RESULTS

The mean preoperative FAO was 79.7 mm (range 62.5-113 mm), with a mean CCD-angle of 128.6° (range 114.5°-145°). The conventional stem could only restore the FAO in 72 of the cases, whereas the short stem restored the FAO in all cases. CCD-angle was not a predictor, but the preoperative FAO was. A cut-off point of 81.25 mm (95% confidence interval of 80.75-84.75 mm) in preoperative FAO was found where the conventional stem was unable to restore the FAO. Reliability of measurements was excellent, with an intra-observer reliability of 0.99 and inter-observer reliability in baseline measurements higher than 0.9 between the three observers.

CONCLUSION

In preoperative planning of FAO restoration in total hip arthroplasty, digital templating shows that short stems with a curve following the medial calcar are potentially better at restoring the FAO compared to conventional stems if the preoperative offset is ≥ 80.0 mm.

Key Words: Offset; Anatomic offset restoration; Total hip arthroplasty; Short hip stem; Conventional hip stem

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Core Tip: This is a retrospective study, consisting of digital templating a short stem and conventional stem in the same X-ray of the hip to see if there is a difference in restoring the femoroacetabular offset. We found that in a larger femoroacetabular offset (> 80 mm) the short stem could provide better restoration when compared to a conventional stem.

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INTRODUCTION

In recent years, failure of anatomical restoration has gained more attention as a reason for persistent complaints after total hip arthroplasty (THA). Despite considerable improvement, up to 22% of the patients experience functional limitations in daily life[1-4]. Since there has been an increase of young and active patients receiving THA, who have higher expectations of their functional outcome[4,5], excellent results are needed. Nowadays, there is more focus on anatomical restoration as related to clinical outcome[6]. An important part of accurate anatomical reconstruction is a restored femoroacetabular offset (FAO). A loss of ≥ 5 mm between the preoperative offset and postoperative offset is associated with altered gait and decreased functional outcome[7,8]. Restoration of offset improves hip stability, range-of-motion, abductor function and reduced wear[9-13].

Conventional stems are the most common choice for elective THA, due to the amount of experience in placement of these stems and good long-term results. However, individual anatomy can hinder proper femoral offset restoration as the diaphyseal anchorage of this type of stem limits placement options. Short hip stems were designed for preservation of proximal bone stock, but it seems that anatomical restoration is also achievable with short stems. As there are many different designs, short stems can be classified based on osteotomy or anchoring principle. Metadiaphyseal anchoring short stems allow for excellent restoration of individual anatomy[6,14,15], as the placement of these curved short stems can be angled in the desired position to follow the natural curvature of the medial calcar. Due to this feature, it mimics the physiological load transfer on the proximal femur[16,17].

For correct placement of the hip stem, digital 2d-templating is common clinical practice and is a reliable method to estimate the correct size of hip stems prior to surgery[18-21]. It provides information on the level of osteotomy, insight on the probable size of components, and whether anatomical restoration can be achieved.

The primary aim of this study was therefore to see if the FAO could be restored by use of preoperative digital 2d-templating with a short metadiaphyseal anchoring stem and a conventional stem, within a wide range of anatomical hip variations. The secondary aim was to examine the

association of secondary measurements required for digital templating, such as the caput-colllum-diaphyseal angle (CCD-angle) and preoperative offset, with offset restoration. Additionally, the intra- and inter-observer reliability of the measurements by use of digital 2d-templating was investigated, as there is limited data on this particular subject and its reliability[21,22].

MATERIALS AND METHODS

Patients

One hundred standardized preoperative hip measurement radiographs of patients were included, with primary or secondary osteoarthritis as indication for THA. The radiographs were randomly chosen from two ongoing cohorts, the Optimys trial (Mathys Ltd, Bettlach, Switzerland) and the CBH trial (Mathys Ltd, Bettlach, Switzerland). Fifty radiographs were randomly selected from either cohort, creating a variability in coxa norma, vara and valga. If preoperative measurement radiographs were missing, containing a magnification marker for determination of the amount of magnification used, these radiographs were excluded. Approval for inclusion has been attained from the medical ethics review committee, under registry numbers NL47055.048.13 and NL48211.048.14.

Radiological evaluation

Standardised preoperative hip radiographs with magnification marker were used for 2D-digital templating. An internal rotation angle of 20° was used to produce the full profile of the femoral neck on anteroposterior radiography[23,24]. Computer-assisted measurements and 2d-templating were performed by use of Orthoview (Materialise NV, Leuven, Belgium)[25,26].

Pre-templating FAO was measured by first determining the femoral offset, defined as the distance of the longitudinal axis of the femur to the center of rotation. The longitudinal axis was determined from a 4-point box in the intramedullary cavity of the femur. The acetabular offset was determined next, defined as the distance from the center of rotation to the lateral edge of the pelvic teardrop[6,23,24,27-29]. The CCD-angle was used to identify the difference in hip-anatomy, *i.e.*, to identify if patients had a coxa vara (< 120°), coxa norma (120°-135°) or coxa valga (> 135°).

Digital templating of the short and conventional stem was then performed, with the cup as fixed factor in both images. The variables were measured again after templating, with femoral offset now being defined as the distance from the longitudinal axis of the femur to the center of rotation of the prosthetic head. The post-templating acetabular offset was defined as the distance from the center of rotation of the cup to the lateral edge of the pelvic teardrop (Figure 1).

Radiological measurements and templating were performed independently by three observers. To assess intra- and inter-observer reliability, the measurements were performed twice by a medical student (Verboom T) and by a resident in orthopaedic surgery (de Waard S), and once by an experienced orthopaedic hip surgeon (Haverkamp D).

Implants

Implants used for templating in this study were the CBH as the conventional stem and the Optimys as the short stem. In both cases the RM Pressfit Vitamys (Mathys Ltd, Bettlach, Switzerland) cup was used. The CBH is a widely used conventional press fit hip stem with a diaphyseal anchorage. Since the CBH hip stem follows the longitudinal femoral axis, femoral offset can only be increased (after determining the correct stem size) by choosing a larger head size and/or a lateral neck.

The Optimys is a short press fit hip stem, which anchors in the metadiaphyse. The shape of the Optimys follows the curvature of the medial calcar and can be placed into varus or valgus position, allowing to increase or decrease the femoral offset as needed. Also, extra femoral offset can be given with head size and a lateral neck.

Statistical analysis

Patient characteristics and outcome variables are described as means with ranges or frequencies with accompanying percentages. Restoration of FAO was dichotomized into "restored" when < 5 mm from baseline or "not restored" when ≥ 5 mm from baseline[7,30]. Differences between the short stem and the conventional stem concerning the proportions of correct restoration of the offset were analyzed by use of McNemar tests. To assess the association between absolute offset restoration and both CCD-angle and preoperative offset, multi-level analyses were performed by use of linear mixed model to account for paired measurements for both hip stems. In case of effect modification of stem type, linear regression analyses were performed for each stem separately. A P value < 0.05 was considered statistically significant.

For the determinants that were significantly associated with offset restoration (CCD-angle or preoperative offset), an operating curve (ROC) -analysis was performed to determine the optimal cutoff point of this independent variable for restoration within the limits of 5 mm. To provide a 95 % confidence interval (CI), bootstrapping procedure was performed. By using a 1000 bootstrap samples

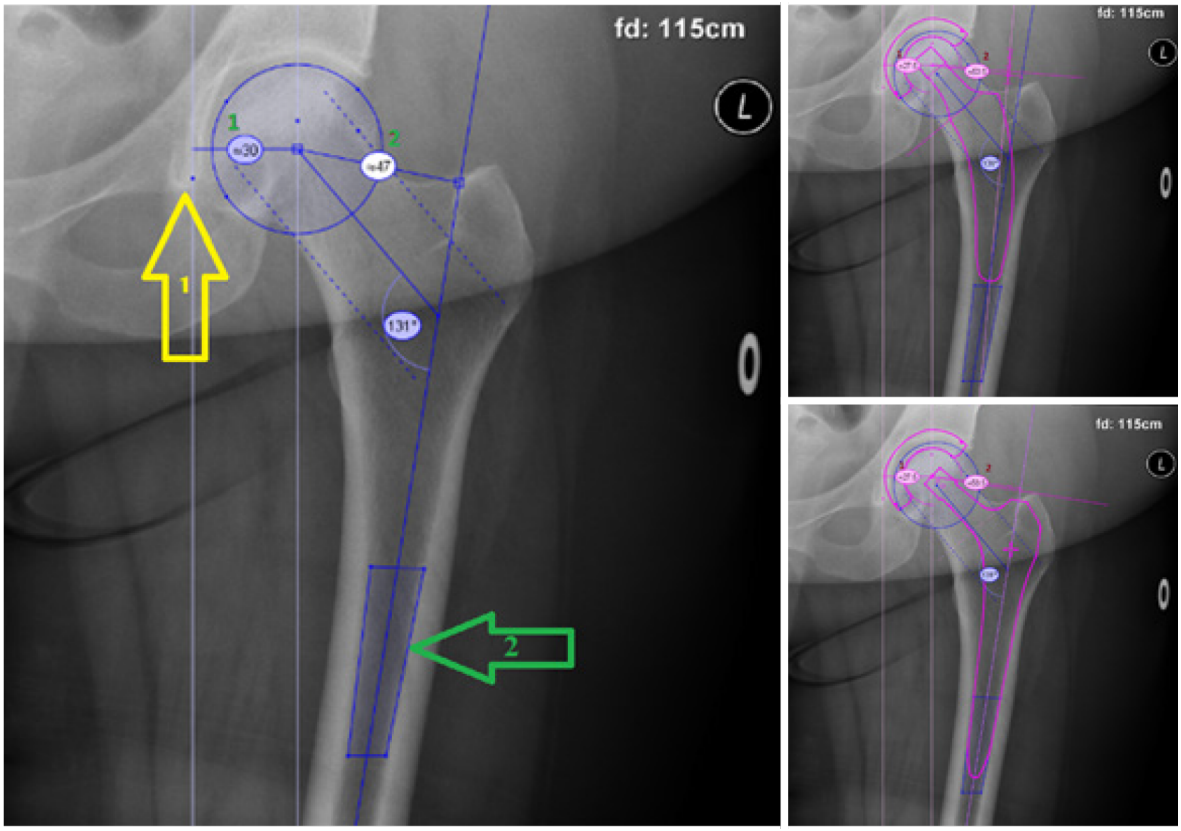


Figure 1 Measurements in digital templating before and after hip stem placement. Arrow 1: Teardrop. Arrow 2: Femoral axis determination box. Line 1: acetabular offset. Line 2: femoral offset.

and calculating their respective cut-off values, the Standard Error was obtained to acquire the 95 %CI of the optimal cut-off point. Accompanying area under the curve (AUC) was calculated as measure of accuracy.

Additionally, to assess inter-observer and intra-observer reliability, intra-class correlation coefficients ($ICC_{2,1}$) were calculated. Statistical analysis was performed using IBM SPSS Statistics, version 24.0 (Armonk, NY: IBM Corp.).

Sample size

A pilot study was performed where 20 radiographs were randomly chosen and evaluated, in which 30% of conventional stems had more than 5 mm loss in FAO. Based on a 10% difference with the short stem being clinically relevant, a sample of 89 radiographs was required to identify superiority of the short stem in FAO restoration when compared to the conventional stem, with an a = 0.05 and a power of 90%. A total of 100 radiographs were included in this study.

RESULTS

Patient characteristics

Radiographs in a total of 100 patients were included, 72 were female. A mean age of 67 years was found, with a mean BMI of 27. Almost all patients were diagnosed with primary coxarthrosis. The mean preoperative FAO was 80mm, with a CCD-angle of 128.6° (Table 1).

Restoring FAO

The short stem reached a post-templating difference of < 5 mm in FAO in all cases (100%) for both student and resident, whereas the conventional stem only achieved this in 76% and 72% of the radiographs for student and resident, respectively. The difference in FAO restoration was significant (P < 0.001), in benefit of the short stem compared to the conventional stem. A varus hip showed a failure rate of 14.3% (n = 4/24) of the non-restored hips, while a valgus hip showed no failure at all (Figure 2).

Significant interactions (P < 0.001 for all analyses) were observed between the stems and the determinants (CCD-angle and preoperative FAO), therefore analyses of the stem types were performed separately. Significant association of the CCD-angle and pre-templating FAO with the FAO restoration

Table 1 Patient and radiological characteristics

Patient characteristic	(*n* = 100)
Female, %	72
Age, mean (range)	66.7 (41-90)
BMI, mean (range)	27.3 (18.7-42.8)
Right hip, %	54
Indication, %	
Primary coxarthrosis	98
Perthes coxarthrosis	1
Posttraumatic coxarthrosis	1
Femoral offset (mm), mean (range)	47 (30.5-67)
Acetabular offset (mm), mean (range)	32.5 (22.5-47.5)
Femoro-acetabular offset (mm), mean (range)	80 (62-113)
CCD-angle (°)	128.6 (114.5-146)

CCD angle: Caput-colllum-diaphyseal angle; CI: Confidence interval.

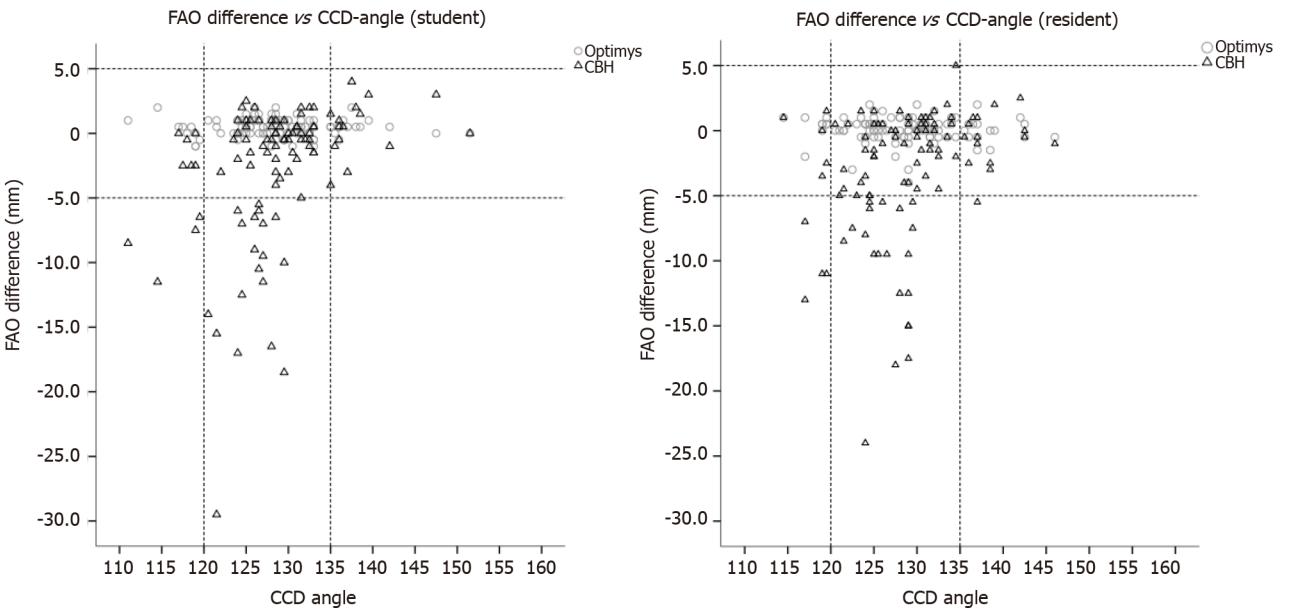


Figure 2 Femoroacetabular offset difference *vs* caput-colllum-diaphyseal angle for student and resident. Reference lines for varus (< 120°) and valgus (> 135°) angles. CCD: Caput-colllum-diaphyseal angle; FAO: Femoroacetabular offset.

was only observed for the conventional stem, with the highest explained variance for the pre-templating FAO of 68% (Table 2).

An FAO of more than 81.25 mm showed a failure in 79% of the templated conventional stems with the resident, compared to the student with a failure rate of 76% above 80.5 mm. A negative trend-line in FAO restoration is seen as the pre-templating FAO increases by both student and resident (Figure 3). For a correct cut-off point for failure in the conventional stem, bootstrapping was performed for a ROC-analysis for the pre-templating FAO with a restoration within 5 mm. The CCD-angle was not used for bootstrapping, as the AUC was smaller than 0.5. After bootstrapping the measurements of the resident, the optimal threshold of the pre-templating FAO was 81.25 mm (95%CI: 80.75-84.75), above which the conventional stem could not restore the FAO (Figure 1), with a sensitivity of 0.96, specificity of 0.79, and an AUC of 0.94.

Post-templating femoral and acetabular offset

The results of the post-templating measurements are shown in Table 3. The short stem restored the

Table 2 Determinants correlated with offset restoration

	β coefficient (95%CI)	R^2	*P* value
Student			
CCD-angle (short stem)	-0.01 (-0.03, -0.02)	0.002	0.62
CCD-angle (conventional stem)	0.34 (0.18, 0.50)	0.15	< 0.001
Pre-templating FAO (short stem)	-0.004 (-0.02, 0.01)	0.002	0.62
Pre-templating FAO (conventional stem)	-0.45 (-0.53, -0.38)	0.63	< 0.001
Resident			
CCD-angle (short stem)	-0.01 (-0.04, 0.02)	0.004	0.55
CCD-angle (conventional stem)	-0.25 (-0.10, 0.41)	0.09	0.002
Pre-templating FAO (short stem)	-0.02 (-0.04, 0.00)	0.03	0.05
Pre-templating FAO (conventional stem)	-0.44 (-0.50, -0.38)	0.68	0.000

FAO: Femoroacetabular offset; CCD angle: Caput-colllum-diaphyseal angle; CI: Confidence interval.

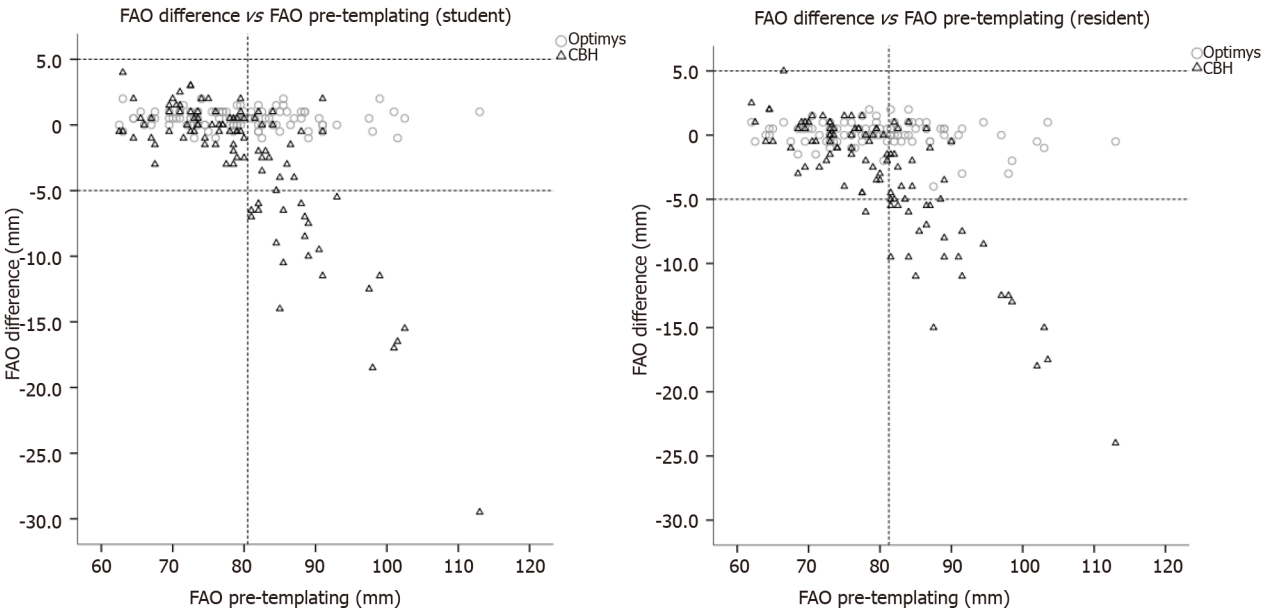


Figure 3 Femoroacetabular offset difference *vs* femoroacetabular offset pre-templating for student and resident. Reference line at cutoff point of 80.5 mm pre-templating Femoroacetabular offset (FAO) for the student, reference line at cutoff point of 81.25 mm pre-templating FAO for the resident. FAO: Femoroacetabular offset.

femoral offset in all cases, whereas the conventional stem restored the femoral offset in 91% of the cases. There was a mean decrease of acetabular offset of -4 mm.

Intra-observer reliability and inter-observer reliability

The intra-reliability of the student and the resident was both 0.99 for the pre-templating FAO. All other reliability scores were > 0.9 for both the student and the resident. Compared to the hip surgeon in pre-templating FAO, the inter-observer reliability was 0.93 and 0.95, between the student *vs* hip surgeon and resident *vs* hip surgeon respectively (Tables 4 and 5).

DISCUSSION

The goal of this study was to determine whether a metadiaphyseal anchoring short stem potentially facilitated a better restoration of FAO in digital templating compared to a conventional hip stem. The FAO was taken as primary measurement and not the femoral offset, as the acetabular offset can decrease postoperative due to medial placement of the acetabular component[31]. Therefore, the

Table 3 Post-templating measurements of radiographs (*n* = 100)

	Short stem	Conventional stem
Post-templating measurements		
Femoral offset (mm), mean (range)	51.5 (3679)	48 (3757.5)
Acetabular offset (mm), mean (range)	28.5 (23.535.5)	28.5 (23.535.5)
Femoro-acetabular offset (mm), mean (range)	80 (62112.5)	76.5 (63.589.5)
Difference pre- and post-templating		
Femoral offset (mm), mean (range)	4 (-2.513)	1 (-11.511)
Acetabular offset (mm), mean (range)	-4 (-142.5)	-4 (-142.5)
Femoro-acetabular offset (mm), mean (range)	0 (-42)	-3 (-245)
Restoration of femoral offset, %	100	91
Restoration of femoro-acetabular offset, %	100	72

Table 4 Intra-observer reliability

	Student	Resident
Pre-templating FAO	0.99	0.99
Post-templating FAO short stem	0.98	0.98
Post-templating FAO conventional stem	0.92	0.93
CCD-angle	0.93	0.94

FAO: Femoroacetabular offset; CCD angle: Caput-colllum-diaphyseal angle.

Table 5 Inter-observer reliability

	Student *vs* Resident	Student *vs* Hip surgeon	Resident *vs* Hip surgeon
Pre-templating FAO	0.98	0.93	0.95
Pre-templating FO	0.97	0.93	0.94
Pre-templating AO	0.97	0.91	0.92
Post-templating FAO short stem	0.97	0.93	0.95
Post-templating FAO conventional stem	0.90	0.84	0.86
CCD-angle	0.87	0.81	0.76

FAO: Femoroacetabular offset; CCD angle: Caput-colllum-diaphyseal angle.

femoral offset must increase additionally to compensate for the loss in acetabular offset or the cup must be placed more lateral. How the acetabular component is placed varies per orthopedic surgeon. However, the acetabular cup used in this study showed an average decrease of 3.7 mm in acetabular offset in literature[32,33]. In this study there was a decrease in acetabular offset of 4 mm, which is comparable to the other studies. The FAO restoration rate within 5 mm limits for the short stem was achieved in all cases, whereas the conventional stem achieved a restoration rate of 72% (resident) and 76% (student) during digital templating. The pre-templating FAO was associated with failure in FAO restoration when using the conventional stem, as pre-templating FAO values > 81 mm had a non-restoration rate of 60% in this group. The cutoff value was determined to use for a future reference standard, as it could provide a cutoff point if clinical relevance is shown. The cutoff point of 80 mm for pre-templating FAO was chosen conservatively, at the found cutoff value (81.25 mm), because of the rapid decrease in restoration rate beyond these points, to account for variance in the general population. The CCD-angle was not clinically relevant for FAO restoration, nor was the pre-templating FAO clinically relevant for the short stem. While it was expected that varus hips would comprise the majority of hips where a conventional stem would prove insufficient in FAO restoration, this was only observed

in 14% (n = 4/24) of the cases. While it stands to reason that a varus angle would increase femoral offset, a varus hip is not the primary reason for failure of FAO restoration. There was no difference in FAO restoration between both stems in valgus hips. Since there is no prior data on this specific subject, these results cannot be compared to other studies.

The short stem used in this study is a metadiaphyseal anchoring stem, with a curved design. It is to be expected that other similar designs are capable to restore the FAO in the same manner, which has previously been shown with the Nanos stem (Smith and Nephew, Marl, Germany)[15]. During surgery, the resection of the femoral neck determines for a large part the placement of the hip stem. In varus hips, a smaller part of the femoral neck will be resected for optimal placement as compared to valgus hips. Thus, a short stem thus can be neck preserving or trochanter sparing, depending on the anatomy of the patient. This is the main reason why the FAO can be restored within the 5 mm limit. Metaphyseal stems are not comparable to our outcomes, due to stem design differences.

Conventional hip stems are anchored in the diaphysis, where placement variability is limited and increasing femoral offset is only facilitated by using a larger head size or a lateral neck. Due to this rigidity in placement options, the results of this study can be interpreted for all conventional hip stems. Conventional stems can be placed into a varus position using smaller stem size, resulting in an increased femoral offset. However, long term survival could be compromised due to increased stress on the tip of the prosthesis. Therefore, this manner of placement is not recommended. In the results between the experienced hip surgeon and resident and medical student, the ICC values were lower for the conventional stem than expected. However, the hip surgeon was inclined to sooner place the conventional stem into a varus position, restoring the FAO better than the resident and medical student.

The high level of inter- and intra-observer reliability is indicative of high accuracy and reproducibility of the measurements. This reliability has also been shown in other templating studies[21,29,34,35], along with a high predictive value for prosthesis placement[6,21]. The found cutoff point may, after further clinical research, be a reason to introduce digital 2d-templating as a tool for stem type selection in combination with clinical considerations. Also, this study shows that preoperative templating can be performed reliably by medical students and orthopedic residents, after a learning curve.

There were some limitations to this study. Firstly, 2d-templating was used to measure 3-dimensional distances, which may cause underestimation of femoral offset and modification of CCD-angles[28,34]. However, radiographic 2d-templating is the method of choice for the majority of hip surgeons due to cost, radiation load, availability and has been shown to be similar in reliability and accuracy to 3d-templating with use of computed tomography[36]. The CCD-angle modification from 2d-templating may have been disadvantageous to the assessment of the CCD-angle as a predicting factor for FAO restoration. Secondly, other characteristics of the femoral canal were not examined in this study. The Dorr classification could help decide on type of femoral stem chosen for the surgery[37]. A Dorr type A with a large offset would be very difficult for a conventional stem to restore the offset, whereas a Dorr type C could lead to inadequate fixation of a short stem.

Another limitation is the fact that no postoperative measurements were done, which means that the results cannot be directly translated to clinical practice. However, the short stem was able to restore the FAO postoperative in the study of Kutzner *et al*[6] and recent studies showed that preoperative digital 2d-templating assured a satisfying restoration of the individual anatomy in short stems[22,26,38].

An advantage in usage of conventional stems over short stems is that there are many available studies with long-term outcomes, while these are only limited for short stems. It may also be preferable to use conventional stems in patients with suboptimal bone quality, as there is a lower load per hip stem surface unit due to the larger diaphyseal anchoring area. Theoretically, short stems could lose initial press-fit in softer bone with a higher chance on subsidence, increasing the risk of implant instability or periprosthetic fractures. Especially in older patients, the advantage of short stems, *i.e.*, preservation of proximal bone stock, is less important and not worth the risk for potentially increasing the risk of complications. Another topic is the costs of hip stems. Conventional stems are less expensive than short stems, which is also relevant once all clinical factors have been properly considered.

The advantage in FAO restoration in this study may contribute to the use of short stems in a broadened patient group with hips with a large offset. Clinical trials will have to show whether the improved restoration in FAO will grant the expected improved functional. Other reasons to choose conventional stems over short stems still may have priority over the advantage found in this study.

CONCLUSION

In preoperative planning of FAO restoration in THA, digital templating shows that short stems with a curve following the medial calcar are potentially better at restoring the FAO compared to conventional stems if the preoperative offset is ≥ 80.0 mm.

ARTICLE HIGHLIGHTS

Research background

The following steps that are necessary to take are the postoperative measurements of the short stem to see if the offset can be restored. Also, a pilot study with gait measurements in a case-matched study of patients with either a short or conventional stem will help to define if there is a difference.

Research motivation

If the native offset was > 80 mm, the short stem was better at restoring FAO than the conventional stem in digital templating. This could indicate that there is a specific patient population that could benefit if a short stem with a curve is chosen as femoral stem instead of the conventional stem.

Research objectives

A FAO more than 80mm showed a large failure rate in restoration in the conventional stems, whereas the short stem could restore the offset in all cases. The reliability of all measurements were good between in both inter- as intra-reliability, with no difference in experience.

Research methods

Digital templating in a standardized X-ray of the hip were used from two ongoing cohorts, varying in hip anatomy. Orthoview was used as digital templating program. Pre-templating FAO was measured, as well as post-templating FAO measurements in the short and conventional stem. The results were divided into restored (< 5 mm difference in offset) or not-restored (> 5 mm difference in offset).

Research results

Primary objective was the femoroacetabular offset restoration in all types of hip anatomy between a short and conventional hip stem, where the acetabular component is used as a fixed parameter. Second objectives were the reliability of the measurements.

Research conclusions

As digital templating is a reliable tool for measuring component sizes in total hip arthroplasty, this is used as measurement to see if there is a difference between a short and conventional hip stem in a wide range of hip anatomy.

Research perspectives

Short stems are gaining popularity, as one of the possible advantages is the restoration of offset. Offset restoration improves functional outcome. This could benefit the younger patient population, as they have higher expectations of their total hip arthroplasty in their more active lifestyle.

FOOTNOTES

Author contributions: de Waard S, Verboom T, Bech NH, Kerkhoffs GM, Haverkamp D drafted the manuscript; de Waard S and Haverkamp D did the measurements; Sierevelt I performed the statistical analysis, de Waard S assisted with data analysis; Sierevelt I, Haverkamp D participated in study design; Kerkhoffs GM and Haverkamp D participated in oversight of the study.

Institutional review board statement: The cohort studies in which the X-rays were chosen from, were reviewed by and approved by the Medical Ethical review committee of the MC Slotervaart hospital in Amsterdam, under registry numbers NL47055.048.13 and NL48211.048.14.

Informed consent statement: All study participants provided informed written consent about personal and medical data collection prior to study enrolment.

Conflict-of-interest statement: There are no conflict of interest from any of the authors regarding this paper.

Data sharing statement: No additional data are available. For information regarding the used data, contact the corresponding author at s.dewaard21@gmail.com.

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REFERENCES

1 **Judge A**, Cooper C, Williams S, Dreinhoefer K, Dieppe P. Patient-reported outcomes one year after primary hip replacement in a European Collaborative Cohort. *Arthritis Care Res (Hoboken)* 2010; **62**: 480-488 [PMID: 20391502 DOI: 10.1002/acr.20038]
2 **Hawker GA**, Badley EM, Borkhoff CM, Croxford R, Davis AM, Dunn S, Gignac MA, Jaglal SB, Kreder HJ, Sale JE. Which patients are most likely to benefit from total joint arthroplasty? *Arthritis Rheum* 2013; **65**: 1243-1252 [PMID: 23459843 DOI: 10.1002/art.37901]
3 **Singh JA**, Lewallen DG. Patient-level clinically meaningful improvements in activities of daily living and pain after total hip arthroplasty: data from a large US institutional registry. *Rheumatology (Oxford)* 2013; **52**: 1109-1118 [PMID: 23382362 DOI: 10.1093/rheumatology/kes416]
4 **Amlie E**, Havelin LI, Furnes O, Baste V, Nordsletten L, Hovik O, Dimmen S. Worse patient-reported outcome after lateral approach than after anterior and posterolateral approach in primary hip arthroplasty. A cross-sectional questionnaire study of 1,476 patients 1-3 years after surgery. *Acta Orthop* 2014; **85**: 463-469 [PMID: 24954494 DOI: 10.3109/17453674.2014.934183]
5 **Skyttä ET**, Jarkko L, Antti E, Huhtala H, Ville R. Increasing incidence of hip arthroplasty for primary osteoarthritis in 30- to 59-year-old patients. *Acta Orthop* 2011; **82**: 1-5 [PMID: 21189098 DOI: 10.3109/17453674.2010.548029]
6 **Kutzner KP**, Kovacevic MP, Roeder C, Rehbein P, Pfeil J. Reconstruction of femoro-acetabular offsets using a short-stem. *Int Orthop* 2015; **39**: 1269-1275 [PMID: 25522801 DOI: 10.1007/s00264-014-2632-3]
7 **Renkawitz T**, Weber T, Dullien S, Woerner M, Dendorfer S, Grifka J, Weber M. Leg length and offset differences above 5mm after total hip arthroplasty are associated with altered gait kinematics. *Gait Posture* 2016; **49**: 196-201 [PMID: 27450670 DOI: 10.1016/j.gaitpost.2016.07.011]
8 **Sariali E**, Klouche S, Mouttet A, Pascal-Moussellard H. The effect of femoral offset modification on gait after total hip arthroplasty. *Acta Orthop* 2014; **85**: 123-127 [PMID: 24564749 DOI: 10.3109/17453674.2014.889980]
9 **McGrory BJ**, Morrey BF, Cahalan TD, An KN, Cabanela ME. Effect of femoral offset on range of motion and abductor muscle strength after total hip arthroplasty. *J Bone Joint Surg Br* 1995; **77**: 865-869 [PMID: 7593096]
10 **Asayama I**, Chamnongkich S, Simpson KJ, Kinsey TL, Mahoney OM. Reconstructed hip joint position and abductor muscle strength after total hip arthroplasty. *J Arthroplasty* 2005; **20**: 414-420 [PMID: 16124955 DOI: 10.1016/j.arth.2004.01.016]
11 **Sakalkale DP**, Sharkey PF, Eng K, Hozack WJ, Rothman RH. Effect of femoral component offset on polyethylene wear in total hip arthroplasty. *Clin Orthop Relat Res* 2001; 125-134 [PMID: 11451111 DOI: 10.1097/00003086-200107000-00019]
12 **Mahmood SS**, Mukka SS, Crnalic S, Wretenberg P, Sayed-Noor AS. Association between changes in global femoral offset after total hip arthroplasty and function, quality of life, and abductor muscle strength. A prospective cohort study of 222 patients. *Acta Orthop* 2016; **87**: 36-41 [PMID: 26471772 DOI: 10.3109/17453674.2015.1091955]
13 **Foucher KC**, Freels S. Preoperative factors associated with postoperative gait kinematics and kinetics after total hip arthroplasty. *Osteoarthritis Cartilage* 2015; **23**: 1685-1694 [PMID: 26028143 DOI: 10.1016/j.joca.2015.05.005]
14 **Kutzner KP**, Freitag T, Donner S, Kovacevic MP, Bieger R. Outcome of extensive varus and valgus stem alignment in short-stem THA: clinical and radiological analysis using EBRA-FCA. *Arch Orthop Trauma Surg* 2017; **137**: 431-439 [PMID: 28154993 DOI: 10.1007/s00402-017-2640-z]
15 **Ettinger M**, Ettinger P, Ezechieli M, Büermann S, Budde S, Calließ T, Petri M, Thorey F. CCD and offset after Nanos short stem in total hip arthroplasty. *Technol Health Care* 2013; **21**: 149-155 [PMID: 23510975 DOI: 10.3233/THC-130716]
16 **Bieger R**, Ignatius A, Reichel H, Dürselen L. Biomechanics of a short stem: In vitro primary stability and stress shielding of a conservative cementless hip stem. *J Orthop Res* 2013; **31**: 1180-1186 [PMID: 23553802 DOI: 10.1002/jor.22349]
17 **Parchi PD**, Cervi V, Piolanti N, Ciapini G, Andreani L, Castellini I, Poggetti A, Lisanti M. Densitometric evaluation of periprosthetic bone remodeling. *Clin Cases Miner Bone Metab* 2014; **11**: 226-231 [PMID: 25568658 DOI: 10.11138/ccmbm/2014.11.3.226]
18 **Sariali E**, Mauprivez R, Khiami F, Pascal-Mousselard H, Catonné Y. Accuracy of the preoperative planning for cementless total hip arthroplasty. A randomised comparison between three-dimensional computerised planning and conventional templating. *Orthop Traumatol Surg Res* 2012; **98**: 151-158 [PMID: 22381566 DOI: 10.1016/j.otsr.2011.09.023]
19 **The B**, Diercks RL, van Ooijen PM, van Horn JR. Comparison of analog and digital preoperative planning in total hip and knee arthroplasties. A prospective study of 173 hips and 65 total knees. *Acta Orthop* 2005; **76**: 78-84 [PMID: 15788312 DOI: 10.1080/00016470510030364]
20 **Shaarani SR**, McHugh G, Collins DA. Accuracy of digital preoperative templating in 100 consecutive uncemented total hip arthroplasties: a single surgeon series. *J Arthroplasty* 2013; **28**: 331-337 [PMID: 22854351 DOI: 10.1016/j.arth.2012.06.009]
21 **Schmidutz F**, Steinbrück A, Wanke-Jellinek L, Pietschmann M, Jansson V, Fottner A. The accuracy of digital templating:

A comparison of short-stem total hip arthroplasty and conventional total hip arthroplasty. *Int Orthop* 2012; **36**: 1767-1772 [PMID: 22476451 DOI: 10.1007/s00264-012-1532-7]

22 **Snijders TE**, van Erp JHJ, de Gast A. Restoring femoral offset and leg length; the potential of a short curved stem in total hip arthroplasty. *J Orthop* 2019; **16**: 396-399 [PMID: 31110402 DOI: 10.1016/j.jor.2019.04.013]

23 **Lecerf G**, Fessy MH, Philippot R, Massin P, Giraud F, Flecher X, Girard J, Mertl P, Marchetti E, Stindel E. Femoral offset: anatomical concept, definition, assessment, implications for preoperative templating and hip arthroplasty. *Orthop Traumatol Surg Res* 2009; **95**: 210-219 [PMID: 19423418 DOI: 10.1016/j.otsr.2009.03.010]

24 **Flecher X**, Ollivier M, Argenson JN. Lower limb length and offset in total hip arthroplasty. *Orthop Traumatol Surg Res* 2016; **102**: S9-20 [PMID: 26797005 DOI: 10.1016/j.otsr.2015.11.001]

25 **Archibeck MJ**, Tripuraneni KR, Carothers JT, Junick DW, Munson NR, Murray-Krezan CM. Prospective, Randomized, Surgeon-Blinded Comparison of Standard Magnification Assumption *vs* Magnification Marker Usage for Preoperative Templating in Total Hip Arthroplasty. *J Arthroplasty* 2017; **32**: 3061-3064 [PMID: 28602530 DOI: 10.1016/j.arth.2017.05.016]

26 **Kutzner KP**, Pfeil J, Kovacevic MP. Preoperative digital planning *vs* postoperative outcomes in total hip arthroplasty using a calcar-guided short stem: frequent valgization can be avoided. *Eur J Orthop Surg Traumatol* 2017; **27**: 643-651 [PMID: 28391517 DOI: 10.1007/s00590-017-1948-2]

27 **Mahmood SS**, Mukka SS, Crnalic S, Wretenberg P, Sayed-Noor AS. Association between changes in global femoral offset after total hip arthroplasty and function, quality of life, and abductor muscle strength. A prospective cohort study of 222 patients. *Acta Orthop* 2016; **87**: 36-41 [PMID: 26471772 DOI: 10.3109/17453674.2015.1091955]

28 **Amenabar T**, Marimuthu K, Hawdon G, Gildone A, McMahon S. Total hip arthroplasty using a short-stem prosthesis: restoration of hip anatomy. *J Orthop Surg (Hong Kong)* 2015; **23**: 90-94 [PMID: 25920653 DOI: 10.1177/230949901502300121]

29 **González Della Valle A**, Comba F, Taveras N, Salvati EA. The utility and precision of analogue and digital preoperative planning for total hip arthroplasty. *Int Orthop* 2008; **32**: 289-294 [PMID: 17404731 DOI: 10.1007/s00264-006-0317-2]

30 **Cassidy KA**, Noticewala MS, Macaulay W, Lee JH, Geller JA. Effect of femoral offset on pain and function after total hip arthroplasty. *J Arthroplasty* 2012; **27**: 1863-1869 [PMID: 22810007 DOI: 10.1016/j.arth.2012.05.001]

31 **Bhaskar D**, Rajpura A, Board T. Current Concepts in Acetabular Positioning in Total Hip Arthroplasty. *Indian J Orthop* 2017; **51**: 386-396 [PMID: 28790467 DOI: 10.4103/ortho.IJOrtho_144_17]

32 **Erivan R**, Aubret S, Villatte G, Mulliez A, Descamps S, Boisgard S. Does using a polyethylene RM press-fit cup modify the preparation of the acetabulum and acetabular offset in primary hip arthroplasty? *Orthop Traumatol Surg Res* 2017; **103**: 669-674 [PMID: 28579018 DOI: 10.1016/j.otsr.2017.03.026]

33 **Meermans G**, Doorn JV, Kats JJ. Restoration of the centre of rotation in primary total hip arthroplasty: the influence of acetabular floor depth and reaming technique. *Bone Joint J* 2016; **98-B**: 1597-1603 [PMID: 27909120 DOI: 10.1302/0301-620X.98B12.BJJ-2016-0345.R1]

34 **Mahmood SS**, Al-Amiry B, Mukka SS, Baea S, Sayed-Noor AS. Validity, reliability and reproducibility of plain radiographic measurements after total hip arthroplasty. *Skeletal Radiol* 2015; **44**: 345-351 [PMID: 25403426 DOI: 10.1007/s00256-014-2055-7]

35 **Bertz A**, Indrekvam K, Ahmed M, Englund E, Sayed-Noor AS. Validity and reliability of preoperative templating in total hip arthroplasty using a digital templating system. *Skeletal Radiol* 2012; **41**: 1245-1249 [PMID: 22588597 DOI: 10.1007/s00256-012-1431-4]

36 **Merle C**, Waldstein W, Pegg EC, Streit MR, Gotterbarm T, Aldinger PR, Murray DW, Gill HS. Prediction of three-dimensional femoral offset from AP pelvis radiographs in primary hip osteoarthritis. *Eur J Radiol* 2013; **82**: 1278-1285 [PMID: 23639771 DOI: 10.1016/j.ejrad.2013.02.040]

37 **Dorr LD**, Faugere MC, Mackel AM, Gruen TA, Bognar B, Malluche HH. Structural and cellular assessment of bone quality of proximal femur. *Bone* 1993; **14**: 231-242 [PMID: 8363862 DOI: 10.1016/8756-3282(93)90146-2]

38 **Erivan R**, Muller AS, Villatte G, Millerioux S, Mulliez A, Boisgard S, Descamps S. Short stems reproduce femoral offset better than standard stems in total hip arthroplasty: a case-control study. *Int Orthop* 2020; **44**: 45-51 [PMID: 31254017 DOI: 10.1007/s00264-019-04355-5]

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ORIGINAL ARTICLE

Clinical Trials Study

Periprosthetic joint infections in femoral neck fracture patients treated with hemiarthroplasty – should we use antibiotic-loaded bone cement?

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Abstract

BACKGROUND

Hemiarthroplasty is the most common treatment in elderly patients with displaced intra-capsular femoral neck fracture (FNF). Prosthetic joint infection (PJI) is one of the most feared and frequent complications post-surgery because of the frail health status of these patients and the need for fast track surgery. Therefore, priorities should lie in effective preventive strategies to mitigate this burden.

AIM

To determine how much the implementation of the routine use of antibiotic-loaded bone cement (ALBC) as a relatively easy-to-apply amendment to the surgical practice reduces the infection rate in our hemiarthroplasty cohort.

METHODS

We retrospectively assessed all demographic, health status and treatment-related

data of our FNF patients undergoing cemented hemiarthroplasty in the period from 2011 to 2017; 241 patients were further analyzed after exclusion of patients with cancer-related sequelae and those who died before the end of the 1-year observation period. The PJI rate as diagnosed on basis of the Musculoskeletal Infection Society (MSIS) criteria 2011 was determined for each included patient and compared in function of the bone cement used for hip stem fixation. Patients were split into a group receiving a plain bone cement in the period from January 2011 to June 2013 (non-ALBC group) and into a group receiving an ALBC in the period July 2013 to December 2017 (ALBC group). Data analysis was performed with statistical software. We further calculated the cost-efficacy of the implementation of routine use of ALBC in the second group balancing the in-hospital infection related treatment costs with the extra costs of use of ALBC.

RESULTS

In total 241 FNF patients who received cemented hemiarthroplasty in the period from January 2011 to January 2017 were eligible for inclusion in this retrospective study. There were 8 PJI cases identified in the ALBC group among n = 94 patients, whereas 28 PJI cases were observed in the non-ALBC group among n = 147 patients. The statistical analysis showed an infection risk reduction of 55.3% (in particular due to the avoidance of chronic delayed infections) in the ALBC group (95%CI: 6.2%-78.7%; P = 0.0025). The cost-evaluation analysis demonstrated a considerable cost saving of 3.500 € per patient, related to the implementation of routine use of ALBC in this group.

CONCLUSION

Use of ALBC is a potent infection preventive factor in FNF patients receiving cemented hemiarthroplasties. It was further found to be highly cost-effective.

Key Words: prosthetic joint infection; Femoral neck fracture patients; Hemiarthroplasty; Antibiotic-loaded bone cement; Prophylaxis; Cost-efficacy

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Core Tip: Routine use of antibiotic-loaded bone cement in cemented hemiarthroplasties of femoral neck fracture patients has the potential of reducing the infection risk to a significant degree. This measure should be considered on top of the implementation of strict protocols of special pre-, peri- and postoperative orthogeriatric care

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INTRODUCTION

Prosthetic joint infection (PJI) is a rare but very dreadful complication of arthroplasty. The incidence is typically in the range of 1%-2% after primary elective joint replacement[1], but easily surpasses 5% in the elderly population of femoral neck fracture (FNF) patients undergoing hemi- or total hip arthroplasty[2]. This high infection rate reflects the fragile health conditions of such patients being on an emergency surgery track and their often suboptimal pre-, peri- and postoperative care. It is expected that the FNF patient numbers will grow significantly in our ageing societies causing high socioeconomic costs and a high burden of morbidity and mortality[3]. In order to mitigate the high risk of complications occurring in this patient cohort, it is therefore mandatory to consider amendments to the routine surgical protocols. This also includes more potent preventive strategies for infections.

The prophylactic use of antibiotic-loaded bone cement (ALBC) is a frequent surgical practice in cemented hip and knee joint replacement aiming at reducing the risk of procedure related infections. The idea behind delivering antibiotics directly into the joint compartment was originally pioneered by Buchholz and Engelbrecht in 1969. They reported high initial peak concentrations of the antibiotic eluted in situ from bone cement which was found to exceed 100-1000 fold the minimum inhibitory concentration (MIC) of the pathogen in the first days without exposing the patient to major risks of side effects[4,5]. Systemically applied antibiotics, by contrast, often do not reach effective concentration

levels in the osteoarticular compartment as a consequence of reduced blood flow in inflamed tissue and limited bone penetration of many antibiotics[6]. Indeed, by implementing this additional prevention measure Buchholz achieved an impressive reduction in deep infections in both, primary and revision hip replacements[7]. Subsequently, the Scandinavian registries and – most recently - the National Joint Registry of UK have demonstrated that the additional use of ALBC to perioperative systemic prophylaxis reduces the revision risk in cemented joint replacement[8-10]. It can be further speculated that this effect might vary if specific cement brands were compared due to brand-specific differences in antibiotic elution as a function of their special polymer contents and porosities[11,12]. Although one would expect from these experiences in elective procedures that hemiarthroplasty patients might benefit equally or even more from additional local antibiotic prophylaxis, data in this patient group are still sparse. To the best of our knowledge there is also no cost evaluation available in fracture patients which calculated the treatment costs of hemiarthroplasty related infections against the extra costs of ALBC use instead of plain cement.

In view of the very high numbers of PJI cases which we observed in the past in our hemiarthroplasty patients we decided to assess the infection preventive effect of the implementation of routine ALBC use for our cemented hemiarthroplasties. By comparing the infection rate before and after this surgical protocol modification we wanted to address the following questions in form of a retrospective clinical study: (1) *(Primary endpoint of the study)* Does the implementation of ALBC instead of plain cement as standard for hip stem fixation reduce the infection rates in this frail patient cohort? (2) Do we observe the highest protective effect, if we switch to an ALBC brand which has been described as a superior antibiotic eluting polymer matrix[13,14]? (3) What is the influence of individual patient risk factors and parameters on the occurrence and course of PJI cases; and (4) *(Secondary endpoint of the study)* Is the implementation of routine use of ALBC cost-effective?

For this purpose we retrospectively analyzed the patients and compared the PJI rate in those hemiarthroplasty procedures which had been cemented in the period from 2011 to 2013 with the plain bone cement Cemex with the PJI rate of those procedures which had been cemented in the subsequent period 2013 to 2017 with the gentamicin loaded bone cement Palacos R+G.

MATERIALS AND METHODS

This study (study approval number 35/17 NoEPA by Hospital Ethical Committee) analyzed all hip fracture patients treated at the University Hospital Central de la Defensa Gómez Ulla in Madrid, Spain, in the period from 2011 to 2017. Patient data and clinical histories were available on paper or in electronic form in the hospital IT program Balmis® (Hewlett Packard, Spain). In total 427 patients with diagnosis of hip fractures were reported. Of these 72 were excluded because of osteosynthesis treatment, 114 patients were further excluded because of periprosthetic or oncologic fractures or because of premature death before completing the 1-year observation period. Finally, 241 patients with intracapsular neck of femur fractures who went on to have cemented hemiarthroplasty either with a mono- or with a bipolar prosthesis in this period were found eligible for study inclusion. All interventions were performed by the same team of surgeons and the same surgical access route to the femur (direct lateral or Hardinge access route). The preoperative parental antibiotic prophylaxis was administered in the following way: either administration of 2 g of cefazolin, initiated 60 min before incision, or administration of 1 g of vancomycin, respectively, in case of contraindications or allergy against cephalosporins. In total 3 additional shots of 1 g of cefazolin, each one in an interval of 8 h, or 1 g of vancomycin, each one in an interval of 12 h, respectively, were administered postoperatively.

The hemiarthroplasty prosthesis used in all patients of this study was the brand Multifit Integrated System® with monopolar Ellittica® head or the bipolar prosthesis head SBA® (both Samobiomedical, Italy). The bone cement used for stem fixation in the period from January 2011 until June 2013 was the antibiotic-free brand Cemex (Tecres Spa, Italy) of high viscosity, mixed under atmospheric conditions and retrogradely injected with aid of a gun. The bone cement subsequently used in the period from July 2013 until the end of the study in December 2017 was the 0.5 g gentamicin containing high viscous cement Palacos R+G (Heraeus-Medical, Germany), prepared in a vacuum-mixing system and retrogradely injected under pressure with aid of a gun.

The following patient data were collected from the files: age, sex, type of intracapsular femur fracture according to the Garden classification, type of trauma (low or high energy impact), form of arrival to the emergency department at the hospital (self-walking, in vehicle of relatives, by ambulance or transfer from another health institution). Presence of risk factors for infections were recorded including inflammatory arthropathies, degree of immunosuppression, diabetes mellitus, previous articular infection, malnutrition, hemophilia and presence of tumors. The health status of all patients was assessed using the American Society of Anesthesiologists (ASA) score, the degree of mobility was assessed according to the Functional Ambulation Category (FAC) score and the Barthel Functional (BF) index for activities of daily living was used to evaluate the level of functional independence. The diagnosis of acute or delayed periprosthetic infections within the observation period of 1 year was done on basis of the MSIS criteria 2011[15] (see Table 1). All data were collected in a Microsoft Excel® speadsheet in strict

Table 1 Criteria for diagnosis of periprosthetic joint infection according to the Musculoskeletal Infection Society Workgroup[15]

PJI exists when
(1) There is a sinus tract communicating with the prosthesis; or (2) A pathogen is isolated by culture from at least two separate tissue or fluid samples obtained from the affected prosthetic joint; or (3) Four of the following six criteria exist: (a) Elevated serum erythrocyte sedimentation rate (ESR) and serum C-reactive protein (CRP) concentration; (b) Elevated synovial leukocyte count; (c) Elevated synovial neutrophil percentage (PMN%); (d) Presence of purulence in the affected joint; (e) Isolation of a microorganism in one culture of periprosthetic tissue or fluid; or (f) Greater than five neutrophils per high-power field in five high-power fields observed from histologic analysis of periprosthetic tissue at 9400 magnification.

PJI: Periprosthetic joint infection.

anonymous form and analyzed using the statistical software package of SPSS®, version 15 (SPSS Inc., Chicago, IL, United States).

We further performed a cost-evaluation in which we compared across both study arms the overall product related costs as well as the costs related to the surgical interventions and to the days of in-hospital care according to the 2014 updated DRG (diagnosis related groups) based hospital reimbursement regulation DEF/2277/2014 for medical services and products in institutions of the Ministry of Defense of Spain. These costs include in detail: (1) Routine and special diagnostic and therapeutic examinations prior to the surgical procedure; (2) All expenses related to complications during the pre-, peri- and post-operative phase; (3) All expenses of surgical reinterventions, if required, because of bad surgical practice and within a period of 2 mo from day of hospital discharge; (4) All medication during the treatment including blood supply and hemoderivates; (5) Nutritional assistance including parenteral or enteral products; (6) Expenses related to the medical team (specialized doctors, nurses and auxillary staff); (7) Expenses for use of theatre and anesthesia; (8) Expenses for all required medical consumables and pre- and postoperative controls including the early ambulatory phase; (9) Expenses related to the days in an individual or shared hospital room; (10) Expenses within the intensive care unit, if required; and (11) Expenses for revision-related procedures after hospital discharge.

RESULTS

In total 241 patients with intracapsular neck of femur fractures who went on to receive cemented hemiarthroplasty in the period from January 2011 to December 2017 were eligible for inclusion in this retrospective study. They were stratified into 2 study groups according to the bone cement used for the fixation of the hip stem, 94 patients received the gentamicin-loaded bone cement (ALBC group) and 147 patients received the plain cement without any added antibiotic (non-ALBC group). The demographic and health status related data for all patients were analyzed in detail and compared between both groups with focus on risk factors for infections (see Table 2). There were 38 patients (25.9%) in the non-ALBC group who had one or several risk factors including inflammatory arthropathies, malnutrition, immunosuppression, diabetes, prior articular infection, tumors or hemophilia. The percentage of risk for infection patients was higher in the ALBC group with 39.4% (n = 47). Use of oral anticoagulants (acenocumarol) was also assessed and compared between the groups (6.8% in the non-ALBC group *vs* 8.5% in the ALBC group, data not shown). The predominant overall ASA status of the patients in both groups was 3 (52.9%) and the predominant FAC mobility score was 4. Distribution of sex and average of patient age were comparable in both groups.

Primary endpoint

The overall incidence of PJI was compared between both groups. The number of infection cases was found to be with 8 cases among 94 patients (8.5%) significantly lower in the ALBC group as opposed to 28 infections among 147 patients in the non-ALBC group (19%) within the observation period of 1 year (see Figure 1A). From the total number of 8 infections occurring in the ALBC group, 4 cases were classified as acute (evolution of symptoms before 3 mo) and 4 cases as chronic delayed (evolution of symptoms after three months). In the non-ALBC group, 8 infections were of acute nature while 20 were delayed (see Figure 1B). This means in the statistical analysis that the use of the gentamicin-loaded bone cement Palacos R+G instead of the plain cement Cemex led to an overall reduction of the infection risk of 55.3% (95%CI: 6.2%-78.7%; P = 0.0025). The number needed to treat was 1.8.

Secondary endpoint

The implementation of routine use of the antibiotic-loaded bone cement Palacos R+G instead of the plain cement Cemex resulted in additional treatment costs. In order to justify these extra costs, we calculated the cost-benefit ratio of this new measure on basis of our routine hemiarthroplasty cost figures and the additional treatment expenses related to the management of the infection cases. The

Table 2 Basic clinical data of included patients in study according to the study arms

Items	Plain cement group (*n* = 147), *n* (%)	ALBC group (*n* = 94), *n* (%)	Both groups, (*n* = 241), *n* (%)
Sex			
Male	42 (28.6)	29 (30.9)	71 (29.5)
Female	105 (71.4)	65 (69.1)	170 (70.5)
Age			
< 80	27 (18.4)	25 (26.6)	52 (21.6)
> 80	120 (81.6)	69 (73.4)	189 (78.4)
Garden classification			
I	4 (2.7)	10 (10.6)	14 (5.8)
II	19 (12.9)	8 (8.5)	27 (11.2)
III	47 (32.0)	35 (37.2)	82 (34.0)
IV	77 (52.4)	41 (43.6)	118 (49.0)
Type of trauma			
High energy	1 (0.7)	0 (0)	1 (0.4)
Low energy	146 (99.3)	94 (100)	240 (99.6)
Arrival at hospital			
Walking	2 (1.4)	5 (5.3)	7 (2.9)
Transferral by relatives	1 (0.7)	1 (1.1)	2 (0.8)
Ambulance	95 (64.6)	75 (79.8)	170 (70.5)
Transferral from other centres	49 (33.3)	13 (13.8)	62 (25.7)
Risk factors for infections			
Yes	38 (25.9)	37 (39.4)	75 (31.1)
No	109 (74.1)	57 (60.6)	166 (68.9)

Presentation of femur neck fracture patient characteristics in each group with focus on sex, age, Garden classification of hip fractures, type of trauma, mode of arrival at hospital and risk factors for infection (focus on: presence of inflammatory arthropathies, degree of immunosuppression, presence of diabetes mellitus, previous articular infection, malnutrition, hemophilia and presence of tumors). ALBC: Antibiotic-loaded bone cement.

documented in-hospital costs for the implantation of a primary cemented hemiprosthesis in our institution are 12.665 €. In case of complications these costs increase significantly to 24.205 € for treatment of acute infections or to 35.746 € for the treatment of chronic delayed infections, reflecting in particular length of stay in the hospital and additional surgical intervention costs. The added costs for each patient receiving ALBC instead of plain cement (+20 € per package of 40 g) were subsequently put in relation to the number of avoided infections in the ALBC group. Based on the above shown numbers of infections occurring in each group with their subsequent treatment costs for both, acute and chronic cases, we calculated an average treatment cost of 14.127 € per patient in the ALBC group and of 17.632 € per patient in the non-ALBC group. These figures represent a cost saving of approximately 3.505 € for each patient after switching to the ALBC Palacos R+G.

DISCUSSION

The occurrence of PJI in the cohort of FNF patients treated with hemiarthroplasty is much more frequent and an even more catastrophic complication than in elective hip replacement patients. The high infection rates reflect the general frailty of the patients presenting at an advanced age, with an acute trauma event and with a high burden of comorbidities[16]. Further risk factors for infections have to be added to this including the operative conditions (junior surgeon, uncemented stems, duration of surgery) and the post-operative management regimen (length of hospitalization, hematoma, prolonged wound drainage and urinary catheterizations) as shown in a recent literature review[17]. The surgical and antibiotic treatment of the infection cases together with the extended immobility period further

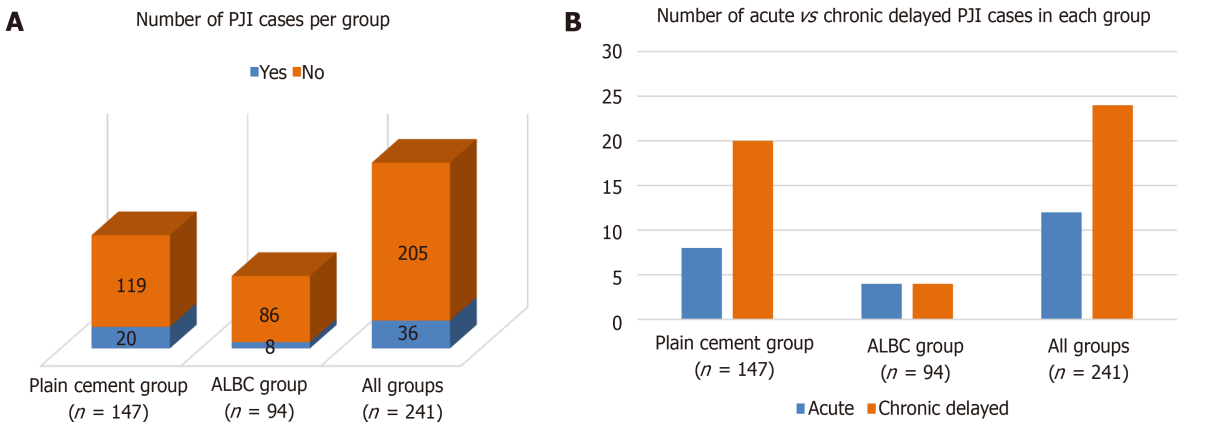


Figure 1 Graphical presentation. A: The number of periprosthetic joint infection (PJI) cases (blue color) *vs* non-infection cases (orange color) in each group within the observation period of 1 yr; B: The number of acute (blue color) *vs* chronic delayed PJI cases (orange color) in each group within the observation period of 1 yr. Staphylococci were the most frequent pathogens (*S. aureus* with higher prevalence in acute infections, coagulase-negative staphylococci with higher prevalence in chronic delayed infections – data not shown). PJI: Periprosthetic joint infection; ALBC: Antibiotic-loaded bone cement.

weakens the organism leading to 1-year mortality rates in the range of 40% to 50%[18,19].

Staphylococcus is the most commonly found microorganism in acute and chronic infections. While the prevalence of *S. aureus* as culprit of PJI is gradually decreasing, coagulase-negative Staphylococci are being found more and more in acute and particularly chronic infections[20]. These bacteria are either directly inoculated through contaminated implants during surgery or postoperatively through contiguous spread from slow healing wounds or through hematogeneous dissemination from more remote bacteremias. Among the anti-straphylococcal weapons available the bactericidal antibiotic gentamicin has still largely retained its antimicrobial efficacy – at least if it is present at high concentrations. Such high peak levels can be expected after initial release of the antibiotic from a well eluting bone cement. Indeed, the analysis of major European arthroplasty registries has shown that the combination of systemic perioperative and local antibiotic prophylaxis *via* gentamicin-loaded bone cement lowers the overall revision risk and protects the implants from early infections[8-10] In a similar way Sanz-Ruiz *et al*[21] recently observed an impressive reduction in their PJI rate (-57% for all cemented primary prostheses and -72.6% for cemented hip replacements) after switching from plain cement to ALBC. Interestingly, the PJI incidence in all their uncemented procedures did not change in the entire observation period, thus suggesting that the outcome was, in fact, due to the change of the bone cement category[21].

One might speculate that the particularly frail population of FNF patients treated with cemented hemiarthroplasty would equally or benefit even more from the presence of an additional antimicrobial "frontline" in situ. However, this hypothesis has not been systematically evaluated in our country. Our present study provides evidence that the implementation of the routine use of ALBC instead of plain cement is a powerful anti-infective measure in this patient cohort. We show here that the number of PJI cases could be significantly reduced by 55% if stems were cemented with ALBC. This effect was even more remarkable in light of the higher percentage of patients with well described risk factors for infections in the ALBC group compared to the non-ALBC group.

We are aware that this finding may not only reflect the switch from an unloaded to an antibiotic-loaded cement category, but may also depend on individual cement brand characteristics. This fits to prior observations showing that the ALBC brand PALACOS R+G has a superior antibiotic elution behaviour compared to other bone cement brands[13,14].

The PJI rate in our hemiarthroplasty patients was found to be much higher than described in the literature, probably reflecting "real world" experiences in our hospital until recently. This refers to the absence of a special orthogeriatric optimization protocol prior and post-surgery as well as to the absence of a routine follow-up of possible complications. Patients were transferred back to their residences or homes and followed by a general practitioner without further hospital consultations in the orthopedic unit where the surgery had been performed. This led to practices where patients with infections were re-admitted to our hospital in an already chronic state, with strong wound dehiscence or even fistula formation and oral antibiotic therapy already initiated. The lessons which we learned from these observations have now triggered the implementation of new protocols. We now routinely improve the pre-operative control of our FNF patients (focus on nutritional status, glycemic control, treatment of urinary tract infections *etc.*), we strictly avoid intraoperative hypothermia and implement postoperative follow-up consultations in the hospital with early diagnosis of possible infection cases. By following these new protocols in combination with the use of ALBC we hope to further decrease the PJI incidence in our FNF patients.

Inspired by recent observations that the antibiotic combinations gentamicin and clindamycin or gentamicin and vancomycin in bone cement exert a stronger and more sustained growth inhibition on many bacteria compared to the gentamicin mono-cement[22,23], we will soon start to test the hypothesis of an even more efficient local antibiotic prophylaxis with dual ALBC in our FNF patients. We therefore want to repeat the here described clinical study comparing in the future PJI incidence between a group receiving the single ALBC Palacos R+G *vs* the PJI rate in a group receiving the dual ALBC Copal G+C (containing 1 g of gentamicin and 1 g of clindamycin). Indeed, Sanz-Ruiz *et al*[24] have recently provided some proof of concept by showing that the routine use of Copal G+C decreased the number of PJI cases in procedures associated with a higher infection risk (aseptic knee revision procedures). The observed risk reduction in the Copal G+C group was 53% compared to the Palacos R+G group. Similarly, Sprowson *et al*[25] also reported a lower infection rate in their highly standardized hemiarthroplasty patient cohorts in the United Kingdom, if allocated to the dual ALBC group. However, it has to be pointed out that the United Kingdom in contrast to many other countries follows a high standard of care for fracture patients by imposing orthogeriatric guidelines on the basis of regular assessments of their national fracture database[26]. Therefore, clinical treatment experiences in the United Kingdom may not be fully transferable to countries with less rigorous orthogeriatric care standards.

Routine use of ALBC is still associated with concerns regarding possible systemic side effects and the risk of resistance development. While caution with high dose ALBC (exceeding concentrations of 3.6 g antibiotic per 40 g of cement – *e.g.*, in spacers during staged septic treatment) appears justified for patients with pre-existing acute kidney injuries[27], there is no evidence for such concerns with low dose ALBC. In fact, we did not observe a higher rate of complications attributed to the use of ALBC in our FNF patients nor a higher rate of *Clostridium difficile* infections. Because of the local mode of antibiotic action there is also no proof so far that ALBC use triggers clinically relevant antibiotic resistance development[28].

Most health systems have come under progressive economic pressure. It is therefore of interest to conclude from our simple cost-benefit evaluations that the relatively easily applicable measure of routine ALBC use in hemiarthroplasty patients has such a cost saving potential in our institution. We could show that approximately 3.500 € could be saved for each patient in the ALBC group. Although this figure will vary from country to country and even from hospital to hospital depending on the price differences between the cements and the hospital-specific PJI treatment costs, we believe that they can provide an indication of what can be achieved.

Our study has several limitations. These refer in the first instance to the retrospective nature of the study and to the limited and not equally balanced number of patients in each study arm. We can also not exclude a cement material related effect because of choosing the plain cement brand from one manufacturer and the ALBC brand from another. However, we would rule out a major patient, procedure and surgical skill related bias between both groups, since patient characteristics, prosthesis use and duration of surgeries as well as the pool of operating surgeons were comparable in the observation periods.

CONCLUSION

The present pilot study has demonstrated that in the absence of good clinical protocols for the frail cohort of FNF patients the relatively easy-to-apply implementation of routine use of ALBC significantly reduces the high number of PJI cases in cemented hemiarthroplasty. This measure was found to be highly cost-effective and leads to considerable savings of treatment costs. The study also brings to attention how important it is to implement orthogeriatric guidelines in a hospital in order to achieve a better pre-, peri- and postoperative care of FNF patients.

Further studies are needed to truly elucidate the effect of ALBC – even loaded with two antibiotics - on a larger scale in FNF patients. Based on our experiences so far we strongly recommend the use of ALBC for cemented arthroplasty in FNF patients.

ARTICLE HIGHLIGHTS

Research background

Use of antibiotic-loaded bone cement (ALBC) for fixation of cemented hip stems in the context of hemiarthroplasties may establish an additional antimicrobial "frontline" in the vulnerable joint compartment.

Research motivation

Given the high periprosthetic joint infection (PJI) rates in this frail patient group of femur neck fracture (FNF), it appears mandatory to consider further effective and easy-to-apply infection preventive measures.

Research objectives

The aim of this study was to compare the PJI rate between patients receiving cemented hip stems with plain cement (non-ALBC group) and patients receiving cemented hip stems with gentamicin-loaded bone cement (ALBC group) in one of the biggest Military hospitals in Spain. The treatment costs of PJI cases in each group were subsequently put in relation to the extra costs related to the routine use of ALBC instead of plain cement.

Research methods

In total 241 FNF patients who went on to receive cemented hemiarthroplasty during the period from January 2011 to December 2017 were eligible for inclusion in this retrospective study. Patients were stratified into 2 study groups according to the bone cement used for the fixation of the hip stem. The number of PJI cases were analyzed and compared between both groups. Infections were further differentiated between early or chronic delayed infections by the onset of symptoms. Treatment costs in each group were compared with the extra costs related to the use of gentamicin-loaded bone cement in the ALBC group.

Research results

Use of ALBC in our hospital setting and in the absence of strict guidelines regulating pre-, peri- and postoperative care of FNF patients has been found to reduce the infection rate by 55%. Despite the extra costs of ALBC use instead of plain cement, this change of surgical practice led to savings of approximately 3500 € per patient.

Research conclusions

Use of ALBC was found to be a potent infection prevention factor in FNF patients receiving cemented hemiarthroplasties. It was further found to be highly cost-effective.

Research perspectives

Further studies validating the generalizability of our findings under different pre-, peri- and postoperative conditions of FNF patient care are warranted. This does also include the use of dual ALBC to further reduce the still high infection rates.

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FOOTNOTES

Author contributions: Crego-Vita D has been the supervisor and principal investigator in this IIT; Aedo-Martin D, García-Canas R, Espigares-Correa A and Sánchez-Pérez C performed the patient consultations, the pre- and postoperative diagnosis and the surgeries; and Berberich C made substantial contributions to the interpretation and discussion of the study and drafted the manuscript.

Institutional review board statement: The first author and principal investigator of the study who submitted the study proposal to the ethics committee received the ethical clearance of this study from the ethical review board of the hospital (see separate certificate).

Informed consent statement: Because of the retrospective nature of the here presented clinical study signed informed consent form is not needed. However, the ethics committee of the Hospital Central de la Defensa Gómez Ulla (Military Hospital Gómez Ulla) has given permission to conduct this study (see certificate).

Conflict-of-interest statement: All authors of this study declare that there is no conflict of interest.

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REFERENCES

1 **Izakovicova P**, Borens O, Trampuz A. Periprosthetic joint infection: current concepts and outlook. *EFORT Open Rev* 2019; **4**: 482-494 [PMID: 31423332 DOI: 10.1302/2058-5241.4.180092]
2 **Gallardo-Calero I**, Larrainzar-Coghen T, Rodriguez-Pardo D, Pigrau C, Sánchez-Raya J, Amat C, Lung M, Carrera L, Corona PS. Increased infection risk after hip hemiarthroplasty in institutionalized patients with proximal femur fracture. *Injury* 2016; **47**: 872-876 [PMID: 26857632 DOI: 10.1016/j.injury.2015.12.032]
3 **Baker PN**, Salar O, Ollivere BJ, Forward DP, Weerasuriya N, Moppett IK, Moran CG. Evolution of the hip fracture population: time to consider the future? *BMJ Open* 2014; **4**: e004405 [PMID: 24747789 DOI: 10.1136/bmjopen-2013-004405]
4 **Buchholz HW**, Elson RA, Heinert K. Antibiotic-loaded acrylic cement: current concepts. *Clin Orthop Relat Res* 1984; 96-108 [PMID: 6386264]
5 **Neut D**, Kluin OS, Thompson J, van der Mei HC, Busscher HJ. Gentamicin release from commercially-available gentamicin-loaded PMMA bone cements in a prosthesis-related interfacial gap model and their antibacterial efficacy. *BMC Musculoskelet Disord* 2010; **11**: 258 [PMID: 21067595 DOI: 10.1186/1471-2474-11-258]
6 **Landersdorfer CB**, Bulitta JB, Kinzig M, Holzgrabe U, Sörgel F. Penetration of antibacterials into bone: pharmacokinetic, pharmacodynamic and bioanalytical considerations. *Clin Pharmacokinet* 2009; **48**: 89-124 [PMID: 19271782 DOI: 10.2165/00003088-200948020-00002]
7 **Buchholz HW**, Elson RA, Engelbrecht E, Lodenkämper H, Röttger J, Siegel A. Management of deep infection of total hip replacement. *J Bone Joint Surg Br* 1981; **63-B**: 342-353 [PMID: 7021561 DOI: 10.1302/0301-620X.63B3.7021561]
8 **Engesaeter LB**, Lie SA, Espehaug B, Furnes O, Vollset SE, Havelin LI. Antibiotic prophylaxis in total hip arthroplasty: effects of antibiotic prophylaxis systemically and in bone cement on the revision rate of 22,170 primary hip replacements followed 0-14 years in the Norwegian Arthroplasty Register. *Acta Orthop Scand* 2003; **74**: 644-651 [PMID: 14763692 DOI: 10.1080/00016470310018135]
9 **Jämsen E**, Huhtala H, Puolakka T, Moilanen T. Risk factors for infection after knee arthroplasty. A register-based analysis of 43,149 cases. *J Bone Joint Surg Am* 2009; **91**: 38-47 [PMID: 19122077 DOI: 10.2106/JBJS.G.01686]
10 **Leong JW**, Cook MJ, O'Neill TW, Board TN. Is the use of antibiotic-loaded bone cement associated with a lower risk of revision after primary total hip arthroplasty? *Bone Joint J* 2020; **102-B**: 997-1002 [PMID: 32731820 DOI: 10.1302/0301-620X.102B8.BJJ-2020-0120.R1]
11 **Kuehn KD**, Ege W, Gopp U. Acrylic bone cements: composition and properties. *Orthop Clin North Am* 2005; **36**: 17-28, v [PMID: 15542119 DOI: 10.1016/j.ocl.2004.06.010]
12 **Vaishya R**, Chauhan M, Vaish A. Bone cement. *J Clin Orthop Trauma* 2013; **4**: 157-163 [PMID: 26403875 DOI: 10.1016/j.jcot.2013.11.005]
13 **Meeker DG**, Cooper KB, Renard RL, Mears SC, Smeltzer MS, Barnes CL. Comparative Study of Antibiotic Elution Profiles From Alternative Formulations of Polymethylmethacrylate Bone Cement. *J Arthroplasty* 2019; **34**: 1458-1461 [PMID: 30935799 DOI: 10.1016/j.arth.2019.03.008]
14 **Hendriks JG**, van Horn JR, van der Mei HC, Busscher HJ. Backgrounds of antibiotic-loaded bone cement and prosthesis-related infection. *Biomaterials* 2004; **25**: 545-556 [PMID: 14585704 DOI: 10.1016/s0142-9612(03)00554-4]
15 **Parvizi J**, Zmistowski B, Berbari EF, Bauer TW, Springer BD, Della Valle CJ, Garvin KL, Mont MA, Wongworawat MD, Zalavras CG. New definition for periprosthetic joint infection: from the Workgroup of the Musculoskeletal Infection Society. *Clin Orthop Relat Res* 2011; **469**: 2992-2994 [PMID: 21938532]
16 **Crego-Vita D**, Sanchez-Perez C, Gomez-Rico JA, de Arriba CC. Intracapsular hip fractures in the elderly. Do we know what is important? *Injury* 2017; **48**: 695-700 [PMID: 28088377 DOI: 10.1016/j.injury.2017.01.022]
17 **Noailles T**, Brulefert K, Chalopin A, Longis PM, Gouin F. What are the risk factors for post-operative infection after hip hemiarthroplasty? *Int Orthop* 2016; **40**: 1843-1848 [PMID: 26611729 DOI: 10.1007/s00264-015-3033-y]
18 **Guren E**, Figved W, Frihagen F, Watne LO, Westberg M. Prosthetic joint infection-a devastating complication of hemiarthroplasty for hip fracture. *Acta Orthop* 2017; **88**: 383-389 [PMID: 28271919 DOI: 10.1080/17453674.2017.1301009]
19 **Edwards C**, Counsell A, Boulton C, Moran CG. Early infection after hip fracture surgery: risk factors, costs and outcome. *J Bone Joint Surg Br* 2008; **90**: 770-777 [PMID: 18539671 DOI: 10.1302/0301-620X.90B6.20194]
20 **Osmon DR**. Microbiology and Antimicrobial Challenges of Prosthetic Joint Infection. *J Am Acad Orthop Surg* 2017; **25** Suppl 1: S17-S19 [PMID: 27922947 DOI: 10.5435/JAAOS-D-16-00639]
21 **Sanz-Ruiz P**, Matas-Diez JA, Sanchez-Somolinos M, Villanueva-Martinez M, Vaquero-Martín J. Is the Commercial Antibiotic-Loaded Bone Cement Useful in Prophylaxis and Cost Saving After Knee and Hip Joint Arthroplasty? *J*

Arthroplasty 2017; **32**: 1095-1099 [PMID: 27919578 DOI: 10.1016/j.arth.2016.11.012]

22 **Ensing GT**, van Horn JR, van der Mei HC, Busscher HJ, Neut D. Copal bone cement is more effective in preventing biofilm formation than Palacos R-G. *Clin Orthop Relat Res* 2008; **466**: 1492-1498 [PMID: 18338216 DOI: 10.1007/s11999-008-0203-x]

23 **Cara A**, Ballet M, Hemery C, Ferry T, Laurent F, Josse J. Antibiotics in Bone Cements Used for Prosthesis Fixation: An Efficient Way to Prevent *Staphylococcus aureus* and *Staphylococcus epidermidis* Prosthetic Joint Infection. *Front Med (Lausanne)* 2020; **7**: 576231 [PMID: 33553196 DOI: 10.3389/fmed.2020.576231]

24 **Sanz-Ruiz P**, Matas-Diez JA, Villanueva-Martínez M, Santos-Vaquinha Blanco AD, Vaquero J. Is Dual Antibiotic-Loaded Bone Cement More Effective and Cost-Efficient Than a Single Antibiotic-Loaded Bone Cement to Reduce the Risk of Prosthetic Joint Infection in Aseptic Revision Knee Arthroplasty? *J Arthroplasty* 2020; **35**: 3724-3729 [PMID: 32682594 DOI: 10.1016/j.arth.2020.06.045]

25 **Sprowson AP**, Jensen C, Chambers S, Parsons NR, Aradhyula NM, Carluke I, Inman D, Reed MR. The use of high-dose dual-impregnated antibiotic-laden cement with hemiarthroplasty for the treatment of a fracture of the hip: The Fractured Hip Infection trial. *Bone Joint J* 2016; **98-B**: 1534-1541 [PMID: 27803231 DOI: 10.1302/0301-620X.98B11.34693]

26 **Ftouh S**, Morga A, Swift C; Guideline Development Group. Management of hip fracture in adults: summary of NICE guidance. *BMJ* 2011; **342**: d3304 [PMID: 21693526 DOI: 10.1136/bmj.d3304]

27 **Dagneaux L**, Limberg AK, Osmon DR, Leung N, Berry DJ, Abdel MP. Acute Kidney Injury When Treating Periprosthetic Joint Infections After Total Knee Arthroplasties with Antibiotic-Loaded Spacers: Incidence, Risks, and Outcomes. *J Bone Joint Surg Am* 2021; **103**: 754-760 [PMID: 33780403 DOI: 10.2106/JBJS.20.01825]

28 **Sanz-Ruiz P**, Berberich C. Infection Risk-Adjusted Antibiotic Prophylaxis Strategies in Arthroplasty: Short Review of Evidence and Experiences of a Tertiary Center in Spain. *Orthop Res Rev* 2020; **12**: 89-96 [PMID: 32821178 DOI: 10.2147/ORR.S256211]

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ORIGINAL ARTICLE

Observational Study

Bone mineral density in fracture neck of femur patients: What's the significance?

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Abstract

BACKGROUND

The National Institute for Health and Care Excellence (NICE) guidelines have advised further research is required into investigating the added prognostic value of bone mineral density (BMD) in the assessment of fracture risk with the Fracture Risk Assessment Tool (FRAX) score.

AIM

To investigate the significance of BMD in fracture neck of femur patients and compare it to the outcome of the FRAX score.

METHODS

Inclusion criteria for this study were all patients who underwent dual-energy X-ray absorptiometry (DXA) scan following fracture neck of femur between 2015 and 2017. Analysis of BMD, FRAX scores and patient demographic data was undertaken.

RESULTS

A total of 69 patients were included in the study, mean age 74.1 years. There was no significant difference between mean BMD of the femoral neck in males (0.65) as compared to females (0.61) (P = 0.364). Analyses showed no significant correlation between BMD and menopause age (r_s = -0.28, P = 0.090). A significant difference was seen of the femoral neck BMD between the different fracture pattern types (P = 0.026). A stronger correlation was observed between BMD of femoral neck and FRAX major score (r_s = -0.64, P < 0.001) than with BMD of lumbar spine and FRAX major score (r_s = -0.37, P = 0.003).

CONCLUSION

This study demonstrated that BMD of the femoral neck measured by DXA scan is of added prognostic value when assessing patients for risk of fracture neck of femur in combination with the FRAX predictive scoring system.

Key Words: Fracture neck of femur; Bone mineral density; Fracture Risk Assessment Tool score; Fragility fracture; Osteoporosis

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Core Tip: The results in this study place more emphasis on bone mineral density (BMD) when assessing fracture risk, in comparison to key factors incorporated into the Fracture Risk Assessment Tool (FRAX) predictive score. Menopause age and female gender had an indeterminate influence on BMD, as well as World Health Organization classification of osteoporosis. Body mass index had a significant influence on BMD. Osteoporosis was more common in patients with extra-capsular hip fracture patterns. This study shows that BMD is significant in assessing risk of fracture neck of femur in comparison to the FRAX predictive score.

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INTRODUCTION

The National Institute for Health and Care Excellence (NICE) define osteoporosis as a disease characterised by low bone mass and structural deterioration of bone tissue, with a consequent increase in bone fragility and susceptibility to fracture[1]. Fractures secondary to osteoporosis may be referred to as fragility fractures; which are described as those resultant from a mechanical force that would not ordinarily be associated with a fracture[2]; further described by the World Health Organization (WHO) where a fracture occurs from forces equal to or less than a fall from a standing height[1].

Osteoporosis may be viewed as primary or secondary. Primary being characterised by age and sex hormone related progressive mineral loss[3]. Secondary osteoporosis occurs as a result of different pathologies and use of specific medication[4].

Osteoporosis is a disease that develops silently, only manifesting on occurrence of a fracture. It is for this reason that the increase in osteoporosis related pathology has been entitled by some as the "silent epidemic"[4]. The WHO considers osteoporosis to be only second to cardiovascular diseases as a crucial healthcare issue[5].

Prevalence of osteoporosis is known to increase with age, from 2% at age 50 years to 25% at age 80 years[1]. There are known to be over three million United Kingdom residents with osteoporosis at present[6], with this figure expected to continue to rise. Subsequently, the burden on healthcare services as a result of osteoporosis is only likely to rise with the ongoing increase in the world population. In the United Kingdom alone; projections suggest that the incidence of fragility fractures is likely to increase by 21% by the year 2020 (230000 per annum), with a resultant overall annual cost upwards of £2.1 billion [6]. In Europe it is estimated that direct costs resulting from osteoporotic fractures to have an overall cost of €76.7 billion[7].

Despite the above figures, it is almost impossible to truly predict the economic burden of osteoporosis and osteoporotic fractures. The consequences are not only that of economic cost to the healthcare system, but also of associated morbidity, impairment, reduced quality of life and mortality. It is therefore paramount that resources and research into fracture prediction and prevention continues, to ensure that efficient allocation of resources may continue in an already stretched healthcare system.

The International Osteoporosis Foundation and the WHO state that fracture risk should be advised as a short-term absolute risk[8]. A period of ten years is agreed upon as this comprises the probable duration of treatment as well as the benefits that may continue once treatment is ceased[4]. There are several different predicting tools used to identify risk of fragility fracture. The fracture risk assessment tool (FRAX®) is a predictive algorithm developed by the University of Sheffield that takes into account clinical risk factors, with or without the addition of bone mineral density (BMD)[9,10]. The FRAX tool provides a 10-year probability of hip or major osteoporotic fracture by means of a percentage likelihood [11]. The clinical risk factors utilised as part of the FRAX predictive tool are displayed in Table 1.

Table 1 Osteoporosis risk factors utilised in Fracture Risk Assessment Tool predictive tool for osteoporotic fractures[29]

Clinical risk factors
Age
Gender
Weight
Height
Previous fracture
Parent fractured hip
Current smoking
Glucocorticoid use
Rheumatoid arthritis
Secondary osteoporosis risk factors — Type I diabetes mellitus, osteogenesis imperfecta, hyperthyroidism, hypogonadism, premature menopause, chronic malnutrition or malabsorption, chronic liver failure
Alcohol — 3 or more units per day
Bone mineral density

BMD is defined as grams per centimetre squared (g/cm^2)[12]. This is measured by means of dual-energy X-ray absorptiometry (DXA) scan. A value of BMD (g/cm^2) is therefore given for the area of bone scanned (most commonly proximal femur and lumbar spine)[12]. Alternatively, the value may be converted to a value in comparison (standard deviation) with the peak bone mass of a Caucasian female aged 30 (T-score), or for the peak bone mass adjusted for age, gender and race (*z*-score)[12]. It is the T-score that is used by the WHO as an objective means of defining osteoporosis in an individual as per DXA scan result; with Osteoporosis being defined as T-score less than or equal to -2.5 (Table 2)[13].

Currently in the United Kingdom it is common practice for the FRAX tool to be used by a primary care physician to give 10-year probability of major osteoporotic fracture. NICE guidelines currently advise if the value is significant, then preventative management is to be initiated immediately, however if the risk is moderate, a DXA scan is advised to further quantify the probability.

A number of recent publications have focused on re-assessment of the importance of clinical risk factors associated with the progression to osteoporosis, including BMD. Trajanoska *et al*[14] conducted a meta-analysis of genome-wide association studies and a two-sample mendelian randomisation approach to assess the role of fifteen clinical risk factors on osteoporotic fracture risk. It was deduced that among clinical risk factors for fracture that were assessed, only BMD was shown to have a major causal effect on fracture. This mendelian randomisation study provides evidence against a causal effect of several proposed clinical risk factors for fractures (*e.g.*, diabetes, glucose, rheumatoid arthritis, and vitamin D)[14].

Findings from the Foundation of the National Institutes of Health (FNIH) Bone Quality Project, a meta-analysis of twenty-two trials, have shown that a twenty-four percent change in BMD, as per DXA measurement, is responsible for a large proportion of the fracture risk reduction across a range of osteoporosis treatment options[15]. The regression analysis conducted as part of the study displayed percentage difference in increase in BMD (change in BMD with treatment minus the change in BMD with placebo) at the hip, femoral neck, and lumbar spine was significantly associated with relative risk reduction of having a fracture[15]. This, in turn, supports the notion that the BMD, as measured per DXA scan, be utilised as a surrogate biomarker in the measurement of disease progression and management of osteoporosis.

As part of recent guidelines, NICE have recommended research to be focused on the added prognostic value of BMD in the assessment of fracture risk with FRAX[1]. NICE state that there is currently not sufficient research, in primary or secondary care, evaluating if the addition of BMD to FRAX improves the accuracy of the predicted fracture risk[1]. More specifically, NICE advise further research is required to ensure that the addition of BMD results in the correct re-classification of risk, *i.e.*, high to low risk and vice versa[1].

The authors hypothesise an increased significance of BMD in comparison to the individual components of the FRAX score. The aim of this study was to investigate the significance of BMD in fracture neck of femur patients and compare it to the outcome of the FRAX score.

Table 2 World Health Organisation classification of osteoporosis[29]

Terminology	T-score definition
Normal	T ≥ -1.0
Osteopenia	-2.5 < T < -1.0
Osteoporosis	T ≤ -2.5
Severe osteoporosis	T ≤ -2.5 in the presence of one or more fragility fracture

MATERIALS AND METHODS

Patients

This retrospective observational cohort study which did not require ethics committee approval. All patients had sustained a fracture neck of femur and managed as appropriate under the admitting on-call consultant orthopaedic surgeon between 2015 to 2017.

All patients underwent a DXA scan following completion of management of the fractured neck of femur. DXA images were taken of the contralateral femoral neck and the lumbar spine (L2, L3, L4), in line with published protocols[5,10,11]. Patients with contralateral hip prosthesis in-situ and with lumbar spine instrumentation were excluded from the study. FRAX scores were calculated for all the patients included in the study.

Fracture pattern classification

Neck of femur fractures were classified as intra-capsular or extra-capsular. Extra-capsular fractures were defined as those at the inter-trochanteric line (fracture line passes through the greater trochanter to the lesser trochanter) or distal to this as assessed on plain radiograph imaging (antero-posterior pelvis and lateral hip). Fractures proximal to the inter-trochanteric line were classified as intra-capsular fractures. This is a validated radiographic classification system of fracture neck of femur pattern[16].

Proposed outcome

The authors aim to investigate the association between BMD and the components of the FRAX score within the cohort.

Statistical analysis

All continuous data variables displayed a skewed distribution (verified by both plotted histograms and the Shapiro-Wilks test). The appropriate non-parametric statistical test was used in their analyses. This includes Mann Whitney *U* test and Kruskall-Wallis *H* test used in the appropriate manner. The Chi-squared test was used for the categorical data analysis of the fracture neck of femur pattern type and the Spearman Rank test was used for the correlation analyses. The level of statistical significance was set at $P < 0.05$. Statistical analysis was performed using SPSS for Windows version 25.0 (IBM Corp., Armonk, New York, United States).

RESULTS

Table 3 displays the demographic data of the study cohort. A total of 69 patients were included in the cohort, all undergoing DXA scan following fracture neck of femur and undergoing a complete FRAX score assessment.

Table 4 shows the fracture neck of femur classification pattern. Table 5 shows the details of the surgical management.

The mean FRAX score for a major osteoporotic fracture amongst the study cohort was 19.87% (SD 11.01%); this score representing the percentage probability of occurrence of fracture of the distal radius, proximal humerus, lumbar spine or neck of femur over a ten-year period (Table 6). In addition, the mean FRAX score for fracture neck of femur amongst the study cohort was 7.75% (SD 8.09%); representing the ten-year percentage probability of fracture neck of femur only (Table 6). BMD of the femoral neck and lumbar spine where used to calculate the corresponding T-score and *z*-score. Table 2 shows the WHO classification of Osteoporosis when interpreting T-score values. None of the patients included in this study fitted the classification grade of osteoporosis as all of them had fragility fractures and so by definition were classified as severe osteoporosis when the T-score ≤ -2.5.

Table 7 shows that there was no statistically significant difference for either BMD of femoral neck or lumbar spine between males and females.

Table 3 Patient demographic data

Patient demographic	
Number of patients (*n*)	69
Age yr (mean, range)	74.1 (61-98)
Height cm (mean, range)	161.9 (141-190)
Weight kg (mean, range)	67.7 (31-150)
BMI (mean, range)	25.7 (16-63)
Gender (male:female)	25:44
Menopause age (mean, range)	46.6 (32-56)
Laterality (left:right)	27:42

BMI: Body mass index.

Table 4 Pattern of fracture neck of femur

	***n* (%)**
Intra-capsular fracture	36 (52.2)
Extra-capsular fracture	33 (47.8)

Table 5 Surgical management of fracture neck of femur

	***n* (%)**
Total hip replacement	24 (34.8)
Hemi-arthroplasty	10 (14.5)
Dynamic hip screw	31 (45.0)
Intra-medullary nail	4 (5.7)

Table 6 Dual-energy X-ray absorptiometry scan results

Dual-energy X-ray absorptiometry scan	
FRAX major (mean ± SD)	19.87 ± 11.01
FRAX hip (mean ± SD)	7.75 ± 8.09
BMD hip (mean ± SD)	0.62 ± 0.13
T-score hip (mean ± SD)	-2.20 ± 1.05
z-score hip (mean ± SD)	-0.60 ± 0.97
BMD spine (mean ± SD)	0.88 ± 0.30
T-score spine (mean ± SD)	-1.36 ± 1.65
z-score spine (mean ± SD)	0.37 ± 1.72

BMD: Bone mineral density; FRAX: Fracture Risk Assessment Tool.

Figure 1 illustrates the scatter plot graph showing no significant correlation between the menopause age of female patients and the BMD of either the femoral neck or lumbar spine.

Tables 8 and 9 show no statistically significant difference between the mean menopause age of female patients and the WHO classification of the femoral neck BMD and the lumbar spine BMD respectively.

Figure 2 shows a significant direct correlation between body mass index (BMI) and BMD for both femoral neck ($r_s = 0.58$; $P < 0.001$) and lumbar spine ($r_s = 0.43$; $P < 0.001$).

Table 7 Comparison of mean bone mineral density femoral neck and lumbar spine in males and females

	Male (*n* = 25)	Female (*n* = 44)	*P* value[1]
BMD femoral neck	0.65	0.61	0.364
BMD lumbar spine	1.01	0.85	0.135

[1]Mann Whitney *U* test. BMD: Bone mineral density.

Table 8 Analysis between World Health Organization classification of femoral neck bone mineral density and mean menopause age of female patients (*n* = 39)

	n	Menopause age (mean ± SD)	*P* value[1]
Normal	5	45.0 ± 7.4	0.086
Osteopenia	16	44.8 ± 5.1	
Severe osteoporosis	18	48.4 ± 5.1	

[1]Kruskal-Wallis *H* test.

Table 9 Analysis between World Health Organization classification of lumbar spine bone mineral density and mean menopause age of female patients (*n* = 40)

	n	Menopause age (mean ± SD)	*P* value[1]
Normal	15	47.2 ± 5.7	0.835
Osteopenia	15	46.1 ± 5.3	
Severe osteoporosis	10	46.3 ± 6.1	

[1]Kruskal-Wallis *H* test.

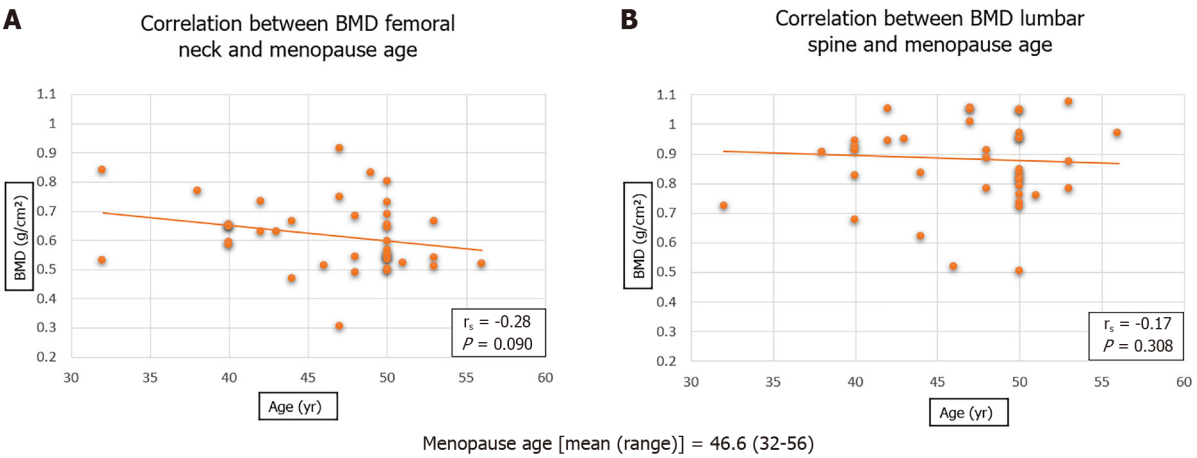


Figure 1 Scatter plot graphs of bone mineral density of femoral neck and lumbar spine with menopause age of female patients (*n* = 44) (Spearman Rank Correlation analysis). A: Femoral neck; B: Lumbar spine. BMD: Bone mineral density.

Table 10 shows a statistically significant difference (P = 0.026) between the pattern of fracture neck of femur and the WHO Classification of femoral neck BMD. Patients with extra-capsular fractures where more likely to have severe osteoporosis than those with intra-capsular fractures.

Figure 3 illustrates a statistically significant inverse correlation between the femoral neck BMD and the lumbar spine BMD with the FRAX major score (percentage likelihood of major osteoporotic fracture in the next ten years). The correlation was stronger with the femoral neck BMD (r_s = -0.64; P < 0.001) than that of the lumbar spine BMD (r_s = -0.37; P < 0.001).

Table 10 Analysis between World Health Organization classification of femoral neck bone mineral density and the pattern of fracture neck of femur (*n* = 62)

	Intra-capsular (*n*)	Extra-capsular (*n*)	*P* value[1]
Normal	6	2	0.026
Osteopenia	17	7	
Severe osteoporosis	10	20	

[1]Chi-Squared test.

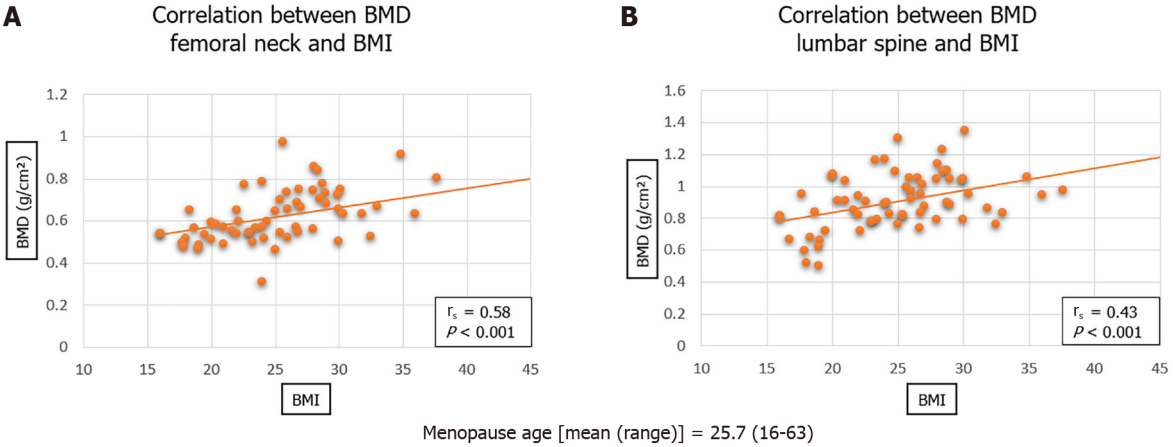


Figure 2 Scatter plot graphs of bone mineral density of femoral neck and lumbar spine with body mass index (*n* = 69) (Spearman Rank Correlation analysis). A: Femoral neck; B: Lumbar spine. BMD: Bone mineral density; BMI: Body mass index.

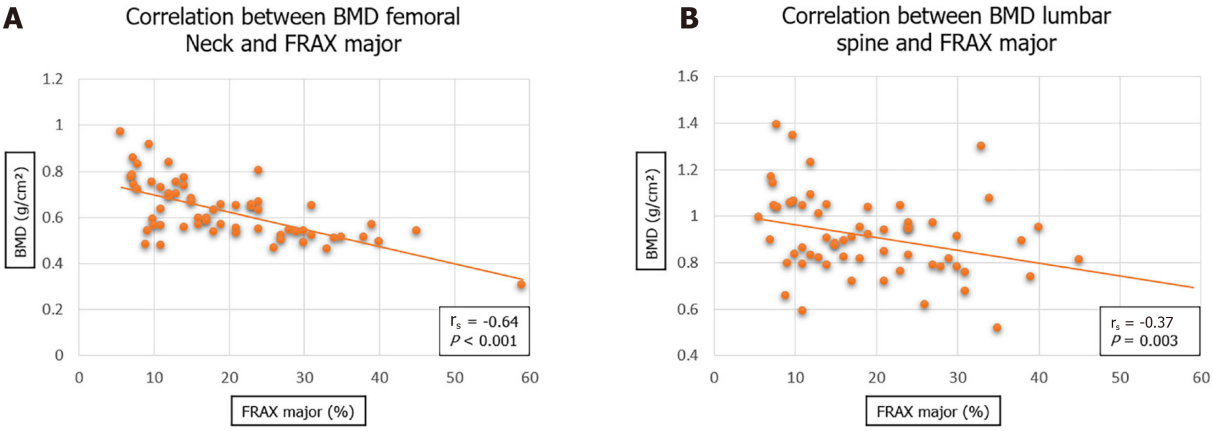


Figure 3 Scatter plot graphs of bone mineral density of femoral neck and lumbar spine with Fracture Risk Assessment Tool major score (*n* = 69) (Spearman Rank Correlation analysis). A: Femoral neck; B: Lumbar spine. BMD: Bone mineral density; FRAX: Fracture Risk Assessment Tool.

DISCUSSION

The main findings of this study were that BMD had a significant correlation with the FRAX score and also with BMI. Neither female gender or early menopause age had a significant influence on BMD. Osteoporosis was more common in patients with extra-capsular hip fracture patterns.

The aetiological factors associated with development of both primary and secondary osteoporosis have been looked at in numerous studies. With the incidence of osteoporosis continuing to rise[17], it is important that new research continues to advance and build upon previous findings.

The clinical risk factors associated with development of osteoporosis have long been agreed upon, with emerging contributory risk factors to secondary osteoporosis being a constant subject of further research[18]. However, the significance of the contribution of certain clinical risk factors to the pathophysiology of the development of primary osteoporosis is less understood. This study aimed to

investigate the significance of BMD in fracture neck of femur patients and compare it to the outcome of the FRAX score.

This study addressed a relatively unique cohort, all patients had sustained a major osteoporotic fracture (*i.e.*, fracture neck of femur). This allowed for research into arguably the most at risk group of individuals in the community. This contrasts to previous literature, whereby major osteoporotic fracture is used as an end-point on patient follow-up[10].

Local clinical guidelines allow for the discretion of the referring clinician with regards to whether DXA scan is appropriate following surgical management and rehabilitation of fracture neck of femur patients. In general, this would be all patients under the age of 75, as well as those patients felt to be independent in all aspects of daily living. This ensures that those included in this cohort will potentially benefit from preventative medical treatments to avert further major osteoporotic fractures. In addition, this ensures that 10-year percentage probability of major osteoporotic fracture data generated is relevant for the cohort.

The majority of patients with intra-capsular fracture neck of femur were managed with total hip arthroplasty, as opposed to hemi-arthroplasty, as displayed in Table 5. This reflects the relatively low mean age of the patients in the cohort. Current National Institute for Health and Care Excellence (NICE) guidelines advise that fracture neck of femur patients be managed surgically by total hip replacement if they are independently mobile and independent in activities of daily living[18]. This, in turn, portrays that the cohort in this study represents a group of individuals who are expected to continue with an independent lifestyle after surgical management, and therefore it is important that further fracture prevention is prioritised by all members of the healthcare team. Osteoporosis was more common in patients with extra-capsular hip fracture patterns in this study. Dynamic hip screw (DHS) is a common internal fixation device used for this fracture pattern. The biomechanical pull-out strength of locking plates is superior to that of conventional plates particularly in osteoporotic bone. It may be more prudent to use DHS implants which have locking plates for screw fixation in the surgical management of patients with an extra-capsular fracture configuration.

The significant (inverse) relationship between femoral neck BMD and lumbar spine BMD with the FRAX score (10-year percentage probability of major osteoporotic fracture) is in agreement with previous literature[17,20]. This supports the ongoing understanding that measures to increase BMD will result in reduced incidence in major osteoporotic fractures[15,21].

The correlation between BMD (both femoral neck and lumbar spine) and BMI is also in agreement with previous literature[22]. This is likely to be explained by a combination of factors, including nutritional status, mechanical load and hormones. It has previously been hypothesised that increased weight, and subsequently increased mechanical load, results in decreased osteoclast activity and increased osteoblast activity, increasing bone strength and bone mineral content[23]. This supports current emphasis on nutritional status of fracture neck of femur patients, not only in aiding rehabilitation, but also in prevention of further fracture.

BMD was noted to have a significant influence on the fracture pattern at the neck of femur. This is also in agreement with previous literature[16], whereby extra-capsular fracture patterns are associated with a lower BMD. However, it is important to emphasis that literature has shown there to be other factors that will have an influence on fracture pattern at the neck of femur[24], most notably intertrochanteric outer diameter and buckling ratio.

Gender difference has long been known to have an influence on both osteoporosis fracture risk and BMD. This is variable is included in the FRAX questionnaire[25]. Interestingly, there was no significant difference between males and females for BMD within the cohort studied. It is important to note that it is not the intention to disprove the influence of gender on BMD, and ultimately osteoporosis. However, it may be argued that the effect of gender is not in isolation, and that other factors that affect BMD (nutrition, mechanical force, genetic predisposition, ethnicity, *etc.*) may outweigh gender's overall role.

It was shown that menopause age did not have a significant association with either BMD or WHO osteoporosis classification. This is in contrast to the majority of published literature[26], whereby it is understood that earlier menopause age is associated with lower BMD, and therefore increased incidence of osteoporosis and fragility fractures[27]. This study does not conclude that age of menopause has no effect on BMD, osteoporosis and fracture risk. However, it emphasises that a multi-faceted approach must be taken when attempting to address the field in question.

Limitations of the study included that much of the presented data focuses on the influence of gender on BMD, and consequently the influence of gender on osteoporosis and fracture risk. One must make note of the differences in frequency between males (n = 25) and females (n = 44). This was appropriately adjusted for in the statistical analyses conducted. This gender discrepancy is explained by the disproportionately higher incidence of fracture neck of femur in females as compared to males[28].

Recommendations for future research include a greater focus on how BMD may help reclassify patient fracture risk when added to the already calculated FRAX score based on 10-year probability of both major osteoporotic fracture and fracture neck of femur. This will aid to ensure osteoporosis preventative management is appropriately prioritised to reduce the incidence of fragility fractures. The findings in this paper also support the requirement for further research into the use of BMD as a surrogate biomarker for both fracture risk and osteoporosis prevention and management. This may be in the context of a cross-sectional study of fragility fractures at differing ages group and further

appropriate stratification as per age, with confounding factors adjusted for.

CONCLUSION

The results in this study place more emphasis on BMD when assessing fracture risk, in comparison to key factors incorporated into the FRAX predictive score. Menopause age and female gender had an indeterminate influence on BMD, as well as WHO classification of osteoporosis. BMI had a significant influence on BMD. Osteoporosis was more common in patients with extra-capsular hip fracture patterns. This study shows that BMD is significant in assessing risk of fracture neck of femur in comparison to the FRAX predictive score.

ARTICLE HIGHLIGHTS

Research background

There has been a steady increase in fragility fractures in the United Kingdom and worldwide. This has been seen in the increased number of patients admitted with fracture neck of femur. It is essential to gain a further understanding of the aetiology to understand preventative measures.

Research motivation

Increased prevalence of osteoporosis fragility fractures in the NHS, causing an increased economic burden.

Research objectives

The aim of this study was to investigate the significance of bone mineral density (BMD) in fracture neck of femur patients and compare it to the outcome of the Fracture Risk Assessment Tool (FRAX) score.

Research methods

Statistical analyses undertaken to ascertain the relationship between BMD and the individual factors included in the FRAX score.

Research results

The results in this study place more emphasis on BMD when assessing fracture risk, in comparison to key factors incorporated into the FRAX predictive score. Menopause age and female gender had an indeterminate influence on BMD, as well as World Health Organization classification of osteoporosis. BMI had a significant influence on BMD. Osteoporosis was more common in patients with extra-capsular hip fracture patterns. This study shows that BMD is significant in assessing risk of fracture neck of femur in comparison to the FRAX predictive score.

Research conclusions

This study demonstrated that BMD of the femoral neck measured by dual-energy X-ray absorptiometry scan is of added prognostic value when assessing patients for risk of fracture neck of femur in combination with the FRAX predictive scoring system.

Research perspectives

The findings in this paper also support the requirement for further research into the use of BMD as a surrogate biomarker for both fracture risk and osteoporosis prevention and management. This may be in the context of a cross-sectional study of fragility fractures at differing ages group and further appropriate stratification as per age, with confounding factors adjusted for.

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FOOTNOTES

Author contributions: Elamin Ahmed H contributed to study design, literature review and manuscript production; Al-Dadah O contributed to study design, literature review, statistical analysis and manuscript production.

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Informed consent statement: Informed consent was obtained from all patients as part of their routine clinical care in this pragmatic study which evaluated the existing clinical practice within the department.

Conflict-of-interest statement: The authors report no conflict of interest.

Data sharing statement: No additional data are available.

STROBE statement: The authors have read the STROBE Statement-checklist of items, and the manuscript was prepared and revised according to the STROBE Statement-checklist of items.

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REFERENCES

1 **The National Institute for Health and Care Excellence**. Osteoporosis - prevention of fragility fractures. [cited 11th November 2020]. In: The National Institute for Health and Care Excellence [Internet]. Available from: https://cks.nice.org.uk/osteoporosis-prevention-of-fragility-fractures#.XYihz9zxKPo.mendeley
2 **Curtis EM**, Moon RJ, Harvey NC, Cooper C. The impact of fragility fracture and approaches to osteoporosis risk assessment worldwide. *Bone* 2017; **104**: 29-38 [PMID: 28119181 DOI: 10.1016/j.bone.2017.01.024]
3 **Albright F**. Annals of internal medicine, Volume 27, 1947: Osteoporosis. *Nutr Rev* 1989; **47**: 85-86 [PMID: 2649807 DOI: 10.1111/j.1753-4887.1989.tb02800.x]
4 **Pisani P**, Renna MD, Conversano F, Casciaro E, Di Paola M, Quarta E, Muratore M, Casciaro S. Major osteoporotic fragility fractures: Risk factor updates and societal impact. *World J Orthop* 2016; **7**: 171-181 [PMID: 27004165 DOI: 10.5312/wjo.v7.i3.171]
5 **Kanis JA**, Delmas P, Burckhardt P, Cooper C, Torgerson D. Guidelines for diagnosis and management of osteoporosis. The European Foundation for Osteoporosis and Bone Disease. *Osteoporos Int* 1997; **7**: 390-406 [PMID: 9373575 DOI: 10.1007/BF01623782]
6 **Burge R**, Worley D, Johansen A, Bhattacharyya S, Bose U. The cost of osteoporotic fractures in the UK: Projections for 2000-2020. *J Med Econ* 2008; **4**: 51-62
7 **Johnell O**, Kanis JA. An estimate of the worldwide prevalence and disability associated with osteoporotic fractures. *Osteoporos Int* 2006; **17**: 1726-1733 [PMID: 16983459 DOI: 10.1007/s00198-006-0172-4]
8 **Kanis JA**, Johnell O, Oden A, De Laet C, Jonsson B, Dawson A. Ten-year risk of osteoporotic fracture and the effect of risk factors on screening strategies. *Bone* 2002; **30**: 251-258 [PMID: 11792594 DOI: 10.1016/s8756-3282(01)00653-6]
9 **Ström O**, Borgström F, Kanis JA, Compston J, Cooper C, McCloskey EV, Jönsson B. Osteoporosis: burden, health care provision and opportunities in the EU: a report prepared in collaboration with the International Osteoporosis Foundation (IOF) and the European Federation of Pharmaceutical Industry Associations (EFPIA). *Arch Osteoporos* 2011; **6**: 59-155 [PMID: 22886101 DOI: 10.1007/s11657-011-0060-1]
10 **Kanis JA**, Oden A, Johnell O, Johansson H, De Laet C, Brown J, Burckhardt P, Cooper C, Christiansen C, Cummings S, Eisman JA, Fujiwara S, Glüer C, Goltzman D, Hans D, Krieg MA, La Croix A, McCloskey E, Mellstrom D, Melton LJ 3rd, Pols H, Reeve J, Sanders K, Schott AM, Silman A, Torgerson D, van Staa T, Watts NB, Yoshimura N. The use of clinical risk factors enhances the performance of BMD in the prediction of hip and osteoporotic fractures in men and women. *Osteoporos Int* 2007; **18**: 1033-1046 [PMID: 17323110 DOI: 10.1007/s00198-007-0343-y]
11 **Watts NB**. The Fracture Risk Assessment Tool (FRAX®): applications in clinical practice. *J Womens Health (Larchmt)* 2011; **20**: 525-531 [PMID: 21438699 DOI: 10.1089/jwh.2010.2294]
12 **Berger A**. Bone mineral density scans. *BMJ* 2002; **325**: 484 [PMID: 12202332 DOI: 10.1136/bmj.325.7362.484]
13 **Kanis JA**, Melton LJ 3rd, Christiansen C, Johnston CC, Khaltaev N. The diagnosis of osteoporosis. *J Bone Miner Res* 1994; **9**: 1137-1141 [PMID: 7976495 DOI: 10.1002/jbmr.5650090802]
14 **Trajanoska K**, Morris JA, Oei L, Zheng HF, Evans DM, Kiel DP, Ohlsson C, Richards JB, Rivadeneira F; GEFOS/GENOMOS consortium and the 23andMe research team. Assessment of the genetic and clinical determinants of fracture risk: genome wide association and mendelian randomisation study. *BMJ* 2018; **362**: k3225 [PMID: 30158200 DOI: 10.1136/bmj.k3225]

15 **Busko M**. Study Finds BMD Can Stand in for Fractures. Will the FDA Agree? [cited 11th November 2020 In: Medscape [Internet]. Available from: https://www.medscape.com/viewarticle/902884

16 **Nakamura N**, Kyou T, Takaoka K, Ohzono K, Ono K. Bone mineral density in the proximal femur and hip fracture type in the elderly. *J Bone Miner Res* 1992; **7**: 755-759 [PMID: 1642144 DOI: 10.1002/jbmr.5650070705]

17 **Kanis JA**. Diagnosis and Clinical Aspects of Osteoporosis. In: Ferrari SL, Roux C. Pocket Reference to Osteoporosis. Cham: Springer International Publishing, 2019: 11-20

18 **Mirza F**, Canalis E. Management of endocrine disease: Secondary osteoporosis: pathophysiology and management. *Eur J Endocrinol* 2015; **173**: R131-R151 [PMID: 25971649 DOI: 10.1530/EJE-15-0118]

19 **Ftouh S**, Morga A, Swift C; Guideline Development Group. Management of hip fracture in adults: summary of NICE guidance. *BMJ* 2011; **342**: d3304 [PMID: 21693526 DOI: 10.1136/bmj.d3304]

20 **Imerci A**, Yalın Kılınç C, Aydogan NH, Karalezli MN, Savran A. Fracture Risk Assessment Tool (FRAX®) Results Calculated With and Without Bone Mineral Density Values for the Evaluation of Fracture Risk in Postmenopausal Women With Osteopenia. *J Clin Densitom* 2018; **21**: 464-471 [PMID: 28781230 DOI: 10.1016/j.jocd.2017.06.027]

21 **Ferrari S**, Libanati C, Lin CJF, Brown JP, Cosman F, Czerwiński E, de Gregório LH, Malouf-Sierra J, Reginster JY, Wang A, Wagman RB, Lewiecki EM. Relationship Between Bone Mineral Density T-Score and Nonvertebral Fracture Risk Over 10 Years of Denosumab Treatment. *J Bone Miner Res* 2019; **34**: 1033-1040 [PMID: 30919997 DOI: 10.1002/jbmr.3722]

22 **Wu SF**, Du XJ. Body Mass Index May Positively Correlate with Bone Mineral Density of Lumbar Vertebra and Femoral Neck in Postmenopausal Females. *Med Sci Monit* 2016; **22**: 145-151 [PMID: 26766815 DOI: 10.12659/msm.895512]

23 **Vincent HK**, Heywood K, Connelly J, Hurley RW. Obesity and weight loss in the treatment and prevention of osteoarthritis. *PM R* 2012; **4**: S59-S67 [PMID: 22632704 DOI: 10.1016/j.pmrj.2012.01.005]

24 **Rivadeneira F**, Zillikens MC, De Laet CE, Hofman A, Uitterlinden AG, Beck TJ, Pols HA. Femoral neck BMD is a strong predictor of hip fracture susceptibility in elderly men and women because it detects cortical bone instability: the Rotterdam Study. *J Bone Miner Res* 2007; **22**: 1781-1790 [PMID: 17638578 DOI: 10.1359/jbmr.070712]

25 **Moberg LME**, Nilsson PM, Holmberg AH, Samsioe G, Borgfeldt C. Primary screening for increased fracture risk by the FRAX® questionnaire-uptake rates in relation to invitation method. *Arch Osteoporos* 2019; **14**: 51 [PMID: 31069544 DOI: 10.1007/s11657-019-0603-4]

26 **Heidari B**, Hosseini R, Javadian Y, Bijani A, Sateri MH, Nouroddini HG. Factors affecting bone mineral density in postmenopausal women. *Arch Osteoporos* 2015; **10**: 15 [PMID: 25972061 DOI: 10.1007/s11657-015-0217-4]

27 **Mishra S**, Manju M, Toora BD, Mohan S, Venkatesh BP. Comparison of bone mineral density and serum minerals in pre and post-menopausal women. *Int J Clin Trials* 2015; **2** [DOI: 10.18203/2349-3259.ijct20151237]

28 **Hedlund R**, Lindgren U. Trauma type, age, and gender as determinants of hip fracture. *J Orthop Res* 1987; **5**: 242-246 [PMID: 3572593 DOI: 10.1002/jor.1100050210]

29 **Kanis JA**, Johnell O, Oden A, Johansson H, McCloskey E. FRAX and the assessment of fracture probability in men and women from the UK. *Osteoporos Int* 2008; **19**: 385-397 [PMID: 18292978 DOI: 10.1007/s00198-007-0543-5]

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ORIGINAL ARTICLE

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Liverpool carpal tunnel scoring system to predict nerve conduction study results: A prospective correlation study

Yuen Chan, Veenesh Selvaratnam, Tharjan Manickavasagar, Vishwanath Shetty, Vishal Sahni

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Abstract

BACKGROUND

Carpal tunnel syndrome (CTS) is one of the most common peripheral nerve compressive neuropathies. The clinical symptoms and physical examinations of CTS are widely recognised, however, there is still debate around what is the best approach for assessment of CTS. Clinical assessment is still considered the gold standard, however, controversies do exist regarding the need for investigations such nerve conduction studies (NCS) to aid with management decisions.

AIM

To correlate the severity of NCS results to a scoring system which included symptoms, signs and risk factors.

METHODS

This was a prospective correlation study. We scored patients' signs and symptoms using our CTS scoring system. This was then correlated with the findings of the NCS. The scoring system included - four symptoms (2 Katz hand diagrams – one for tingling and one for numbness; nocturnal paresthesia and bilateral symptoms) and four clinical signs (weak thumb abduction test; Tinel's sign; Phalen sign and hypoalgesia in median nerve territory) and two risk factors (age more than 40 years and female sex). We classified the NCS results to normal, mild, moderate and severe.

RESULTS

There were 61 scores in 59 patients. The mean scores for the categories were as

follows: 6.75 for normal NCS; 5.50 for mild NCS; 9.17 for moderate NCS and 9 for severe NCS. All scores of 8 or more matched with NCS results of moderate and severe intensity apart from three scores which were greater than seven that had normal NCS. Eta score was 0.822 for the CTS score being the dependent value and the NCS category being the independent variable showing a strong association between the scoring system and the NCS group.

CONCLUSION
We feel that this simple scoring system can be used to predict and correlate the severity of NCS in patients with CTS.

Key Words: Carpal tunnel syndrome; Nerve; Compression neuropathy; Median nerve; Scoring

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Core Tip: The use of our simple scoring method can help determine if patients with carpal tunnel syndrome need nerve conduction studies. Patients scoring less than 8 may have mild or moderate carpal tunnel syndrome and in these patients we recommend the use of nerve conduction studies. In patients scoring 8 or more, we do not recommend the use of nerve conduction studies for the diagnosis of carpal tunnel syndrome.

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INTRODUCTION

Carpal tunnel syndrome (CTS) is one of the most common peripheral nerve compressive neuropathies. The prevalence of CTS in the United Kingdom is 7%-16%. A General Practice Research Database found that 88 men and 193 women present as new cases per 100000 population per year[1]. The clinical symptoms and physical examinations are widely recognised, however there is still debate around what is the best approach for the assessment of carpal tunnel syndrome. Clinical assessment is considered the gold standard; however, controversies exist regarding the need for investigations such as nerve conduction studies (NCS) to aid with management decisions[2].

NCS is the investigation of choice when clinical diagnosis is inconclusive. It is also used to confirm the diagnosis of CTS. NCS have been found to be highly sensitive and specific for the diagnosis of CTS [3]. However, NCS can be painful and expensive. The reported false negative rate of NCS is between 1.5% to 16%[4,5]. The reported false positive rate is up to 46%[6]. The evaluation of NCS for CTS involves the measurement of conduction velocity across the carpal tunnel, as well as determination of the amplitude of sensory and motor responses. Focal demyelination can occur with increased median nerve compression. This results in local conduction block and slowing of motor and sensory conduction across the wrist. The axons of the median nerve can be damaged with even greater compression resulting in reduced amplitudes.

The grading of severity of CTS is as follows: Mild - prolonged sensory nerve action potential (SNAP), and/or slightly reduced SNAP amplitude. Moderate - abnormal median SNAP as above, plus prolonged median motor distal latency. Severe - prolonged median motor and sensory distal latencies, plus either an absent SNAP or low amplitude or absent thenar compound muscle action potential. Needle examination often reveal fibrillation, reduced recruitment, and motor unit potential charges[7,8].

There are validated measures such as the Boston Carpal Tunnel Syndrome Questionnaire which quantify symptoms and disability; however, this does not include clinical examinations. One study found that the clinical-neurophysiologic relationships are very strong when they evaluated the clinical picture with the disability scale of the Boston Carpal Tunnel Syndrome Questionnaire as well as clinical examinations findings. Conversely, the clinical-neurophysiologic relationship is not so clear and simple when they compared it with the symptoms only[9]. Other scoring systems include use of hand diagrams such as the Katz[10] hand diagram (looking at distribution of symptoms in the hand) and the CTS-6 scale (looking at symptoms and examination)[11]. A systematic review found there are limited evidence to support the use of these scoring systems[12].

Numerous patients with CTS have severe symptoms but no NCS changes, therefore we hypothesised that a scoring system combining symptoms, signs and risk factors can help with the diagnosis of CTS. The aim of the study was to correlate the severity of NCS results to a scoring system which included

symptoms, signs and risk factors.

MATERIALS AND METHODS

We prospectively collected data for fifty-nine patients who were referred to our hand unit with symptoms of carpal tunnel syndrome. All patients who were referred and diagnosed with CTS clinically were included in the study. Patient with symptoms but diagnosed with other diagnoses were excluded. All patients who clinically showed symptoms of CTS had the ten-point scoring system and NCS carried out. We prospectively collected data for 61 hands (59 patients) over a ten-month period.

We reviewed existing scoring systems and examination signs to develop a scoring system. We developed a 10-point scoring system which included symptoms, signs and risk factors. We scored our patients using the ten-point scoring system. The scoring system included; four symptoms (2 Katz[10] hand diagram – for tingling and numbness, nocturnal paresthesia and bilateral symptoms), four clinical signs (weak thumb abduction test, Tinel's sign, Phalen sign and hypoalgesia in median nerve territory) and two risk factors (age more than 40 years and female sex). We classified the NCS to normal, mild, moderate and severe as described above[8].

This study was conducted prospectively. Local clinical governance approval was obtained. All patients who underwent the ten-point scoring system and had NCS was included. Our ten-point scoring system (Table 1) was applied to patients with symptoms of CTS prior to NCS. The score of the ten-point scoring system was then correlated with the severity results of the NCS. The score was used to correlate with the NCS results but was not used to decide on treatment. As the scoring depended on the signs and symptoms no blinding could be applied to the assessors or the patients. The assessors of clinical signs and symptoms were not involved in the statistical analysis of the results. The data analysis was carried out by a member of authors who were blinded to the patients and tests.

The ten-point scoring system included tingling and numbness on a Katz hand diagram. Nocturnal paresthesia is defined as night numbness and tingling or wakening. Bilateral symptoms imply symptoms involving both hands. Signs included weak thumb abduction; Tinel's sign which is reproduction of the symptoms on tapping over the carpal tunnel; Phalen's sign which is reproduction of the symptoms for CTS on flexion of the wrist for 60 s. Hypoalgesia is defined as reduced sensitivity to a painful stimulus in the median nerve distribution.

Other data collected were age, sex, laterality of hand affected, NCS results and duration of symptoms. It was our common practice in our hospital to refer a patient for a NCS in suspected cases of CTS prior to surgical intervention. All patients in this study were from a single upper limb surgeon's practice. Statistical analysis was done using SPSS. Eta value was used to determine the association between NCS category and CTS score. Eta of 0 is no association and Eta of 1 is perfect association. One way ANOVA test was used to test difference between the groups. The partial Eta squared was used to test how much variability of the scores was accounted for by the NCS severity. Post hoc analysis was carried out to determine which NCS groups have differences between each other. The post hoc analysis used in this study was Scheffe.

RESULTS

There were 61 scores in 59 patients. There were 43 female and 18 male patients. The mean duration of symptoms was 17 mo (range 2-84 mo). Thirty-two were left hands and twenty-nine were right hands. There were 8 patients in the normal NCS category, 14 patients in the mild NCS category, 12 patients in the moderate NCS category and 27 patients in the severe NCS category. The mean age was 60 years (range 37-91 years).

The mean score for the categories were as follows: 6.75 for normal NCS, 5.50 for mild NCS, 9.17 for moderate NCS and 9 for severe NCS. All scores of 8 or more matched with NCS of moderate and severe intensity apart from three scores which were greater than seven that were normal on NCS (Table 2).

One of the three patients who had a score over 7 but had normal NCS was found to have a cervical disc herniation after a magnetic resonance imaging of the cervical spine. This patient underwent cervical disc decompression and had resolution of her symptoms. She did not require a carpal tunnel decompression. The other two patients with a score of 8 and 9 respectively underwent a carpal tunnel decompression despite normal NCS as clinically they were both symptomatic. Both patients reported resolution of symptoms post carpal tunnel decompression.

An Eta coefficient test was performed to determine the strength of correlation between the scores and the NCS categories of normal, mild, moderate and severe. An Eta score was 0.822 for the CTS score being the dependent value and the NCS category being the independent variable shows a strong association between the score and the NCS categories. A one-way ANOVA test showed there were a significant statistical difference between the severity groups ($P < 0.001$). The partial Eta squared was 0.676 meaning that 67.6% of the variability of the CTS score is accounted for by the severity of their CTS.

Table 1 The Liverpool ten-point carpal tunnel syndrome scoring system

	1 point	1 point	0 point
Symptoms			
Tingling (Katz hand diagram)	Classic pattern	Probable pattern	Unlikely pattern
Numbness (Katz hand diagram)	Classic pattern	Probable pattern	Unlikely pattern
Nocturnal paresthesia	Yes		No
Bilateral symptoms	Yes		No
Signs			
Weak thumb abduction	Yes		No
Tinels sign	Yes		No
Phalen's sign	Yes		No
Hypoalgesia	Yes		No
Risk factors			
Age > 40 yr	Yes		No
Female	Yes		No

Table 2 Correlation between our carpal tunnel syndrome scoring and nerve conduction studies results

Score/NCS	Normal	Mild	Moderate	Severe
0				
1				
2		1		
3				
4		2		
5	2	3		
6	2	4		
7	1	4		
8	2		3	9
9	1		4	9
10			5	9

NCS: Nerve conduction studies.

A post hoc analysis showed there were statistical significance between the CTS scores of patients with normal NCS and patients with moderate and severe NCS ($P < 0.001$). There was statistical significance between the CTS scores of patients with mild NCS compared with CTS scores of patients with moderate and severe NCS ($P < 0.001$). There was no significant statistical difference between CTS scores of patients with moderate NCS findings compared with severe NCS findings ($P < 0.979$).

DISCUSSION

An appropriate diagnosis of carpal tunnel syndrome is important as it is a common condition. There is no consensus on whether to base treatment decisions on clinical history and assessment only, or NCS should be done in every case. Within the UK, different areas have different rules on diagnosis and treatment. The British Orthopaedic Association guidelines states NCS is not routinely needed and should only be used if clinical examination and history are equivocal, if there is persistent or recurrent carpal tunnel syndrome or if there is an unclear diagnosis suggesting peripheral neuropathy[13].

NCS may not always be positive in patients who are symptomatic. Not every clinician request NCS because of the costs and delays associated with NCS[14]. One study looking at just history and examination findings concluded that the majority of patients who have CTS on the basis of their scoring system, further NCS studies did not change the probability of diagnosing the condition[11]. Another study looked at using a web-based CTS questionnaire prior to the patient's appointment and found that it provided a sufficiently accurate prediction of the likelihood of CTS to help in the initial planning, investigation and treatment of CTS[15].

A CTS scoring can help in planning and streamlining of services which is of significant importance especially in light of the current pandemic. We should aim to get the right diagnosis as effectively and as efficiently as possible and to use resources such as NCS in a cost-effective way.

The reported sensitivity and specificity for each of our sign and symptoms are as follows; classic or probable Katz hand diagram pattern (0.64, 0.73 respectively), nocturnal paraesthesia (0.51, 0.68 respectively), bilateral symptoms (0.61, 0.58 respectively), weak thumb abduction test (0.66, 0.66 respectively), Tinel sign (0.60, 0.80 respectively), Phalen sign (0.91, 0.86 respectively), hypoalgesia in median nerve (0.51, 0.93 respectively), age more than 40 years (0.80, 0.41 respectively)[10,16-21]. Female sex has an increased risk of developing CTS[22]. This may be due to females being over-represented in jobs that have a high risk of developing CTS. When the occupational exposure is truly similar, the risk of developing CTS is similar between both genders. In our cohort, 71% of patients were females. We did not obtain job specifications for our patients.

This study shows our simple ten-point scoring system have a high correlation with the NCS results. Our CTS score differentiated between patients with normal/mild NCS symptoms to patients with moderate/severe NCS findings. The difference is significant between patients with normal/mild NCS findings compared with patients with moderate/severe NCS findings. We have CTS in patients across the range of the CTS scores but the aim of the scoring system is to identify patients who would most likely benefit from NCS prior to carpal tunnel decompression as their clinical findings are equivocal.

We did not find a difference between patients with moderate and severe NCS findings or between patients with normal and mild NCS findings. However, clinically we feel both the moderate and severe group would be treated with a carpal tunnel decompression, therefore it is more important to differentiate between patients with normal and mild vs. moderate and severe NCS. In patients with normal and mild NCS, treatment will also depend on their symptoms. If symptoms are severe then they will more likely receive surgical intervention otherwise they would initially undergo a period of conservative management. Surgical intervention would only be undertaken should the patient fail their trial of conservative management.

The strength of our study is having a scoring system that combines signs, symptoms and risk factors. There are limitations to our study. It was a relatively small number of patients and we would need further studies to validate our scoring system. We did not have the co-morbidities or occupation of the patients and we did not re-do the scores after surgical decompression to see if the score can be used to monitor outcome post CTD. Further studies looking to include these factors would be beneficial.

CONCLUSION

We feel that this simple scoring system can be used to predict and correlate the severity of NCS in patients with CTS. Based on our study, we believe that patients who score less than eight may require NCS to confirm the diagnosis of CTS. However, patient who score more than 7 have a 93% chance of having moderate to severe CTS on NCS. Use of our simple scoring methods can help determine patients with moderate and severe CTS. In this group of patients, we recommend not using NCS. Patients scoring less than 8 may have mild or moderate CTS and, in this group of patients, we recommend the use of NCS. Further studies, looking to validate the scoring system clinically would be useful.

ARTICLE HIGHLIGHTS

Research background

There is still debate around what is the best approach for assessment of Carpal tunnel syndrome (CTS). Controversies do exist regarding the need for investigations such as the need for nerve conduction studies (NCS) to aid with management decisions.

Research motivation

We hypothesised that a scoring system combining symptoms, signs and risk factors can help with the diagnosis of carpal tunnel syndrome and whether nerve conduction studies would be required.

Research objectives
The aim of the study was to correlate the severity of nerve conduction study results to a scoring system which included symptoms, signs and risk factors.

Research methods
We scored patients' signs and symptoms using our CTS scoring system. This was then correlated with the findings of the NCS. The scoring system included - four symptoms and four clinical signs and two risk factors. We classified the NCS results to normal, mild, moderate and severe.

Research results
All scores of 8 or more matched with NCS results of moderate and severe intensity apart from three scores which were greater than seven that had normal NCS. Eta score was 0.822 for the CTS score being the dependent value and the NCS category being the independent variable showing a strong association between the scoring system and the NCS group.

Research conclusions
Based on our study, we believe that patients who score less than 8 may require NCS to confirm the diagnosis of CTS. However, patients who score more than 7 have a 93% chance of having moderate to severe CTS on NCS. The use of our simple scoring methods can help determine patients with moderate and severe CTS. In this group of patients, we recommend not using NCS. Patients scoring less than 8 may have mild or moderate CTS and in this group of patients, we recommend the use of NCS.

Research perspectives
The use of our Liverpool carpal tunnel scoring system can have the potential to be used to help determine if NCS is required. Further studies looking into the validation of the scoring system is required.

FOOTNOTES

Author contributions: Chan Y and Selvaratnam V wrote and edited the manuscript and were involved in the analysis of the study; Selvaratnam V, Manickavasagar T, Shetty V, and Sahni V were involved in the collection of data and editing of the manuscript.

Institutional review board statement: This study was approved by Southport and Ormskirk NHS Hospital.

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REFERENCES

1 **Latinovic R**, Gulliford MC, Hughes RA. Incidence of common compressive neuropathies in primary care. *J Neurol Neurosurg Psychiatry* 2006; **77**: 263-265 [PMID: 16421136 DOI: 10.1136/jnnp.2005.066696]

2 **Padua L**, Coraci D, Erra C, Pazzaglia C, Paolasso I, Loreti C, Caliandro P, Hobson-Webb LD. Carpal tunnel syndrome: clinical features, diagnosis, and management. *Lancet Neurol* 2016; **15**: 1273-1284 [PMID: 27751557 DOI: 10.1016/S1474-4422(16)30231-9]

3 **Jablecki CK**, Andary MT, Floeter MK, Miller RG, Quartly CA, Vennix MJ, Wilson JR; American Association of Electrodiagnostic Medicine; American Academy of Neurology; American Academy of Physical Medicine and Rehabilitation. Practice parameter: Electrodiagnostic studies in carpal tunnel syndrome. Report of the American Association of Electrodiagnostic Medicine, American Academy of Neurology, and the American Academy of Physical Medicine and Rehabilitation. *Neurology* 2002; **58**: 1589-1592 [PMID: 12058083 DOI: 10.1212/wnl.58.11.1589]

4 **Löscher WN**, Auer-Grumbach M, Trinka E, Ladurner G, Hartung HP. Comparison of second lumbrical and interosseus latencies with standard measures of median nerve function across the carpal tunnel: a prospective study of 450 hands. *J Neurol* 2000; **247**: 530-534 [PMID: 10993495 DOI: 10.1007/s004150070152]

5 **Uncini A**, Di Muzio A, Awad J, Manente G, Tafuro M, Gambi D. Sensitivity of three median-to-ulnar comparative tests in diagnosis of mild carpal tunnel syndrome. *Muscle Nerve* 1993; **16**: 1366-1373 [PMID: 8232394 DOI: 10.1002/mus.880161215]

6 **Redmond MD**, Rivner MH. False positive electrodiagnostic tests in carpal tunnel syndrome. *Muscle Nerve* 1988; **11**: 511-518 [PMID: 3374521 DOI: 10.1002/mus.880110515]

7 **Yazdanpanah P**, Aramesh S, Mousavizadeh A, Ghaffari P, Khosravi Z, Khademi A. Prevalence and severity of carpal tunnel syndrome in women. *Iran J Public Health* 2012; **41**: 105-110 [PMID: 23113142]

8 **Stevens JC**. AAEM minimonograph #26: the electrodiagnosis of carpal tunnel syndrome. American Association of Electrodiagnostic Medicine. *Muscle Nerve* 1997; **20**: 1477-1486 [PMID: 9390659 DOI: 10.1002/(sici)1097-4598(199712)20:12<1477::aid-mus1>3.0.co;2-5]

9 **Padua L**, Padua R, Lo Monaco M, Aprile I, Tonali P. Multiperspective assessment of carpal tunnel syndrome: a multicenter study. Italian CTS Study Group. *Neurology* 1999; **53**: 1654-1659 [PMID: 10563608 DOI: 10.1212/wnl.53.8.1654]

10 **Katz JN**, Stirrat CR, Larson MG, Fossel AH, Eaton HM, Liang MH. A self-administered hand symptom diagram for the diagnosis and epidemiologic study of carpal tunnel syndrome. *J Rheumatol* 1990; **17**: 1495-1498 [PMID: 2273490]

11 **Graham B**. The value added by electrodiagnostic testing in the diagnosis of carpal tunnel syndrome. *J Bone Joint Surg Am* 2008; **90**: 2587-2593 [PMID: 19047703 DOI: 10.2106/JBJS.G.01362]

12 **Dabbagh A**, MacDermid JC, Yong J, Macedo LG, Packham TL. Diagnosing Carpal Tunnel Syndrome: Diagnostic Test Accuracy of Scales, Questionnaires, and Hand Symptom Diagrams-A Systematic Review. *J Orthop Sports Phys Ther* 2020; **50**: 622-631 [PMID: 32938312 DOI: 10.2519/jospt.2020.9599]

13 **British Orthopaedic Association**; Royal College of Surgeons of England. Commissioning Guide: Treatment of Carpal Tunnel Syndrome. 2017

14 **Hui ACF**, Wong SM, Griffith J. Carpal Tunnel Syndrome. *Pract Neurol* 2005; **5**: 210 [DOI: 10.1111/j.1474-7766.2005.00312.x]

15 **Bland JD**, Rudolfer S, Weller P. Prospective analysis of the accuracy of diagnosis of carpal tunnel syndrome using a web-based questionnaire. *BMJ Open* 2014; **4**: e005141 [PMID: 25142261 DOI: 10.1136/bmjopen-2014-005141]

16 **Buch-Jaeger N**, Foucher G. Correlation of clinical signs with nerve conduction tests in the diagnosis of carpal tunnel syndrome. *J Hand Surg Br* 1994; **19**: 720-724 [PMID: 7706873 DOI: 10.1016/0266-7681(94)90244-5]

17 **Kuhlman KA**, Hennessey WJ. Sensitivity and specificity of carpal tunnel syndrome signs. *Am J Phys Med Rehabil* 1997; **76**: 451-457 [PMID: 9431262 DOI: 10.1097/00002060-199711000-00004]

18 **Heller L**, Ring H, Costeff H, Solzi P. Evaluation of Tinel's and Phalen's signs in diagnosis of the carpal tunnel syndrome. *Eur Neurol* 1986; **25**: 40-42 [PMID: 3940864 DOI: 10.1159/000115985]

19 **Golding DN**, Rose DM, Selvarajah K. Clinical tests for carpal tunnel syndrome: an evaluation. *Br J Rheumatol* 1986; **25**: 388-390 [PMID: 3779325 DOI: 10.1093/rheumatology/25.4.388]

20 **De Smet L**, Steenwerckx A, Van den Bogaert G, Cnudde P, Fabry G. Value of clinical provocative tests in carpal tunnel syndrome. *Acta Orthop Belg* 1995; **61**: 177-182 [PMID: 8525813]

21 **Katz JN**, Larson MG, Sabra A, Krarup C, Stirrat CR, Sethi R, Eaton HM, Fossel AH, Liang MH. The carpal tunnel syndrome: diagnostic utility of the history and physical examination findings. *Ann Intern Med* 1990; **112**: 321-327 [PMID: 2306060 DOI: 10.7326/0003-4819-112-5-321]

22 **Harris-Adamson C**, Eisen EA, Dale AM, Evanoff B, Hegmann KT, Thiese MS, Kapellusch JM, Garg A, Burt S, Bao S, Silverstein B, Gerr F, Merlino L, Rempel D. Personal and workplace psychosocial risk factors for carpal tunnel syndrome: a pooled study cohort. *Occup Environ Med* 2013; **70**: 529-537 [PMID: 23645610 DOI: 10.1136/oemed-2013-101365]

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ORIGINAL ARTICLE

Prospective Study

Clinical efficacy of the Ankle Spacer for the treatment of multiple secondary osteochondral lesions of the talus

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Abstract

BACKGROUND

The Ankle Spacer was developed as a joint-sparing alternative to invasive end-stage surgeries. Currently, there are no clinical studies on the Ankle Spacer.

AIM

To describe the operative technique and the clinical efficacy of the Ankle Spacer for the treatment of multiple, cystic osteochondral lesions of the talus in patients with failed prior operative treatment.

METHODS

This is a prospective study during which patients were assessed preoperatively, at 2- and 6 wk, and at 3, 6, 12 and 24 mo postoperatively. Patients with multiple, cystic or large (≥ 15 mm) osteochondral lesions of the talus after failed prior surgery were included. The primary outcome measure was the numeric rating scale (NRS) for pain during walking at 2 years postoperatively. Secondary outcome measures included the NRS in rest and during stair climbing, the American Orthopaedic Foot and Ankle Society Hindfoot Score, the Foot and Ankle Outcome Score, the Short- Form 36 physical and mental component scale, and the Range of Motion (ROM). Radiographic evaluations were conducted to evaluate prosthetic loosening and subsidence. Revision rates and complications were also assessed.

RESULTS

Two patients underwent an Ankle Spacer implantation on the talus. The NRS during walking improved from 6 and 7 preoperatively to 2 and 2 points postoper-

atively at 2 years, in patient 1 and 2, respectively. The other patient-reported outcome measures also improved substantially. There were no re-operations nor complications. Radiological imaging showed no loosening of the implant and no change of implant position.

CONCLUSION

The Ankle Spacer showed clinically relevant pain reduction during walking, improvement in clinical outcomes as assessed with PROMs, and no complications or re-operations. This treatment option may evolve as a joint-sparing alternative to invasive end-stage surgeries.

Key Words: Hemi-arthroplasty; Ankle Spacer; Talar surface implant; Osteochondral lesions of the talus; End-stage

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Core Tip: Our aim was to provide an overview of the clinical efficacy of a novel implant system that is a hemi-arthroplasty of the ankle. This device can be used for multiple, secondary osteochondral lesions of the talus and isolated osteo-arthritis of the talar dome. In this prospective case series, it was shown that this novel device showed promising clinical outcomes and can be considered safe.

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INTRODUCTION

Osteochondral lesions of the Talus (OLT) are pathologic lesions of the talar cartilage and the subchondral bone. These lesions can occur in up to 50% of acute ankle fractures and sprains[1]. For OLTs of larger size (*i.e.*, above 10 or 15 mm in diameter) and of non-fragmentous morphology, the 'standard' operative treatment options such as autologous chondrocyte implantation, osteochondral autograft transfer systems, and a Talar OsteoPeriostic grafting from the Iliac Crest procedure may result in satisfactory clinical outcomes[2-4]. However, in some patients, there are multiple secondary lesions present of large and cystic nature. For these lesions, it is not always possible to harvest an osteo(chondral) autograft that is large enough to replace all the diseased osteochondral tissue of the talus without damaging the donor site or compromising the congruency of the ankle joint. Allograft treatment could be considered for the treatment of these type of lesions. However, these contain the disadvantages of loss of viability and stability in one-third of the grafts, and possibly clinically fail due to immunological reactions[5,6]. However, when there are multiple secondary (*i.e.*, failed prior surgery) lesions present on the talar articular surface in combination with a large and cystic nature, the above-described operative interventions are to be expected to result in relatively inferior outcomes.

To avoid inferior surgical outcomes in patients with persisting complaints after previous unsuccessful conservative management and operative therapy, other effective operative interventions are performed including an ankle arthrodesis or a total ankle prosthesis[7-9]. An (arthroscopic) ankle arthrodesis results in satisfactory clinical outcomes mostly concerning pain[10-12]. However, the operative intervention in question can result in functional limitations due to loss of the range of motion (ROM) of the ankle[13]. Furthermore, an ankle arthrodesis may potentially result in an increased long-term risk of arthritis in adjacent hindfoot joints, particularly the subtalar joint[14]. An alternative option is the placement of a total ankle prosthesis, for which a substantial amount of bone needs to be resected[15]. In order to address the problem of decreased joint motion (in the case of an ankle arthrodesis) and major bone resection (in the case of a prosthesis), a one-piece hemi-arthroplasty covering the talar surface, and leaving the tibia plafond untouched, can be a potential solution to the aforementioned challenges.

Although previous operative interventions similar to such a hemi-arthroplasty have been described in the literature, the studies applied operative techniques with resection of a substantial part of the talar cortical bone and cartilage in order to verify fitting of the implant thereby taking away a potential successful ankle arthrodesis in case of clinical failure[16-18]. Consequently, a novel bone-sparing hemi-prosthesis has been developed (The Ankle Spacer) to enable resurfacing of the talar dome and simultaneously preserving the ROM and potentially optimize physical functioning. Potential advantages include preservation of ankle motion, decreased stress on the midfoot and subtalar joints, and the possibility to perform an ankle fusion after failed hemi-arthroplasty. Up to now, no operative technique description

combined with the first clinical outcomes has been described in the literature. It is therefore the purpose of the present study to describe the operative technique and the clinical efficacy of the Ankle Spacer for the treatment of multiple, cystic OLTs in patients with failed prior operative treatment. Despite the fact that no clinical trials have been published on this specific implant, it is hypothesized that the 2-year postoperative follow-up will show a clinically relevant pain reduction and prosthesis survival.

MATERIALS AND METHODS

Study design

The study concerns a non-randomized, non-blinded, non-comparative prospective trial, with a 2-year follow-up period at the outpatient clinic aiming at assessing pain, function and implant survival, and thereby investigating the clinical efficacy of the Ankle Spacer. The study was approved by the local Medical Ethics Committee (Internal Review Board, IRB) of the Amsterdam University Medical Centre with reference number MEC 2017_175 and was performed in accordance with the principles of the Declaration of Helsinki and the medical Research Involving Human Subjects Act. The study was sponsored by Arthrex as a post market study with reference number EMEA-17037.

Patient selection

All patients eligible for operative implantation of the Ankle Spacer visiting the outpatient clinic between March 2017 and March 2019 for an OLT with a diameter of 15mm or more (anterior-posterior or medial-lateral), an OLT that failed prior operative intervention(s) or patients with multiple OLTs on the talar dome surface, were requested if they were willing to participate in the present clinical trial. If they were interested, patients were informed about this study and were given two wk to decide upon participation. In case patients provided their consent, they were screened for meeting the inclusion and exclusion criteria (Table 1).

Timeframe and outcome assessment

Preoperatively, standing weight bearing conventional radiographs and a computed tomography scan (CT) were taken. Preoperative patient-reported outcome measures (PROMs) consisted of the Numeric Rating Scale (NRS) of pain (during walking, in rest and during stairclimbing), patient satisfaction regarding complaints, activity and treatment, the American Orthopaedic Foot and Ankle Society (AOFAS) Hindfoot Score, Foot and Ankle Outcome Score (FAOS) and the Short-Form 36 (SF-36 physical and mental component scale). The AOFAS score physician subscale and ROM were assessed by an independent researcher who was not involved in the operative procedure[19,20]. Follow-up assessment was performed at two and six weeks, three and six months, one-year and two years postoperatively. At these follow-up moments the patients were requested to fill out a questionnaire consisting of the above-mentioned PROMs and a physical examination was performed to test the ROM (expect for the postoperative visits at 2 wk and 6 wk after the surgery). Radiographs were taken one day, 6 wk, one year and two years postoperatively. At one-year of follow-up, a CT-scan was made (Figure 1 describes the flow-chart outlining the study procedures). In addition, postoperative complications were recorded. Demographic data were also collected. The primary outcome measure in question was the NRS of pain during walking at 2-years follow-up and implant survival. All other outcome measures described above were secondary outcomes.

Description of the device

The Arthrex Ankle Spacer is a one-piece implant system that replaces the talar side of the tibio-talar joint (Figure 2). The Ankle Spacer replaces the articulating upper surface of the talus and offers several implant sizes in millimeters (18, 20, 22, 24, 26, 28) in order to fit to the different sizes of the talus. It is anatomically designed to the native talar dome to provide an optimal fit to the distal articular tibial surface. The implant is polished to a mirror effect on the articulating surface and has a rough titanium plasma spray (TPS) coated under surface with two posts and spikes for implant fixation (US10,350,079 B2). The rough surface enables secondary fixation due to bone ingrowth. Spikes at the posterior part of the prosthesis allow for further fixation to the bone. The weight of the ankle spacer weighs varies from 11 to 22 g, depending on the size of the spacer.

Operative technique

Before receiving the Ankle Spacer, the patient received 2 g of cefazoline pre-operatively. The procedure was carried out under general anesthesia. The patient was placed in the supine position with a tourniquet applied around the thigh and a rolled-up apron underneath the lateral malleolus to facilitate eversion of the foot to improve exposure of the talus. A longitudinal incision between 10 and 15 cm was centered over the ankle immediately lateral to the tibialis anterior tendon. The incision was deepened to the ankle joint while retracting the extensor hallucis longus and the neurovascular bundle laterally. If present, the osteophytes on the anterior tibia edge were removed. Subsequently, the cartilage was

Table 1 Inclusion and exclusion criteria

Patient	Gender	Age	BMI (kg/m²)	Prior procedures
1	M	36	27	2013: Removal of anterior bony ankle impingement
				2013: Arthroscopic screw fixation of talar osteochondral lesion
				2014: Screw removal
				2015: Hyaluronic acid injections (multiple)
				2016: Arthroscopic Bone Marrow Stimulation for talar osteochondral lesion
2	F	56	23	2005: Spongiosaplasty for talar osteochondral lesion
				2008: Arthroscopic bone marrow stimulation for talar osteochondral lesions
				2014: Retrograde drilling for talar osteochondral lesion
				2017: Hyaluronic acid injections (multiple)

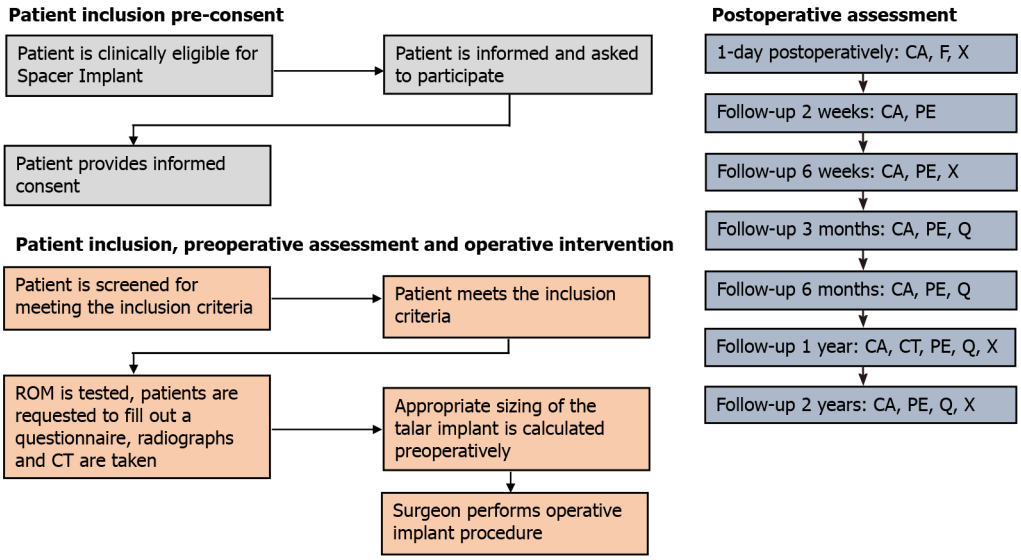


Figure 1 Flow-chart of the study design and main procedures participants will undergo during this study. CA: Complication assessment; CT: Computed tomography; PE: Physical examination; Q: Questionnaires; ROM: Range of motion; X: Mortise and lateral radiographs.

removed (Figure 3A) on the upper talar surface as well as part of the underlying subchondral bone (Figure 3B).

Additionally, microfracturing was performed to support ingrowth for secondary ankle spacer fixation (Figure 3C).

The tibiotalar joint was manually distracted and the appropriate trial Ankle Spacer was inserted into the joint. The trial Ankle Spacer was placed in a central position in the medial-lateral direction. The trial was fixated in the slotted hole with a K-wire and the trial inserter was removed afterwards.

Then, dynamic dorsi- and plantarflexion of the ankle was performed as this allowed self-alignment of the temporarily fixed trial. Afterwards, the trial spacer was fixated with a K-wire in the second hole in order to prevent dislocation, after which both K-wires were advanced bi-cortically in order to achieve proper fixation. Fluoroscopy was used to confirm proper sizing and positioning of the trial Ankle Spacer.

The double drill sleeve was aligned to the two holes on the Ankle Spacer and were maintained in a perpendicular angle relative to the surface of the ankle spacer. Subsequently, drilling was started with the first drill until the moment it stopped on the drill sleeve. This first drill was left for fixation in the drill hole, and then the second drill was to drill the second hole, in exactly the same manner.

Then all instruments were removed. Prior to inserting the Ankle Spacer, the prepared bone bed was thoroughly cleaned and inspected. The Ankle Spacer was inserted on the talar dome using the ankle space inserter, while placing the two posts on the bottom of the Ankle Spacer into the prepared drill holes for fixation. The implant was impacted with an impactor until the posts were fully seated in the drill holes (Figure 4A and Figure 4B). The joint capsule was closed and the layers were closed subsequently.

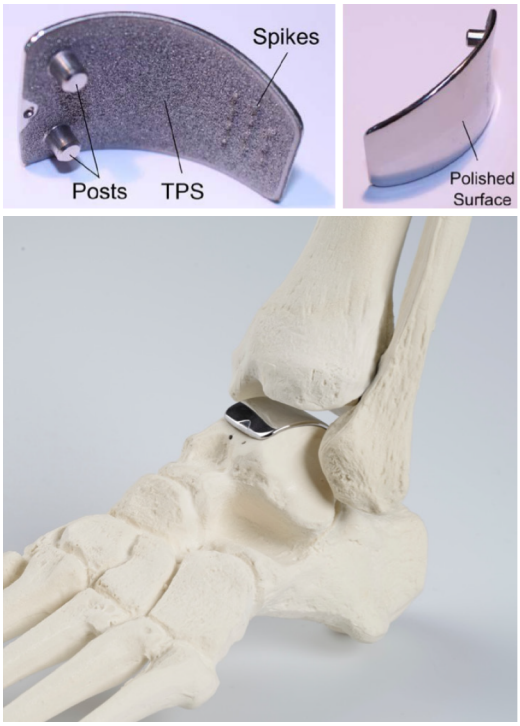


Figure 2 The Ankle Spacer Implant.

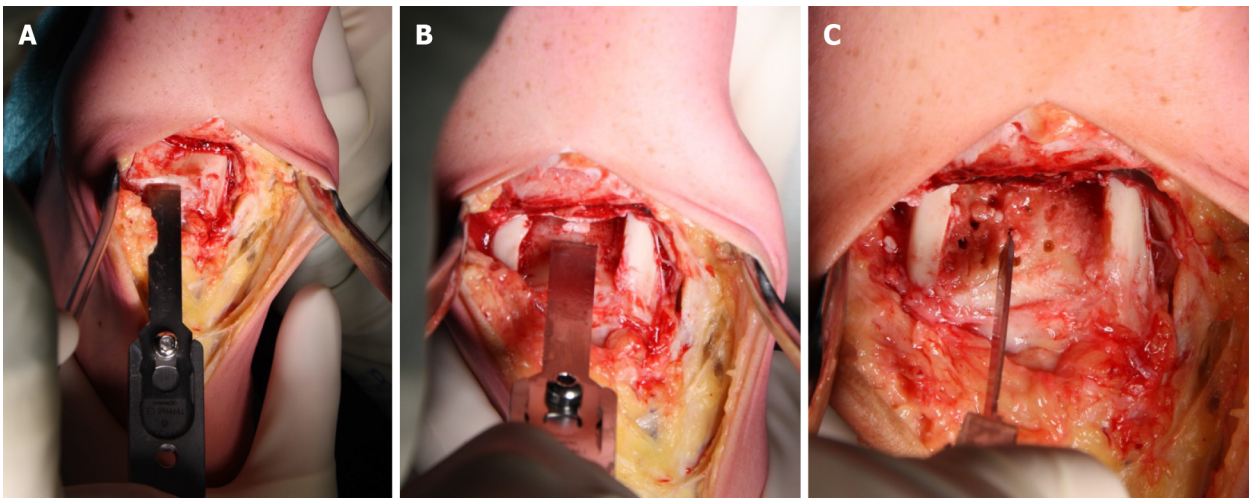


Figure 3 Preparation of cartilage and bone prior to insertion. A: Removal of the talar cartilage; B: Removal of the subchondral bone; C: Bone marrow stimulation of the subchondral bone.

Post-operative protocol

Postoperatively, wound dressing with adequate padding was applied. At hospital discharge a removable lower leg splint was applied. Careful active and passive dorsi- and plantarflexion motion (flexion-extension exercises) without weight bearing monitored by a physiotherapist were started two days after surgery. After two wk of non-weight bearing, depending on the degree of wound and soft tissue healing, mobilization was started with progressive weight bearing to tolerance in a Walker. Flexion-extension exercises were continued. Six wk after surgery, intensive physiotherapy and rehabilitation was started for at least a period of 6 wk.

Power calculation and study population

A power analysis was conducted to estimate the needed sample size for this prospective non-comparative trial using the NRS for pain as primary outcome measure with a clinical relevant difference of 1 point and a standard deviation of 1.5 points. Additionally, in this calculation a standard p-value of 0.05 ($\alpha = 0.05$) and a power of 80% were used. This indicated that a total of 20 patients would need to be included in the trial in order to detect a clinically important difference in pain comparing pre- and

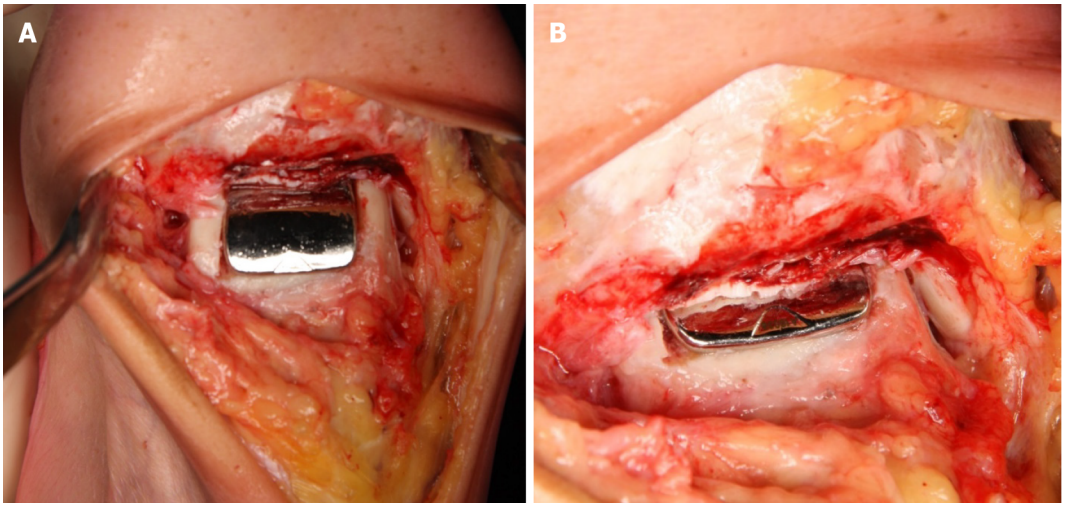


Figure 4 After the insertion of the Ankle Spacer. A: End-result after the insertion of the Ankle Spacer; B: End-result after the insertion of the Ankle Spacer.

postoperative NRS scores. Due to the relative rarity of patients presenting at our outpatient department with the exact above-described inclusion and exclusion criteria, two patients could be identified with fitting indications who were operated on with the implantation of the Ankle Spacer. The age of these patients was 36 and 56 years old (one male, one female). No patients were lost to follow-up. Prior procedures that were performed are listed in Table 2 alongside demographic factors. The pre-operative CT scans of the patients as presented in Figures 5 and 6.

Statistical analysis

All statistical analyses were performed by means of SPSS version 20.0 (SPSS Inc., Chicago, IL, United States). Data will be presented as descriptive analyses through qualitative comparisons in the different patients. Consequently, data will be presented per patient, aiming at presenting changes in scores preoperatively *vs* postoperatively.

RESULTS

Primary outcome

The primary outcome measure, the NRS of pain during walking improved from 6 preoperatively to 2 points at 2 years follow-up in patient 1, and from 7 preoperatively to 2 points postoperatively at 2 years follow-up in patient 2. This entails an improvement of 4 points and 5 points in patient 1 and 2, respectively (Figure 7).

Secondary outcomes

The other PROMs can be appreciated in Table 3. There were no complications and no reoperations. Radiologically, for all postoperative radiographs and CT-scans it was concluded that there were no indications of loosening of the implant, no implant migration, and no subsidence was noted (Figure 8). The ROM assessments were described in Table 4.

DISCUSSION

This is the first study describing the results of the newly developed Ankle Spacer. The Ankle Spacer is a one-piece implant system that replaces the talar side of the tibiotalar joint, and can therefore be considered a hemi-arthroplasty procedure. The implant had been designed in order to overcome a number of downsides that are associated with the current treatment options for large, cystic, or multiple osteochondral lesions of the talus that have failed prior operative intervention(s). One of these treatment option being applied in the younger patient population is an arthroscopic ankle arthrodesis which results in highly satisfactory clinical outcomes mostly concerning pain outcomes[10-12]. The downside of this operative intervention is that it results in functional limitations due to loss of ROM of the ankle [13]. Furthermore, an ankle arthrodesis increases the long-term risk of (radiographic) osteoarthritis in adjacent hindfoot joints, particularly in the subtalar joint[14,21]. An alternative option is the placement of a total ankle prosthesis, for which a substantial amount of bone needs to be resected[15,22]. In order to tackle the downsides of these treatment options, develop a bone-sparing procedure and resurfacing

Table 2 Patient characteristics

Inclusion criteria	Exclusion criteria
Age ranging from 18 to 80 yr	Severe ankle malalignment (more than 5° varus or valgus)
Failed previous conservative treatment	Suspicion of grade two or higher (Kellgren-Lawrence-Score) ankle joint degeneration on the tibia side
Complaints for at least 6 mo	Ankle Fracture less than 6 mo ago
Talar osteochondral lesions (multiple degenerative talar cysts present, and/or prior failed operative treatment and/or multiple defects and/or a diameter of 15mm or more)	Tendinitis
	Advanced osteoporosis
	Adiposity grade I (BMI of 30 kg/m^2 or more)
	Diabetes mellitus / reumathoid arthritis / severe neuro-arthropathy
	Blood supply limitations and active infections, which may retard healing
	Foreign-body sensitivity
	Currently participating in an investigational drug or another device study that clinically interferes with the current study endpoints

BMI: Body mass index; F: Female; M: Male.

the talar dome to preserve ROM and potentially optimize physical functioning, the Ankle Spacer, a novel bone-sparing hemi-prosthesis, has been developed. The outcomes of treatment with the Ankle Spacer were described in the present article. Potential advantages include preservation of ankle motion, decreased stress on the midfoot and subtalar joints, and the possibility to perform an ankle fusion after failed hemi-arthroplasty.

It is therefore clear that the Ankle Spacer is a new and innovative device. The current study is the first clinical trial performed investigating the efficacy of the Ankle Spacer, and therefore there is no clinical literature on this particular prosthetic device at this time to compare our clinical results to. Our current clinical results must therefore be compared to similar devices having been researched over the past decade. An articular and subchondral bone resurfacing implant procedure on one side of the joint (hemi-arthroplasty) can be considered a relatively novel operative intervention. Promising clinical results have been reported for similar treatment in the femoral and humeral head, as well as the first metatarsal and patellar surface. [16,23-27]. Van Bergen *et al*[17,18,28] showed that a focal resurfacing implant is a promising treatment for talar OLTs that have failed prior operative treatment[28]. They concluded that in a patient series including 38 patients the clinical results at a mean follow-up of three years were satisfactory. A different study by Holton *et al*[29] demonstrated that the use of a different resurfacing implant in the form of an articular resurfacing component maintained a good clinical improvement for patients at mid-term follow-up. A study by Brunner *et al*[30] which is less clinically comparable as it replaces the whole entity of the ankle, as opposed to the resurfacing of the talar surface as done by the Ankle Spacer or as opposed to the resurfacing implant as used by van Bergen *et al*[4,6,31], showed that short- term to mid-term results for patients treated with the Scandinavian Total Ankle Replacement (STAR) prosthesis have been encouraging. The long-term results were clinically inferior compared to the short-term and mid-term results. Additionally, studies on the Total Ankle Replacement (TAR), which is, to a certain though limited extent, comparable to the Ankle Spacer, have shown that long-term results demonstrated improved pain scores as it was observed to be a viable and durable operative implantation option[32,33]. Another implantation technique in the form of a Tornier Salto Talaris Anatomic Ankle has been described in the literature. Mid- term results showed that the survivorship of this implant was calculated to be around 95%[34,35]. A study by Queen *et al*[36] found that at a follow-up of 2 years investigating 51 patients after a fixed-bearing Total Ankle Replacement significant improvements in gait mechanics, pain reduction and functioning were observed.

As an objective conclusive remark on the evidence found on similar operative techniques, one can state that similar operative techniques yielded favorable clinical, radiological and safety outcomes. When comparing these three aspects to our results it can be concluded that in our treated patients, similar outcomes were found. Postoperative improvement was especially clear in the observed primary outcome measure which was the NRS pain during walking. This outcome measures typically describes the state and magnitude of pain in patients with OLTs of the talus as these patients experience pain especially when performing weight bearing activities, but often are unable to participate in sports due to complaints[4]. It was shown that this primary outcome measure improved from 6 and 7 preoperatively

Table 3 Preoperative and postoperative outcomes for patients 1 and 2

Patient 1						
Time-Point	FAOS	SF-36	AOFAS ankle hindfoot score	NRS satisfaction with current activity level	NRS satisfaction with daily functioning despite any complaints	NRS satisfaction with treatment so far
Preoperatively	Pain: 56; Symptoms: 46; ADL: 68; Sports: 20 QoL: 25	PCS: 28; MCS: 61	61	3	3	8
3 mo postoperatively	Pain: 86; Symptoms: 82; ADL: 91; Sports: 40 QoL: 63	PCS: 44; MCS: 55	82	7	8	9
6 mo postoperatively	Pain: 79; Symptoms: 86 ; ADL: 93; Sports: 60 QoL: 63	PCS: 45; MCS: 53	75	7	8	9
1 year postoperatively	Pain: 46; Symptoms: 67; ADL: 79; Sports: 25 QoL: 44	PCS: 39; MCS: 56	77	6	4	7
2 years postoperatively	Pain: 62; Symptoms: 81; ADL: 90; Sports: 55 QoL: 69	PCS: 51; MCS: 52	100	8	8	9
Patient 2						
Preoperative	Pain: 81; Symptoms: 79; ADL: 91; Sports: N.A. QoL: 25	PCS: 44; MCS: 56	72	5	6	7
3 mo postoperatively	Pain: 64; Symptoms: 68; ADL: 66; Sports: 30 QoL: 0	PCS: 33; MCS: 41	69	2	2	2
6 mo postoperatively	Pain: 68; Symptoms: 69 ; ADL: 72; Sports: 30 QoL: 13	PCS: 29; MCS: 54	71	1	5	1
1 year postoperatively	Pain: 72; Symptoms: 50; ADL: 72; Sports: 30 QoL: 19	PCS: 33; MCS: 51	68	2	5	2
2 years postoperatively	Pain: 81; Symptoms: 68; ADL: 78; Sports: 55 QoL: 50	PCS: 43; MCS: 53	88	9	9	8

ADL: Activities in daily living; AOFAS: American Orthopaedic Foot and Ankle Society; FAOS: Foot and ankle outcome score; MCS: Mental component scale; NRS: Numeric rating scale; PCS: Physical component scale; QoL: Quality of life; SF-36: Short-form 36.

to 2 and 2 postoperatively at 2 years, in patient 1 and 2, respectively. As a result, we can conclude that for both patients a minimal clinically important difference was reached when comparing the preoperative state of pain to the postoperative state of pain at 2 years after the surgery. As an improvement of at least −1.0 on the NRS scale of 0 to 10 points is significantly associated with the concept of a "better improvement", and an improvement of -2.0 on this scale is associated with a "much better improvement"[31]. The improvement was also reflected in the radiological outcomes and the subjective satisfaction scores that were taken both preoperatively and postoperatively at the different follow-up moments in which it was clear that the patients stated that they were satisfied with their level of activity. Moreover, this was also reflected in the postoperative AOFAS Hindfoot Scale, which ranged from 88 to 100, scores that can be considered to represent a successful surgery.

Furthermore, it was observed that there were no complications, no reoperations nor revisions, which implicates that, when extrapolating these results for a larger population based on our experience, the insertion of the Ankle Spacer can be regarded a safe procedure. This outcome should be interpreted in the light of the high re-intervention rates that are associated with Total Talar Prostheses, as some studies report that up to 38% of the patients need revision surgery within the first year after total ankle arthroplasty[37]. With regards to ROM, it was shown that the ROM did not decrease in the patients, potentially due to the fact that patients received adequate postoperative physiotherapy and because of the fact that the Ankle Spacer was inserted just below the level of the subchondral bone plater not affecting joint congruency. This is clinically relevant to take into account when comparing ROM outcomes after placement of the Ankle Spacer to outcomes after an ankle arthrodesis procedure[38].

This study should be interpreted in light of its strengths and weaknesses. Strengths of this study include its prospective and thorough methodology, completeness of follow-up, and the use of various validated outcome measures in the assessment of a not yet studied resurfacing implant. Limitations

Table 4 Preoperative and postoperative range of motion outcomes patient 1 and 2

	Patient 1		Patient 2	
	Dorsiflexion in degrees (affected/unaffected side)	Plantarflexion in degrees (affected/unaffected side)	Dorsiflexion in degrees (affected/unaffected side)	Plantarflexion in degrees (affected/unaffected side)
Preoperative	5 / 10	35 / 40	5 / 5	40 / 40
2 wk postoperatively	5 / 15	20 / 40	2 / 15	25 / 40
6 wk postoperatively	7 / 10	35 / 40	5 / 10	35 / 40
3 mo postoperatively	10 / 10	35 / 45	5 / 10	35 / 40
6 mo postoperatively	10 / 10	35 / 45	10 / 10	35 / 40
1 yr postoperatively	10 / 10	35 / 45	10 / 10	35 / 40
2 yr postoperatively	10 / 10	35 / 45	7 / 10	35 / 40



Figure 5 Pre-operative computed tomography scan of patient number 1: Upper part shows coronal slides with the images from left to right going into the posterior to anterior direction. The lower part shows sagittal slides with the images from left to right going from lateral to medial.

include the absence of a controlled group, lack of long-term follow-up outcomes ranging past the two years follow-up, and the small series of patients. However, we have found in our tertiary referral clinic that operates in an academic setting with the status of an official (inter)national expertise center for the treatment of OLTs in the ankle that the indication for an Ankle Spacer implantation is highly rare, even though we receive a high number of patients on a yearly basis. As a result, it was therefore noted that the Ankle Spacer has been removed from the market due to limited indications and strict regulatory

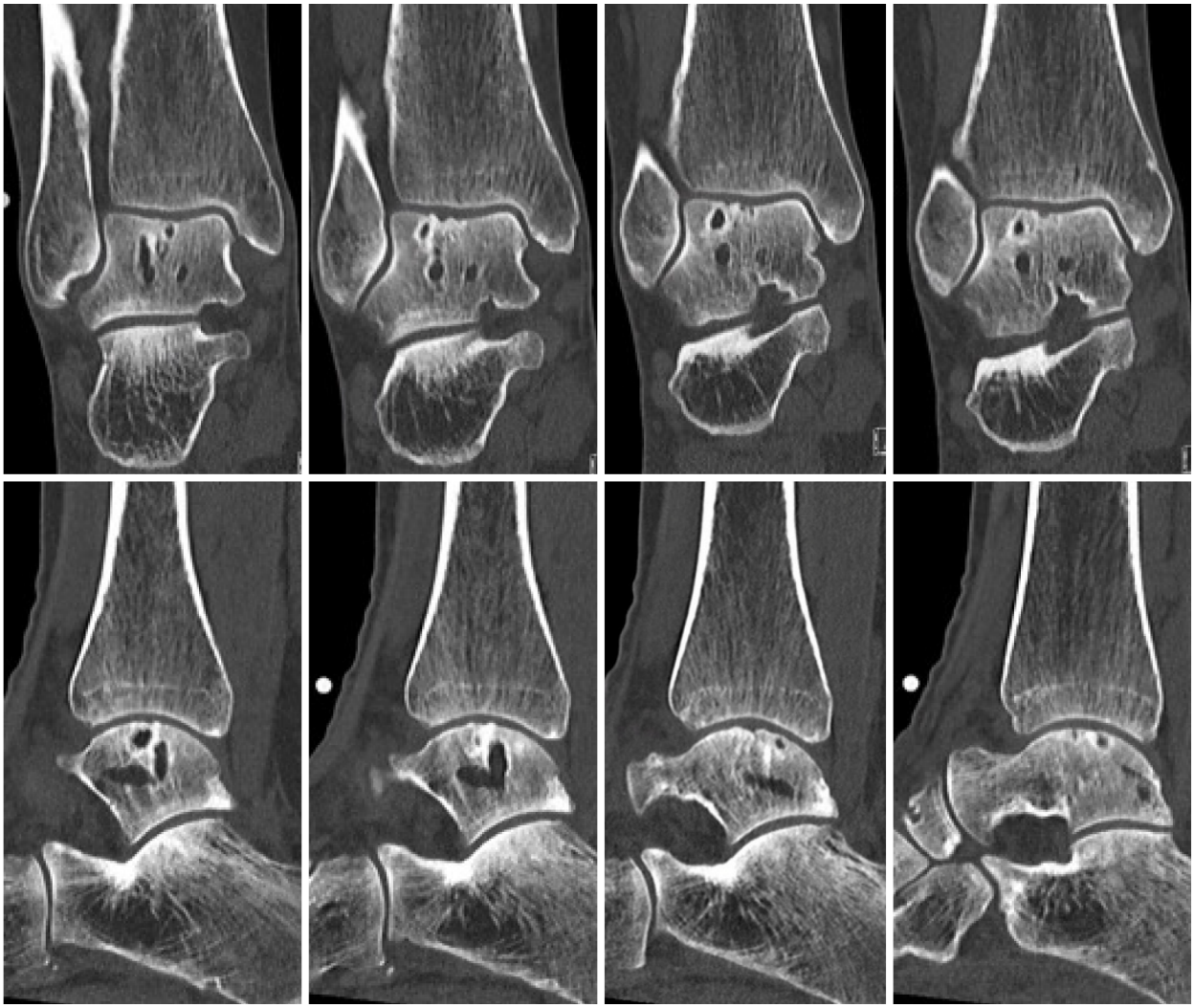


Figure 6 Pre-operative computed tomography scan of patient number 2: Upper part shows coronal slides with the images from left to right going into the posterior to anterior direction. The lower part shows sagittal slides with the images from left to right going from lateral to medial.

requirements.

The clinical relevance of the present study can be interpreted in the light of the highly specific indication for the implantation of the Ankle Spacer. This device is particularly suited for patients with multiple OLTs of the talar dome having failed prior operative intervention(s) with an unaffected distal tibial part of the ankle joint. This study shows that the Ankle Spacer is effective for this particular and rare patient group, thereby functioning as a joint-sparing alternative to more invasive operative interventions, such as an ankle arthrodesis or total ankle arthroplasty.

CONCLUSION

The Ankle Spacer showed clinically relevant pain reduction during walking, improvement in clinical outcomes as assessed with PROMs, and no complications or re-operations. This treatment option may therefore evolve as a joint-sparing alternative to an ankle arthrodesis, a total talar implant or a total ankle arthroplasty/resurfacing.

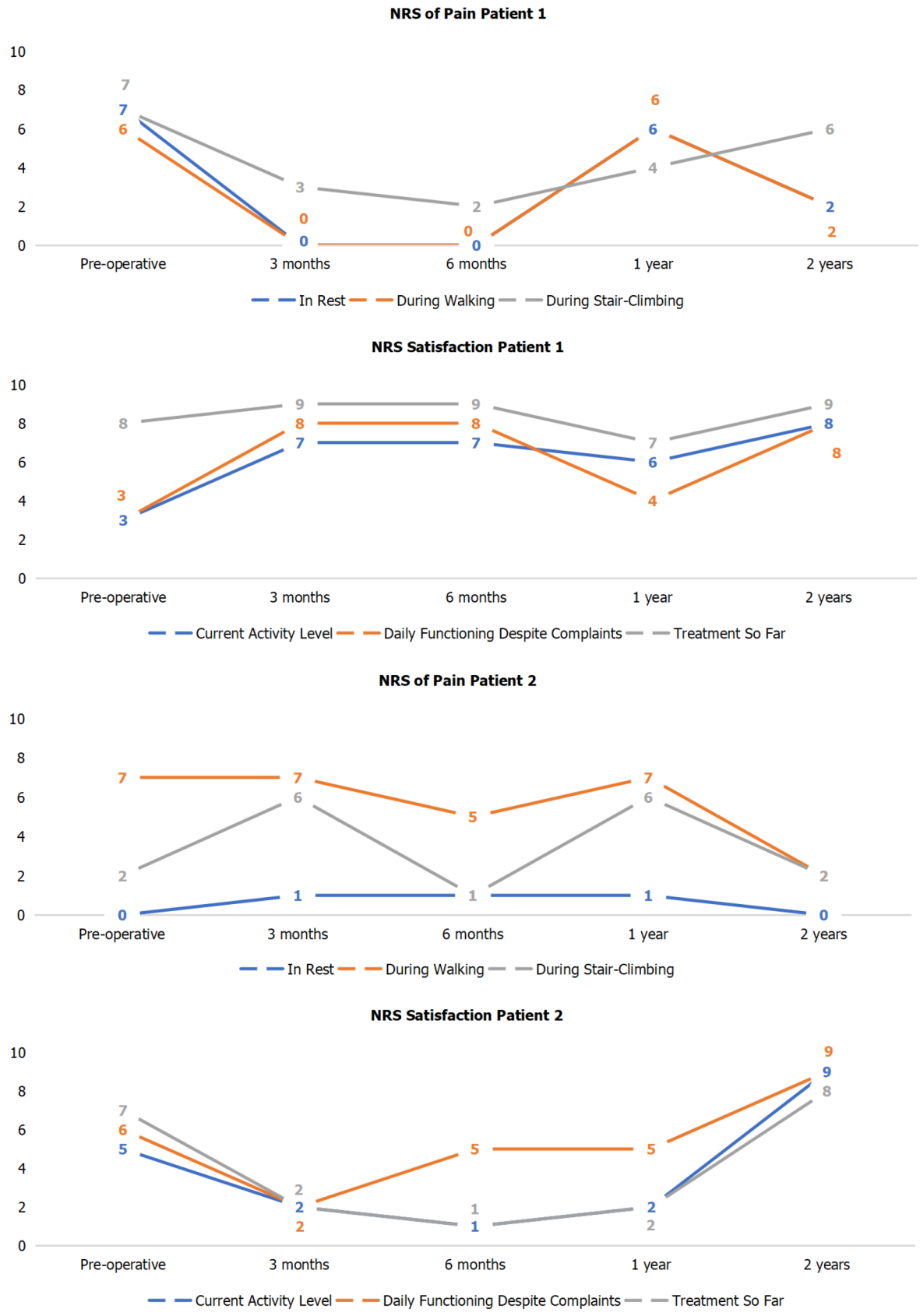


Figure 7 Pre-and postoperative Numeric Rating Scale scores of pain and satisfaction for patients 1 and 2.

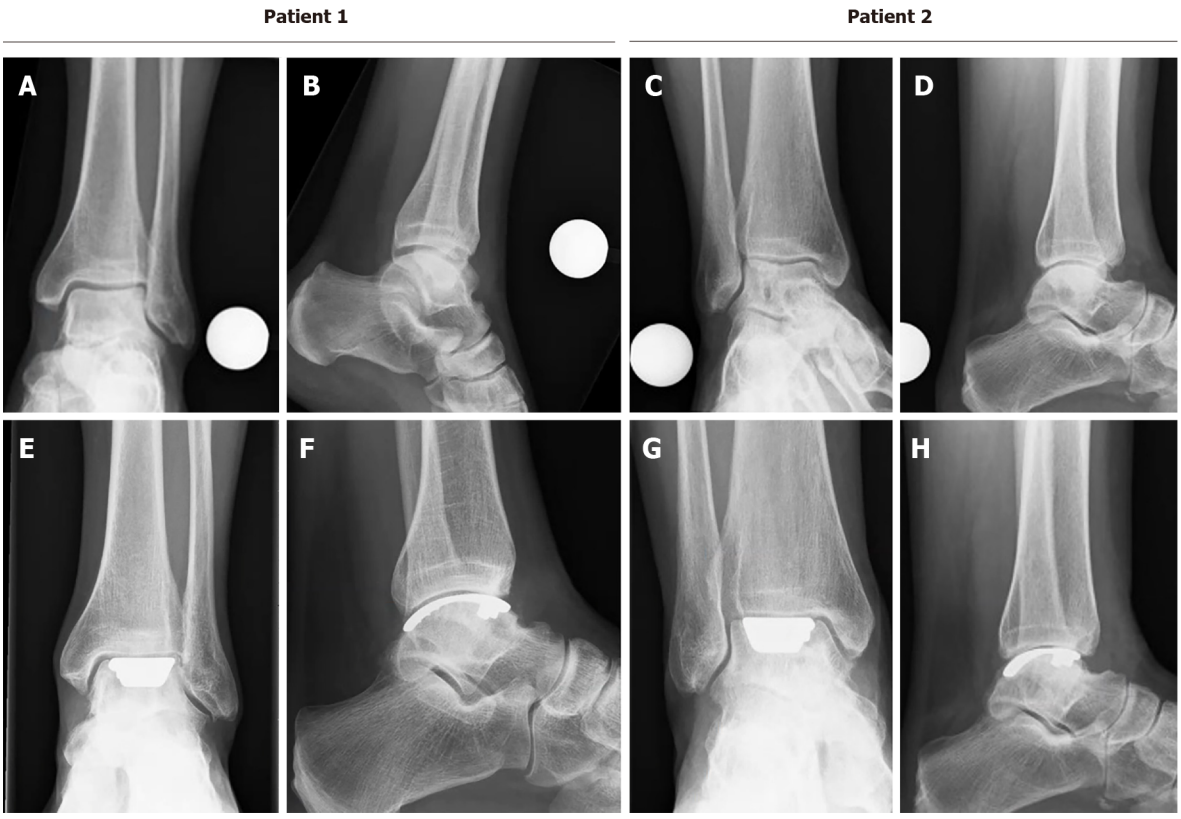


Figure 8 Preoperative and postoperative radiographs. A and C: Preoperative mortise radiographs; B and D: Preoperative lateral radiograph; E and G: Postoperative mortise radiograph (2-years); F and H: Postoperative radiograph.

ARTICLE HIGHLIGHTS

Research background

Osteochondral lesions of the Talus (OLT) are pathologic lesions of the talar cartilage and the subchondral bone. These lesions can occur in up to 50% of acute ankle fractures and sprains. For OLTs of larger size (*i.e.*, above 10 or 15 mm in diameter) and of non-fragmentous morphology, the 'standard' operative treatment options such as autologous chondrocyte implantation, osteochondral autograft transfer systems, and a Talar OsteoPeriostic grafting from the Iliac Crest procedure may result in satisfactory clinical outcomes. However, in some patients, there are multiple secondary lesions present of large and cystic nature. For these lesions, it is not always possible to harvest an osteo(chondral) autograft that is large enough to replace all the diseased osteochondral tissue of the talus without damaging the donor site or compromising the congruency of the ankle joint. Allograft treatment could be considered for the treatment of these type of lesions. However, these contain the disadvantages of loss of viability and stability in one-third of the grafts, and possibly clinically fail due to immunological reactions. However, when there are multiple secondary (*i.e.*, failed prior surgery) lesions present on the talar articular surface in combination with a large and cystic nature, the above-described operative interventions are to be expected to result in relatively inferior outcomes.

Research motivation

Currently, it is difficult to treat patients with osteochondral lesions of the ankle that are of multiple, cystic and secondary nature. This is because the lesions are considered relatively large and difficult to treat. For this indication, it was usually performed to fuse the ankle joint. However, in the past 2 to 5 years, novel innovative surgical options have been developed, such as the Ankle Spacer, in order to overcome an ankle fusion or ankle prosthesis.

Research objectives

To describe the operative technique and the clinical efficacy of the Ankle Spacer for the treatment of multiple, cystic OLTs in patients with failed prior operative treatment.

Research methods

In a prospective study including patients with multiple, cystic or large osteochondral lesions of the talus were included who failed previous surgical treatment. We looked at the numeric rating scale (NRS) for

pain during walking at 2 years after implantation of the Ankle Spacer and we also assessed the NRS in rest and during stair-climbing, the American Orthopaedic Foot and Ankle Outcome Score, the Foot and Ankle Outcome Score, the Short-Form 36 and the range of motion of the ankles both pre-operatively as well as post-operatively. Radiographic evaluations were conducted to evaluate prosthetic loosening and subsidence. Revision rates and complications were also assessed.

Research results

In this prospective study, two patients underwent the implantation of an Ankle Spacer for osteochondral damage on the talar dome. We found that there were clinically relevant pain reductions during walking as well as important improvements in clinical outcomes as assessed with the patient-reported outcome measures. Furthermore, it was found that there were no complications nor re-operations.

Research conclusions

The Ankle Spacer showed good clinical outcomes and clinically relevant pain reduction during walking, improvement in clinical outcomes as assessed with PROMs, and no complications or re-operations. This treatment option may therefore evolve as a joint-sparing alternative to an ankle arthrodesis, a total talar implant or a total ankle arthroplasty/resurfacing.

Research perspectives

Future research should be focused at the development of a prospective, self-learning algorithm taking into account the individual patient factors influencing outcomes after conservative and surgical treatment so that we can assess which patients would benefit most from which treatment options.

FOOTNOTES

Author contributions: Dahmen J, Altink JN, Vuurberg G, Wijdicks C, Stufkens S and Kerkhoffs G have made substantial contributions to conception and design, acquisition of data, analysis and interpretation of data, and have been involved in drafting the manuscript; Dahmen J and Altink JN have been involved in the acquisition of data; all authors have been involved in revising the manuscript, critically for important intellectual content, and have given final approval of the version to be published.

Institutional review board statement: The study was approved by the local Medical Ethics Committee (Internal Review Board, IRB) of the Amsterdam University Medical Centre with reference number MEC 2017_175 and was performed in accordance with the principles of the Declaration of Helsinki and the medical Research Involving Human Subjects Act (WMO).

Informed consent statement: All patients provided informed consent prior to the participation in the study.

Conflict-of-interest statement: The study was sponsored by Arthrex as a post market study with reference number EMEA-17037.

Data sharing statement: No additional data available.

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REFERENCES

1 **Martijn HA**, Lambers KTA, Dahmen J, Stufkens SAS, Kerkhoffs GMMJ. High incidence of (osteo)chondral lesions in

ankle fractures. *Knee Surg Sports Traumatol Arthrosc* 2021; **29**: 1523-1534 [PMID: 32761358 DOI: 10.1007/s00167-020-06187-y]
2 **Dahmen J**, Lambers KT, Reilingh ML, van Bergen CJ, Stufkens SA, Kerkhoffs GM. No superior treatment for primary osteochondral defects of the talus. *Knee Surg Sports Traumatol Arthrosc* 2017; **26**: 2142-2157
3 **Kerkhoffs GMMJ**, Altink JN, Stufkens SAS, Dahmen J. Talar OsteoPeriostic grafting from the Iliac Crest (TOPIC) for large medial talar osteochondral defects : Operative technique. *Oper Orthop Traumatol* 2021; **33**: 160-169 [PMID: 32902691 DOI: 10.1007/s00064-020-00673-9]
4 **Rikken QGH**, Kerkhoffs GMMJ. Osteochondral Lesions of the Talus: An Individualized Treatment Paradigm from the Amsterdam Perspective. *Foot Ankle Clin* 2021; **26**: 121-136 [PMID: 33487235 DOI: 10.1016/j.fcl.2020.10.002]
5 **Haene R**, Qamirani E, Story RA, Pinsker E, Daniels TR. Intermediate outcomes of fresh talar osteochondral allografts for treatment of large osteochondral lesions of the talus. *J Bone Joint Surg Am* 2012; **94**: 1105-1110 [PMID: 22717829 DOI: 10.2106/JBJS.J.02010]
6 **Pomajzl RJ**, Baker EA, Baker KC, Fleischer MM, Salisbury MR, Phillips DM, Fortin PT. Case Series With Histopathologic and Radiographic Analyses Following Failure of Fresh Osteochondral Allografts of the Talus. *Foot Ankle Int* 2016; **37**: 958-967 [PMID: 27272267 DOI: 10.1177/1071100716651963]
7 **Brodsky JW**, Scott DJ, Ford S, Coleman S, Daoud Y. Functional Outcomes of Total Ankle Arthroplasty at a Mean Follow-up of 7.6 Years: A Prospective, 3-Dimensional Gait Analysis. *J Bone Joint Surg Am* 2021 [DOI: 10.2106/jbjs.20.00659]
8 **Usuelli FG**, Indino C, Leardini A, Manzi L, Ortolani M, Caravaggi P. Range of motion of foot joints following total ankle replacement and subtalar fusion. *Foot Ankle Surg* 2021; **27**: 150-155 [PMID: 32381452 DOI: 10.1016/j.fas.2020.03.015]
9 **Usuelli FG**, Indino C, Maccario C, Manzi L, Romano F, Aiyer A, Kaplan JRM. A Modification of the Fibular Osteotomy for Total Ankle Replacement Through the Lateral Transfibular Approach. *J Bone Joint Surg Am* 2019; **101**: 2026-2035 [PMID: 31764365 DOI: 10.2106/JBJS.19.00307]
10 **de Leeuw PA**, Hendrickx RP, van Dijk CN, Stufkens SS, Kerkhoffs GM. Midterm results of posterior arthroscopic ankle fusion. *Knee Surg Sports Traumatol Arthrosc* 2016; **24**: 1326-1331 [PMID: 26759153 DOI: 10.1007/s00167-015-3975-z]
11 **Hendrickx RP**, Kerkhoffs GM, Stufkens SA, van Dijk CN, Marti RK. Ankle fusion using a 2-incision, 3-screw technique. *Oper Orthop Traumatol* 2011; **23**: 131-140 [PMID: 21455740 DOI: 10.1007/s00064-011-0015-0]
12 **Hendrickx RP**, Stufkens SA, de Bruijn EE, Sierevelt IN, van Dijk CN, Kerkhoffs GM. Medium- to long-term outcome of ankle arthrodesis. *Foot Ankle Int* 2011; **32**: 940-947 [PMID: 22224322 DOI: 10.3113/FAI.2011.0940]
13 **Sealey RJ**, Myerson MS, Molloy A, Gamba C, Jeng C, Kalesan B. Sagittal plane motion of the hindfoot following ankle arthrodesis: a prospective analysis. *Foot Ankle Int* 2009; **30**: 187-196 [PMID: 19321094 DOI: 10.3113/FAI.2009.0187]
14 **Wang Y**, Wong DW, Tan Q, Li Z, Zhang M. Total ankle arthroplasty and ankle arthrodesis affect the biomechanics of the inner foot differently. *Sci Rep* 2019; **9**: 13334 [PMID: 31527781 DOI: 10.1038/s41598-019-50091-6]
15 **Hintermann B**, Zwicky L, Knupp M, Henninger HB, Barg A. HINTEGRA revision arthroplasty for failed total ankle prostheses. *J Bone Joint Surg Am* 2013; **95**: 1166-1174 [PMID: 23824384 DOI: 10.2106/JBJS.L.00538]
16 **Reilingh ML**, Van Bergen CJA, Van Dijk CN. Novel metal implantation technique for osteochondral defects of the medial talar dome. *Techniques in Foot and Ankle Surgery* 2012; **11**: 45-49 [DOI: 10.1097/btf.0b013e31824696d7]
17 **van Bergen CJ**, van Eekeren IC, Reilingh ML, Sierevelt IN, van Dijk CN. Treatment of osteochondral defects of the talus with a metal resurfacing inlay implant after failed previous surgery: a prospective study. *Bone Joint J* 2013; **95-B**: 1650-1655 [PMID: 24293595 DOI: 10.1302/0301-620X.95B12.32455]
18 **van Bergen CJA**, van Eekeren ICM, Reilingh ML, Gerards RM, Dijk CNV. The use of HemiCAP for the treatment of osteochondral lesions. *Operative Techniques in Orthopaedics* 2014; **24**: 190-194 [DOI: 10.1053/j.oto.2014.04.003]
19 **Kitaoka HB**, Alexander IJ, Adelaar RS, Nunley JA, Myerson MS, Sanders M. Clinical rating systems for the ankle-hindfoot, midfoot, hallux, and lesser toes. *Foot Ankle Int* 1994; **15**: 349-353 [PMID: 7951968 DOI: 10.1177/107110079401500701]
20 **Reilingh ML**, van Bergen CJ, Gerards RM, van Eekeren IC, de Haan RJ, Sierevelt IN, Kerkhoffs GM, Krips R, Meuffels DE, van Dijk CN, Blankevoort L. Effects of Pulsed Electromagnetic Fields on Return to Sports After Arthroscopic Debridement and Microfracture of Osteochondral Talar Defects: A Randomized, Double-Blind, Placebo-Controlled, Multicenter Trial. *Am J Sports Med* 2016; **44**: 1292-1300 [PMID: 26903214 DOI: 10.1177/0363546515626544]
21 **Valderrabano V**, Horisberger M, Russell I, Dougall H, Hintermann B. Etiology of ankle osteoarthritis. *Clin Orthop Relat Res* 2009; **467**: 1800-1806 [PMID: 18830791 DOI: 10.1007/s11999-008-0543-6]
22 **Hopgood P**, Kumar R, Wood PL. Ankle arthrodesis for failed total ankle replacement. *J Bone Joint Surg Br* 2006; **88**: 1032-1038 [PMID: 16877602 DOI: 10.1302/0301-620X.88B8.17627]
23 **Anderson DD**, Tochigi Y, Rudert MJ, Vaseenon T, Brown TD, Amendola A. Effect of implantation accuracy on ankle contact mechanics with a metallic focal resurfacing implant. *J Bone Joint Surg Am* 2010; **92**: 1490-1500 [PMID: 20516325 DOI: 10.2106/JBJS.I.00431]
24 **Davidson PA**, Rivenburgh D. Focal anatomic patellofemoral inlay resurfacing: theoretic basis, surgical technique, and case reports. *Orthop Clin North Am* 2008; **39**: 337-346, vi [PMID: 18602562 DOI: 10.1016/j.ocl.2008.02.003]
25 **Hasselman CT**, Shields N. Resurfacing of the first metatarsal head in the treatment of hallux rigidus. *Techniques in Foot and Ankle Surgery* 2008; **7**: 31-40 [DOI: 10.1097/btf.0b013e318165c356]
26 **Uribe JW**, Botto-van Bemden A. Partial humeral head resurfacing for osteonecrosis. *J Shoulder Elbow Surg* 2009; **18**: 711-716 [PMID: 19186078 DOI: 10.1016/j.jse.2008.10.016]
27 **Van Stralen RA**, Haverkamp D, Van Bergen CJ, Eijer H. Partial resurfacing with varus osteotomy for an osteochondral defect of the femoral head. *Hip Int* 2009; **19**: 67-70 [PMID: 19455506 DOI: 10.1177/112070000901900113]
28 **Vuurberg G**, Reilingh ML, van Bergen CJA, van Eekeren ICM, Gerards RM, van Dijk CN. Metal Resurfacing Inlay Implant for Osteochondral Talar Defects After Failed Previous Surgery: A Midterm Prospective Follow-up Study. *Am J Sports Med* 2018; **46**: 1685-1692 [PMID: 29624081 DOI: 10.1177/0363546518764916]
29 **Holton C**, Gudipati S, Budgen A. Mid-term follow-up of talar dome resurfacing surgery using the HemiCAP device for osteochondral lesions: review of 3 cases. *Foot & ankle* 2013 [DOI: 10.1016/j.fas.2016.05.206]

30 **Brunner S**, Barg A, Knupp M, Zwicky L, Kapron AL, Valderrabano V, Hintermann B. The Scandinavian total ankle replacement: long-term, eleven to fifteen-year, survivorship analysis of the prosthesis in seventy-two consecutive patients. *J Bone Joint Surg Am* 2013; **95**: 711-718 [PMID: 23595069 DOI: 10.2106/JBJS.K.01580]

31 **Salaffi F**, Stancati A, Silvestri CA, Ciapetti A, Grassi W. Minimal clinically important changes in chronic musculoskeletal pain intensity measured on a numerical rating scale. *Eur J Pain* 2004; **8**: 283-291 [PMID: 15207508 DOI: 10.1016/j.ejpain.2003.09.004]

32 **Alvine FG**, Conti SF. [The AGILITY ankle: mid- and long-term results]. *Orthopade* 2006; **35**: 521-526 [PMID: 16598491 DOI: 10.1007/s00132-006-0939-5]

33 **Knecht SI**, Estin M, Callaghan JJ, Zimmerman MB, Alliman KJ, Alvine FG, Saltzman CL. The Agility total ankle arthroplasty. Seven to sixteen-year follow-up. *J Bone Joint Surg Am* 2004; **86**: 1161-1171 [PMID: 15173288]

34 **Bonnin M**, Judet T, Colombier JA, Buscayret F, Graveleau N, Piriou P. Midterm results of the Salto Total Ankle Prosthesis. *Clin Orthop Relat Res* 2004; 6-18 [DOI: 10.1097/01.blo.0000132407.75881.a0]

35 **Schweitzer KM**, Adams SB, Viens NA, Queen RM, Easley ME, Deorio JK, Nunley JA. Early prospective clinical results of a modern fixed-bearing total ankle arthroplasty. *J Bone Joint Surg Am* 2013; **95**: 1002-1011 [PMID: 23780538 DOI: 10.2106/JBJS.L.00555]

36 **Queen RM**, De Biassio JC, Butler RJ, DeOrio JK, Easley ME, Nunley JA. J. Leonard Goldner Award 2011: changes in pain, function, and gait mechanics two years following total ankle arthroplasty performed with two modern fixed-bearing prostheses. *Foot Ankle Int* 2012; **33**: 535-542 [PMID: 22835389 DOI: 10.3113/FAI.2012.0535]

37 **Criswell BJ**, Douglas K, Naik R, Thomson AB. High revision and reoperation rates using the Agility™ Total Ankle System. *Clin Orthop Relat Res* 2012; **470**: 1980-1986 [PMID: 22270469 DOI: 10.1007/s11999-012-2242-6]

38 **Wang Y**, Li Z, Wong DW, Zhang M. Effects of Ankle Arthrodesis on Biomechanical Performance of the Entire Foot. *PLoS One* 2015; **10**: e0134340 [PMID: 26222188 DOI: 10.1371/journal.pone.0134340]

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SYSTEMATIC REVIEWS

COVID-19 pandemic: An update on the reaction attitude of the spine societies and their members worldwide

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Abstract

BACKGROUND

All surgical specialties have been influenced by the coronavirus disease 2019 (COVID-19) pandemic, and substantial changes have been determined in medical assistance, especially in elective surgery. Several spine societies have published recommendations to provide optimal care during this unique situation.

AIM

To discuss the recommendations by many spine societies for the management of spinal diseases during the COVID-19 pandemic.

METHODS

The present study was performed according to the PRISMA guidelines. A review of the MEDLINE database (PubMed – National Library of Medicine), Google, and Google Scholar was performed from March 2020 to date for articles published in the English Language.

RESULTS

Spine associations and societies worldwide were divided into three groups: Continental, specialty and country-based societies. A total of 27 spine associations were included in this review. There were eight major continental associations, but only one-third of these had published guidelines and recommendations on this topic. On the other hand, the specialty-based societies have not addressed the topic, except in two cases.

CONCLUSION

The national spine societies showed the deepest concern on this topic with several publications in scientific journals influenced by the local epidemiological severity. Contrarily, continental and specialty-based societies showed less interest in this topic.

Key Words: COVID-19; Pandemic; Spine surgery; Spine society; Guidelines; Recommendations

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Core Tip: We designed a review to verify the reaction of the worldwide spine societies to the coronavirus disease 2019 pandemic. Twenty-seven associations were identified. Continental and specialty-based companies showed less reaction attitude than the regional scientific societies, probably due to the local epidemiological severity of the disease.

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INTRODUCTION

With the start of the global pandemic of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in December of 2019, governments and healthcare providers were put on alert, fearing this novel virus that would ultimately lead to the declaration of a global pandemic on March 11.

This naturally resulted in healthcare systems around the world bracing for impact. The biggest hurdle that these systems expected was the need to accommodate a huge surge of patients requiring intensive care (early data suggested that 15%-35% of patients affected with the virus would need admission to the intensive care units). This load would effectively break a healthcare system.

The scientific community has continued to study SARS-CoV-2 to understand its pathogenicity while also trying to avoid the collapse of the healthcare structure and decrease the number of collateral deaths.

Several studies on the recommendations have been published by the major spine scientific societies worldwide[1-5]. The concluding observations of this review highlighted how these surgical scientific communities had promptly reacted to the emergency by issuing documents and guidelines. Here we review the literature concerning the release of documents, guidelines, or recommendations by spine societies, providing a comprehensive overview on these topics, thus providing a useful resource for spine surgeons worldwide.

MATERIALS AND METHODS

According to the PRISMA guidelines, a review of the MEDLINE database (PubMed - National Library of Medicine), Google, and Google scholar were performed on Monday, March 2, 2020, to date, for articles published in the English language. Search terms included: COVID-19 coronavirus AND pandemic AND spine AND surgery AND spine societies AND guidelines AND recommendations (Figure 1). We reviewed search results to assess the relevance of documents on these topics, including editorials, letters, and webpages. References were reviewed to locate other articles of interest.

RESULTS

Twenty-eight associations and societies deal with the scientific aspects and interventional treatment of spine disorders. Spine associations and societies worldwide were divided into three groups: Continental (C) (n = 8), specialty (Sb) (n = 7), and country-based (Cb) (n = 12) societies. There were eight C-companies (Table 1), but only three [North America Spine Society (NASS), World Spine Column Society (WSCS), Asia Pacific Spine Society] published guidelines in international scientific journals. The Sb societies (Table 2) seem not to have addressed the topic. Only the Spine Intervention Society (SIS) published an online paper on their website with its guidelines. Furthermore, the AO spine website shows different strategies for maintaining internal research and training.

All 12 Cb (Table 3) produced a publication: seven in scientific journals (French Spine Surgery Society), Saudi Spine Society (Saudi SS), Singapore Spine Society, Chinese Spine Society, The Japanese Society for Spine Surgery and Related Research, Egyptian Spine Association, Brazilian Spine Society) and the remaining five in websites or editorial documents (British Association of Spine Surgeons, Italian Spine Society, Association of Spine Surgeons of India, German Spine Society, Canadian Spine Society).

Table 1 List of the 8 spinal continental societies

Continental societies	Links
World Spinal Column Society	https://www.worldspinalcolumn.org/
The Africa Spinal Cord Injury Network	http://www.afscin.org/afscin-4-2020
Asian Spinal Cord Network	https://ascon.info/
International Spinal Cord Society	https://www.iscos.org.uk/
North American Spine Society	https://www.spine.org/
European Spine Society	https://www.eurospine.org/
Asia Pacific Spine Society	https://www.apssonline.org/
Latin America	https://www.silaco.org/acerca

Table 2 List of the 7 specialty-based societies

Specialty-based societies	Links
International Society for the Advancement of Spine Surgery	https://www.isass.org/
AOSpine	https://aospine.aofoundation.org
Society for Minimally Invasive Spine Surgery	http://ismiss.com/1-0-Home.html
Scoliosis Research Society	https://www.srs.org/
Cervical Spine Research Society	https://www.csrs.org/
The International Society for the Study of the Lumbar Spine	https://www.issls.org/
Spine Intervention Society	https://www.spineintervention.org/

Table 3 List of the 12 country-based societies

Country-based societies	Links
Italian Spine Society	https://www.gis-italia.org/
Saudi Spine Society	http://saudispine.org/
Association of Spine Surgeons of India	http://assi.in
Singapore Spine Society	https://www.singaporespinesociety.org.sg/
German Spine Society	https://www.dwg.org/startseite/
French Spine Society	http://scfr.it
Egyptian Spine Association	https://www.facebook.com/Egyspine/
Chinese Spine Society	https://www.apssonline.org/
Iranian Spine Surgery	http://www.aicnss.com/
British Ass. Spine Surgeons	https://spinesurgeons.ac.uk/
Canadian Spine Society	https://spinecanada.ca/
Brazilian Spine Society	http://www.plataformainterativa2.com/coluna/

The literature search yielded a sum of 28 articles that were relevant to spine surgery and coronavirus disease 2019 (COVID-19) (Table 4). We were able to identify four main topics developed in these papers.

DISCUSSION

COVID-19, also known as acute respiratory disease, is an infectious respiratory disease caused by SARS-CoV-2. The first cases were identified in China, and after that, diffused around the world through respiratory droplets, with a high lethality rate. In this scenario, the COVID-19 pandemic has changed

Table 4 Selection of 28 articles from members of the spine societies

Article title	Journal	Society/Country	Ref.
Triaging Spine Surgery in the COVID-19 Era	*Journal of Spinal Disorders and Techniques*	AO Spine	[1]
Triaging Spine Surgery and Treatment during the COVID-19 Pandemic	*Journal of Orthopaedics and Traumatology*	USA	[2]
French Spine Surgery Society guidelines for management of spinal surgeries during COVID-19 pandemic	*World Journal of Clinical Cases*	French	[3]
Strategy for the Practice of Spine Oncological Surgery During the Covid-19 Pandemic	*Spine*	Italy	[6]
Spine Surgery and COVID-19: The Influence of Practice Type on Preparedness, Response, and Economic Impact	*Global Spine Journal*	AO Spine	[7]
Spine Surgery and COVID-19: Challenges and Strategies from the Front Lines	*Journal of Bone and Joint Surgery*	Singapore	[8]
Spine Surgery and COVID-19: Early Experiences From Singapore	*Spine*	Singapore	[9]
COVID-19 Nonessential Surgery Restrictions and Spine Surgery: A German Experience	*Spine*	Germany	[10]
The Impact of COVID-19 pandemic on Spine Surgeons: An Asia Pacific Spine Society (APSS) Survey	*Spine*	Asia Pacific	[11]
COVID-19 and Spine Surgery: A Review and Evolving Recommendations	*Global Spine Journal*	USA	[4]
Spine surgery in Atlantic Canada in the COVID-19 era: lessons learned so far	*Spine*	Canada	[12]
Spine Surgery in Italy in the COVID-19 Era: Proposal for Assessing and Responding to the Regional State of Emergency	*World Neurosurgery*	Italy	[13]
The Saudi Spine Society guidelines on spinal surgery during the COVID-19 pandemic	*Journal of Orthopaedics and Research*	Saudi	[5]
Recommendations for resuming elective spine surgery in the COVID-19 era	*British Journal of Anaesthesiology*	USA	[14]
Principles for Managing Patients with Spinal Ailments in the Coronavirus Disease 2019 Era: What Do We Know So Far? An Evidence-Based, Narrative Review	*Asian Spine Journal*	India	[15]
Medical care for spinal diseases during the COVID-19 pandemic	*Clinics*	Brazil	[28]
The management of emergency spinal surgery during the COVID-19 pandemic in Italy	*Bone and Joint Journal*	Italy	[16]
Scoring System to Triage Patients for Spine Surgery in the Setting of Limited Resources: Application to the Coronavirus Disease 2019 (COVID-19) Pandemic and Beyond	*World Neurosurgery*	USA	[17]
Management of Spine Trauma in COVID-19 Pandemic: A Preliminary Report	*Archives of Bone and Joint Surgery*	Iran	[18]
Advice on Standardized Diagnosis and Treatment for Spinal Diseases during the Coronavirus Disease 2019 Pandemic	*Asian Spine Journal*	China	[19]
The Role of Spine Surgeons in the Era of COVID-19 Outbreak	*Neurospine*	China	[20]
Addressing Coronavirus Disease 2019 in Spine Surgery: A Rapid National Consensus Using the Delphi Method *via* Teleconference	*Asian Spine Journal*	Singapore	[21]
Adapting Policy Guidelines for Spine Surgeries During COVID-19 Pandemic in View of Evolving Evidences: An Early Experience From a Tertiary Care Teaching Hospital	*Cureus*	India	[22]
Addressing a national crisis: the spine hospital and department's response to the COVID-19 pandemic in New York City	*Spine Journal*	USA	[23]
Essential Spine Surgery During the COVID-19 Pandemic: A Comprehensive Framework for Clinical Practice from a Specialty Orthopedic Hospital in New York City	*HSS Journal*	USA	[24]
Impact of the COVID-19 pandemic on spinal surgery in Singapore	*Singapore Medical Journal*	Singapore	[25]
The Novel Corona Virus COVID-19 and Spinal Surgery Practice: Review and Updates	*The Egyption Spine Journal*	Egypt	[26]
Spine Surgery: Precautions and Strategies to Minimize Perioperative Risks Amid COVID-19 Outbreak	*Spine Surgery and Related Research*	Japan	[27]

COVID-19: Coronavirus disease 2019.

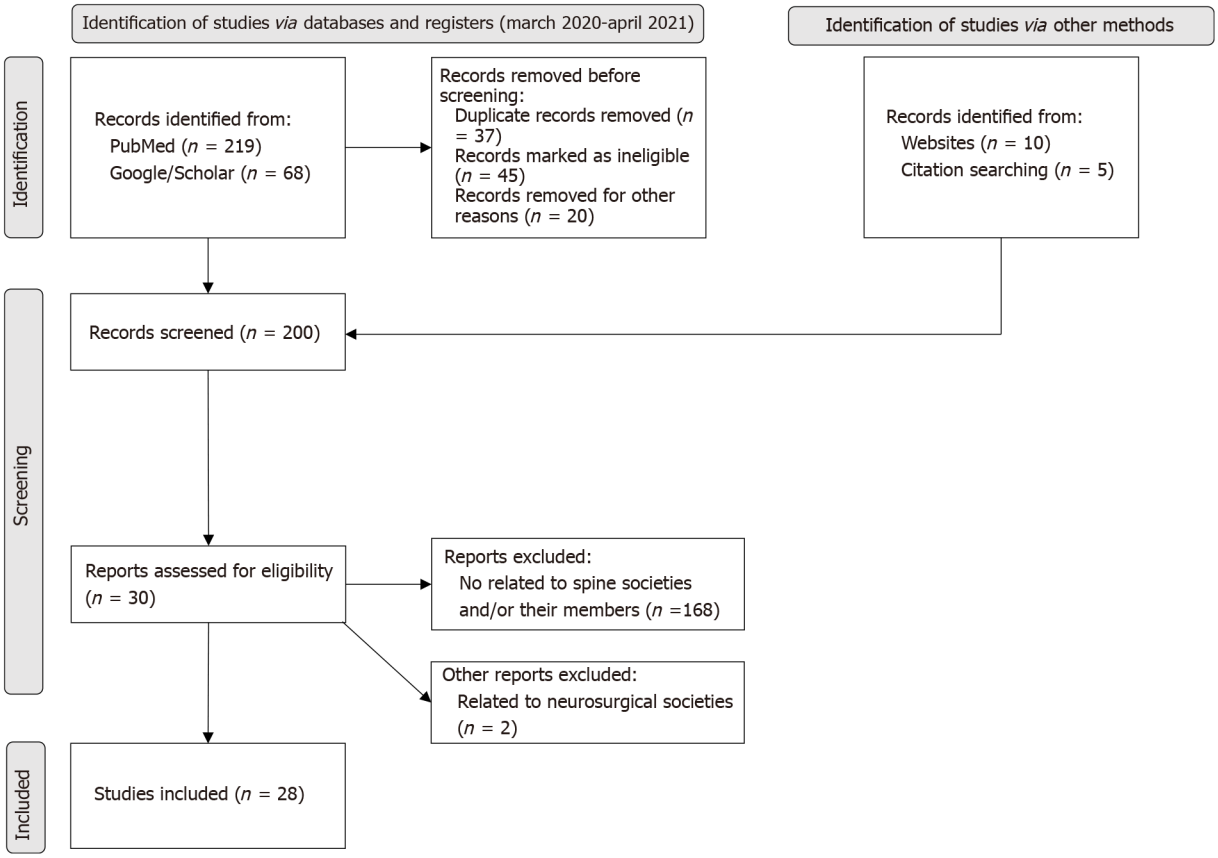


Figure 1 PRISMA flow chart.

medical and surgical practices worldwide. Major scientific societies have issued guidelines and recommendations to optimize resources and ensure treatment without putting patients' lives at risk. Urgent or non-deferrable emergency interventions were favoured, postponing those in the election but seeking their reactivation as soon as possible[6,10,12,14,18]. These changes have had a significant socio-economic impact. Specialty-based societies have also taken action, and in particular, the neurosurgical scientific community has promptly developed recommendations for managing patients with cranial or spinal pathologies[29]. A group of Italian neurosurgeons summarized these guidelines in a recent publication[30]. They discussed the "grey zone" left by the generalized guidelines regarding neurosurgery and how they should be acting to resume control.

Similarly, we wanted to verify the reaction of the worldwide spine societies to this emergency. This topic, to our knowledge, has not previously been addressed in the literature. Twenty-six associations, present on the web as companies or networks that deal with the interventional treatment of spinal pathologies, were identified. Three out of eight (37.5%) major continental companies (Saudi SS, NASS, WSCS) had issued guidelines in the form of scientific work in a journal or document. In particular, the NASS guidance, released on April 22, probably remains the most cited and applied document in subsequent scientific paper[21,26-28]: "*……after reviewing the recommendations regarding procedures and treatments developed by the Centers for Medicare and Medicaid Services (CMS) and the American College of Surgeons (ACS), NASS convened a multidisciplinary task force of orthopaedic surgeons, neurosurgeons and PM&R/pain specialists to provide spine-care specific guidance for procedures*" (see the entire document by the link in Table 2). The Asia Pacific society published a survey about the impact of a pandemic on surgical activity[11]: a total of 222 respondents from 19 countries completed the questionnaire. The mean reduction of clinic volume for all countries was 48.1%. Surgical theatres were closed, reduced, or limited to semi-emergency and emergency surgeries, and spine surgeons were moderately concerned about contracting COVID-19 during their clinical practice extremely concerned to transmit the disease to their family members.

Most Sb societies seem not to have addressed the topic. Only the SIS published a website document with its guidance. The AO spine website shows some corporate strategies for maintaining internal research and training. The greatest interest was from 12 Cb, with publications in journals, websites, or editorial documents. However, other regional societies are lacking. Four themes were seen recurring in our review of 28 articles relating to the new proposed guidelines and line of action. The highest recurring theme, which was seen in 100% of the articles, was the use of protective personal equipment and protocols to follow with COVID positive and COVID suspected patients to curb the spread and limit the transmission (Table 4).

The second was the use of a multidisciplinary panel to evaluate each patient admitted and the urgency[8,9,13]: doctors would have to decide based on the COVID burden imposed on the healthcare system and hospitals[15,17,19,24].

The third theme aimed to decrease the general activity of the healthcare system, increasing the number of hospital intensive care and departments able to treat infected people and the expected wave of patients. This topic was further discussed in detail the distinction of patients concerning their clinical picture and severity[20,22,23,25,27], given priority and urgency in treatment.

The fourth and last theme, which was seen only in seven articles, was the use of a team-based approach: each team could act independent, developing its own schedule and location, reducing work delay and decreasing the mixing of the different teams. A minimal effect on their department's function was recorded. When viewing the Cb spine societies, we found different approaches to achieve similar objectives, ensuring a treatment activity on the most urgent patients or patients who cannot be postponed without increasing the risks of exposure or contact with the virus.

Most of the approaches were directed towards a "second phase", which defines a period when the healthcare system is not overburdened by the pandemic. One point shared was the distinction and separation of patients based on clinical urgency and COVID status, resulting in the avoidance of unneeded risk. Checklists and forms, along with history taking and evaluation of the physician to both the patient's condition and the system's utilization, were extremely useful. The evaluation of the system was carried out by taking into consideration risks and resources. These were respectively weighted on the patient's history and system capabilities, for example, by checking the ability of a healthcare facility to deal with an emergency situation. Surgery was chosen only when possible and needed, while a deferral was preferred to elective and low urgency cases. To guarantee patients during the hospital stay, hygiene, self-isolation rules, and restrictions on companionship rules were adopted. Fast-track recovery and online follow-up restricted the number of unneeded people in the hospital.

CONCLUSION

Only one-third of continental spine societies have issued recommendations. The international specialist companies have little addressed the topic, except for the SIS and partly the AO spine. Paradoxically, the national companies were more stimulated to issue their guidelines. The local epidemiological severity has likely influenced the reactive corporate attitude. Spine specialists at different levels realized the liability of not addressing spinal cases and the possible liabilities that could arise if taken up during a pandemic. Articles and online video conferences presented real-life scenarios that proved the gravity of the situation. The discussed guidelines and seminars showed their efficacy to control the spread of COVID-19 and the efficiency of the healthcare system. The points raised by the spine worldwide societies may not solve all issues related to spinal case management in the COVID era, but at least they have set forward a relevant ground to raise possible questions for the future's sake, as well as the possibilities of reflecting upon these ideas on other similar areas of medicine. As a doctor of the Singaporean Spine Society commented, "We are all in the same storm, just different boats, and we should all work together to save each other".

ARTICLE HIGHLIGHTS

Research background

During the second phase of the coronavirus disease 2019 (COVID-19) pandemic, some authors have felt the need to summarize and order data on the recommendations issued by the major surgical scientific societies in the world. The concluding observations of this review highlighted how these surgical scientific communities had promptly reacted to the emergency by issuing documents and guidelines. In particular, the neurosurgical scientific community has promptly developed recommendations for managing patients with cranial or spinal pathologies.

Research motivation

We designed a review of the literature concerning the release of documents, guidelines, or recommendations by the spine societies in the world, intending to offer an overview on these topics to which spine surgeons worldwide can easily refer.

Research objectives

This study aimed to discuss the recommendations by many spine societies for the management of spinal diseases during the COVID-19 pandemic.

Research methods
A review of the MEDLINE database according to the PRISMA guidelines.

Research results
We identified 28 associations present on the Internet as companies or networks that deal with the interventional treatment of spinal pathologies. We distinguished societies, associations, or networks worldwide into three groups. The literature search yielded a sum of 28 articles that were relevant to spine surgery and COVID-19.

Research conclusions
Only one-third of continental spine societies have issued recommendations. The international specialist companies have dealt little or nothing with the topic, except the SIS and partly AO spine. Paradoxically, the national companies were more stimulated to issue their guidelines. The local epidemiological severity has likely influenced the reactive corporate attitude.

Research perspectives
Articles and online video conferences presented real-life scenarios that proved the gravity of the situation. The discussed guidelines and seminars showed their efficacy to control the spread of COVID-19 and the efficiency of the healthcare system. The discussing points by the spine worldwide societies may not solve all issues related to spinal case management in the COVID era, but at least they have set forward a relevant ground to raise possible questions for the future's sake, as well as the possibilities of reflecting upon these ideas on other similar areas of medicine.

FOOTNOTES

Author contributions: Ramieri A and Miscusi M designed the research; Alshafeei O and Trungu S performed the research; Ramieri A and Alshafeei O analyzed the data; Alshafeei O and Ramieri A wrote the paper; Costanzo G and Raco A supervised the paper; all authors read and approved the final manuscript.

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REFERENCES

1 **Donnally CJ 3rd**, Shenoy K, Vaccaro AR, Schroeder GD, Kepler CK. Triaging Spine Surgery in the COVID-19 Era. *Clin Spine Surg* 2020; **33**: 129-130 [PMID: 32235170 DOI: 10.1097/BSD.0000000000000988]
2 **Rizkalla JM**, Hotchkiss W, Clavenna A, Dossett A, Syed IY. Triaging Spine Surgery and Treatment during the COVID-19 Pandemic. *J Orthop* 2020; **20**: 380-385 [PMID: 32764857 DOI: 10.1016/j.jor.2020.06.015]
3 **Prost S**, Charles YP, Allain J, Barat JL, d'Astorg H, Delhaye M, Eap C, Zairi F, Guigui P, Ilharreborde B, Meyblum J, Le Huec JC, Lonjon N, Lot G, Hamel O, Riouallon G, Litrico S, Tropiano P, Blondel B; French Spine Surgery Society. French Spine Surgery Society guidelines for management of spinal surgeries during COVID-19 pandemic. *World J Clin Cases* 2020; **8**: 1756-1762 [PMID: 32518767 DOI: 10.12998/wjcc.v8.i10.1756]
4 **Jain NS**, Alluri RK, Schopler SS, Hah R, Wang JC. COVID-19 and Spine Surgery: A Review and Evolving Recommendations. *Global Spine J* 2020; **10**: 528-533 [PMID: 32677557 DOI: 10.1177/2192568220923655]

5 **Alturkistany A**, Abduljabbar FH, Alhelal F, Dajim NB, Khalifah S, Konbaz F, Aleissa S, Al-Habib A, Kattan M, Alqahtani Y, Alatassi R. The Saudi Spine Society guidelines on spinal surgery during the COVID-19 pandemic. *J Orthop Surg Res* 2020; **15**: 211 [PMID: 32513216 DOI: 10.1186/s13018-020-01732-4]

6 **Berjano P**, Vanni D, Fariselli L, Cecchinato R, Boriani S. Strategy for the Practice of Spine Oncological Surgery During the Covid-19 Pandemic. *Spine (Phila Pa 1976)* 2020; **45**: 1386-1394 [PMID: 32756271]

7 **Weiner JA**, Swiatek PR, Johnson DJ, Louie PK, Harada GK, McCarthy MH, Germscheid N, Cheung JPY, Neva MH, El-Sharkawi M, Valacco M, Sciubba DM, Chutkan NB, An HS, Samartzis D. Spine Surgery and COVID-19: The Influence of Practice Type on Preparedness, Response, and Economic Impact. *Global Spine J* 2020; 2192568220949183 [PMID: 32762354 DOI: 10.1177/2192568220949183]

8 **Soh TLT**, Ho SWL, Yap WMQ, Oh JY. Spine Surgery and COVID-19: Challenges and Strategies from the Front Lines. *J Bone Joint Surg Am* 2020; **102**: e56 [PMID: 32559051 DOI: 10.2106/JBJS.20.00503]

9 **Soh TLT**, Ding BTK, Yap WMQ, Oh JY. Spine Surgery and COVID-19: Early Experiences From Singapore. *Spine (Phila Pa 1976)* 2020; **45**: 786-788 [PMID: 32479716 DOI: 10.1097/BRS.0000000000003532]

10 **Mehta AI**, Chiu RG. COVID-19 Nonessential Surgery Restrictions and Spine Surgery: A German Experience. *Spine (Phila Pa 1976)* 2020; **45**: 942-943 [PMID: 32604352 DOI: 10.1097/BRS.0000000000003571]

11 **Chan CYW**, Chiu CK, Cheung JPY, Cheung PWH, Gani SMA, Kwan MK. The Impact of COVID-19 pandemic on Spine Surgeons: An Asia Pacific Spine Society (APSS) Survey. *Spine (Phila Pa 1976)* 2020; **45**: 1285-1292 [PMID: 32756270 DOI: 10.1097/BRS.0000000000003622]

12 **El Helou A**. Spine surgery in Atlantic Canada in the COVID-19 era: lessons learned so far. *Spine J* 2020; **20**: 1379-1380 [PMID: 32389734 DOI: 10.1016/j.spinee.2020.04.027]

13 **Rispoli R**, Diamond ME, Balsano M, Cappelletto B. Spine Surgery in Italy in the COVID-19 Era: Proposal for Assessing and Responding to the Regional State of Emergency. *World Neurosurg* 2021; **145**: e1-e6 [PMID: 32777401 DOI: 10.1016/j.wneu.2020.08.001]

14 **Wilson LA**, Zhong H, Poeran J, Liu J, Memtsoudis SG. Recommendations for resuming elective spine surgery in the COVID-19 era. *Br J Anaesth* 2020; **125**: e339-e341 [PMID: 32631616 DOI: 10.1016/j.bja.2020.06.022]

15 **Viswanathan VK**, Subramanian S, Rao AK. Principles for Managing Patients with Spinal Ailments in the Coronavirus Disease 2019 Era: What Do We Know So Far? *Asian Spine J* 2020; **14**: 572-580 [PMID: 32493004]

16 **Giorgi PD**, Villa F, Gallazzi E, Debernardi A, Schirò GR, Crisà FM, Talamonti G, D'Aliberti G. The management of emergency spinal surgery during the COVID-19 pandemic in Italy. *Bone Joint J* 2020; **102-B**: 671-676 [PMID: 32323563 DOI: 10.1302/0301-620X.102B6.BJJ-2020-0537]

17 **Sciubba DM**, Ehresman J, Pennington Z, Lubelski D, Feghali J, Bydon A, Chou D, Elder BD, Elsamadicy AA, Goodwin CR, Goodwin ML, Harrop J, Klineberg EO, Laufer I, Lo SL, Neuman BJ, Passias PG, Protopsaltis T, Shin JH, Theodore N, Witham TF, Benzel EC. Scoring System to Triage Patients for Spine Surgery in the Setting of Limited Resources: Application to the Coronavirus Disease 2019 (COVID-19) Pandemic and Beyond. *World Neurosurg* 2020; **140**: e373-e380 [PMID: 32479913 DOI: 10.1016/j.wneu.2020.05.233]

18 **Chehrassan M**, Ebrahimpour A, Ghandhari H, Sanei Taheri M, Athari B, Sadighi M, Jafari KafiAbadi M, Karami A, Zali A. Management of Spine Trauma in COVID-19 Pandemic: A Preliminary Report. *Arch Bone Jt Surg* 2020; **8**: 270-276 [PMID: 32733982 DOI: 10.22038/abjs.2020.47882.2368]

19 **Zou J**, Yu H, Song D, Niu J, Yang H. Advice on Standardized Diagnosis and Treatment for Spinal Diseases during the Coronavirus Disease 2019 Pandemic. *Asian Spine J* 2020; **14**: 258-263 [PMID: 32222720 DOI: 10.31616/asj.2020.0122]

20 **Wang B**. The Role of Spine Surgeons in the Era of COVID-19 Outbreak. *Neurospine* 2020; **17**: 342-343 [PMID: 32408725 DOI: 10.14245/ns.2040206.103]

21 **Tan KA**, Thadani VN, Chan D, Oh JY, Liu GK. Addressing Coronavirus Disease 2019 in Spine Surgery: A Rapid National Consensus Using the Delphi Method *via* Teleconference. *Asian Spine J* 2020; **14**: 373-381 [PMID: 32403894 DOI: 10.31616/asj.2020.0224]

22 **Verma V**, Nagar M, Jain V, Santoshi JA, Dwivedi M, Behera P, Selvanayagam R, Pal D, Singh K. Adapting Policy Guidelines for Spine Surgeries During COVID-19 Pandemic in View of Evolving Evidences: An Early Experience From a Tertiary Care Teaching Hospital. *Cureus* 2020; **12**: e9147 [PMID: 32789084 DOI: 10.7759/cureus.9147]

23 **Lombardi JM**, Bottiglieri T, Desai N, Riew KD, Boddapati V, Weller M, Bourgois C, McChrystal S, Lehman RA. Addressing a national crisis: the spine hospital and department's response to the COVID-19 pandemic in New York City. *Spine J* 2020; **20**: 1367-1378 [PMID: 32492529 DOI: 10.1016/j.spinee.2020.05.539]

24 **Soffin EM**, Reisener MJ, Sama AA, Beckman JD, Liguori GA, Lebl DR, Girardi FP, Cammisa FP, Hughes AP. Essential Spine Surgery During the COVID-19 Pandemic: A Comprehensive Framework for Clinical Practice from a Specialty Orthopedic Hospital in New York City. *HSS J* 2020; 1-7 [PMID: 32929320 DOI: 10.1007/s11420-020-09786-0]

25 **Tan BJ**, Teo HLT, Loo WL, Dinesh SK. Impact of the COVID-19 pandemic on spinal surgery in Singapore. *Singapore Med J* 2020; **61**: 624-625 [PMID: 32460452 DOI: 10.11622/smedj.2020081]

26 **Elkazaz MK**, Abou-Madawi AM, Khattab MF, Elkhatib E, Alshatoury HA. The Novel Corona Virus COVID-19 and Spinal Surgery Practice: Review and Updates. *Egy Spine J* 2020; **34**: 2-12 [DOI: 10.21608/esj.2020.31620.1137]

27 **Wang TV**, Ito M. Spine Surgery: Precautions and Strategies to Minimize Perioperative Risks Amid COVID-19 Outbreak. *Spine Surg Relat Res* 2020; **4**: 192-198 [PMID: 32864484 DOI: 10.22603/ssrr.2020-0076]

28 **Silva RTE**, Cristante AF, Marcon RM, Barros-Filho TEP. Medical care for spinal diseases during the COVID-19 pandemic. *Clinics (Sao Paulo)* 2020; **75**: e1954 [PMID: 32401963 DOI: 10.6061/clinics/2020/e1954]

29 **Ricciardi L**, Trungu S, Scerrati A, DE Bonis P, Miscusi M, Raco A. Neurosurgery at the time of COVID-19: how this pandemic infectious disease is influencing neurosurgical activities and patient management. *J Neurosurg Sci* 2021; **65**: 216-217 [PMID: 32347683 DOI: 10.23736/S0390-5616.20.04976-0]

30 **Germanò A**, Raffa G, Angileri FF, Cardali SM, Tomasello F. Coronavirus Disease 2019 (COVID-19) and Neurosurgery: Literature and Neurosurgical Societies Recommendations Update. *World Neurosurg* 2020; **139**: e812-e817 [PMID: 32360733 DOI: 10.1016/j.wneu.2020.04.181]

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SCIENTOMETRICS

Assessing the academic achievement of United States orthopaedic departments

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Abstract

BACKGROUND

Assessing academic productivity allows academic departments to identify the strengths of their scholarly contribution and provides an opportunity to evaluate areas for improvement.

AIM

To provide objective benchmarks for departments seeking to enhance academic productivity and identify those with significant improvement in recent past.

METHODS

Our study retrospectively analyzed a cohort of orthopaedic faculty at United States-based academic orthopaedic programs. 5502 full-time orthopaedic faculty representing 178 programs were included in analysis. Variables included for analysis were National Institutes of Health funding (2014-2018), leadership positions in orthopaedic societies (2018), editorial board positions of top orthopaedic journals (2018), total number of publications and Hirsch-index. A weighted algorithm was used to calculate a cumulative score for each academic program. This study was performed at a large, United States medical school.

RESULTS

All 178 programs included in analysis were evaluated using the comprehensive weighted algorithm. The five institutions with the highest cumulative score, in decreasing order, were: Washington University in St. Louis, the Hospital for Special Surgery, Sidney Kimmel Medical College (SKMC) at Thomas Jefferson University, the University of California, San Francisco (UCSF) and Massachusetts General Hospital (MGH)/Brigham and Women's/Harvard. The five institutions

with the highest score *per* capita, in decreasing order, were: Mayo Clinic (Rochester), Washington University in St. Louis, Rush University, Virginia Commonwealth University (VCU) and MGH/Brigham and Women's/Harvard. The five academic programs that had the largest improvement in cumulative score from 2013 to 2018, in decreasing order, were: VCU, SKMC at Thomas Jefferson University, UCSF, MGH/Brigham and Women's/Harvard, and Brown University.

CONCLUSION

This algorithm can provide orthopaedic departments a means to assess academic productivity, monitor progress, and identify areas for improvement as they seek to expand their academic contributions to the orthopaedic community.

Key Words: Bibliometrics; Academic achievement; Number of publications; National Institutes of Health funding; Hirsch-index

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Core Tip: Assessing academic productivity allows academic departments to identify the strengths of their scholarly contribution and provides an opportunity to evaluate areas for improvement. By identifying measures of academic productivity for full-time faculty at academic orthopaedic programs in the United States, we were able to establish a comprehensive weighted algorithm for valuation of the scholarly achievement of each program. Furthermore, by establishing and documenting the findings and methodology of this algorithm, programs have the opportunity to assess, monitor, and identify areas of growth as they seek to expand their academic contributions to the orthopaedic community.

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INTRODUCTION

The evaluation of academic orthopaedic surgery programs based on scholarly contribution is difficult to assess. Faculty are often measured by bibliometric variables that represent their academic productivity such as citation indices, number of publications and amount of research funding[1-3]. Our study aimed to measure the current scholarly productivity of orthopaedic departments in the United States. The results of this analysis are an assessment of orthopaedic programs based on the academic contributions of their faculty. In addition to recognizing highly academic departments, our study aims to provide orthopaedic departments with a tool that can be continually utilized to monitor academic productivity and, thus, identify areas for improvement.

There are many difficulties associated with evaluating the academic productivity of orthopaedic surgery programs. The subjective nature of certain metrics, such as national reputation and faculty satisfaction, used in rankings like *Doximity* or *U.S. News & World Report*[4-7] often make standardizing academic achievement difficult. Furthermore, current productivity is not always accurately reflected, as the productivity of alumni for the preceding 15 years are included in these rankings[4]. Another difficulty in evaluating academic achievement is the lack of consensus as to the weight that different objective bibliometric measures should have when determining overall academic contribution.

Efforts to quantify academic achievement have gained popularity amongst various specialties over the past decade. Publicly available metrics such as National Institutes of Health (NIH) funding, faculty Hirsch-indices (h-index) and number of publications have been used in plastic surgery, ophthalmology, dermatology, urology and a variety of other medical specialties to provide a measurement of an institution's academic prowess[8-15]. The h-index is a well validated tool to accurately measure academic output and has been lauded in the orthopaedic community[16-18]. The h-index is defined as the number of publications (h) an individual has that receive at least h citations, with each other publication having < h citations[19]. Therefore, the h-index can never exceed the number of publications a faculty member has and considers both quality and quantity of a faculty member's publications. NIH funding has also been validated as an accurate measure of scholarly impact across different specialties [9,20].

Previous studies in other specialties have utilized algorithms that weigh metrics of academic achievement to ultimately rank programs based on their academic productivity[12,21,22]. Our current study uses data from 2014-2018 to provide a five-year updated, enhanced analysis of our previous study [23], and continue to assess orthopaedic programs based on the academic output of their faculty. Cumulative statistics as well as *per* capita statistics, which help to highlight both programs with a large volume of academic output as well as smaller programs with a high academic yield, were used in this study. Furthermore, in order to acknowledge programs that have improved their scholarly productivity, we quantified the change in cumulative score from our previous paper that used data from 2013 to our current study that uses data from 2014-2018. As scholarly productivity is often linked with academic promotion, the ability to attract talented faculty and other important factors[3], standardized methods are necessary to accurately assess the academic achievement of orthopaedic surgery programs. The authors believe that the establishment of a consistent and representative algorithm of program achievement can be used as a tool to continually monitor progress over time and, importantly, provide guidance to individual programs on target areas to enhance overall scholarly productivity.

MATERIALS AND METHODS

Programs included for analysis were identified through a search of the Accreditation Council for Graduate Medical Education website[24]. Faculty included for analysis were identified using faculty lists on individual departmental websites. An email was subsequently sent to program directors and coordinators for each institution to verify that the list of faculty on the department website was accurate and up to date. In an effort to standardize faculty lists, only faculty with a full-time appointment in the respective department of orthopaedic surgery were included for analysis. This included research faculty but did not include surgeons from other specialties, house staff, co-appointed faculty, part-time faculty or emeritus faculty as depicted on individual departmental websites. All inputted data and calculations were reviewed by multiple authors independently to ensure accuracy.

Our current study includes the same bibliometrics as our prior study[23] to quantify academic productivity for each faculty member. While some of these metrics are cumulative over a faculty member's career, including total number of publications and h-index, other metrics such as NIH funding from 2014-2018, leadership society membership for 2018 and journal editorial board membership for 2018 provide a more current evaluation of academic productivity. As NIH funding can fluctuate dramatically, five years of NIH funding was analyzed. The bibliometrics of each faculty member within an orthopaedic surgery department were cumulated. A weighted algorithm was subsequently used to compute a score for each academic institution to assess their scholarly contribution. Change in cumulative score for each program from 2013 to 2018 was then calculated.

The weighted score was calculated as follows. For each of the five categories, each academic program was assigned a score from zero to one, with the program with the highest score in an individual category assigned a one. The category-specific score for each academic institution was calculated by dividing the value of a specific outcome measure attained by an institution by the value of that outcome measure attained by the highest achieving institution. That score was then either multiplied by 2.0 for the category of NIH funding, 1.0 for the categories of number of publications and h-index or 0.5 for the categories of leadership society membership and journal editorial board membership. Thus, NIH funding accounted for 40% of the total score, number of publications and h-index each accounted for 20% and society leadership and journal editorial board membership each accounted for 10% (Figure 1). For example, the faculty from the University of Iowa accounted for 2789 total publications. This was divided by the highest number of publications (13494) achieved by any institution (the Hospital for Special Surgery, Cornell) and multiplied by 1.0 (weighing factor for number of publications). A score of 0.207 was then given to the University of Iowa for the "number of publications" category. The same computation was then repeated with each bibliometric being divided by the number of full-time faculty within a department to calculate the *per* capita measurement.

The validated Scopus database was used to determine the total number of publications and h-index for each individual faculty member[25,26]. Scopus was chosen to analyze the total number of publications as Scopus only includes peer-reviewed literature and has the broadest coverage of any database [25]. Our analysis of total number of publications will therefore include all types of publications from an individual's career. The NIH Research Portfolio Online Reporting Tool was used to obtain NIH funding from 2014-2018[27].

Our analysis also included the two largest general orthopaedic societies in the United States: The Orthopaedic Research Society (ORS) and the American Academy of Orthopaedic Surgeons (AAOS) as well as the preeminent society from each orthopaedic subspecialty to stay consistent with our prior study. These societies were chosen to give an equal representation to all orthopaedic subspecialties. In an effort to decrease inherent bias, no societies that are nomination-dependent were included for analysis. Faculty on editorial boards of American orthopaedic journals with an impact factor over 2.5 were included for analysis. These journals included all journals from our previous study as well as the *Orthopaedic Journal of Sports Medicine* and *Clinical Research on Foot and Ankle.*

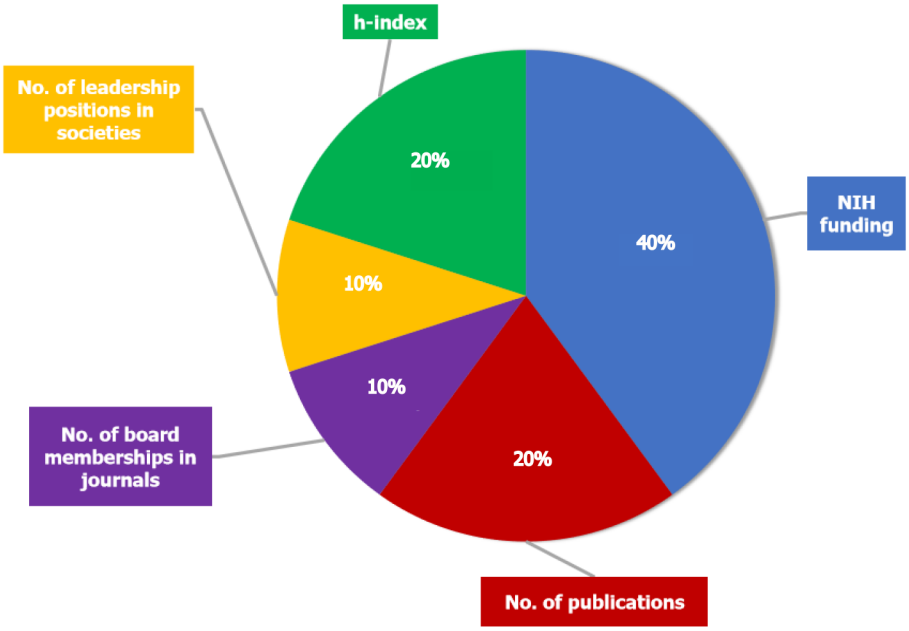


Figure 1 Weighted algorithm showing overall academic achievement. The five criteria used to evaluate each academic orthopaedic program's contributions are shown. Metrics of original academic thought-National Institutes of Health funding (2014-2018), h-index and total number of publications-were weighted to each represent 40%, 20% and 20%, respectively, of the overall score. Metrics of leadership-editorial positions and society leadership in 2018-were weighted to each represent 10% of the overall score. Each programs' individual score in each category was multiplied by the weight of the criteria and summed to create a weighted score of overall academic achievement. h-index: Hirschberg-index; NIH: National Institutes of Health.

RESULTS

Of 181 academic orthopaedic programs with an accredited residency program were included for data analysis. Three institutions were excluded due to the lack of a list of faculty members on departmental websites and limited contacts to find this information. 36 out of the remaining 178 programs responded to the authors' email for a response rate of 20.2%.

Programs received cumulative NIH grant funding between 2014-2018 ranging from $31.9 million [University of California, San Francisco (UCSF)] to no NIH funding. Washington University in St. Louis ($29.3 million), Virginia Commonwealth University (VCU) ($28.6 million), University of Rochester ($23.0 million), Brown University ($22.1 million) and Sidney Kimmel Medical College (SKMC) at Thomas Jefferson University ($18.2 million) represent the next five institutions with the highest NIH funding during this period (Table 1).

The total number of publications for full-time faculty of an orthopaedic department ranged from 12 to 13494 at the Hospital for Special Surgery (Cornell). The five institutions with the most publications following the Hospital for Special Surgery were SKMC at Thomas Jefferson University (9259), Mayo Clinic (Rochester) (8735), Washington University in St. Louis (6616), Massachusetts General Hospital (MGH)/Brigham and Women's/Harvard (6421), and Rush University (5661) (Table 2).

The Hospital for Special Surgery had the highest cumulative h-index with 3318, followed by SKMC at Thomas Jefferson University which had a h-index of 1988 (Table 3).

Fifty-two programs had faculty members holding at least one leadership position in orthopaedic surgery societies in the United States, representing 29.2% of the 178 programs evaluated. Full-time faculty at MGH/Brigham and Women's/Harvard garnered the most leadership positions with seven, followed by Duke University with six. Four leadership positions were held by faculty at the Hospital for Special Surgery, Johns Hopkins University, Mayo Clinic (Rochester), Rush University, and SKMC at Thomas Jefferson University (Table 4).

Full-time faculty at the Hospital for Special Surgery held the most editorial board positions at top orthopaedic and subspecialty journals with 20 positions, followed by MGH/Brigham and Women's/Harvard with 19 positions and Washington University in St. Louis with 18 editorial board positions (Table 5).

All 178 programs were evaluated using the comprehensive weighted algorithm. Based on this algorithm, Washington University in St. Louis was shown to be the most academically productive orthopaedic surgery program in the United States. The following five most academically productive orthopaedic programs were: The Hospital for Special Surgery, SKMC at Thomas Jefferson University, the UCSF, MGH/Brigham and Women's/Harvard and Mayo Clinic (Rochester) (Figure 2).

Table 1 Ten United States orthopaedic surgery residency programs with the largest total Dollar amount of National Institutes of Health funding received from 2014-2018

Institution	NIH funding	Points (weighted)
University of California, San Francisco	$31928483	2
Washington University in St. Louis	$29320191	1.836616603
Virginia Commonwealth University	$28619478	1.792723945
University of Rochester	$23035238	1.442927182
Brown University	$22064165	1.382099175
SKMC at Thomas Jefferson University	$18237937	1.142424274
University of Pennsylvania	$17252775	1.080713731
Mayo Clinic (Rochester)	$16801697	1.052458208
University of Utah	$16762167	1.049982049
Yale University	$16184261	1.01378202

SKMC: Sidney Kimmel Medical College; NIH: National Institutes of Health.

Table 2 Ten United States orthopaedic surgery residency programs with the highest total number of publications by institutional full-time faculty, 2018

Institution	Publications	Points (weighted)
Hospital for Special Surgery (Cornell)	13494	1
SKMC at Thomas Jefferson University	9259	0.68615681
Mayo Clinic (Rochester)	8735	0.64732474
Washington University in St. Louis	6616	0.49029198
MGH/Brigham and Women's/Harvard	6421	0.47584111
Rush University	5661	0.41951979
New York University	4882	0.36179043
University of Pennsylvania	4603	0.34111457
University of Pittsburgh	4407	0.3265896
Stanford University	3903	0.28923966

MGH: Massachusetts General Hospital; SKMC: Sidney Kimmel Medical College.

Based on per-capita measurements of academic achievement that accounts for the number of full-time faculty in each program, the most academically productive orthopaedic surgery programs were: Mayo Clinic (Rochester), Washington University in St. Louis, Rush University, VCU, MGH/Brigham and Women's/Harvard, and Duke University (Figure 3).

VCU had the largest improvement in their score from 2013 with a 1.62 point change. SKMC at Thomas Jefferson University (1.40), UCSF (1.39), MGH/Brigham and Women's/Harvard (1.31), Brown University (1.23) and Icahn School of Medicine at Mount Sinai (0.92) were the next five institutions with the largest improvement in cumulative score since 2013 (Table 6).

DISCUSSION

This study aims to assess the scholarly contribution of orthopaedic departments using objective bibliometrics from 2014 to 2018. With so many metrics available to assess academic achievement, this is admittedly both difficult and controversial. In light of the financial, reputational and academic pressures surrounding academic productivity, our goal was to (1) Acknowledge academic institutions for their scientific contribution; (2) Allow academic departments to communicate best practices to one another; and (3) Provide a method to longitudinally monitor academic improvement to facilitate a discussion as

Table 3 Ten United States orthopaedic surgery residency programs with the highest cumulative h-index of institutional full-time faculty, 2018

Institution	h-index	Points (weighted)
Hospital for Special Surgery (Cornell)	3318	1
SKMC at Thomas Jefferson University	1988	0.59915612
Washington University in St. Louis	1680	0.50632911
Mayo Clinic (Rochester)	1627	0.49035564
MGH/Brigham and Women's/Harvard	1454	0.43821579
University of California, San Francisco	1178	0.35503315
University of Pittsburgh	1126	0.33936106
New York University	1109	0.33423749
University of California, Los Angeles	1101	0.3318264
Rush University	1078	0.32489451

h-index: Hirschberg-index; MGH: Massachusetts General Hospital; SKMC: Sidney Kimmel Medical College.

Table 4 Eleven United States orthopaedic surgery residency programs with the highest amount of full-time faculty holding leadership positions in the two largest general orthopaedic surgery societies in the United States and a subspecialty society for each of the nine orthopaedic subspecialties, 2018

Institution	Leadership positions	Points (weighted)
MGH/Brigham and Women's/Harvard	7	0.500
Duke University	6	0.429
Hospital for Special Surgery (Cornell)	4	0.286
Johns Hopkins University	4	0.286
Mayo Clinic (Rochester)	4	0.286
Rush University	4	0.286
SKMC at Thomas Jefferson University	4	0.286
University of North Carolina	3	0.214
Cleveland Clinic	3	0.214
Washington University in St. Louis	3	0.214
Yale University	3	0.214

Two largest general orthopaedic surgery societies in the United States: AAOS and ORS; Nine orthopaedic subspecialties: ASES, AOSSM, MSTS, AAHS, AAHKS, OTA, NASS, POSNA, and AOFAS. AAOS: American Academy of Orthopaedic Surgeons; ORS: Orthopaedic Research Society; AAAHKS: American Association of Hip and Knee Surgeons; AAHS: American Association for Hand Surgery; AOFAS: American Orthopaedic Foot & Ankle Society; ASES: American Shoulder and Elbow Surgeons; AOSSM: American Orthopaedic Society for Sports Medicine; MSTS: Musculoskeletal Tumor Society; NASS: North American Spine Society; OTA: Orthopaedic Trauma Association; POSNA: Pediatric Orthopaedic Society of North America; MGH: Massachusetts General Hospital; SKMC: Sidney Kimmel Medical College.

to the definition of academic success.

It is imperative to consider that the mission of orthopaedic programs and faculty is not always rooted in academic achievement, but rather is based on operative and clinical capability, outreach to underserved populations, teaching and mentorship, and/or technological innovation. Undoubtedly, there are metrics other than academic productivity that define a program's "success." Although many of the results of this study are organized numerically, the findings are not intended for comparison against one another. The purpose of this study was not to "rank" orthopaedic departments, but rather to establish a tool that programs may use to assess their own academic productivity against their respective baseline values established in this study. The conclusions reached in this study only pertain to academic productivity as related to the specific bibliometrics analyzed. Additionally, departments inherently differ in size and maturity of research infrastructure. Nonetheless, in a culture that is

Table 5 Nine United States orthopaedic surgery residencyprograms with the highest amount of editorial board positions held by institutional full-time faculty in 2018

Institution	Editorial board positions	Points (weighted)
Hospital for Special Surgery (Cornell)	20	0.5
MGH/Brigham and Women's/Harvard	19	0.475
Washington University in St. Louis	18	0.45
SKMC at Thomas Jefferson University	16	0.4
University of Pittsburgh	15	0.375
Johns Hopkins University	11	0.275
Columbia University	11	0.275
Stanford University	11	0.275
University of Michigan	11	0.275

The journals included were the *American Journal of Sports Medicine*; *Osteoarthritis and Cartilage*; *Journal of Bone and Joint Surgery*; *Arthroscopy*; *Journal of Orthopaedic Research*; *Clinical Orthopaedics and Related Research*; *Knee Surgery, Sports Traumatology, Arthroscopy*; *Orthopaedic Journal of Sports Medicine*; *Bone and Joint Journal*; *Spine Journal*; *Spine*; *Clinical Research on Foot and Ankle*; *Journal of the American Academy of Orthopaedic Surgeons*; *Journal of Arthroplasty*; and *Journal of Shoulder and Elbow Surgery*. MGH: Massachusetts General Hospital; SKMC: Sidney Kimmel Medical College.

Table 6 Ten United States orthopaedic surgery residency programs with the largest positive change in weighted points from 2013

Institution	Change in points from 2013
Virginia Commonwealth University	1.62
SKMC at Thomas Jefferson University	1.40
University of California, San Francisco	1.39
MGH/Brigham and Women's/Harvard	1.31
Brown University	1.23
Icahn School of Medicine at Mount Sinai	0.92
University of Utah	0.90
Hospital for Special Surgery (Cornell)	0.86
Cleveland Clinic Foundation Program	0.83
Columbia University	0.76

MGH: Massachusetts General Hospital; SKMC: Sidney Kimmel Medical College.

constantly interested in evaluations, analyzing academic productivity using objective metrics remains an important factor to appraise orthopaedic departments.

There are several limitations of this study to consider. One important limitation to our study is the subjective nature by which the weighted algorithm was formulated. The authors believe that our previous study[23] did not place enough emphasis on the effect that basic science research has on academic productivity. Although other sources of basic science funding such as the Department of Defense and the Orthopaedic Research and Education Foundation exist, the NIH is the largest public funder of biomedical research worldwide[27]. Therefore, as basic science is a large portion of the NIH portfolio[27], NIH funding was given additional weight (40% of cumulative score) relative to other bibliometrics included. As the distribution of points in our current study slightly differs from our previous paper, our calculation of score improvement from 2013 to 2018 is subject to limitations. Given that any choice of variables for a weighted algorithm will have an element of subjectivity to it, the authors accept these limitations. The authors also acknowledge that it may be difficult to identify part-time, co-appointed or emeritus faculty based solely on departmental websites. Furthermore, there are undoubtedly changes in faculty lists over from 2013 to 2018. However, universities and academic centers have different criteria for "joint appointments." As such, in an effort to decrease inherent bias, part-time or co-appointed faculty were not included. All 178 programs were also contacted in an attempt to confirm faculty lists.

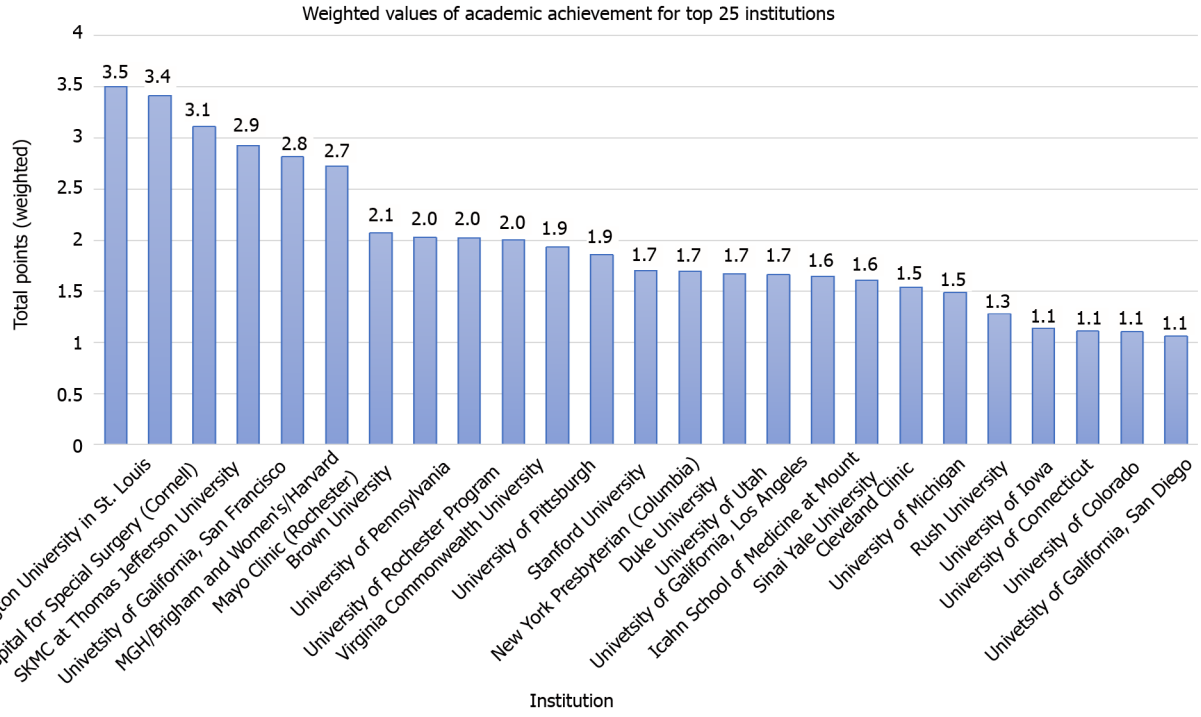


Figure 2 A total of 176 United States academic orthopaedic surgery programs received points using a weighted algorithm. The overall order of the 25 most cumulatively academically productive programs using data from 2014-2018 is shown.

Further limitations of this study lie in the actual bibliometrics used. The h-index has been validated both within and outside of the orthopaedic community[16-18], however it is not without its criticisms. The h-index does not proportionally reflect the impact of authors who have published a small number of highly cited studies, nor does it proportionally reflect the impact of authors who have published a large number of scarcely cited studies. The h-index and the total number of publications also do not take into account the order that authors are listed and thus, the impact that each author had[28,29]. Augmentations of the h-index have been proposed[28-30], however until they are widely accepted and publicly available, the authors believe that the h-index remains the best metric. Furthermore, the authors only reported journal editorial board members and leaders in orthopaedic academic societies for the 2018 calendar year as most journals and societies do not have this data for prior years publicly available. This excluded either of these metrics for years prior. In an effort to minimize this limitation, editorial board and society leadership each only accounted for 10% of the overall score. While the authors believe a snapshot of recent academic productivity is important when evaluating recent academic achievement, it is imperative to understand how the availability of prior data would affect these results.

Based on this algorithm, Washington University in St. Louis, the Hospital for Special Surgery, SKMC at Thomas Jefferson University, the UCSF and MGH/Brigham and Women's/Harvard are currently the five most cumulatively academically productive orthopaedic surgery programs. The Mayo Clinic (Rochester), Washington University in St. Louis, Rush University, VCU and MGH/Brigham and Women's/Harvard are currently the five most academically productive orthopaedic surgery programs *per* capita. The five academic programs that had the largest improvement in cumulative score from 2013 to 2018 were: VCU, SKMC at Thomas Jefferson University, UCSF, MGH/Brigham and Women's/Harvard, and Brown University.

CONCLUSION

This algorithm is easily reproducible and provides a metric that departments can use to track their academic productivity over time as well as identify areas for improvement. These reported bibliometrics can continually be updated in upcoming years as a measure of changing scholarly contribution. Programs that have shown dramatic improvement in scholarly contribution since our 2013 study can be seen as model programs. Programs striving for similar improvement would have other programs identified to serve as roadmaps, opening up an avenue for communication. Furthermore, as factors affecting academic promotion are often difficult to assess, this standardized algorithm may, importantly, aid academic medical centers to determine promotion. This is not a list of the "best" orthopaedic surgery institutions as clinical care metrics were not included in the analysis. This analysis

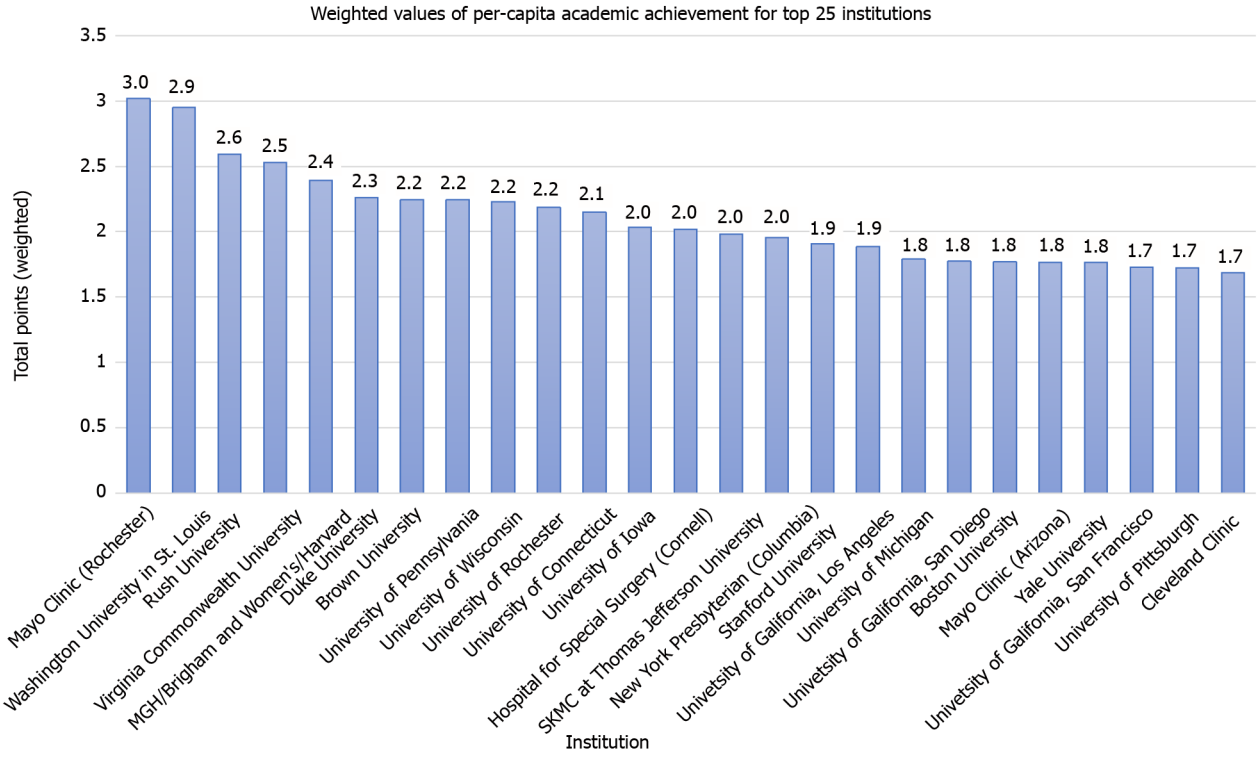


Figure 3 A total of 176 United States academic orthopaedic surgery programs received points using a weighted algorithm. The overall order of the 25 most academically productive programs using data from 2014-2018 and normalizing for the number of faculty *per* program is shown.

did not attempt to take into account the quality of clinical care provided, or the clinical education provided to medical students, residents or fellows, therefore the authors would like to reiterate that this algorithm was not used to rank orthopaedic departments.

ARTICLE HIGHLIGHTS

Research background

Orthopaedic surgery faculty are often measured by bibliometric variables that represent their academic productivity such as citation indices, number of publications and amount of research funding.

Research motivation

Assessing academic productivity allows academic departments to identify the strengths of their scholarly contribution and provides an opportunity to evaluate areas for improvement.

Research objectives

To provide objective benchmarks for departments seeking to enhance academic productivity and identify those with improvement in recent past.

Research methods

Our study retrospectively analyzed a cohort of orthopaedic faculty at United States-based academic orthopaedic programs. Variables included for analysis were National Institutes of Health funding (2014-2018), leadership positions in orthopaedic societies (2018), editorial board positions of top orthopaedic journals (2018), total number of publications and Hirsch-index. A weighted algorithm was used to calculate a cumulative score for each academic program.

Research results

The five institutions with the highest cumulative score, in decreasing order, were: Washington University in St. Louis, the Hospital for Special Surgery, Sidney Kimmel Medical College (SKMC) at Thomas Jefferson University, the University of California, San Francisco (UCSF) and Massachusetts General Hospital (MGH)/Brigham and Women's/Harvard. The five institutions with the highest score *per* capita, in decreasing order, were: Mayo Clinic (Rochester), Washington University in St. Louis, Rush University, Virginia Commonwealth University (VCU) and MGH/Brigham and Women's/Harvard.

The five academic programs that had the largest improvement in cumulative score from 2013 to 2018, in decreasing order, were: VCU, SKMC at Thomas Jefferson University, UCSF, MGH/Brigham and Women's/Harvard, and Brown University.

Research conclusions

This algorithm can provide orthopaedic departments a means to assess academic productivity, monitor progress, and identify areas for improvement as they seek to expand their academic contributions to the orthopaedic community.

Research perspectives

The authors would like to reiterate that this is in no way a ranking system as there are many unique challenges that institutions face. We hope that this provides a tool that programs may use to assess and improve their own academic productivity, while simultaneously providing an opportunity to praise the growth and achievement of institutions on a cumulative as well as *per* capita basis.

FOOTNOTES

Author contributions: The above authors were each included in substantial contributions to research design, or the acquisition, analysis or interpretation of data, drafting the paper or revising it critically, approval of the submitted and final versions.

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REFERENCES

1 **Hohmann E**, Glatt V, Tetsworth K. Orthopaedic Academic Activity in the United States: Bibliometric Analysis of Publications by City and State. *J Am Acad Orthop Surg Glob Res Rev* 2018; **2**: e027 [PMID: 30280140 DOI: 10.5435/JAAOSGlobal-D-18-00027]
2 **Tetsworth K**, Fraser D, Glatt V, Hohmann E. Use of Google Scholar public profiles in orthopedics. *J Orthop Surg (Hong Kong)* 2017; **25**: 2309499017690322 [PMID: 28228048 DOI: 10.1177/2309499017690322]
3 **Valsangkar NP**, Zimmers TA, Kim BJ, Blanton C, Joshi MM, Bell TM, Nakeeb A, Dunnington GL, Koniaris LG. Determining the Drivers of Academic Success in Surgery: An Analysis of 3,850 Faculty. *PLoS One* 2015; **10**: e0131678 [PMID: 26177096 DOI: 10.1371/journal.pone.0131678]
4 **Residency Navigator Methodology**. Doximity. [cited 16 July 2019]. Available from: https://residency.doximity.com/methodology
5 **U.S. News and World Reports**. Best Orthopedic Hospitals. [cited 16 July 2019]. Available from: https://health.usnews.com/best-hospitals/rankings/orthopedics
6 **The Active Times**. Unique Luxury Stargazing Domes-See the Stars and planet Mars. [cited 16 July 2019]. Available from: http://www.theactivetimes.com/best-orthopedichospitals-us
7 **The Leapfrog Group**. Search Leapfrog's Hospital and Surgery Center Ratings. [cited 16 July 2019]. Available from: http://www.leapfroggroup.org/cp
8 **Blumenthal KG**, Huebner EM, Banerji A, Long AA, Gross N, Kapoor N, Blumenthal DM. Sex differences in academic rank in allergy/immunology. *J Allergy Clin Immunol* 2019; **144**: 1697-1702.e1 [PMID: 31279008 DOI: 10.1016/j.jaci.2019.06.026]
9 **Colaco M**, Svider PF, Mauro KM, Eloy JA, Jackson-Rosario I. Is there a relationship between National Institutes of Health

funding and research impact on academic urology? *J Urol* 2013; **190**: 999-1003 [PMID: 23466241 DOI: 10.1016/j.juro.2013.02.3186]

10 **LaRocca CJ**, Wong P, Eng OS, Raoof M, Warner SG, Melstrom LG. Academic productivity in surgical oncology: Where is the bar set for those training the next generation? *J Surg Oncol* 2018; **118**: 397-402 [PMID: 30125359 DOI: 10.1002/jso.25143]

11 **McDermott M**, Gelb DJ, Wilson K, Pawloski M, Burke JF, Shelgikar AV, London ZN. Sex Differences in Academic Rank and Publication Rate at Top-Ranked US Neurology Programs. *JAMA Neurol* 2018; **75**: 956-961 [PMID: 29610899 DOI: 10.1001/jamaneurol.2018.0275]

12 **Namavar AA**, Marczynski V, Choi YM, Wu JJ. US dermatology residency program rankings based on academic achievement. *Cutis* 2018; **101**: 146-149 [PMID: 29554158]

13 **Svider PF**, Lopez SA, Husain Q, Bhagat N, Eloy JA, Langer PD. The association between scholarly impact and National Institutes of Health funding in ophthalmology. *Ophthalmology* 2014; **121**: 423-428 [PMID: 24070807 DOI: 10.1016/j.ophtha.2013.08.009]

14 **Yang HY**, Rhee G, Xuan L, Silver JK, Jalal S, Khosa F. Analysis of H-index in Assessing Gender Differences in Academic Rank and Leadership in Physical Medicine and Rehabilitation in the United States and Canada. *Am J Phys Med Rehabil* 2019; **98**: 479-483 [PMID: 30624239 DOI: 10.1097/PHM.0000000000001129]

15 **Therattil PJ**, Hoppe IC, Granick MS, Lee ES. Application of the h-Index in Academic Plastic Surgery. *Ann Plast Surg* 2016; **76**: 545-549 [PMID: 25422983 DOI: 10.1097/SAP.0000000000000382]

16 **Bastian S**, Ippolito JA, Lopez SA, Eloy JA, Beebe KS. The Use of the h-Index in Academic Orthopaedic Surgery. *J Bone Joint Surg Am* 2017; **99**: e14 [PMID: 28196042 DOI: 10.2106/JBJS.15.01354]

17 **Martinez M**, Lopez S, Beebe K. Gender Comparison of Scholarly Production in the Musculoskeletal Tumor Society Using the Hirsch Index. *J Surg Educ* 2015; **72**: 1172-1178 [PMID: 26232946 DOI: 10.1016/j.jsurg.2015.06.020]

18 **Nowak JK**, Lubarski K, Kowalik LM, Walkowiak J. H-index in medicine is driven by original research. *Croat Med J* 2018; **59**: 25-32 [PMID: 29498495 DOI: 10.3325/cmj.2018.59.25]

19 **Hirsch JE**. An index to quantify an individual's scientific research output. *Proc Natl Acad Sci U S A* 2005; **102**: 16569-16572 [PMID: 16275915 DOI: 10.1073/pnas.0507655102]

20 **Svider PF**, Mauro KM, Sanghvi S, Setzen M, Baredes S, Eloy JA. Is NIH funding predictive of greater research productivity and impact among academic otolaryngologists? *Laryngoscope* 2013; **123**: 118-122 [PMID: 22991270 DOI: 10.1002/lary.23659]

21 **Benway BM**, Kalidas P, Cabello JM, Bhayani SB. Does citation analysis reveal association between h-index and academic rank in urology? *Urology* 2009; **74**: 30-33 [PMID: 19567283 DOI: 10.1016/j.urology.2008.10.045]

22 **Ponce FA**, Lozano AM. Academic impact and rankings of American and Canadian neurosurgical departments as assessed using the h index. *J Neurosurg* 2010; **113**: 447-457 [PMID: 20380531 DOI: 10.3171/2010.3.JNS1032]

23 **Namavar AA**, Loftin AH, Khahera AS, Stavrakis AI, Hegde V, Johansen D, Zoller S, Bernthal N. Evaluation of US Orthopaedic Surgery Academic Centers Based on Measurements of Academic Achievement. *J Am Acad Orthop Surg* 2019; **27**: e118-e126 [PMID: 30199475 DOI: 10.5435/JAAOS-D-16-00536]

24 **Accrediation Council for Graduate Medical Education (ACGME)**. Public Advanced Program Search. [cited 04 April 2019]. Available from: https://apps.acgme.org/ads/Public/Programs/Search

25 **Scopus**. Scopus Database. [cited 16 July 2019]. Available from: http://www.scopus.com/

26 **Walker B**, Alavifard S, Roberts S, Lanes A, Ramsay T, Boet S. Inter-rater reliability of h-index scores calculated by Web of Science and Scopus for clinical epidemiology scientists. *Health Info Libr J* 2016; **33**: 140-149 [PMID: 27168256 DOI: 10.1111/hir.12140]

27 **Gillum LA**, Gouveia C, Dorsey ER, Pletcher M, Mathers CD, McCulloch CE, Johnston SC. NIH disease funding levels and burden of disease. *PLoS One* 2011; **6**: e16837 [PMID: 21383981 DOI: 10.1371/journal.pone.0016837]

28 **Post A**, Li AY, Dai JB, Maniya AY, Haider S, Sobotka S, Choudhri TF. c-index and Subindices of the h-index: New Variants of the h-index to Account for Variations in Author Contribution. *Cureus* 2018; **10**: e2629 [PMID: 30027021 DOI: 10.7759/cureus.2629]

29 **Thompson DF**, Callen EC, Nahata MC. New indices in scholarship assessment. *Am J Pharm Educ* 2009; **73**: 111 [PMID: 19885080 DOI: 10.5688/aj7306111]

30 **Zhang CT**. The h'-index, effectively improving the h-index based on the citation distribution. *PLoS One* 2013; **8**: e59912 [PMID: 23565174 DOI: 10.1371/journal.pone.0059912]



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The primary aim of *World Journal of Orthopedics* (*WJO*, *World J Orthop*) is to provide scholars and readers from various fields of orthopedics with a platform to publish high-quality basic and clinical research articles and communicate their research findings online.

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REVIEW

Conservative treatment of knee osteoarthritis: A review of the literature

Wei Boon Lim, Oday Al-Dadah

Specialty type: Orthopedics

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Abstract

Knee osteoarthritis (KOA) is a common chronic debilitating disease with an estimated prevalence of 23.9% in the general adult population. The condition is characterised by joint pain, functional impairment and significant reduction in quality of life. Management for KOA can generally be divided into conservative (non-operative) and surgical (operative) measures. Conservative management broadly compromises pharmacological and non-pharmacological options and is conventionally the first line treatment to avoid or delay the need for surgical management. The aim of this study is to provide an overview of the current recommendations, efficacy and safety profile of different conservative treatments through a review of the literature.

Key Words: Osteoarthritis; Knee; Conservative; Non-surgical; Treatment; Management

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Core Tip: Conservative management is conventionally used as the first line treatment to avoid or delay the need for surgical management in knee osteoarthritis. However, it remains under-utilised and recommendations of different conservative management options can vary greatly among different international guidelines. Hence, this study aims to provide an overview of the current recommendations, efficacy and safety profile of different conservative management options so as to better understand the value of each treatment option.

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INTRODUCTION

Traditionally, osteoarthritis is considered a degenerative disease that leads to loss of articular cartilage, bone remodelling (osteophyte formation), subchondral sclerosis and subchondral cysts. Articular cartilage is a shock-absorbent connective tissue that provides a smooth surface to minimise friction upon joint movement. The above changes lead to joint dysfunction and hence pain worsened upon activity, stiffness and loss of function. However, more recent studies[1,2] have shown that the pathogenesis is much more complex with metabolic and inflammatory aspects to it.

TREATMENT OPTIONS

The main overarching aim of conservative treatment is to provide symptomatic relief of the disease and slow its progression to avoid or forestall end-stage surgical options (*i.e.* total knee placement). The various conservative treatment options include exercise, weight loss, pharmacological agents and orthotics.

EXERCISE

Exercise therapy is core treatment in knee osteoarthritis (KOA) with the benefits of exercise having been linked to muscle strengthening and hypertrophy, weight management and even potential disease-modifying effects. The 2007 Osteoarthritis Research Society International (OARSI) guidelines[3] for management of KOA stated that exercise was strongly endorsed with 21 items recommending aerobic and strengthening exercises and a further 8 items recommending water-based exercises. Currently, an exercise regime is strongly recommended as 1st line treatment by international guidelines with strong evidence supporting its effectiveness[4,5]. Uthman *et al*[6] concluded that it is unlikely further clinical trials comparing exercise *vs* non-exercise will ever contradict the clear benefit of the former. Consequently, this review will focus on the effectiveness of mind-body exercises, balance exercises and general recreational physical activity (*i.e.* walking) that are often under-reported.

Mind body exercises

Mind-body exercises, including Tai Chi and Yoga, combine physical activity, mental focus and controlled breathing. In a single-blinded randomised controlled trial (RCT) comparing Tai Chi with standard physical therapy for KOA, Wang *et al*[7] concluded that both interventions showed improvements in Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) scores and most secondary outcomes at the post-intervention period and 52 wk follow-up. Notably, the Tai Chi group demonstrated superiority in terms of depression and the physical component in quality of life. Secondary analysis of the same trial concluded that patients begin to notice the improvements after 2-5 wk[8]. Other studies have also supported the effectiveness of yoga in KOA. In a RCT of 113 patients older than 60 years with self-reported KOA, Cheung *et al*[9] reported that both yoga and the control aerobic/strengthening exercises resulted in improved pain relief and physical function. Moreover, perhaps due to the inclusion of meditation and standing-up exercises, the 8-wk yoga program was superior in terms of improving anxiety and fear of falling. As a result, the above studies show the potential of mind-body exercises over traditional standard physical therapy for a more holistic approach.

Balance training

Balance training has been shown to be effective for KOA in improving mobility and reduce pain and falls risk. Liao *et al*[10] in a RCT reported that addition of balance exercises to conventional training further improved function such as stair climbing and standing from a seated position. Balance training has also been shown to be as effective in pain reduction as strength training in a RCT by Chaipninyo *et al*[11]. Holistic exercise programmes that incorporate balance exercises have also been shown to reduce falls risk in a systemic review by Sherrington *et al*[12].

Non-strenuous activities

The benefits of recreational non-strenuous activity such as walking differ based on the pre-existing severity of KOA and length of activity. In a RCT by Wallis *et al*[13] of 46 patients with severe KOA, a 12-wk walking program of 70 min per week was not effective in decreasing knee pain as compared to the control group receiving standard care. They concluded that walking may have cardiovascular benefits without relieving knee pain. However, it must be noted that the patients recruited had grade III or IV osteoarthritis and hence walking might not have significant benefits at a severe stage. In addition, excessive recreational physical activity might lead to worsening outcomes. In a clinical study assessing the dose response of walking for patients with severe KOA (Grade III and IV), Wallis *et al*[14] found that there was a higher risk of adverse events leading to worsening knee pain beyond 70 min per week of supervised walking. However, in a RCT of patients with mild to moderate KOA, Alghadir *et al*[15] concluded that a 6-wk walking program of 30 min a week resulted in greater pain relief, physical function and quadriceps muscle strength. Farrokhi *et al*[16] recommended shorter interval bouts of walking over continuous and longer sessions due to reported knee pain and undesirable knee loading when patients walk continuously for 30 min or more. Therefore, increased general activity might be more effective in mild to moderate KOA at a lower dose to prevent adverse symptoms.

However, most research trials tend to recruit patients who are physically inactive and it is questionable whether patients who are already physically fit can expect to experience the same magnitude of benefits. In the data analysis of 12796 patients in the nationwide physical exercise program for patients with KOA in Denmark, Skou *et al*[17] concluded that all patients regardless of baseline physical activity level can expect to see similar pain reduction at both post-intervention and the 12 mo mark.

Exercise regimen prescription

Prescription of an exercise regime can also be further complicated by the large number of exercises available and variable dosage in terms of frequency, sets and repetition. In addition, there have been far less research done that directly compares different exercises due to the cost and sheer number of exercises available. In a recent systematic review and network meta-analysis, Goh *et al*[18] classified exercises into aerobic, mind-body, strengthening, flexibility/skill and mixed types. Overall, mixed exercises that targeted multiple physical domains were the least effective for unknown reasons whereas other exercises were superior in some target outcomes.

In a single-blinded RCT of 78 patients with grade II or III KOA, Kabiri *et al*[19] reported that a supervised exercise program including resistance training and aerobic training resulted in significant improvements in pain relief and physical function. However, the arm ergometer group demonstrated superior reduction in Visual Analogue Scale (VAS) and change of function in the Knee injury and Osteoarthritis Outcome Score dimension while the treadmill group was superior in the timed up and go test. Therefore, this reinforces the possibility of customising exercises to better target desired outcomes in patients. Moreover, in a RCT of elderly patients with pre-radiographic KOA, Suzuki *et al*[20] concluded that a well-rounded program that targeted overall muscle strength with flexibility was more effective than targeting certain groups.

Aquatic exercises

It has been proposed that aquatic exercises have certain advantages over land-based ones such as pain reduction and reduced joint loading due to the buoyancy of the water. However, in a single-blinded randomised trial comparing land based *vs* water based exercise, Wang *et al*[21] concluded that both types of exercises demonstrate benefits in pain relief, physical function and quality of life without significant differences between them. Instead, they recommended that choice should be based on the patient's preference and convenience.

Mode of delivery of exercises

Despite the proven benefits of exercise therapy in KOA, several studies have noted low compliance rates. An important factor affecting compliance is mode of delivery which can include supervised or internet or home based. In a randomised clinical trial comparing internet *vs* supervised based sessions, Allen *et al*[22] identified baseline body mass index (BMI) and symptom duration as factors that affected the effectiveness of the program. Data analysis from the study showed that patients with low BMI had greater improvements through internet-based exercise sessions while those with high BMI and longer history of symptoms benefitted more from physical therapy. In another RCT comparing a month of supervised exercise in the clinic *vs* unsupervised sessions at home for KOA, Deyle *et al*[23] reported that both were effective but the supervised sessions was twice as effective in terms of pain, stiffness and function. Therefore, it might be more appropriate to use supervised sessions when KOA is more severe or patient has greater co-morbidities or low compliance. Another mode to consider would be group *vs* individual therapy. In a single-blinded randomised clinical trial comparing group *vs* individual approach, Allen *et al*[24] found that 12 wk of both approaches were effective in improving WOMAC and physical performance without significant difference between them.

Integration of exercise and patient education

ESCAPE-knee pain rehabilitation program is a community-based exercise rehabilitation program that combines exercise and patient-education to encourage self-management of osteoarthritis and patient empowerment. The program is supported by National Health Service England and widely available across the United Kingdom. In a RCT by Hurley *et al*[25] concluded that the ESCAPE program was effective, cost-efficient and resulted in better functional outcomes over conventional primary care. The clinical and cost benefits persisted 30 mo after completion of the rehabilitation program. The program was also equally effective regardless of being implemented on an individual or collective group basis. An RCT by Jessep *et al*[26] also supported the economic efficiency of the program over outpatient physiotherapy. While both methods had similar clinical benefits, the ESCAPE program had a lower cost per person and healthcare utilisation cost. Qualitative interviews by Hurley *et al*[27] concluded that the ESCAPE program enables patients to have greater confidence in the safety, effectiveness and applicability of exercising to improve their condition. Hence, it is evident that a holistic exercise program is able to achieve both physiological improvements and psychosocial benefits that fosters health beliefs and behaviours.

WEIGHT LOSS IN KNEE OSTEOARTHRITIS

The OARSI guidelines[28] for KOA noted that 13 international guidelines recommended weight loss as a core treatment. High BMI is a risk factor for developing KOA and has been associated with worse outcomes following knee replacement surgery.

Many studies have shown the effectiveness of weight management. In a randomised trial of 80 obese patients with KOA, Christensen *et al*[29] found that a low energy diet was significantly superior over the control education group in improving physical function over 8 wk. In addition, they concluded that body fat reduction was significantly associated with increase in function and a 10% bodyweight reduction would result in a 28% increase in function. In another clinical study by Coriolano *et al*[30] they found that weight loss of 16.5% in bodyweight through a diet program resulted in significant pain and function improvement. The benefits of the diet program were sufficient for patients to postpone their need for total knee replacement surgery. In addition, in the long-term Osteoarthritis Initiative cohort study, Gersing *et al*[31] reported that weight loss was associated with slower cartilage deterioration especially in the medial compartment. It should be noted that the benefits for cartilage loss was only seen in groups that had lost weight through dieting as opposed to exercise. Hence, it is evident that weight loss is effective in treating KOA, both short-term and long-term.

The benefits of weight loss might be linked to reduce joint loading. In a secondary analysis of data from the CAROT trial, Aaboe *et al*[32] found that every kilogram lost in bodyweight resulted in 2.2 kg reduction in the peak knee joint loading. Weight loss has also been linked to inflammatory and interstitial turnover changes. Loeser *et al*[33] in a RCT of 429 patients with symptomatic KOA found that weight loss through diet decreased biomechanical markers of interstitial matrix inflammation and turnover (IL-6, C1M, C3M and CRPM). However, the limitation of this study was that the biochemical results do not show a relationship with change in physical function or radiographic progression of osteoarthritis.

Weight loss is often promoted in tandem with exercise therapy and the combination of both interventions has been shown to be more effective. In a single-blinded RCT of 316 patients with symptomatic KOA, Messier *et al*[34] compared the effectiveness of exercise and weight reduction measured in primary (WOMAC function index) and secondary (functional tests, pain and stiffness score, joint space width) outcomes. The clinical study concluded that a combination of both interventions was superior over either intervention alone in self-reported pain and function, and physical performance. The benefits were maintained for 12 additional months. Moreover, in the Osteoarthritis Initiative, it was noted that slower cartilage loss was seen in the diet and diet plus exercise group, but not in the exercise only group[31]. Therefore, this highlights the increased effectiveness in combining both weight loss and exercise intervention.

However, there have been doubts about the viability of weight loss programs in the long run due to the possibility of regaining weight or potentially negative side-effects of weight cycling. Weight cycling refers to periods of weight loss followed by weight gain which can lead to adverse events such as increased metabolic risk. However, in a randomised trial comparing intermittent weight cycling through low-energy diet *vs* steady weight loss through daily meal replacements over 3 years, Christensen *et al*[35] concluded that both strategies with dietary counselling were equally viable and effective with a good safety profile. Firstly, both structured diet programs were effective in maintaining weight loss without rebounding. In addition, the benefits of weight loss on symptom relief and cardiovascular disease risks were maintained over 3 years. Hence, this emphasises the effectiveness of weight loss as long as a structured program is in place to ensure patient compliance.

PHARMACOLOGICAL MANAGEMENT IN OSTEOARTHRITIS

Originally, the World Health Organisation (WHO) analgesic pain ladder was established for treatment of cancer pain in 1986. The WHO ladder consisted of the following steps: Step I with non-opioid analgesics [acetaminophen or nonsteroidal anti-inflammatory drug (NSAIDs)], Step II with weak opioids and step III with strong opioids. This approach has been extrapolated to pain management for osteoarthritis and involves going to the next step if the current step was inadequate for pain relief. However, such an approach has now been questioned due to the multiple pain modalities present in KOA.

Acetaminophen/paracetamol

Even though acetaminophen is often recommended as first-line analgesia, its effectiveness is questionable and it was not recommended in the most recent OARSI guidelines[4] for KOA. In a double-blinded RCT involving 779 patients with KOA, Miceli-Richard *et al*[36] concluded that acetaminophen at 4 g/day taken over 6 wk did not demonstrate statistically superior results over placebo in terms of knee pain intensity and assessment of their condition. The use of acetaminophen was well-tolerated with a good safety profile. In a separate double-blinded RCT by Case *et al*[37], acetaminophen similarly did not demonstrate statistically or clinically meaningful results over placebo as assessed by the WOMAC index. Although other trials by Prior *et al*[38] and Altman *et al*[39] do support the effectiveness of acetaminophen, the Cochrane systematic review for paracetamol in KOA concludes that the benefits for pain and physical function are small and are clinically unimportant[40]. Therefore, recommendation of acetaminophen as first-line analgesic medication should be reconsidered.

However, acetaminophen might be valuable for its advantageous synergistic effect when combined with other analgesics for pain relief. Pareek *et al*[41] in a randomised multicentre study demonstrated that the combination of aceclofenac and acetaminophen was superior over monotherapy in rapid pain relief for osteoarthritic flare-ups. However, Doherty *et al*[42] in a randomised double-blinded study concluded that while the combination of paracetamol and ibuprofen was superior for pain relief over paracetamol alone, it was not significantly superior over ibuprofen alone. In addition, patients taking two ibuprofen/paracetamol tablets were found to be at greater risk of reduction in haemoglobin levels due to gastrointestinal (GI) blood loss than either monotherapy alone. This suggests a synergistic interaction between paracetamol and ibuprofen in causing GI complications.

NSAIDs

NSAIDs work by inhibiting cyclo-oxygenase enzymes, and in turn reducing prostaglandin levels. Hence, this leads to a reduction in pain and inflammation. NSAIDs can be classified into non-selective or selective COX-2 inhibitors, as well as topical and oral formulations. The National Institute for Health and Care Excellence (NICE)[43] recommends topical NSAIDs before systemic analgesics (oral NSAIDs, COX-2 inhibitors and opioids) for KOA. The OARSI guidelines[44] also consider topical NSAIDs to be safer and better tolerated than oral NSAIDs.

Comparison of selective and non-selective NSAIDs

Head-to-head trials have shown both classes to have comparable effectiveness. In a 6-wk RCT comparing efficacy of celecoxib (COX-2 selective NSAID) *vs* ibuprofen (non-selective NSAID) for KOA, Gordo *et al*[45] concluded that both were similarly effective and well-tolerated. Pooled results from two placebo-controlled trials[46] showed that both Naproxen (non-selective NSAID) and Celecoxib (COX-2 selective NSAID) resulted in early significant pain relief based on WOMAC score by the second day of treatment and analgesic effect was maintained for 12 wk. However, while both treatments were statistically superior over placebo at week 6 based on the OMERACT-OARSI response, Naproxen remained superior at week 12 but Celecoxib was not.

Instead, the bigger difference would be tolerability and safety profile. COX-2 selective inhibitors have been thought to cause fewer GI side-effects as the inhibition of COX-1 is responsible for the associated GI toxicity. In the CONDOR randomised trial, Chan *et al*[47] reported that the risk of GI complications was lower in the patient group taking COX-2 selective NSAIDs than in patients taking non-selective NSAIDs with a proton pump inhibitor. There is an increased risk of GI complications with prolonged intake and in patients over 70 years of age.

In terms of cardiovascular risks, both classes appear to have similar risks. Two population-based analysis studies in Taiwan and Finland reported that use of all NSAIDs increase the risks of cardiovascular events[48,49]. A meta-analysis[50] concluded that naproxen, out of all the NSAIDs, is associated with the least vascular risks. Overall, NSAIDs have varying safety profiles and prescription of the most appropriate drug should be done based on the balance of benefits *vs* risks to the individual patient. In a network meta-analysis[51], Naproxen was ranked as the most effective conservative treatment of KOA, coupled with its good relative safety and low cost to improve pain and function.

Oral vs topical NSAIDs

Despite oral NSAIDs being a step-up in pharmacological pain management, oral NSAIDs are not shown

to be superior in studies. Tugwell *et al*[52] in a RCT reported that oral and topical preparations of diclofenac were equivalent in symptomatic relief of KOA. While the topical form resulted in minor local skin irritation, the oral form had significantly greater systemic side-effects and abnormal laboratory tests (liver function tests, haemoglobin and creatinine clearance). In the TOIB RCT comparing topical and oral ibuprofen for chronic knee pain, Underwood *et al*[53] reinforced that both formulations were similar in effectiveness but oral NSAIDs produced more instances of minor adverse side-effects. However, neither resulted in significant improvements in WOMAC scores from baseline to follow-up at one year, hence this shows that neither preparation is particularly effective in some patients.

Opioids: Evidence regarding the safety and effectiveness of opioids are still contradictory based on current literature with mixed recommendations from guidelines. The latest OARSI guidelines[4] strongly recommends against opioid use due to the risk of potential dependency, be it transdermal or oral form. However, the latest American College of Rheumatology guidelines[5] conditionally recommends Tramadol over non-Tramadol opioids if opioids are considered. Non-tramadol opioids are only recommended if alternatives are exhausted and should be used at the lowest possible dose for the shortest possible time.

Opioids can generally be classified as weak or strong (Table 1).

Weak opioids: Research has generally supported the effectiveness of weak and strong opioids over placebo for pain relief. Peloso *et al*[54] in a RCT reported that controlled release codeine was statistically superior over placebo in improving pain, stiffness and physical function based on the WOMAC subscales. Also, in a non-inferiority trial, Conaghan *et al*[55] concluded that buprenorphine patches with oral paracetamol and co-codamol tablets were effective in significantly reducing patients' pain over 7 d of treatment. However, over 80% of patients in both groups reported adverse events and the study was limited by its high withdrawal rate in both groups.

Tramadol: Tramadol's mechanism of action is unique as it is not only a weak opioid receptor agonist, but also modulates norepinephrine and serotonin levels. Current clinical trials have shown tramadol to have mixed effectiveness. In a RCT of 1020 adults with osteoarthritis of the knees or hips, Gana *et al*[56] reported that tramadol at 200-300 mg once daily was statistically superior over placebo for improvements on pain, physical functioning but did not reach significance for subject global assessment of disease activity. Post-hoc data analysis by Kosinski *et al*[57] revealed tramadol also improved sleep quality and decreased pain-related sleep disturbance. However, in another RCT by DeLemos *et al*[58], the 100 mg and 200 mg dosages were not superior over placebo in any of the primary end-points. As for the 300 mg dose, significant improvements were achieved in patient global assessment of disease activity but not in WOMAC pain and physical function scores. Addition of tramadol at 200 mg per day has also been shown to allow significant naproxen dose reduction in patients taking them based on a placebo-controlled study by Schnitzer *et al*[59].

Due to the mixed effectiveness shown, the paper looked towards systematic reviews to ascertain effectiveness of tramadol. In the latest Cochrane review for tramadol[60], tramadol alone or combined with acetaminophen is not likely to be clinically important in improving pain or function in patients, but an additional 5% of patients do report a clinically important improvement of 20% or more in pain relief compared to placebo.

Head to head trials have also shown tramadol to be comparable to other opioids. In a randomised parallel trial comparing tramadol and dihydrocodeine, Wilder-Smith *et al*[61] reported that strong osteoarthritic pain insufficiently controlled by NSAIDs alone was controlled by both medication by the second day. While tramadol was superior for analgesia at rest and interfered less with GI function, it resulted in greater sedation and drowsiness as compared to dihydrocodeine. Karlsson *et al*[62] in a randomised non-inferiority trial of patients with chronic osteoarthritis pain reported that tramadol tablets were comparable to buprenorphine patches.

Strong opioids: In a randomised controlled study by Matsumoto *et al*[63], oxymorphone resulted in superior pain relief and functional improvements over placebo in patients with osteoarthritic pain uncontrolled by other non-opioid analgesia. However, 83% of patients reported at least one adverse event which were mild to moderate and was the biggest reason for patient withdrawal. Conversely, Caldwell *et al*[64] in an RCT reported that morphine sulphate only resulted in statistically significant pain relief but not physical function. While opioids have been shown to maintain their analgesic effect in the long-term for open-label extension studies, Bialas *et al*[65] concluded that such studies are limited due to the low-quality evidence and high dropout rates.

Opioids in general: Despite opioids being recommended as a last pharmacological resort when all alternatives fail, their use has not been shown to be superior over non-opioid in non-inferiority trials. In the SPACE trial comparing non-opioids and opioids for moderate to severe chronic osteoarthritis, Krebs *et al*[66] concluded that opioid therapy should not be initiated as they were not superior for pain relief, function and quality of life. Instead, the opioid group had significantly more medication-related side-effects and higher pain intensity over 12 mo. Beaulieu *et al*[67] also reported that tramadol and diclofenac were equally effective in pain relief and functional improvement. In another systematic

Table 1 Strength of opioids

Weak opioids	Strong opioids
Codeine	Morphine
Dihydrocodeine	Methadone
Tramadol	Fentanyl
	Oxycodone
	Tapentadol
	Oxymorphone

review comparing pain reduction, Smith *et al*[68] reported that NSAIDs, strong and weak opioids all have similar analgesic. Therefore, the lack of a demonstrable difference between strong and weak opioids suggests the need for more comparative trials in chronic non-cancer pain. Elderly patients prescribed opioids as opposed to NSAIDs also have a significantly greater risk of falls and fractures by 4.1 times[69].

Despite lack of evidence for clinical superiority over placebo, meta-regression in systematic reviews [70,71] have shown them to have small or no clinical impact on pain relief and functional improvements. Their effectiveness is also compromised by their high incidence of adverse events and side-effects as demonstrated by the high withdrawal rates in clinical studies although this can be partially mitigated by titration as many clinical studies often start with a non-titrated dose. Side-effects include GI adverse events (constipation, nausea, vomiting); central nervous system events (sedation, dizziness); dermatological events (pruritus, rashes)[72].

Opioid use also leads to poor long-term outcomes and result in both peri-operative and post-operative complications. In terms of post-operative complications, pre-operative opioid use has been linked to a greater likelihood of chronic opioid use following surgery[73]; greater risk of adverse outcomes that includes peri-prosthetic joint infection[74], higher hospital readmission rates[75] and post-operative pain[76]. The higher risk of complications would further obfuscate management as patients would need to wean or reduce their opioid use for several months prior to the surgery[77]. In terms of peri-operative complications, long-term opioid use can result in hyperalgesia and tolerance [78]. This would make it more difficult to provide adequate peri-operative and post-operative analgesia in patients undergoing knee replacement (or any form of) surgery.

Intra-articular corticosteroids: Intra-articular corticosteroids (IACs) are frequently-used as an adjunctive treatment for pain control in KOA due to its anti-inflammatory effect. Recommendation for use of IACs in treatment of KOA is variable. While the American Academy of Orthopaedic Surgeons[79] found it inconclusive, other organisations such as NICE[43], OARSI[80] and American College of Rheumatology[5] have recommended or conditionally recommended its use.

Clinical studies have affirmed the effectiveness of IACs as an adjunctive therapy for short-term pain relief and the effectiveness of IACs in the literature has varied from 4 wk up to 26 wk. A network meta-analysis of conservative treatments[51] concluded that IACs provided the greatest short-term pain relief from 4 to 6 wk. In a RCT comparing a single intra-articular injection of hyaluronic acid and triamcinolone acetonide, Tammachote *et al*[81] concluded that IACs resulted in improved pain, function and knee range of motion without any serious adverse events that was present in the 1st week and lasted for 6 mo. However, Yavuz *et al*[82] reported in a prospective study that all three IACs (methylprednisolone, betamethasone and triamcinolone) were effective but their benefits declined at week 12. Regarding the choice of corticosteroid administered, the literature has been mixed. Lomonte *et al*[83] supported that both methylprednisolone and triamcinolone were equally effective for sustained improvement in pain and function up to 24 wk whereas Yavuz *et al*[82], reported that Methylprednisolone also provided better analgesia until the 6th week. The effectiveness of IACs is also independent of the injection site. In a RCT of 60 patients with KOA receiving IACs, Parrilla *et al*[84] concluded that corticosteroids resulted in a clinically significant pain improvement regardless of the injection site.

However, IACs have not shown synergistic benefits when combined with other conservative treatments. A RCT by Henrikson *et al*[85] concluded that addition of IACs to physical therapy provided no further benefits. Another RCT by Deyle *et al*[86] also showed that physical therapy was superior over IACs in the long-term with less pain and functional disability.

Furthermore, the effectiveness of repeated IACs has been shown to be variable. In a randomised placebo-controlled trial, McAlindon *et al*[87] concluded that repeated IACs every 3 mo did not result in superior knee pain control over saline injections. However, intra-articular injections of triamcinolone acetonide at the same dose resulted in significant improvement in knee pain and stiffness over 2 years in a RCT by Raynauld *et al*[88].

IACs have shown a good safety profile but long-term safety profile of IACs has been inconclusive. Raynauld *et al*[88] in a RCT comparing intra-articular injections of steroids against saline, concluded that long-term IACs was safe and did not negatively affect the knee joint. However, McAlindon *et al*[87] concluded that IACs resulted in significantly greater loss of cartilage volume compared to intra-articular injection of saline. In the recent Osteoarthritis Initiative observation study[89], IACs and especially repeated IACs may be associated with greater risk of radiographic KOA progression.

Intra-articular hyaluronic acid: Hyaluronic acid is a glycosaminoglycan naturally found within the knee joint that decreases with the progression of osteoarthritis. Its anti-arthritic effects have been hypothesised to be due to multiple mechanisms of action including chondroprotection, joint lubrication, shock absorption, anti-inflammation and immune cells modulation. Intra-articular hyaluronic acid (IAHA) is an alternative to IACs but recommendation among national and international guidelines for its use in KOA remains inconclusive. The OARSI guidelines[4] state that IAHA treatment is conditionally recommended for longer term treatment effects in patients with KOA whereas NICE guidelines[43] do not recommend it.

Research studies have shown IAHA and IACs to have comparable efficacy with IACs providing greater pain relief in the short-term while IAHA provide greater pain relief in the long-term. In a randomised non-inferiority study by Tammachote *et al*[81], they concluded that both groups had similar symptomatic improvement by the end of six months. However, IACs resulted in better pain relief in the first week and greater functional improvement in the second week. In a multi-centre prospective study, Leighton *et al*[90] reported that IACs and IAHA were comparable throughout the first 12 wk but IAHA was superior for pain, stiffness and function from the 12th to 26th week. Bannuru *et al*[80] in a systematic review concluded that current evidence suggests corticosteroids to be more effective in the short term up to 4 wk, whereas hyaluronic acid is more effective beyond the 4th week. Therefore, the differing therapeutic trajectory plays a key role in clinical prescription based on the patients' symptoms and expectations. A randomised study by Ozturk *et al*[91] reported that the combination of IAHA and IACs was superior over hyaluronic acid alone, resulting in more rapid pain relief and to a lower level. This shows the potential of synergistic effects of combining both therapies. However, it should also be noted that available research trials have been criticised for publication bias and risk of selective reporting of outcomes in an analysis of randomised trials[92].

Repeated use of hyaluronic acid has also been shown to be effective with a good safety profile. In the AMELIA randomised controlled study, Navarro-Sarabia *et al*[93] found that patient responsiveness increased throughout the 40-mo study with repeated injections. In terms of symptom improvement, IAHA not only improve symptoms in-between injections but also had a carry-over effect that lasted for at least 1 year after the last injection. As for safety, incidence of adverse events did not differ from that of placebo's and there were no serious adverse events. Neustadt *et al*[94] also reported that five injections of hyaluronic acid at weekly intervals up to 26 wk was associated with an excellent safety profile and only had minor local adverse reactions. Follow-up at 24 mo still supported the excellent safety profile of the injection.

Overall, the current literature suggests that hyaluronic is an effective alternative to corticosteroid injections with an excellent safety profile.

Topical capsaicin: Capsaicin has been recommended by NICE[43] for adjunctive pain management in KOA. Its mechanism of action is *via* selective depression of type-C nociceptive fibres.

Initial research regarding its effectiveness dates back to 1991 where Deal *et al*[95] reported that topical application four times daily resulted in significant pain relief compared to placebo. This was supported by subsequent research trials. In a double-blinded RCT, Kosuwon *et al*[96] further reported that 0.0125% capsaicin gel was effective for improving stiffness and function in patients with grade II and III Kellgren-Lawrence KOA. In a long-term extension trial of a RCT by Schnitzer *et al*[97] concluded that capsaicin cream was effective in all three primary end-points for patients with mild to moderate KOA who were already taking NSAID or COX-2 inhibitors. The efficacy was also maintained up to a year of continuous use. McCleane *et al*[98] has also highlighted the potential of combining capsaicin with glyceryl nitrate which resulted in reduced localised burning sensation and superior analgesic effects even in patients with osteoarthritis uncontrolled by other pharmacological treatments. However, the study did include patients with osteoarthritis in other joints besides knees which would affect the generalisability of its results.

Capsaicin also has a good safety profile due to its lack of systemic absorption. The main side-effect is a localised burning sensation but withdrawals due to this has been low in the afore mentioned research trials.

As a result, topical capsaicin is effective for mild to moderate KOA. More research would need to be done for patients with severe KOA or other co-morbidities as they are excluded in afore mentioned trials.

Flexiseq gel: Flexiseq gel is marketed as an adjunctive analgesia that contains phospholipid vesicles that passes into the knee synovial joint where it provides lubrication to minimise friction between cartilage and hence reduces pain. In a RCT of 1395 patients with osteoarthritic knee pain, Conaghan *et al*[99] reported that Flexiseq gel was superior to oral placebo with comparable efficacy to oral celecoxib in pain

reduction and functional improvement. There have also been an additional three clinical studies that used Flexiseq gel as a treatment arm[99-102]. However, these clinical studies have shown low quality of evidence. All three of these clinical studies also involve Flexiseq gel as the topical placebo arm and there has been no comparison of Flexiseq gel against a true inactive topical gel to date to account for placebo effects. Furthermore, all the trials have the potential to introduce funding bias as they are sponsored by pharmaceutical companies. There is also limited evidence base for the analgesic mode of action as stated in NICE guidelines[103].

TRANSCUTANEOUS ELECTRICAL NERVE STIMULATION

Transcutaneous electrical nerve stimulation (TENS) therapy involves passing of electrical currents through electrodes placed on the targeted area to stimulate peripheral nerves for pain control. Delivery of the electrical currents can be of varying frequencies and intensity. Clinical studies examining the effectiveness of TENS therapy have shown that it is mostly ineffective with little clinical benefits for patients.

In a double-blinded RCT of 203 patients with KOA by Atamaz *et al*[104], application of TENS therapy did not result in a statistically significant or superior results in pain intensity or physical functioning over placebo treatments. While it was suggested that the lower intake of paracetamol in treatment groups suggested pain relief, lower intake was only present in the first 3 mo for the TENS group and did not persist to the end of the study. In addition, it would be difficult to attribute the improvements in assessment parameters to application of physical agents as every group also had a structured exercise and education program. In another RCT by Cheing *et al*[105], the combination of TENS and exercise training resulted in the best overall improvements in physical outcomes but this was not significantly superior over placebo stimulation. Another randomised placebo-controlled study by Fary *et al*[106] similarly showed that 26 wk of pulsed electrical stimulation was not more effective than placebo. Hence, the current literature does show that TENS therapy at best has small benefits that are not likely to be clinically meaningful.

KNEE BRACING

Knee bracing is often recommended as an adjunctive treatment in KOA. Proposed mechanisms of action for knee bracing include unloading of the medial compartment, or through general biomechanical and neuromuscular effects that lead to improved proprioception and joint stability.

However, clinical studies do not support the theoretical benefit of knee braces. In a RCT of 117 patients with unicompartmental KOA, Brouwer *et al*[107] found that benefits in using the brace was small and compliance was low due to ineffectiveness and skin irritation. In a separate 52 wk observation study of 204 patients with KOA, Yu *et al*[108] found that that neither patellofemoral or tibiofemoral customised bracing resulted in a significant difference in overall pain and functional improvements compared to the control unbraced group. Rather, a multidisciplinary program with a multidisciplinary approach was effective and sufficient for symptomatic improvements. However, limitations of this study included high dropout rate with less than 60% participating in the final assessment and potential recall bias. Survey results by Squyer *et al*[109] also indicated low compliance use of knee brace in patients which is 28% after the first year and 25% after the second year. No patient or radiographic factors were identified in the survey to predict usage or discontinuation of the knee brace.

Due to the lack of research supporting its efficacy and poor-quality evidence, the OARSI guidelines[4] now recommended against knee bracing.

FOOT ORTHOSES

Laterally-wedged insoles have also been recommended in the treatment of medial KOA because of their potential to reduce the knee adduction moment (KAM) (medial-to-lateral knee loading). Research has shown that an increased external knee adduction moment (EKAM) causes an increase in risk of structural deterioration over time of the medial knee compartment. Therefore, insoles might have the potential to minimise the rate of deterioration and help relieve symptoms.

However, several clinical studies have shown that laterally-wedged insoles might not confer any beneficial biomechanical effect and symptom relief. In a secondary analysis of data from a RCT study, Duivenvoorden *et al*[110] concluded that neither valgus brace nor laterally wedged insoles resulted in clinically relevant biomechanical alterations. Unloading of the medial compartment was only present in laterally wedged insoles at baseline and did not persist beyond six weeks. However, the unloading effect at baseline was small and might not be clinically relevant. Another randomised study assessing

the relationship between KAM and knee pain in 70 patients with medial KOA by Jones *et al*[111] concluded that lateral wedges did reduce the average EKAM but changes in EKAM had no clear-cut relationship with knee pain reduction. Instead, some subjects experience paradoxical pain reduction even though EKAM increased. This finding was further supported by a three-month RCT by Lewinson *et al*[112] Their study concluded that the magnitude of KAM reduction was not associated with the same magnitude of change in pain.

Several studies have shown little difference between laterally wedged insoles and neutral insoles. In a 6 mo prospective RCT of 156 patients with symptomatic medial KOA, Pham *et al*[113] concluded that lateral wedged insoles was not superior over neutral insoles in terms of pain, stiffness and physical functioning with the exception of decrease NSAIDs consumption. Neither neutral nor lateral wedged insoles demonstrated disease-modifying effects. Bennell *et al*[114] double-blinded RCT of 200 subjects with mild to moderately severe medial KOA also similarly reported that lateral wedge insoles demonstrated no additional benefit over flat insoles in symptom improvement or disease modifying effect.

Effectiveness of insoles also depends on patient factors. Shimda *et al*[115] in a prospective study analyzing the gait of 42 patients reported that laterally wedged insoles were most effective in reducing KAM in patients with early and mild osteoarthritis. Toda *et al*[116] concluded that insoles are more effective for younger patients and those with higher lean body mass. Conversely, use of insoles are less effective for older patients with sarcopenia.

Overall, insoles and knee bracing have similar effectiveness. However, insoles do have an advantage because of higher compliance, lower cost and ease of use. Therefore, clinicians and allied health professionals should take this into consideration if they wish to recommend foot orthoses as an adjunctive treatment.

THERMOTHERAPY

Thermotherapy involves superficial application of heat or cold to improve symptoms. Cryotherapy is thought to help in pain management by vasoconstriction of blood vessels and blocking of nerve impulses in the joint. This would be useful in reduction of inflammation, oedema of the joint and pain. Alternatively, heat therapy has been proposed to help by relaxing muscles and increasing blood circulation to the applied area. This would then result in pain and stiffness reduction, as well as improving mobility.

Evidence to support use of thermotherapy has been inconclusive. An early RCT by Clarke *et al*[117] in 1974 reported that use of ice packs for three weeks did not result in statistically significant or clinically important pain relief compared to the control group. Subsequently, Hecht *et al*[118] found that ten treatment sessions of cold pack application resulted in oedema reduction while hot packs did not. However, the clinical importance of oedema reduction was unclear. Yurtkuran *et al*[119] reported that ice massage for 20 min at 5 sessions per week was clinically superior over control in increasing quadriceps strength. No difference was seen for function, joint range of motion or knee oedema. In a recent RCT, Aciksoz *et al*[120] concluded that both hot and cold applications in addition to standard treatment resulted in mild improvements for pain, function and quality of life. However, the improvement was not sufficient to be statistically superior over the control group.

Overall, the current literature has been inconclusive with contradicting results. However, given that the thermotherapy is easily implemented and relatively safe, there is no harm in its recommendation as an adjunctive therapy. The decision on heat or cold application would heavily depend on patient's preference as Denegar *et al*[121] in a randomised trial reported greater improvements in pain and function when patients used their preferred treatment.

ORAL SUPPLEMENTS

Glucosamine and chondroitin are two of the most popular dietary supplements marketed for effective management of symptoms of osteoarthritis and improvement of joint health.

Clegg *et al*[122] in a large RCT of 1583 patients concluded that neither glucosamine nor chondroitin sulfate taken alone or together reduced pain effectively and was not significantly better than placebo. Part of the centres of the above GAIT trial also participated in an ancillary study whereby Swaitzke *et al*[123] reported that neither glucosamine nor chondroitin sulfate alone or in combination had a predefined clinically important difference on progress of joint width space narrowing. However, they did note that patients with Kellgren-Lawrencegrade II KOA showed the greatest potential for disease-modifying effect by these treatments. In a more recent RCT by Fransen *et al*[124] the study similarly reinforced the ineffectiveness of glucosamine and chondroitin for symptomatic benefit over placebo. However, patients taking the glucosamine-chondroitin combination had a statistically significant reduction in progress of joint space narrowing at 24 mo. This could be due to the lower percentage of patients with moderate to severe KOA compared to the GAIT trial.

However, the preparation of the supplements does impact the effectiveness. In the CONCEPT trial, Reginster *et al*[125] concluded that pharmaceutical-grade chondroitin at 800 mg/day over 6 mo was superior to placebo and similar to celecoxib in pain reduction and improvement in function. Similarly, Hochberg *et al*[126] in a randomised double-blinded study reported that a combination of prescription-grade chondroitin and glucosamine had comparable efficacy to oral celecoxib in symptomatic relief for KOA after six months of use. However, this study does have several limitations. The study compared the supplementation against oral celecoxib which did not demonstrate superior results over placebo in the GAIT trial. Furthermore, sponsorship of this study by a pharmaceutical company could have introduced bias.

In terms of safety profile, the above research trials show both glucosamine and chondroitin to have a good safety profile. In fact, a recent prospective cohort study across the United Kingdom reported that glucosamine supplements might even be beneficial and associated with lower cardiovascular disease risks[127]. However, follow-up analysis of the osteoarthritis initiative reported that long-term data showed that chondroitin sulfate and glucosamine supplementation could be associated with higher risks of radiographic osteoarthritis and subsequent knee replacements[128].

Overall, glucosamine and chondroitin have shown promise for potential of disease progression and symptomatic relief. However, efficacy would depend on the preparation of the supplements and severity of the disease. More research would also need to be done regarding the long-term safety profile of the supplements. Several meta-analysis and systematic reviews have also criticised that trials supporting large symptomatic benefits often have poor quality, publication bias and small samples while more robust methodologically sound studies have found small to no benefits.

DRY NEEDLING

Dry needling involves the use of fine needles to penetrate the skin and deactivate myofascial trigger points. The mechanism of action has been linked to activation of descending pain pathways that inhibit nociceptive processing[129].

Studies by Ceballos-Laita *et al*[130] and Itoh *et al*[131] have shown dry needling to be effective in improving function and pain intensity for osteoarthritis in the short term when compared to patients receiving control sham treatment. However, limitations of the above studies include low number of dry needling treatments and lack of long-term follow ups to examine the long-term benefits.

Moreover, the effectiveness of dry needling as part of a multidisciplinary approach remains questionable. Romero *et al*[132,133] examined the benefits of adding dry needling to a structured exercise program in KOA in two separate RCTs from a short-term and long-term perspective. However, dry needling failed to show improvements in function and pain intensity in the treatment group for both studies at the 3-mo and one-year mark respectively. The correlation between trigger points and intensity of KOA pain has also shown to be poor based on a secondary analysis by Romero *et al*[134]. Overall, more studies, especially with longer term results, are required to support the effectiveness of dry needling as part of a multidisciplinary approach.

CONCLUSION

Based on the current literature available to date, a multidisciplinary and a multimodal approach with a key focus on exercise, weight loss and pharmacological pain management would be the most appropriate. Out of the multiple pharmacological options available, chronic pain management through topical NSAIDs with intermittent intra-articular injections of corticosteroids or hyaluronic acid provides a reasonable balance between benefit and risk. Topical capsaicin can also be effective in mild to moderate KOA. Acetaminophen has not been shown to be an effective analgesic. Opioids, preferably tramadol, would have to be evaluated on a case-by-case basis due to their potent side-effects which are sufficiently detrimental to negate their benefits. While the post-operative negative impact is clear, more research is needed around the optimal adjunctive peri-operative analgesia and the effect of opioid tolerance on patients undergoing surgery.

There are numerous types of effective exercise therapy available, including a well-structured physical therapy program. Alternate interventions such as thermotherapy, leg orthoses or TENS have shown conflicting results and perhaps only conditionally recommended on an individual basis. Further research is required regarding the effectiveness of chondroitin and glucosamine.

FOOTNOTES

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important intellectual content. All of the authors reviewed and approved the final manuscript as submitted.

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REFERENCES

1 **June RK**, Liu-Bryan R, Long F, Griffin TM. Emerging role of metabolic signaling in synovial joint remodeling and osteoarthritis. *J Orthop Res* 2016; **34**: 2048-2058 [PMID: 27605370 DOI: 10.1002/jor.23420]
2 **Mobasheri A**, Rayman MP, Gualillo O, Sellam J, van der Kraan P, Fearon U. The role of metabolism in the pathogenesis of osteoarthritis. *Nat Rev Rheumatol* 2017; **13**: 302-311 [PMID: 28381830 DOI: 10.1038/nrrheum.2017.50]
3 **Zhang W**, Moskowitz RW, Nuki G, Abramson S, Altman RD, Arden N, Bierma-Zeinstra S, Brandt KD, Croft P, Doherty M, Dougados M, Hochberg M, Hunter DJ, Kwoh K, Lohmander LS, Tugwell P. OARSI recommendations for the management of hip and knee osteoarthritis, part I: critical appraisal of existing treatment guidelines and systematic review of current research evidence. *Osteoarthritis Cartilage* 2007; **15**: 981-1000 [PMID: 17719803 DOI: 10.1016/j.joca.2007.06.014]
4 **Bannuru RR**, Osani MC, Vaysbrot EE, Arden NK, Bennell K, Bierma-Zeinstra SMA, Kraus VB, Lohmander LS, Abbott JH, Bhandari M, Blanco FJ, Espinosa R, Haugen IK, Lin J, Mandl LA, Moilanen E, Nakamura N, Snyder-Mackler L, Trojian T, Underwood M, McAlindon TE. OARSI guidelines for the non-surgical management of knee, hip, and polyarticular osteoarthritis. *Osteoarthritis Cartilage* 2019; **27**: 1578-1589 [PMID: 31278997 DOI: 10.1016/j.joca.2019.06.011]
5 **Kolasinski SL**, Neogi T, Hochberg MC, Oatis C, Guyatt G, Block J, Callahan L, Copenhaver C, Dodge C, Felson D, Gellar K, Harvey WF, Hawker G, Herzig E, Kwoh CK, Nelson AE, Samuels J, Scanzello C, White D, Wise B, Altman RD, DiRenzo D, Fontanarosa J, Giradi G, Ishimori M, Misra D, Shah AA, Shmagel AK, Thoma LM, Turgunbaev M, Turner AS, Reston J. 2019 American College of Rheumatology/Arthritis Foundation Guideline for the Management of Osteoarthritis of the Hand, Hip, and Knee. *Arthritis Rheumatol* 2020; **72**: 220-233 [PMID: 31908163 DOI: 10.1002/art.41142]
6 **Uthman OA**, van der Windt DA, Jordan JL, Dziedzic KS, Healey EL, Peat GM, Foster NE. Exercise for lower limb osteoarthritis: systematic review incorporating trial sequential analysis and network meta-analysis. *Br J Sports Med* 2014; **48**: 1579 [PMID: 25313133 DOI: 10.1136/bjsports-2014-5555rep]
7 **Wang C**, Schmid CH, Iversen MD, Harvey WF, Fielding RA, Driban JB, Price LL, Wong JB, Reid KF, Rones R, McAlindon T. Comparative Effectiveness of Tai Chi Versus Physical Therapy for Knee Osteoarthritis: A Randomized Trial. *Ann Intern Med* 2016; **165**: 77-86 [PMID: 27183035 DOI: 10.7326/M15-2143]
8 **Lee AC**, Harvey WF, Price LL, Han X, Driban JB, Iversen MD, Desai SA, Knopp HE, Wang C. Dose-Response Effects of Tai Chi and Physical Therapy Exercise Interventions in Symptomatic Knee Osteoarthritis. *PM R* 2018; **10**: 712-723 [PMID: 29407226 DOI: 10.1016/j.pmrj.2018.01.003]
9 **Cheung C**, Wyman JF, Bronas U, McCarthy T, Rudser K, Mathiason MA. Managing knee osteoarthritis with yoga or aerobic/strengthening exercise programs in older adults: a pilot randomized controlled trial. *Rheumatol Int* 2017; **37**: 389-398 [PMID: 27913870 DOI: 10.1007/s00296-016-3620-2]
10 **Liao CD**, Lin LF, Huang YC, Huang SW, Chou LC, Liou TH. Functional outcomes of outpatient balance training following total knee replacement in patients with knee osteoarthritis: a randomized controlled trial. *Clin Rehabil* 2015; **29**: 855-867 [PMID: 25552523 DOI: 10.1177/0269215514564086]
11 **Chaipinyo K**, Karoonsupcharoen O. No difference between home-based strength training and home-based balance training on pain in patients with knee osteoarthritis: a randomised trial. *Aust J Physiother* 2009; **55**: 25-30 [PMID: 19226239 DOI: 10.1016/s0004-9514(09)70057-1]
12 **Sherrington C**, Whitney JC, Lord SR, Herbert RD, Cumming RG, Close JC. Effective exercise for the prevention of falls: a systematic review and meta-analysis. *J Am Geriatr Soc* 2008; **56**: 2234-2243 [PMID: 19093923 DOI: 10.1111/j.1532-5415.2008.02014.x]
13 **Wallis JA**, Webster KE, Levinger P, Singh PJ, Fong C, Taylor NF. A walking program for people with severe knee osteoarthritis did not reduce pain but may have benefits for cardiovascular health: a phase II randomised controlled trial. *Osteoarthritis Cartilage* 2017; **25**: 1969-1979 [PMID: 28011099 DOI: 10.1016/j.joca.2016.12.017]
14 **Wallis JA**, Webster KE, Levinger P, Singh PJ, Fong C, Taylor NF. The maximum tolerated dose of walking for people with severe osteoarthritis of the knee: a phase I trial. *Osteoarthritis Cartilage* 2015; **23**: 1285-1293 [PMID: 25882926 DOI: 10.1016/j.joca.2015.04.001]

15 **Alghadir AH**, Anwer S, Sarkar B, Paul AK, Anwar D. Effect of 6-week retro or forward walking program on pain, functional disability, quadriceps muscle strength, and performance in individuals with knee osteoarthritis: a randomized controlled trial (retro-walking trial). *BMC Musculoskelet Disord* 2019; **20**: 159 [PMID: 30967128 DOI: 10.1186/s12891-019-2537-9]

16 **Farrokhi S**, Jayabalan P, Gustafson JA, Klatt BA, Sowa GA, Piva SR. The influence of continuous versus interval walking exercise on knee joint loading and pain in patients with knee osteoarthritis. *Gait Posture* 2017; **56**: 129-133 [PMID: 28544950 DOI: 10.1016/j.gaitpost.2017.05.015]

17 **Skou ST**, Bricca A, Roos EM. The impact of physical activity level on the short- and long-term pain relief from supervised exercise therapy and education: a study of 12,796 Danish patients with knee osteoarthritis. *Osteoarthritis Cartilage* 2018; **26**: 1474-1478 [PMID: 30076884 DOI: 10.1016/j.joca.2018.07.010]

18 **Goh SL**, Persson MSM, Stocks J, Hou Y, Welton NJ, Lin J, Hall MC, Doherty M, Zhang W. Relative Efficacy of Different Exercises for Pain, Function, Performance and Quality of Life in Knee and Hip Osteoarthritis: Systematic Review and Network Meta-Analysis. *Sports Med* 2019; **49**: 743-761 [PMID: 30830561 DOI: 10.1007/s40279-019-01082-0]

19 **Kabiri S**, Halabchi F, Angoorani H, Yekaninejad S. Comparison of three modes of aerobic exercise combined with resistance training on the pain and function of patients with knee osteoarthritis: A randomized controlled trial. *Phys Ther Sport* 2018; **32**: 22-28 [PMID: 29677565 DOI: 10.1016/j.ptsp.2018.04.001]

20 **Suzuki Y**, Iijima H, Tashiro Y, Kajiwara Y, Zeidan H, Shimoura K, Nishida Y, Bito T, Nakai K, Tatsumi M, Yoshimi S, Tsuboyama T, Aoyama T. Home exercise therapy to improve muscle strength and joint flexibility effectively treats pre-radiographic knee OA in community-dwelling elderly: a randomized controlled trial. *Clin Rheumatol* 2019; **38**: 133-141 [PMID: 30167975 DOI: 10.1007/s10067-018-4263-3]

21 **Wang TJ**, Lee SC, Liang SY, Tung HH, Wu SF, Lin YP. Comparing the efficacy of aquatic exercises and land-based exercises for patients with knee osteoarthritis. *J Clin Nurs* 2011; **20**: 2609-2622 [PMID: 21539629 DOI: 10.1111/j.1365-2702.2010.03675.x]

22 **Allen KD**, Arbeeva L, Callahan LF, Golightly YM, Goode AP, Heiderscheit BC, Huffman KM, Severson HH, Schwartz TA. Physical therapy vs internet-based exercise training for patients with knee osteoarthritis: results of a randomized controlled trial. *Osteoarthritis Cartilage* 2018; **26**: 383-396 [PMID: 29307722 DOI: 10.1016/j.joca.2017.12.008]

23 **Deyle GD**, Allison SC, Matekel RL, Ryder MG, Stang JM, Gohdes DD, Hutton JP, Henderson NE, Garber MB. Physical therapy treatment effectiveness for osteoarthritis of the knee: a randomized comparison of supervised clinical exercise and manual therapy procedures versus a home exercise program. *Phys Ther* 2005; **85**: 1301-1317 [PMID: 16305269]

24 **Allen KD**, Bongiorni D, Bosworth HB, Coffman CJ, Datta SK, Edelman D, Hall KS, Lindquist JH, Oddone EZ, Hoenig H. Group Versus Individual Physical Therapy for Veterans With Knee Osteoarthritis: Randomized Clinical Trial. *Phys Ther* 2016; **96**: 597-608 [PMID: 26586865 DOI: 10.2522/ptj.20150194]

25 **Hurley MV**, Walsh NE, Mitchell H, Nicholas J, Patel A. Long-term outcomes and costs of an integrated rehabilitation program for chronic knee pain: a pragmatic, cluster randomized, controlled trial. *Arthritis Care Res (Hoboken)* 2012; **64**: 238-247 [PMID: 21954131 DOI: 10.1002/acr.20642]

26 **Jessep SA**, Walsh NE, Ratcliffe J, Hurley MV. Long-term clinical benefits and costs of an integrated rehabilitation programme compared with outpatient physiotherapy for chronic knee pain. *Physiotherapy* 2009; **95**: 94-102 [PMID: 19627690 DOI: 10.1016/j.physio.2009.01.005]

27 **Hurley MV**, Walsh N, Bhavnani V, Britten N, Stevenson F. Health beliefs before and after participation on an exercised-based rehabilitation programme for chronic knee pain: doing is believing. *BMC Musculoskelet Disord* 2010; **11**: 31 [PMID: 20149236 DOI: 10.1186/1471-2474-11-31]

28 **King LK**, March L, Anandacoomarasamy A. Obesity & osteoarthritis. *Indian J Med Res* 2013; **138**: 185-193 [PMID: 24056594]

29 **Christensen P**, Bliddal H, Riecke BF, Leeds AR, Astrup A, Christensen R. Comparison of a low-energy diet and a very low-energy diet in sedentary obese individuals: a pragmatic randomized controlled trial. *Clin Obes* 2011; **1**: 31-40 [PMID: 25586973 DOI: 10.1111/j.1758-8111.2011.00006.x]

30 **Coriolano K**, Aiken A, Harrison M, Pukall C, Brouwer B, Groll D. Changes in knee pain, perceived need for surgery, physical function and quality of life after dietary weight loss in obese women diagnosed with knee osteoarthritis. *Osteoarthritis Cartilage* 2013; **21**: S261 [DOI: 10.1016/j.joca.2013.02.542]

31 **Gersing AS**, Schwaiger BJ, Nevitt MC, Zarnowski J, Joseph GB, Feuerriegel G, Jungmann PM, Guimaraes JB, Facchetti L, McCulloch CE, Link TM. Weight loss regimen in obese and overweight individuals is associated with reduced cartilage degeneration: 96-month data from the Osteoarthritis Initiative. *Osteoarthritis Cartilage* 2019; **27**: 863-870 [PMID: 30825611 DOI: 10.1016/j.joca.2019.01.018]

32 **Aaboe J**, Bliddal H, Messier SP, Alkjær T, Henriksen M. Effects of an intensive weight loss program on knee joint loading in obese adults with knee osteoarthritis. *Osteoarthritis Cartilage* 2011; **19**: 822-828 [PMID: 21440076 DOI: 10.1016/j.joca.2011.03.006]

33 **Loeser RF**, Beavers DP, Bay-Jensen AC, Karsdal MA, Nicklas BJ, Guermazi A, Hunter DJ, Messier SP. Effects of dietary weight loss with and without exercise on interstitial matrix turnover and tissue inflammation biomarkers in adults with knee osteoarthritis: the Intensive Diet and Exercise for Arthritis trial (IDEA). *Osteoarthritis Cartilage* 2017; **25**: 1822-1828 [PMID: 28756278 DOI: 10.1016/j.joca.2017.07.015]

34 **Messier SP**, Loeser RF, Miller GD, Morgan TM, Rejeski WJ, Sevick MA, Ettinger WH Jr, Pahor M, Williamson JD. Exercise and dietary weight loss in overweight and obese older adults with knee osteoarthritis: the Arthritis, Diet, and Activity Promotion Trial. *Arthritis Rheum* 2004; **50**: 1501-1510 [PMID: 15146420 DOI: 10.1002/art.20256]

35 **Christensen P**, Henriksen M, Bartels EM, Leeds AR, Meinert Larsen T, Gudbergsen H, Riecke BF, Astrup A, Heitmann BL, Boesen M, Christensen R, Bliddal H. Long-term weight-loss maintenance in obese patients with knee osteoarthritis: a randomized trial. *Am J Clin Nutr* 2017; **106**: 755-763 [PMID: 28747328 DOI: 10.3945/ajcn.117.158543]

36 **Miceli-Richard C**, Le Bars M, Schmidely N, Dougados M. Paracetamol in osteoarthritis of the knee. *Ann Rheum Dis* 2004; **63**: 923-930 [PMID: 15249319 DOI: 10.1136/ard.2003.017236]

37 **Case JP**, Baliunas AJ, Block JA. Lack of efficacy of acetaminophen in treating symptomatic knee osteoarthritis: a randomized, double-blind, placebo-controlled comparison trial with diclofenac sodium. *Arch Intern Med* 2003; **163**: 169-178 [PMID: 12546607 DOI: 10.1001/archinte.163.2.169]

38 **Prior MJ**, Harrison DD, Frustaci ME. A randomized, double-blind, placebo-controlled 12 week trial of acetaminophen extended release for the treatment of signs and symptoms of osteoarthritis. *Curr Med Res Opin* 2014; **30**: 2377-2387 [PMID: 25121804 DOI: 10.1185/03007995.2014.949646]

39 **Altman RD**, Zinsenheim JR, Temple AR, Schweinle JE. Three-month efficacy and safety of acetaminophen extended-release for osteoarthritis pain of the hip or knee: a randomized, double-blind, placebo-controlled study. *Osteoarthritis Cartilage* 2007; **15**: 454-461 [PMID: 17142063 DOI: 10.1016/j.joca.2006.10.008]

40 **Leopoldino AO**, Machado GC, Ferreira PH, Pinheiro MB, Day R, McLachlan AJ, Hunter DJ, Ferreira ML. Paracetamol versus placebo for knee and hip osteoarthritis. *Cochrane Database Syst Rev* 2019; **2**: CD013273 [PMID: 30801133 DOI: 10.1002/14651858.CD013273]

41 **Pareek A**, Chandurkar N, Sharma VD, Desai M, Kini S, Bartakke G. A randomized, multicentric, comparative evaluation of aceclofenac-paracetamol combination with aceclofenac alone in Indian patients with osteoarthritis flare-up. *Expert Opin Pharmacother* 2009; **10**: 727-735 [PMID: 19351223 DOI: 10.1517/14656560902781931]

42 **Doherty M**, Hawkey C, Goulder M, Gibb I, Hill N, Aspley S, Reader S. A randomised controlled trial of ibuprofen, paracetamol or a combination tablet of ibuprofen/paracetamol in community-derived people with knee pain. *Ann Rheum Dis* 2011; **70**: 1534-1541 [PMID: 21804100 DOI: 10.1136/ard.2011.154047]

43 **National Clinical Guideline Centre (UK)**. Osteoarthritis: Care and Management in Adults. London: National Institute for Health and Care Excellence (UK); 2014 [PMID: 25340227]

44 **McAlindon TE**, Bannuru RR, Sullivan MC, Arden NK, Berenbaum F, Bierma-Zeinstra SM, Hawker GA, Henrotin Y, Hunter DJ, Kawaguchi H, Kwoh K, Lohmander S, Rannou F, Roos EM, Underwood M. OARSI guidelines for the non-surgical management of knee osteoarthritis. *Osteoarthritis Cartilage* 2014; **22**: 363-388 [PMID: 24462672 DOI: 10.1016/j.joca.2014.01.003]

45 **Gordo AC**, Walker C, Armada B, Zhou D. Efficacy of celecoxib versus ibuprofen for the treatment of patients with osteoarthritis of the knee: A randomized double-blind, non-inferiority trial. *J Int Med Res* 2017; **45**: 59-74 [PMID: 28222627 DOI: 10.1177/0300060516673707]

46 **Holt RJ**, Fort JG, Grahn AY, Kent JD, Bello AE. Onset and durability of pain relief in knee osteoarthritis: Pooled results from two placebo trials of naproxen/esomeprazole combination and celecoxib. *Phys Sportsmed* 2015; **43**: 200-212 [PMID: 26313454 DOI: 10.1080/00913847.2015.1074852]

47 **Chan FK**, Lanas A, Scheiman J, Berger MF, Nguyen H, Goldstein JL. Celecoxib versus omeprazole and diclofenac in patients with osteoarthritis and rheumatoid arthritis (CONDOR): a randomised trial. *Lancet* 2010; **376**: 173-179 [PMID: 20638563 DOI: 10.1016/S0140-6736(10)60673-3]

48 **Huang SP**, Wen YC, Huang ST, Lin CW, Wang TD, Hsiao FY. Nonsteroidal Anti-Inflammatory Drugs and Risk of First Hospitalization for Heart Failure in Patients with No History of Heart Failure: A Population-Based Case-Crossover Study. *Drug Saf* 2019; **42**: 67-75 [PMID: 30232741 DOI: 10.1007/s40264-018-0720-9]

49 **Helin-Salmivaara A**, Virtanen A, Vesalainen R, Grönroos JM, Klaukka T, Idänpään-Heikkilä JE, Huupponen R. NSAID use and the risk of hospitalization for first myocardial infarction in the general population: a nationwide case-control study from Finland. *Eur Heart J* 2006; **27**: 1657-1663 [PMID: 16731535 DOI: 10.1093/eurheartj/ehl053]

50 **Coxib and traditional NSAID Trialists' (CNT) Collaboration**, Bhala N, Emberson J, Merhi A, Abramson S, Arber N, Baron JA, Bombardier C, Cannon C, Farkouh ME, FitzGerald GA, Goss P, Halls H, Hawk E, Hawkey C, Hennekens C, Hochberg M, Holland LE, Kearney PM, Laine L, Lanas A, Lance P, Laupacis A, Oates J, Patrono C, Schnitzer TJ, Solomon S, Tugwell P, Wilson K, Wittes J, Baigent C. Vascular and upper gastrointestinal effects of non-steroidal anti-inflammatory drugs: meta-analyses of individual participant data from randomised trials. *Lancet* 2013; **382**: 769-779 [PMID: 23726390 DOI: 10.1016/S0140-6736(13)60900-9]

51 **Jevsevar DS**, Shores PB, Mullen K, Schulte DM, Brown GA, Cummins DS. Mixed Treatment Comparisons for Nonsurgical Treatment of Knee Osteoarthritis: A Network Meta-analysis. *J Am Acad Orthop Surg* 2018; **26**: 325-336 [PMID: 29688920 DOI: 10.5435/JAAOS-D-17-00318]

52 **Tugwell PS**, Wells GA, Shainhouse JZ. Equivalence study of a topical diclofenac solution (pennsaid) compared with oral diclofenac in symptomatic treatment of osteoarthritis of the knee: a randomized controlled trial. *J Rheumatol* 2004; **31**: 2002-2012 [PMID: 15468367]

53 **Underwood M**, Ashby D, Carnes D, Castelnuovo E, Cross P, Harding G, Hennessy E, Letley L, Martin J, Mt-Isa S, Parsons S, Spencer A, Vickers M, Whyte K. Topical or oral ibuprofen for chronic knee pain in older people. The TOIB study. *Health Technol Assess* 2008; **12**: iii-iiv, ix [PMID: 18505668 DOI: 10.3310/hta12220]

54 **Peloso PM**, Bellamy N, Bensen W, Thomson GT, Harsanyi Z, Babul N, Darke AC. Double blind randomized placebo control trial of controlled release codeine in the treatment of osteoarthritis of the hip or knee. *J Rheumatol* 2000; **27**: 764-771 [PMID: 10743822]

55 **Conaghan PG**, O'Brien CM, Wilson M, Schofield JP. Transdermal buprenorphine plus oral paracetamol vs an oral codeine-paracetamol combination for osteoarthritis of hip and/or knee: a randomised trial. *Osteoarthritis Cartilage* 2011; **19**: 930-938 [PMID: 21477658 DOI: 10.1016/j.joca.2011.03.011]

56 **Gana TJ**, Pascual ML, Fleming RR, Schein JR, Janagap CC, Xiang J, Vorsanger GJ; 023 Study Group. Extended-release tramadol in the treatment of osteoarthritis: a multicenter, randomized, double-blind, placebo-controlled clinical trial. *Curr Med Res Opin* 2006; **22**: 1391-1401 [PMID: 16834838 DOI: 10.1185/030079906X115595]

57 **Kosinski M**, Janagap C, Gajria K, Schein J, Freedman J. Pain relief and pain-related sleep disturbance with extended-release tramadol in patients with osteoarthritis. *Curr Med Res Opin* 2007; **23**: 1615-1626 [PMID: 17559754 DOI: 10.1185/030079907x199493]

58 **DeLemos BP**, Xiang J, Benson C, Gana TJ, Pascual ML, Rosanna R, Fleming B. Tramadol hydrochloride extended-release once-daily in the treatment of osteoarthritis of the knee and/or hip: a double-blind, randomized, dose-ranging trial. *Am J Ther* 2011; **18**: 216-226 [PMID: 20215961 DOI: 10.1097/MJT.0b013e3181cec307]

59 **Schnitzer TJ**, Kamin M, Olson WH. Tramadol allows reduction of naproxen dose among patients with naproxen-responsive osteoarthritis pain: a randomized, double-blind, placebo-controlled study. *Arthritis Rheum* 1999; **42**: 1370-1377 [PMID: 10403264 DOI: 10.1002/1529-0131(199907)42:7<1370::AID-ANR10>3.0.CO;2-T]

60 **Puljak L**. Can tramadol help adults with osteoarthritis? *J Musculoskelet Neuronal Interact* 2020; **20**: 1-3 [PMID: 32131364]

61 **Wilder-Smith CH**, Hill L, Osler W, O'Keefe S. Effect of tramadol and morphine on pain and gastrointestinal motor function in patients with chronic pancreatitis. *Dig Dis Sci* 1999; **44**: 1107-1116 [PMID: 10389680 DOI: 10.1023/a:1026607703352]

62 **Karlsson M**, Berggren AC. Efficacy and safety of low-dose transdermal buprenorphine patches (5, 10, and 20 microg/h) versus prolonged-release tramadol tablets (75, 100, 150, and 200 mg) in patients with chronic osteoarthritis pain: a 12-week, randomized, open-label, controlled, parallel-group noninferiority study. *Clin Ther* 2009; **31**: 503-513 [PMID: 19393841 DOI: 10.1016/j.clinthera.2009.03.001]

63 **Matsumoto AK**, Babul N, Ahdieh H. Oxymorphone extended-release tablets relieve moderate to severe pain and improve physical function in osteoarthritis: results of a randomized, double-blind, placebo- and active-controlled phase III trial. *Pain Med* 2005; **6**: 357-366 [PMID: 16266356 DOI: 10.1111/j.1526-4637.2005.00057.x]

64 **Caldwell JR**, Rapoport RJ, Davis JC, Offenberg HL, Marker HW, Roth SH, Yuan W, Eliot L, Babul N, Lynch PM. Efficacy and safety of a once-daily morphine formulation in chronic, moderate-to-severe osteoarthritis pain: results from a randomized, placebo-controlled, double-blind trial and an open-label extension trial. *J Pain Symptom Manage* 2002; **23**: 278-291 [PMID: 11997197 DOI: 10.1016/s0885-3924(02)00383-4]

65 **Bialas P**, Maier C, Klose P, Häuser W. Efficacy and harms of long-term opioid therapy in chronic non-cancer pain: Systematic review and meta-analysis of open-label extension trials with a study duration ≥26 weeks. *Eur J Pain* 2020; **24**: 265-278 [PMID: 31661587 DOI: 10.1002/ejp.1496]

66 **Krebs EE**, Gravely A, Nugent S, Jensen AC, DeRonne B, Goldsmith ES, Kroenke K, Bair MJ, Noorbaloochi S. Effect of Opioid vs Nonopioid Medications on Pain-Related Function in Patients With Chronic Back Pain or Hip or Knee Osteoarthritis Pain: The SPACE Randomized Clinical Trial. *JAMA* 2018; **319**: 872-882 [PMID: 29509867 DOI: 10.1001/jama.2018.0899]

67 **Beaulieu AD**, Peloso PM, Haraoui B, Bensen W, Thomson G, Wade J, Quigley P, Eisenhoffer J, Harsanyi Z, Darke AC. Once-daily, controlled-release tramadol and sustained-release diclofenac relieve chronic pain due to osteoarthritis: a randomized controlled trial. *Pain Res Manag* 2008; **13**: 103-110 [PMID: 18443672 DOI: 10.1155/2008/903784]

68 **Smith SR**, Deshpande BR, Collins JE, Katz JN, Losina E. Comparative pain reduction of oral non-steroidal anti-inflammatory drugs and opioids for knee osteoarthritis: systematic analytic review. *Osteoarthritis Cartilage* 2016; **24**: 962-972 [PMID: 26844640 DOI: 10.1016/j.joca.2016.01.135]

69 **Rolita L**, Spegman A, Tang X, Cronstein BN. Greater number of narcotic analgesic prescriptions for osteoarthritis is associated with falls and fractures in elderly adults. *J Am Geriatr Soc* 2013; **61**: 335-340 [PMID: 23452054 DOI: 10.1111/jgs.12148]

70 **Osani MC**, Lohmander LS, Bannuru RR. Is There Any Role for Opioids in the Management of Knee and Hip Osteoarthritis? *Arthritis Care Res (Hoboken)* 2021; **73**: 1413-1424 [PMID: 32583972 DOI: 10.1002/acr.24363]

71 **Welsch P**, Petzke F, Klose P, Häuser W. Opioids for chronic osteoarthritis pain: An updated systematic review and meta-analysis of efficacy, tolerability and safety in randomized placebo-controlled studies of at least 4 weeks double-blind duration. *Eur J Pain* 2020; **24**: 685-703 [PMID: 31876347 DOI: 10.1002/ejp.1522]

72 **Fuggle N**, Curtis E, Shaw S, Spooner L, Bruyère O, Ntani G, Parsons C, Conaghan PG, Corp N, Honvo G, Uebelhart D, Baird J, Dennison E, Reginster JY, Cooper C. Safety of Opioids in Osteoarthritis: Outcomes of a Systematic Review and Meta-Analysis. *Drugs Aging* 2019; **36**: 129-143 [PMID: 31073926 DOI: 10.1007/s40266-019-00666-9]

73 **Politzer CS**, Kildow BJ, Goltz DE, Green CL, Bolognesi MP, Seyler TM. Trends in Opioid Utilization Before and After Total Knee Arthroplasty. *J Arthroplasty* 2018; **33**: S147-S153.e1 [PMID: 29198871 DOI: 10.1016/j.arth.2017.10.060]

74 **Bell KL**, Shohat N, Goswami K, Tan TL, Kalbian I, Parvizi J. Preoperative Opioids Increase the Risk of Periprosthetic Joint Infection After Total Joint Arthroplasty. *J Arthroplasty* 2018; **33**: 3246-3251.e1 [PMID: 30054211 DOI: 10.1016/j.arth.2018.05.027]

75 **Weick J**, Bawa H, Dirschl DR, Luu HH. Preoperative Opioid Use Is Associated with Higher Readmission and Revision Rates in Total Knee and Total Hip Arthroplasty. *J Bone Joint Surg Am* 2018; **100**: 1171-1176 [PMID: 30020122 DOI: 10.2106/JBJS.17.01414]

76 **Smith SR**, Bido J, Collins JE, Yang H, Katz JN, Losina E. Impact of Preoperative Opioid Use on Total Knee Arthroplasty Outcomes. *J Bone Joint Surg Am* 2017; **99**: 803-808 [PMID: 28509820 DOI: 10.2106/JBJS.16.01200]

77 **Brock JL**, Jain N, Phillips FM, Malik AT, Khan SN. Postoperative opioid cessation rates based on preoperative opioid use: analysis of common orthopaedic procedures. *Bone Joint J* 2019; **101-B**: 1570-1577 [PMID: 31787005 DOI: 10.1302/0301-620X.101B12.BJJ-2019-0080.R2]

78 **DuPen A**, Shen D, Ersek M. Mechanisms of opioid-induced tolerance and hyperalgesia. *Pain Manag Nurs* 2007; **8**: 113-121 [PMID: 17723928 DOI: 10.1016/j.pmn.2007.02.004]

79 **Jevsevar DS**, Brown GA, Jones DL, Matzkin EG, Manner PA, Mooar P, Schousboe JT, Stovitz S, Sanders JO, Bozic KJ, Goldberg MJ, Martin WR 3rd, Cummins DS, Donnelly P, Woznica A, Gross L; American Academy of Orthopaedic Surgeons. The American Academy of Orthopaedic Surgeons evidence-based guideline on: treatment of osteoarthritis of the knee, 2nd edition. *J Bone Joint Surg Am* 2013; **95**: 1885-1886 [PMID: 24288804 DOI: 10.2106/00004623-201310160-00010]

80 **Bannuru RR**, Vaysbrot EE, Sullivan MC, McAlindon TE. Relative efficacy of hyaluronic acid in comparison with NSAIDs for knee osteoarthritis: a systematic review and meta-analysis. *Semin Arthritis Rheum* 2014; **43**: 593-599 [PMID: 24216297 DOI: 10.1016/j.semarthrit.2013.10.002]

81 **Tammachote N**, Kanitnate S, Yakumpor T, Panichkul P. Intra-Articular, Single-Shot Hylan G-F 20 Hyaluronic Acid Injection Compared with Corticosteroid in Knee Osteoarthritis: A Double-Blind, Randomized Controlled Trial. *J Bone Joint Surg Am* 2016; **98**: 885-892 [PMID: 27252432 DOI: 10.2106/JBJS.15.00544]

82 **Yavuz U**, Sökücü S, Albayrak A, Oztürk K. Efficacy comparisons of the intraarticular steroidal agents in the patients with knee osteoarthritis. *Rheumatol Int* 2012; **32**: 3391-3396 [PMID: 22057944 DOI: 10.1007/s00296-011-2188-0]

83 **Lomonte AB**, de Morais MG, de Carvalho LO, Zerbini CA. Efficacy of Triamcinolone Hexacetonide versus Methylprednisolone Acetate Intraarticular Injections in Knee Osteoarthritis: A Randomized, Double-blinded, 24-week Study. *J Rheumatol* 2015; **42**: 1677-1684 [PMID: 26136485 DOI: 10.3899/jrheum.150297]

84 **Dávila-Parrilla A**, Santaella-Santé B, Otero-López A. Does Injection Site Matter? *Bol Asoc Med P R* 2015; **107**: 78-81 [PMID: 26434090]

85 **Henriksen M**, Christensen R, Klokker L, Bartholdy C, Bandak E, Ellegaard K, Boesen MP, Riis RG, Bartels EM, Bliddal H. Evaluation of the benefit of corticosteroid injection before exercise therapy in patients with osteoarthritis of the knee: a randomized clinical trial. *JAMA Intern Med* 2015; **175**: 923-930 [PMID: 25822572 DOI: 10.1001/jamainternmed.2015.0461]

86 **Deyle GD**, Gill NW, Rhon DI, Allen CS, Allison SC, Hando BR, Petersen EJ, Dusenberry DI, Bellamy N. A multicenter randomised, 1-year comparative effectiveness, parallel-group trial protocol of a physical therapy approach compared to corticosteroid injection on pain and function related to knee osteoarthritis (PTA Trial). *BMJ Open* 2016; **6**: e010528 [PMID: 27033961 DOI: 10.1136/bmjopen-2015-010528]

87 **McAlindon TE**, LaValley MP, Harvey WF, Price LL, Driban JB, Zhang M, Ward RJ. Effect of Intra-articular Triamcinolone vs Saline on Knee Cartilage Volume and Pain in Patients With Knee Osteoarthritis: A Randomized Clinical Trial. *JAMA* 2017; **317**: 1967-1975 [PMID: 28510679 DOI: 10.1001/jama.2017.5283]

88 **Raynauld JP**, Buckland-Wright C, Ward R, Choquette D, Haraoui B, Martel-Pelletier J, Uthman I, Khy V, Tremblay JL, Bertrand C, Pelletier JP. Safety and efficacy of long-term intraarticular steroid injections in osteoarthritis of the knee: a randomized, double-blind, placebo-controlled trial. *Arthritis Rheum* 2003; **48**: 370-377 [PMID: 12571845 DOI: 10.1002/art.10777]

89 **Zeng C**, Lane NE, Hunter DJ, Wei J, Choi HK, McAlindon TE, Li H, Lu N, Lei G, Zhang Y. Intra-articular corticosteroids and the risk of knee osteoarthritis progression: results from the Osteoarthritis Initiative. *Osteoarthritis Cartilage* 2019; **27**: 855-862 [PMID: 30703543 DOI: 10.1016/j.joca.2019.01.007]

90 **Leighton R**, Akermark C, Therrien R, Richardson JB, Andersson M, Todman MG, Arden NK; DUROLANE Study Group. NASHA hyaluronic acid vs. methylprednisolone for knee osteoarthritis: a prospective, multi-centre, randomized, non-inferiority trial. *Osteoarthritis Cartilage* 2014; **22**: 17-25 [PMID: 24185114 DOI: 10.1016/j.joca.2013.10.009]

91 **Ozturk C**, Atamaz F, Hepguler S, Argin M, Arkun R. The safety and efficacy of intraarticular hyaluronan with/without corticosteroid in knee osteoarthritis: 1-year, single-blind, randomized study. *Rheumatol Int* 2006; **26**: 314-319 [PMID: 15703953 DOI: 10.1007/s00296-005-0584-z]

92 **Johansen M**, Bahrt H, Altman RD, Bartels EM, Juhl CB, Bliddal H, Lund H, Christensen R. Exploring reasons for the observed inconsistent trial reports on intra-articular injections with hyaluronic acid in the treatment of osteoarthritis: Meta-regression analyses of randomized trials. *Semin Arthritis Rheum* 2016; **46**: 34-48 [PMID: 27139169 DOI: 10.1016/j.semarthrit.2016.02.010]

93 **Navarro-Sarabia F**, Coronel P, Collantes E, Navarro FJ, de la Serna AR, Naranjo A, Gimeno M, Herrero-Beaumont G; AMELIA study group. A 40-month multicentre, randomised placebo-controlled study to assess the efficacy and carry-over effect of repeated intra-articular injections of hyaluronic acid in knee osteoarthritis: the AMELIA project. *Ann Rheum Dis* 2011; **70**: 1957-1962 [PMID: 21852252 DOI: 10.1136/ard.2011.152017]

94 **Neustadt D**, Caldwell J, Bell M, Wade J, Gimbel J. Clinical effects of intraarticular injection of high molecular weight hyaluronan (Orthovisc) in osteoarthritis of the knee: a randomized, controlled, multicenter trial. *J Rheumatol* 2005; **32**: 1928-1936 [PMID: 16206349]

95 **Deal CL**, Schnitzer TJ, Lipstein E, Seibold JR, Stevens RM, Levy MD, Albert D, Renold F. Treatment of arthritis with topical capsaicin: a double-blind trial. *Clin Ther* 1991; **13**: 383-395 [PMID: 1954640]

96 **Kosuwon W**, Sirichatiwapee W, Wisanuyotin T, Jeeravipoolvarn P, Laupattarakasem W. Efficacy of symptomatic control of knee osteoarthritis with 0.0125% of capsaicin versus placebo. *J Med Assoc Thai* 2010; **93**: 1188-1195 [PMID: 20973322]

97 **Schnitzer TJ**, Pelletier JP, Haselwood DM, Ellison WT, Ervin JE, Gordon RD, Lisse JR, Archambault WT, Sampson AR, Fezatte HB, Phillips SB, Bernstein JE. Civamide cream 0.075% in patients with osteoarthritis of the knee: a 12-week randomized controlled clinical trial with a longterm extension. *J Rheumatol* 2012; **39**: 610-620 [PMID: 22089461 DOI: 10.3899/jrheum.110192]

98 **McCleane G**. The analgesic efficacy of topical capsaicin is enhanced by glyceryl trinitrate in painful osteoarthritis: a randomized, double blind, placebo controlled study. *Eur J Pain* 2000; **4**: 355-360 [PMID: 11124007 DOI: 10.1053/eujp.2000.0200]

99 **Conaghan PG**, Dickson J, Bolten W, Cevc G, Rother M. A multicentre, randomized, placebo- and active-controlled trial comparing the efficacy and safety of topical ketoprofen in Transfersome gel (IDEA-033) with ketoprofen-free vehicle (TDT 064) and oral celecoxib for knee pain associated with osteoarthritis. *Rheumatology (Oxford)* 2013; **52**: 1303-1312 [PMID: 23542612 DOI: 10.1093/rheumatology/ket133]

100 **Kneer W**, Rother M, Mazgareanu S, Seidel EJ; European IDEA-033 study group. A 12-week randomized study of topical therapy with three dosages of ketoprofen in Transfersome® gel (IDEA-033) compared with the ketoprofen-free vehicle (TDT 064), in patients with osteoarthritis of the knee. *J Pain Res* 2013; **6**: 743-753 [PMID: 24187510 DOI: 10.2147/JPR.S51054]

101 **Rother M**, Conaghan PG. A randomized, double-blind, phase III trial in moderate osteoarthritis knee pain comparing topical ketoprofen gel with ketoprofen-free gel. *J Rheumatol* 2013; **40**: 1742-1748 [PMID: 23996292 DOI: 10.3899/jrheum.130192]

102 **Rother M**, Lavins BJ, Kneer W, Lehnhardt K, Seidel EJ, Mazgareanu S. Efficacy and safety of epicutaneous ketoprofen in Transfersome (IDEA-033) versus oral celecoxib and placebo in osteoarthritis of the knee: multicentre randomised controlled trial. *Ann Rheum Dis* 2007; **66**: 1178-1183 [PMID: 17363401 DOI: 10.1136/ard.2006.065128]

103 **National Institute for Health and Care Excellence**. FLEXISEQ for osteoarthritis. 2016 [cited 2021 Mar 24]. Available

fom: www.nice.org.uk/guidance/mib80

104 **Atamaz FC**, Durmaz B, Baydar M, Demircioglu OY, Iyiyapici A, Kuran B, Oncel S, Sendur OF. Comparison of the efficacy of transcutaneous electrical nerve stimulation, interferential currents, and shortwave diathermy in knee osteoarthritis: a double-blind, randomized, controlled, multicenter study. *Arch Phys Med Rehabil* 2012; **93**: 748-756 [PMID: 22459699 DOI: 10.1016/j.apmr.2011.11.037]

105 **Cheing GL**, Tsui AY, Lo SK, Hui-Chan CW. Optimal stimulation duration of tens in the management of osteoarthritic knee pain. *J Rehabil Med* 2003; **35**: 62-68 [PMID: 12691335 DOI: 10.1080/16501970306116]

106 **Fary RE**, Carroll GJ, Briffa TG, Briffa NK. The effectiveness of pulsed electrical stimulation in the management of osteoarthritis of the knee: results of a double-blind, randomized, placebo-controlled, repeated-measures trial. *Arthritis Rheum* 2011; **63**: 1333-1342 [PMID: 21312188 DOI: 10.1002/art.30258]

107 **Brouwer RW**, van Raaij TM, Verhaar JA, Coene LN, Bierma-Zeinstra SM. Brace treatment for osteoarthritis of the knee: a prospective randomized multi-centre trial. *Osteoarthritis Cartilage* 2006; **14**: 777-783 [PMID: 16563810 DOI: 10.1016/j.joca.2006.02.004]

108 **Yu SP**, Williams M, Eyles JP, Chen JS, Makovey J, Hunter DJ. Effectiveness of knee bracing in osteoarthritis: pragmatic trial in a multidisciplinary clinic. *Int J Rheum Dis* 2016; **19**: 279-286 [PMID: 26558446 DOI: 10.1111/1756-185X.12796]

109 **Squyer E**, Stamper DL, Hamilton DT, Sabin JA, Leopold SS. Unloader knee braces for osteoarthritis: do patients actually wear them? *Clin Orthop Relat Res* 2013; **471**: 1982-1991 [PMID: 23378240 DOI: 10.1007/s11999-013-2814-0]

110 **Duivenvoorden T**, van Raaij TM, Horemans HL, Brouwer RW, Bos PK, Bierma-Zeinstra SM, Verhaar JA, Reijman M. Do laterally wedged insoles or valgus braces unload the medial compartment of the knee in patients with osteoarthritis? *Clin Orthop Relat Res* 2015; **473**: 265-274 [PMID: 25267266 DOI: 10.1007/s11999-014-3947-5]

111 **Jones RK**, Chapman GJ, Forsythe L, Parkes MJ, Felson DT. The relationship between reductions in knee loading and immediate pain response whilst wearing lateral wedged insoles in knee osteoarthritis. *J Orthop Res* 2014; **32**: 1147-1154 [PMID: 24903067 DOI: 10.1002/jor.22666]

112 **Lewinson RT**, Vallerand IA, Collins KH, Wiley JP, Lun VMY, Patel C, Woodhouse LJ, Reimer RA, Worobets JT, Herzog W, Stefanyshyn DJ. Reduced knee adduction moments for management of knee osteoarthritis:: A three month phase I/II randomized controlled trial. *Gait Posture* 2016; **50**: 60-68 [PMID: 27580080 DOI: 10.1016/j.gaitpost.2016.08.027]

113 **Pham T**, Maillefert JF, Hudry C, Kieffert P, Bourgeois P, Lechevalier D, Dougados M. Laterally elevated wedged insoles in the treatment of medial knee osteoarthritis. A two-year prospective randomized controlled study. *Osteoarthritis Cartilage* 2004; **12**: 46-55 [PMID: 14697682 DOI: 10.1016/j.joca.2003.08.011]

114 **Bennell KL**, Bowles KA, Payne C, Cicuttini F, Williamson E, Forbes A, Hanna F, Davies-Tuck M, Harris A, Hinman RS. Lateral wedge insoles for medial knee osteoarthritis: 12 month randomised controlled trial. *BMJ* 2011; **342**: d2912 [PMID: 21593096 DOI: 10.1136/bmj.d2912]

115 **Shimada S**, Kobayashi S, Wada M, Uchida K, Sasaki S, Kawahara H, Yayama T, Kitade I, Kamei K, Kubota M, Baba H. Effects of disease severity on response to lateral wedged shoe insole for medial compartment knee osteoarthritis. *Arch Phys Med Rehabil* 2006; **87**: 1436-1441 [PMID: 17084116 DOI: 10.1016/j.apmr.2006.08.018]

116 **Toda Y**, Segal N, Kato A, Yamamoto S, Irie M. Correlation between body composition and efficacy of lateral wedged insoles for medial compartment osteoarthritis of the knee. *J Rheumatol* 2002; **29**: 541-545 [PMID: 11908570]

117 **Clarke GR**, Willis LA, Stenners L, Nichols PJ. Evaluation of physiotherapy in the treatment of osteoarthrosis of the knee. *Rheumatol Rehabil* 1974; **13**: 190-197 [PMID: 4445714 DOI: 10.1093/rheumatology/13.4.190]

118 **Hecht PJ**, Bachmann S, Booth RE Jr, Rothman RH. Effects of thermal therapy on rehabilitation after total knee arthroplasty. A prospective randomized study. *Clin Orthop Relat Res* 1983; 198-201 [PMID: 6883850]

119 **Yurtkuran M**, Kocagil T. TENS, electroacupuncture and ice massage: comparison of treatment for osteoarthritis of the knee. *Am J Acupunct* 1999; **27**: 133-140 [PMID: 10729968]

120 **Aciksoz S**, Akyuz A, Tunay S. The effect of self-administered superficial local hot and cold application methods on pain, functional status and quality of life in primary knee osteoarthritis patients. *J Clin Nurs* 2017; **26**: 5179-5190 [PMID: 28880416 DOI: 10.1111/jocn.14070]

121 **Denegar CR**, Dougherty DR, Friedman JE, Schimizzi ME, Clark JE, Comstock BA, Kraemer WJ. Preferences for heat, cold, or contrast in patients with knee osteoarthritis affect treatment response. *Clin Interv Aging* 2010; **5**: 199-206 [PMID: 20711439 DOI: 10.2147/cia.s11431]

122 **Clegg DO**, Reda DJ, Harris CL, Klein MA, O'Dell JR, Hooper MM, Bradley JD, Bingham CO 3rd, Weisman MH, Jackson CG, Lane NE, Cush JJ, Moreland LW, Schumacher HR Jr, Oddis CV, Wolfe F, Molitor JA, Yocum DE, Schnitzer TJ, Furst DE, Sawitzke AD, Shi H, Brandt KD, Moskowitz RW, Williams HJ. Glucosamine, chondroitin sulfate, and the two in combination for painful knee osteoarthritis. *N Engl J Med* 2006; **354**: 795-808 [PMID: 16495392 DOI: 10.1056/NEJMoa052771]

123 **Sawitzke AD**, Shi H, Finco MF, Dunlop DD, Bingham CO 3rd, Harris CL, Singer NG, Bradley JD, Silver D, Jackson CG, Lane NE, Oddis CV, Wolfe F, Lisse J, Furst DE, Reda DJ, Moskowitz RW, Williams HJ, Clegg DO. The effect of glucosamine and/or chondroitin sulfate on the progression of knee osteoarthritis: a report from the glucosamine/chondroitin arthritis intervention trial. *Arthritis Rheum* 2008; **58**: 3183-3191 [PMID: 18821708 DOI: 10.1002/art.23973]

124 **Fransen M**, Agaliotis M, Nairn L, Votrubec M, Bridgett L, Su S, Jan S, March L, Edmonds J, Norton R, Woodward M, Day R; LEGS study collaborative group. Glucosamine and chondroitin for knee osteoarthritis: a double-blind randomised placebo-controlled clinical trial evaluating single and combination regimens. *Ann Rheum Dis* 2015; **74**: 851-858 [PMID: 24395557 DOI: 10.1136/annrheumdis-2013-203954]

125 **Reginster JY**, Dudler J, Blicharski T, Pavelka K. Pharmaceutical-grade Chondroitin sulfate is as effective as celecoxib and superior to placebo in symptomatic knee osteoarthritis: the ChONdroitin versus CElecoxib versus Placebo Trial (CONCEPT). *Ann Rheum Dis* 2017; **76**: 1537-1543 [PMID: 28533290 DOI: 10.1136/annrheumdis-2016-210860]

126 **Hochberg MC**, Martel-Pelletier J, Monfort J, Möller I, Castillo JR, Arden N, Berenbaum F, Blanco FJ, Conaghan PG, Doménech G, Henrotin Y, Pap T, Richette P, Sawitzke A, du Souich P, Pelletier JP; MOVES Investigation Group.

Combined chondroitin sulfate and glucosamine for painful knee osteoarthritis: a multicentre, randomised, double-blind, non-inferiority trial versus celecoxib. *Ann Rheum Dis* 2016; **75**: 37-44 [PMID: 25589511 DOI: 10.1136/annrheumdis-2014-206792]

127 **Ma H**, Li X, Sun D, Zhou T, Ley SH, Gustat J, Heianza Y, Qi L. Association of habitual glucosamine use with risk of cardiovascular disease: prospective study in UK Biobank. *BMJ* 2019; **365**: l1628 [PMID: 31088786 DOI: 10.1136/bmj.l1628]

128 **Demehri S**, Hafezi Nejad N, Roemer F, Guermazi A. Chondroitin sulfate and glucosamine supplementation is associated with higher incidence of radiographic knee osteoarthritis and subsequent knee replacement: nine years of follow-up data from the osteoarthritis initiative. *Osteoarthritis Cartilage* 2016; **24**: S307 [DOI: 10.1016/j.joca.2016.01.554]

129 **Cagnie B**, Dewitte V, Barbe T, Timmermans F, Delrue N, Meeus M. Physiologic effects of dry needling. *Curr Pain Headache Rep* 2013; **17**: 348 [PMID: 23801002 DOI: 10.1007/s11916-013-0348-5]

130 **Ceballos-Laita L**, Jiménez-Del-Barrio S, Marín-Zurdo J, Moreno-Calvo A, Marín-Boné J, Albarova-Corral MI, Estébanez-de-Miguel E. Effects of dry needling in HIP muscles in patients with HIP osteoarthritis: A randomized controlled trial. *Musculoskelet Sci Pract* 2019; **43**: 76-82 [PMID: 31352178 DOI: 10.1016/j.msksp.2019.07.006]

131 **Itoh K**, Hirota S, Katsumi Y, Ochi H, Kitakoji H. Trigger point acupuncture for treatment of knee osteoarthritis--a preliminary RCT for a pragmatic trial. *Acupunct Med* 2008; **26**: 17-26 [PMID: 18356795 DOI: 10.1136/aim.26.1.17]

132 **Sánchez-Romero EA**, Pecos-Martín D, Calvo-Lobo C, Ochoa-Sáez V, Burgos-Caballero V, Fernández-Carnero J. Effects of dry needling in an exercise program for older adults with knee osteoarthritis: A pilot clinical trial. *Medicine (Baltimore)* 2018; **97**: e11255 [PMID: 29952993 DOI: 10.1097/MD.0000000000011255]

133 **Sánchez Romero EA**, Fernández-Carnero J, Calvo-Lobo C, Ochoa Sáez V, Burgos Caballero V, Pecos-Martín D. Is a Combination of Exercise and Dry Needling Effective for Knee OA? *Pain Med* 2020; **21**: 349-363 [PMID: 30889250 DOI: 10.1093/pm/pnz036]

134 **Sánchez Romero EA**, Fernández Carnero J, Villafañe JH, Calvo-Lobo C, Ochoa Sáez V, Burgos Caballero V, Laguarta Val S, Pedersini P, Pecos Martín D. Prevalence of Myofascial Trigger Points in Patients with Mild to Moderate Painful Knee Osteoarthritis: A Secondary Analysis. *J Clin Med* 2020; **9** [PMID: 32784592 DOI: 10.3390/jcm9082561]

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MINIREVIEWS

Patient-specific instrumentation in total ankle arthroplasty

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Abstract

The recent increase in the adoption of total ankle arthroplasty (TAA) reflects the improvements in implant designs and surgical techniques, including the use of preoperative navigation system and patient-specific instrumentation (PSI), such as custom-made cutting guides. Cutting guides are customized with respect to each patient's anatomy based on preoperative ankle computed tomography scans, and they drive the saw intra-operatively to improve the accuracy of bone resection and implant positioning. Despite some promising results, the main queries in the literature are whether PSI improves the reliability of achieving neutral ankle alignment and more accurate implant sizing, whether it is actually superior over standard techniques, and whether it is cost effective. Moreover, the advantages of PSI in clinical outcomes are still theoretical because the current literature does not allow to confirm its superiority. The purpose of this review article is therefore to assess the current literature on PSI in TAA with regard to current implants with PSI, templating and preoperative planning strategies, alignment and sizing, clinical outcomes, cost analysis, and comparison with standard techniques.

Key Words: Total ankle arthroplasty; Total ankle replacement; Patient-specific instrumentation; Ankle computer navigation system; Preoperative navigation; Prophecy; Infinity; INBONE II

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Core Tip: The recent increase in the adoption of total ankle arthroplasty (TAA) reflects the improvements in implant designs and surgical techniques, including the use of preoperative navigation system and patient-specific instrumentation (PSI). The outcomes of TAA have generally been less satisfactory compared to those of other arthroplasties. Preoperative planning using PSI theoretically improves implant positioning and alignment. This review article assess the current literature regarding PSI in TAA.

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INTRODUCTION

The recent increase in the adoption of total ankle arthroplasty (TAA) reflects the improvements in implant designs and surgical techniques. Nonetheless, the outcomes of TAA have commonly been less satisfactory compared to those of other arthroplasties[1]. Thus, the search for successful TAA continues, and in fact, the interest in implementing this new technology is growing.

The literature on the subject has shown that proper implant positioning and alignment are necessary for achieving good results in TAA. Even the mispositioning of a small implant component has a relevant impact on motion and contact pressure, which may lead to failure[2,3].

As a matter of fact, most of the current TAA instrumentations do not really address patient's variable anatomical features. When using a traditional system, the main parameter considered for tibial cutting block is represented by the tibial tuberosity as proximal reference and the middle of the anterior border of the tibiotalar joint as distal reference. The talar resection is performed with the foot in a visual neutral position[2,3]. This technique allows an experienced surgeon to adopt a good implant positioning; however, many other factors should be considered in order to fully re-establish gait symmetry and natural ankle motion.

Much as with hip and knee arthroplasty, large efforts have been devoted to improving TAA surgical techniques, including the use of preoperative plans based on computer software, and patient-specific instrumentation (PSI), such as custom-made cutting guides. Cutting guides are customized with respect to each patient's anatomy based on preoperative ankle computed tomography (CT) scans, and they drive the saw intra-operatively to improve the accuracy of bone resection and implant posi-tioning.

Nevertheless, there is no unanimous agreement regarding the indication and efficacy of PSI in TAA [4]. The purpose of this review article is therefore to assess the current literature on PSI in TAA. In particular, we will discuss the following topics: (1) Current implants with PSI; (2) Templating and preoperative planning strategies; (3) Alignment and sizing; (4) Clinical outcomes; (5) Cost analysis; and (6) Comparison with standard techniques.

TYPES OF IMPLANTS

Only three implants with PSI for TAA are currently available (Table 1): The INFINITY TAA (Wright Medical Technology Inc, Arlington, TN, United States). The INBONE II Total Ankle System (Wright Medical Technology Inc), and a custom-made version of the BOX TAA (MatOrtho, Ltd., Leatherhead, United Kingdom).

The INFINITY TAA

This implant has a 2-component fixed bearing design, with a low-profile tibia and talar resurfacing, and requires minimal bone resection. The tibial resurfacing component is made of titanium alloy and presents three angled pegs, whilst the talar component has two pegs and is made of cobalt chrome alloy. The INFINITY TAA can be implanted using a CT scan-derived PSI through the PROPHECY Preoperative Navigation System (Wright Medical Technology Inc)[5,6].

The INBONE II total ankle system

This implant is an evolution of the original INBONE design and consists of an intramedullary fixed-bearing two-component design with a polyethylene bearing surface locked into the tibial baseplate. The system retains some main features of the INBONE I design and instrumentations, including the modular tibial stems, thicker polyethylene bearings, and intramedullary guidance. In addition, the INBONE II total ankle system has certain enhancements, including sulcus articulation, additional talar fixation, anteroposterior long tibial trays, trial reduction placement of the talar component, and bone

Table 1 Summary of all actual studies about patient-specific instrumentation in total ankle arthroplasty

Author	Implant type	Study type	No patients	Navigation system	Tibial implant size predicted	Talar implant size predicted	Implant positioning accuracy	Neutral alignment	Comparison with standard technique
Berlet *et al* [10] (2014)	INBONE	Cadaveric study	15 lower limb	PROPHECY			Within 3 degree and translational within 2 mm		
Hsu *et al* [11] (2015)	INBONE II *vs* INFINITY	Retrospective case series	42	PROPHECY	100% INBONEII *vs* 92% INFINITY	76% INBONEII *vs* 46% INFINITY	± 3° coronal and sagittal	100%	
Hanselman *et al*[12] (2015)	INBONE II	Case report	1	PROPHECY				Yes	
Daigre *et al* [13] (2017)	INBONE II	Retrospective multicenter study	44	PROPHECY	98%	80%	< 3° (79.5%), < 4° (88.6%), < 5° (100%)	93.2%	
Saito *et al*[1] (2019)	INFINITY	Retrospective study	99 (75 PSI - 24 SRG)	PROPHECY	73%	51%	Coronal: SRG: 88% < 3°, 8% from 3° to 5°, 4% > 5°; PSI: 85.3% < 3°, 3.3% from 3° to 5°, 1.3% > 5°. Sagittal: SRG: 88% < 3°, 8% from 3° to 5°, 4% > 5°; PSI: 85% < 3° of deviation, 11% from 3° to 5°, 4 % > 5°	100% in PSI *vs* 96% in SRG	$P = 0.884$ not statistically different
Faldini *et al* [8] (2020)	BOX	Case report	1	GEOMAGIC CONTROL	-	-	-	Yes	-

PSI: Patient-specific instrumentation; SRG: Standard Referencing Guide.

removal instrumentation. This new sulcus design has twice as much coronal plane stability as the saddle design of the INBONE I TAA; moreover, it has two 4-mm anterior pegs in addition to the single talar stem design of the INBONE I component, resulting in increased rotational stability[7]. The INBONE II total ankle system can be implanted using a CT scan-derived PSI through the PROPHECY Preoperative Navigation System (Wright Medical Technology Inc).

Custom-made version of the BOX TAA

A three-component implant, with cast cobalt-chrome-molybdenum alloy components fixed to the body of the talus and the distal portion of the tibia, along with an interposed mobile biconcave meniscal bearing, designed to be compatible with the movements of isometric fibers within the calcaneofibular and tibiocalcaneal ankle ligaments[8,9]. The custom-made BOX TAA can be implanted using a CT scan-derived PSI with GeoMagic Control (3D Systems, Inc).

Considering the low number of implants available on the market, there are also few studies in the pertaining literature regarding PSI for TAA, as reported in Table 1.

TEMPLATING AND PREOPERATIVE PLANNING STRATEGIES

Templating in joint prosthetic surgery facilitates alignment optimization, helps in the selection of the correct implant size, and leads to more reliable and consistent prosthesis placement, theoretically lowering the risk of intra-operative complications.

While pre-operative templating is of great importance in planning hip and knee arthroplasty, its role in TAA is less clear.

Traditional preoperative planning methods for TAA are based on antero-posterior (AP) and lateral weight-bearing radiographs. Standard technique uses the tibial tuberosity as a point of reference and is based on the principle that the mechanical axis of the tibia (MAT) should equal the anatomical axis of the tibia (AAT)[14].

Differently from standard techniques, preoperative planning using PSI for TAA is initiated by obtaining preoperative ankle CT imaging, according to manufacturer established protocols, in order to create the patient-specific 3D model. Although with some differences, all computer navigation systems require preoperative CT scans from the knee through the mid-foot.

CT scans allow us to assess preoperative coronal plane deformity, sagittal plane deformity, and rotational deformity, as well as permitting an evaluation of MAT, and AAT alignments.

On the coronal plane, varus or valgus deformity should be determined (neutral alignment is considered as less than 5 degrees of varus or valgus[4]). The tibial slope must be measured in the sagittal plane considering the anterior distal tibial angle, the angle between the AAT, and the line connecting the distal points on the anterior and posterior tibial articular surface (normal values: 83.0 ± 3.6 degrees)[15].

All these measurements can deviate significantly depending on several factors, such as congenital or post-traumatic femoral or/and tibial deformities[16]. More frequently, in the presence of coronal deformity, AAT deviation from the MAT is accentuated.

In the past, ankle coronal and sagittal plane deformities represented a contraindication to TAA[17]. The recent literature shows a trend toward extending the indication of TAA even in the case of severe deformities. During the templating, deformity correction must be evaluated and addressed. Realignment procedures can be performed before TAA surgery or simultaneously to the prosthesis implantation, acting on bone or soft tissue structures depending on patho-anatomy[18,19].

In addition, during pre-operative planning, the prosthesis size and corresponding bone cuts to prepare implant accommodation and its best possible position should always be considered[8].

Very few reports have evaluated the reliability of templating with PSI. In 2007, Adams *et al*[20] were the first to apply computer-assisted surgery for TAA in a cadaver study. Seven matched-pair lower extremities were used. One leg from each pair was randomized for the conventional tibial preparation arm of the study, using the external alignment guide and tibial cutting block from the Scandinavian Total Ankle Replacement system (STAR, Waldemar Link GmbH & Co., Hamburg, Germany). Since dedicated TAA software did not exist at the time of the study, the other leg from each matched pair underwent computer-assisted tibial cut preparation using the VectorVision navigation system (BrainLAB, Munich, Germany) with total knee arthroplasty software. Pre-operative CT data was used to assess the tibial mechanical axis. In both groups, the accuracy of the tibial plafond preparation relative to the tibial shaft axis in both the coronal and sagittal planes was determined by fluoroscopic, radiographic, and CT analysis. Although the conventional and the computer-assisted measurements were not statistically different when compared to one another, the development of computer-navigation software specific to TAA continued.

The first PSI system for TAA that was able to provide a preoperative plan is the PROPHECY INBONE II and PROPHECY INFINITY Preoperative Navigation System. As in other forms of navigation-assisted surgery, the software generates a highly accurate rendering of the patient's bony anatomy. This technology allows the surgeon to interact with the computer model and develop the surgical strategy through stepwise considerations. This process identifies loose bodies, the osteophytes' location, size, and shape, the presence of bone deficits, the 3-plane nature of any preexisting deformity, and the desired features, position, and size of the final implants.

The PROPHECY template calculates the preoperative deformity and the MAT *vs* the AAT based on anatomic landmarks. Anatomic landmarks are established in order to determine tibia/talus alignment achieving neutral axes. According to Berlet *et al*[10], the tibia landmarks are: The proximal tibia, the distal tibia, the proximal anatomic canal, and the distal medial and lateral gutter. The talus landmarks are: The talar neck, and the proximal medial and lateral gutter. These landmarks are used to combine the 3D bone model with 3D computer-assisted design (CAD) models of the implants and instrumentation to perform a virtual TAA implantation. Implant positioning is usually based on the AAT[13], but the choice is at the discretion of the surgeon[17]. Once templating and preoperative planning are approved, patient-specific guides that reference bony anatomy are built through selective laser sintering.

The first study using the PROPHECY system was conducted by Berlet *et al*[10] in 2014 in order to evaluate the reproducibility of tibia and talus patient-specific guide placement and variation between the pre-operative plan and real component position. Fifteen cadaveric lower extremities were scanned and imported into a CAD environment which created the 3D models based on the ankle CT scan. The 3D bone models were combined with the 3D CAD models of the implants and instrumentation to perform a virtual TAA after choosing the appropriate implant size and position. Patient-specific guides were then manufactured to define the resection planes, and the final implant position was recorded. Mean deviation among pre- and post-operative implant position was less than 2° and 1.4 mm[10].

This preoperative planning strategy has been proposed in other clinical studies, demonstrating overall positive accuracy and reproducibility[1,11,13].

More recently, a new and complete TAA customization process was introduced by Faldini *et al*[8], consisting of patient-specific 3D-printed implants and instrumentation. Images obtained from a CT scan were processed for a 3D customized model of the ankle and the BOX ankle prosthesis (MatOrtho, United Kingdom). Using GeoMagic Control (3D Systems, SC), TAA was performed virtually by selecting the most suitable size for each implant according to the dimensions of the joint about to be replaced. Through the use of GeoMagic Control, it was possible to retrieve the corresponding bone resections and the corresponding PSI, designed to perfectly fit the frontal bone of the ankle and embed all required guides for bone preparation. The obtained models were printed in Acrylonitrile Butadiene Styrene by additive manufacturing for a final check. Upon approval of the planning procedure, the

models were sent for final state-of-the-art additive manufacturing (the metal components using cobalt-chromium-molybdenum powders, and the guides using polyamide).

Overall, preoperative three-dimensional bone imaging, and MAT and AAT axis determination are important aspects of planning and templating for PSI.

Several issues regarding PSI templating and preoperative planning strategies must still be addressed. First, different PSI image acquisition methodologies may influence the results. As a matter of fact, cutting guides are usually produced from a non-weightbearing preoperative CT scan. A weight-bearing CT scan, such as cone beam CT, may produce changes to the plan.

Other factors should also be considered: Dissimilar CT image resolutions and planning software, differences in the production methods used for the cutting blocks and their types, margin of error on the part of the manufacturer, and surgeon learning curve may affect the PSI outcomes, and influence the results.

Full-length weight-bearing lower limb imaging is rarely considered, though a complete lower limb alignment evaluation seems to be crucial in order to provide the most appropriate ankle alignment[14].

Lastly, it would be interesting to clarify whether pre-operative templating is more accurately performed using an AP radiograph or 3D imaging using CT scans, and to investigate if preoperative weight-bearing radiographs correlate with the PSI guide measurements.

ALIGNMENT AND SIZING

PSI was introduced as an innovative approach to also improve ankle alignment, and the accuracy and reproducibility of implant placement and sizing.

The literature has already shown that adequate TAA implant alignment and positioning are essential for achieving good clinical results[15,21]. Even a small implant component malpositioning could result in a significant impact on motion and contact pressure, which may determine its failure[2].

Kakkar *et al*[22] described how an implant misalignment could result in eccentric overloads. Traditionally, every arthroplasty system purpose is to reach a neutral axis[23]. According to certain authors[24,25], neutral coronal ankle alignment is defined as less than 5 degrees of valgus to less than 5 degrees of varus.

There is still a good amount of controversial debate in the literature regarding whether PSI improves the reliability of achieving neutral ankle alignment and more accurate implant sizing.

In the cadaver-based study performed by Berlet *et al*[10], PSI led to a reliable and reproducible position of TAA component and ankle alignment. The mean prosthesis alignment variations between pre-operative plans and final location were all within ± 3 degrees.

Hsu *et al*[11] reported similar results in a retrospective case series of 42 consecutive TAAs using preoperative CT scan-derived patient-specific plans and guides (PROPHECY). Of the 42 TAAs, 29 intramedullary referencing implants (INBONE II) and 13 low-profile tibia and talar resurfacing implants (INFINITY) were used. The study revealed that postoperative weight-bearing alignments were in a range of ± 3° from the expected coronal and sagittal alignments reported in the surgical plans following CT scans. Moreover, neutral alignments were gained for all TAAs, independently of preoperative coronal deformity.

Surgical plans have forecasted the real tibial component size utilized in 29 of 29 (100%) INBONE II cases and in 12 of 13 (92%) INFINITY cases. Conversely, plans were more inaccurate for talar component and predicted the real talar component size utilized in 22 of 29 (76%) INBONE II cases and 6 of 13 (46%) INFINITY cases. In all cases of predicted tibia or talar size mismatch, surgical plans estimated one implant size larger than the one that was actually used.

In 2015, Hanselman *et al*[12] reported the case of a 54-year-old man with a 29° varus hindfoot deformity treated by TAA using an INBONE II implant with PROPHECY PSI. Three months post operation, a neutral alignment was achieved, with a coronal plane angle of 1.8°.

In 2017, Daigre *et al*[13] reported on a retrospective multicenter study of 44 TAAs (INBONE II) using PROPHECY PSI. In 79.5% of cases, the postoperative tibial implant position corresponded to the preoperative plan within 3° of the planned aim, within 4° in 88.6% and 5° in 100% of cases. The preoperative navigation system aided to reach a postoperative neutral alignment in 93.2% of cases. The tibial component coronal size was properly predicted in 98% of cases, whereas the talar component was correctly predicted in 80% of cases.

When comparing PSI with the Standard Referencing Guide (SRG) on a retrospective analysis of 99 INFINITY TAAs, Saito *et al*[1] reported that the absolute variation of the tibial component from the intended alignment was 1.6 ± 1.2 degrees in the coronal plane, and 1.9 ± 1.5 degrees in the sagittal plane.

The PSI preoperative plan correctly predicted the implant size in 73% of cases for the tibial component, and in 51% for the talar component, whereas among the mismatched cases, the plan tended to predict an implant size larger than what was actually utilized for both implants.

Considering the reported data, imprecision of the computerized navigation system in predicting the talar implant size still exists. Some authors propose to justify the talar component mismatch with the matter of gutter debridement: An aggressive debri-dement may affect the sizing of the talar component,

leading to smaller talar sizes[1,11,13].

CLINICAL OUTCOMES

Theoretically, the advantages that PSI confers on TAA should translate into impro-vements in clinical outcomes. However, given that PSI is still a novel technique, the current literature is lacking in long-term studies that can assess the differences in instrumentation techniques.

A single case report deals with clinical outcomes. Hanselman *et al*[12] reported good clinical results at 8 mo in a 54-year-old man using the INBONE II Prophecy TAA system. The patient was ambulating without assistance and the ankle range of motion was 40°.

The advantages of PSI in clinical outcomes are still theoretical and need to be confirmed. Conversely to primary arthritis of the hip and knee, end-stage ankle arthritis was frequently post-traumatic and generally involves younger patients. For this reason, looking at the joint replacement, ankle patients are reported to produce greater common physical demands than hip and knee ones; hence, the duration of implants for ankle patients needs to be increased by roughly 10 years. Therefore, obtaining a more accurate anatomic alignment with PSI may reduce the incidence of eccentric wear, component loosening, subsidence, and failure, and indirectly improve longevity and clinical outcomes[10].

COMPARISON WITH STANDARD TECHNIQUES

Advocates for PSI in TAA argue that the advantages conferred by patient-specific cutting block also translate to subsequent improvements in implant positioning, reduced surgical time, and clinical outcomes.

Adams *et al*[20] compared computer-assisted tibia preparation with standard techniques in a cadaveric study. Results showed that the conventional and computer-navigated tibial measurements were not different in the 95% confidence interval for CT, fluoroscopy, or radiographic assessments.

In 2019, Saito *et al*[1] performed a retrospective analysis of 99 patients comparing the utilization of PSI with the SRG. The accuracy of the tibial component placement was similar between the two groups. Neutral ankle alignment was obtained postoperatively for all cases in the PSI group, and for all but one patient in the SRG group, who had 5.7° of varus deviation post operation. The use of PSI had to be abandoned intraoperatively in three cases (3.8%). Operative time (167 *vs* 190 min, $P = 0.040$) and fluoroscopy time (85 *vs* 158 s, $P < 0.001$) were significantly decreased in the PSI group.

COST ANALYSIS

Any new technology, in addition to demonstrating clinical improvements, must undergo an economic analysis to reveal the added cost to the healthcare system in relation to its expected benefits.

Promoters of PSI suggest that PSI will reduce the overall costs of TAA. Although this technology has added associated costs, mostly because of preoperative CT imaging and the creation of custom-made cutting guides, the reduced operative time, the lower processing costs due to fewer sterile trays, the decrease in radiation exposure[4], the reduction in perioperative complications[26], and the better alignment leading to fewer revision surgeries represent the main advantages that can translate to reduced healthcare costs.

Only one study analyzed the costs of PSI in TAA. Hamid *et al*[1] identified a cost-savings threshold of $863 below which PSI was less costly than SR instrumentation. However, only the objective reduction of costs resulting from a decrease in operative time was considered.

CONCLUSION

PSI for TAA may represent an additional tool for surgeons and patients. However, the current literature does not allow us to confirm the superiority of PSI over standard techniques, and there are still several questions to be answered.

Surgical experience is always necessary in order to consider all the factors influencing lower limb alignment, and bone, soft tissue, or ligament balancing. Moreover, blindly trusting PSI can potentially lead to mistakes in implant placement and sizing. For this reason, a surgeon should always know the SR and select a different implant size or abandon PSI when necessary.

Based on the current data from the pertaining literature, the main strengths of PSI for TAA are represented by good reproducibility and accuracy of implant positioning, good neutral alignment and correction of pre-existing deformities[27], shorter operative and fluoroscopy exposure time, and

therefore, a potential decreased risk of complications as well as cost reductions[1].

The insufficiency of corroborating literature and scarcity of studies (in two cases financed by the manufacturer)[10,13] represent the current and main limitations of PSI. Moreover, it is not clear whether PSI may be more useful in order to restore ankle neutral alignment when dealing with complex deformities involving the whole lower limb.

Further prospective, randomized, and multicenter studies are therefore necessary to better evaluate PSI and confirm its routine use in TAA.

FOOTNOTES

Author contributions: Mazzotti A and Arceri A conceived the presented idea; Mazzotti A made substantial contributions to study conception and design, and data acquisition, analysis, and interpretation, drafted the manuscript, and revised it critically; Arceri A coordinated and supervised manuscript preparation; Zielli S provided documentation, and helped shape the research, analysis, and manuscript; Bonelli S provided documentation and critical feedback; Viglione V contributed to the design and implementation of the research; Faldini C revised the manuscript critically and gave final approval of the version to be published; and all authors read and approved the final manuscript.

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REFERENCES

1 **Saito GH**, Sanders AE, O'Malley MJ, Deland JT, Ellis SJ, Demetracopoulos CA. Accuracy of patient-specific instrumentation in total ankle arthroplasty: A comparative study. *Foot Ankle Surg* 2019; **25**: 383-389 [PMID: 30321969 DOI: 10.1016/j.fas.2018.02.008]
2 **Cenni F**, Leardini A, Cheli A, Catani F, Belvedere C, Romagnoli M, Giannini S. Position of the prosthesis components in total ankle replacement and the effect on motion at the replaced joint. *Int Orthop* 2012; **36**: 571-578 [PMID: 21789498 DOI: 10.1007/s00264-011-1323-6]
3 **Reb CW**, Berlet GC. Experience with Navigation in Total Ankle Arthroplasty. Is It Worth the Cost? *Foot Ankle Clin* 2017; **22**: 455-463 [PMID: 28502357 DOI: 10.1016/j.fcl.2017.01.011]
4 **Cody EA**, Scott DJ, Easley ME. Total Ankle Arthroplasty: A Critical Analysis Review. *JBJS Rev* 2018; **6**: e8 [PMID: 30153245 DOI: 10.2106/JBJS.RVW.17.00182]
5 **Rushing CJ**, Kibbler K, Hyer CF, Berlet GC. The INFINITY Total Ankle Prosthesis: Outcomes at Short-Term Follow-up. *Foot Ankle Spec* 2020; 1938640020946199 [PMID: 32772552 DOI: 10.1177/1938640020946199]
6 **King A**, Bali N, Kassam AA, Hughes A, Talbot N, Sharpe I. Early outcomes and radiographic alignment of the Infinity total ankle replacement with a minimum of two year follow-up data. *Foot Ankle Surg* 2019; **25**: 826-833 [PMID: 30638815 DOI: 10.1016/j.fas.2018.11.007]
7 **Scott RT**, Witt BL, Hyer CF. Design comparison of the INBONE I versus INBONE II total ankle system. *Foot Ankle Spec* 2013; **6**: 137-140 [PMID: 23349379 DOI: 10.1177/1938640012473148]
8 **Faldini C**, Mazzotti A, Belvedere C, Durastanti G, Panciera A, Geraci G, Leardini A. A new ligament-compatible patient-specific 3D-printed implant and instrumentation for total ankle arthroplasty: from biomechanical studies to clinical cases. *J Orthop Traumatol* 2020; **21**: 16 [PMID: 32876778 DOI: 10.1186/s10195-020-00555-7]
9 **Giannini S**, Romagnoli M, O'Connor JJ, Catani F, Nogarin L, Magnan B, Malerba F, Massari L, Guelfi M, Milano L, Volpe A, Rebeccato A, Leardini A. Early clinical results of the BOX ankle replacement are satisfactory: a multicenter feasibility study of 158 ankles. *J Foot Ankle Surg* 2011; **50**: 641-647 [PMID: 21840736 DOI: 10.1053/j.jfas.2011.06.003]
10 **Berlet GC**, Penner MJ, Lancianese S, Stemniski PM, Obert RM. Total Ankle Arthroplasty Accuracy and Reproducibility Using Preoperative CT Scan-Derived, Patient-Specific Guides. *Foot Ankle Int* 2014; **35**: 665-676 [PMID: 24719401 DOI: 10.1177/1071100714531232]
11 **Hsu AR**, Davis WH, Cohen BE, Jones CP, Ellington JK, Anderson RB. Radiographic Outcomes of Preoperative CT Scan-

Derived Patient-Specific Total Ankle Arthroplasty. *Foot Ankle Int* 2015; **36**: 1163-1169 [PMID: 25941196 DOI: 10.1177/1071100715585561]

12 **Hanselman AE**, Powell BD, Santrock RD. Total ankle arthroplasty with severe preoperative varus deformity. *Orthopedics* 2015; **38**: e343-e346 [PMID: 25901630 DOI: 10.3928/01477447-20150402-91]

13 **Daigre J**, Berlet G, Van Dyke B, Peterson KS, Santrock R. Accuracy and Reproducibility Using Patient-Specific Instrumentation in Total Ankle Arthroplasty. *Foot Ankle Int* 2017; **38**: 412-418 [PMID: 27920333 DOI: 10.1177/1071100716682086]

14 **Najefi AA**, Malhotra K, Goldberg A. Mechanical and anatomical axis of the lower limb in total ankle arthroplasty. *Foot (Edinb)* 2020; **44**: 101666 [PMID: 32172139 DOI: 10.1016/j.foot.2020.101666]

15 **Barg A**, Elsner A, Anderson AE, Hintermann B. The effect of three-component total ankle replacement malalignment on clinical outcome: pain relief and functional outcome in 317 consecutive patients. *J Bone Joint Surg Am* 2011; **93**: 1969-1978 [PMID: 22048091 DOI: 10.2106/JBJS.J.01415]

16 **Sikorski JM**. Alignment in total knee replacement. *J Bone Joint Surg Br* 2008; **90**: 1121-1127 [PMID: 18757949 DOI: 10.1302/0301-620X.90B9.20793]

17 **Waly FJ**, Yeo NE, Penner MJ. Computed Navigation Guidance for Ankle Replacement in the Setting of Ankle Deformity. *Clin Podiatr Med Surg* 2018; **35**: 85-94 [PMID: 29156170 DOI: 10.1016/j.cpm.2017.08.004]

18 **Franz AC**, Krähenbühl N, Ruiz R, Susdorf R, Horn-Lang T, Barg A, Hintermann B. Hindfoot balancing in total ankle replacement: the role of supramalleolar osteotomies. *Int Orthop* 2020; **44**: 1859-1867 [PMID: 32725295 DOI: 10.1007/s00264-020-04681-z]

19 **Barg A**, Knupp M, Henninger HB, Zwicky L, Hintermann B. Total ankle replacement using HINTEGRA, an unconstrained, three-component system: surgical technique and pitfalls. *Foot Ankle Clin* 2012; **17**: 607-635 [PMID: 23158373 DOI: 10.1016/j.fcl.2012.08.006]

20 **Adams SB Jr**, Spritzer CE, Hofstaetter SG, Jakoi AM, Pietrobon R, Nunley JA 2nd, Easley ME. Computer-assisted tibia preparation for total ankle arthroplasty: a cadaveric study. *Int J Med Robot* 2007; **3**: 336-340 [PMID: 18200622 DOI: 10.1002/rcs.163]

21 **Tochigi Y**, Rudert MJ, Brown TD, McIff TE, Saltzman CL. The effect of accuracy of implantation on range of movement of the Scandinavian Total Ankle Replacement. *J Bone Joint Surg Br* 2005; **87**: 736-740 [PMID: 15855381 DOI: 10.1302/0301-620X.87B5.14872]

22 **Kakkar R**, Siddique MS. Stresses in the ankle joint and total ankle replacement design. *Foot Ankle Surg* 2011; **17**: 58-63 [PMID: 21549973 DOI: 10.1016/j.fas.2011.02.002]

23 **Bonner TJ**, Eardley WG, Patterson P, Gregg PJ. The effect of post-operative mechanical axis alignment on the survival of primary total knee replacements after a follow-up of 15 years. *J Bone Joint Surg Br* 2011; **93**: 1217-1222 [PMID: 21911533 DOI: 10.1302/0301-620X.93B9.26573]

24 **Hsu AR**, Haddad SL. Early clinical and radiographic outcomes of intramedullary-fixation total ankle arthroplasty. *J Bone Joint Surg Am* 2015; **97**: 194-200 [PMID: 25653319 DOI: 10.2106/JBJS.N.00227]

25 **Queen RM**, Adams SB Jr, Viens NA, Friend JK, Easley ME, Deorio JK, Nunley JA. Differences in outcomes following total ankle replacement in patients with neutral alignment compared with tibiotalar joint malalignment. *J Bone Joint Surg Am* 2013; **95**: 1927-1934 [PMID: 24196462 DOI: 10.2106/JBJS.L.00404]

26 **Simonson DC**, Roukis TS. Incidence of Complications During the Surgeon Learning Curve Period for Primary Total Ankle Replacement: A Systematic Review. *Clin Podiatr Med Surg* 2015; **32**: 473-482 [PMID: 26407734 DOI: 10.1016/j.cpm.2015.06.011]

27 **Saltzman CL**, Salamon ML, Blanchard GM, Huff T, Hayes A, Buckwalter JA, Amendola A. Epidemiology of ankle arthritis: report of a consecutive series of 639 patients from a tertiary orthopaedic center. *Iowa Orthop J* 2005; **25**: 44-46 [PMID: 16089071]

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MINIREVIEWS

Diagnosis, treatment and complications of radial head and neck fractures in the pediatric patient

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Abstract

Radial head and neck fractures represent up to 14% of all pediatric elbow fractures and can be a difficult challenge in the pediatric patient. In up to 39% of proximal radius fractures, there is a concomitant fracture, which can easily be overlooked on the initial standard radiographs. The treatment options for proximal radius fractures in children range from non-surgical treatment, such as immobilization alone and closed reduction followed by immobilization, to more invasive options, including closed reduction with percutaneous pinning and open reduction with internal fixation. The choice of treatment depends on the degree of angulation and displacement of the fracture and the age of the patient; an angulation of less than 30 degrees and translation of less than 50% is generally accepted, whereas a higher degree of displacement is considered an indication for surgical intervention. Fractures with limited displacement and non-surgical treatment generally result in superior outcomes in terms of patient-reported outcome measures, range of motion and complications compared to severely displaced fractures requiring surgical intervention. With proper management, good to excellent results are achieved in most cases, and long-term sequelae are rare. However, severe complications do occur, including radio-ulnar synostosis, osteonecrosis, rotational impairment, and premature physeal closure with a malformation of the radial head as a result, especially after more invasive procedures. Adequate follow-up is therefore warranted.

Key Words: Radial head; Proximal radius; Fracture; Pediatrics; Closed fracture reduction; Open reduction fracture; Fracture fixation; Synostosis; Osteonecrosis

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Core Tip: This article presents the latest evidence-based insights in pediatric proximal radius fractures. A stepwise progression of treatment is warranted, starting with closed reduction and immobilization, and progressing to more invasive measures in case of unsuccessful reduction. Open reduction with internal fixation is left as the last option due to the high risk of complications and inferior functional results.

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INTRODUCTION

Radial head or neck fractures can be a difficult challenge in the pediatric patient. Limited data are published on the subject, and there is controversy surrounding the optimal treatment and expected results[1,2]. This article aims to provide an overview of the currently available literature on the diagnosis, classification, treatment, outcomes and complications of proximal radius fractures in the pediatric patient.

Development and anatomy of the radial head and neck

Ossification of the radial head occurs between the ages of 3 years and 5 years, and the radial head fuses with the radial shaft between the ages of 14 years and 17 years[2,3]. The epiphysis of the radial head is covered by the annular ligament, which lies in continuity with the joint capsule. The capsule extends to the proximal metaphysis. Therefore, part of the radial neck is localized outside of the joint capsule. The blood supply to the radial head enters through the metaphysis to retrogradely perfuse the radial head. The posterior interosseous nerve, which provides innervation to the digital extensor muscles, runs directly over the radial neck. The anatomic angle of the radial neck relative to the radial shaft is up to 15 degrees valgus and 10 degrees apex posterior[2]. Knowledge of this anatomy is essential when evaluating a fracture and indicating the appropriate treatment.

Epidemiology of proximal radius fractures

Elbow fractures represent 10% of all fractures occurring in the pediatric population[4]. Unlike in adults, proximal radius fractures are relatively rare, representing up to 14% of all pediatric elbow fractures[4,5]. Radial head and neck fractures occur most frequently in children aged 7 years to 12 years[3,6]. The majority of proximal radius fractures are radial neck fractures (89%), and these fractures occur more frequently in younger patients compared to radial head fractures[7]. A concomitant fracture occurs in up to 39% of radial head or neck fractures, and can easily be missed on the initial interpretation of the radiographs[5,7].

Trauma mechanism

The most common trauma mechanism for radial head and neck fractures is valgus loading with the elbow in extension, such as a fall on an outstretched hand. The force through the lateral capitellum compresses the radial head, causing it to break at the weakest point, which is often the radial neck at the metaphysis. A second injury mechanism is a radial head dislocation, which is most commonly seen in relation to radial head fractures[4].

CLINICAL PRESENTATION

Children with a proximal radius fracture present with symptoms of pain and limited range of motion after a fall or other type of trauma. Patients generally refuse to move the affected elbow. In some cases, pain may be referred to the wrist. Physical examination shows swelling, and pain exacerbated by motion, particularly with attempted pronation and supination. There is tenderness on palpation of the proximal radius[2,8,9]. Neurovascular examination should be performed, with specific consideration to the posterior interosseous nerve[10,11]. Attention should also be paid to soft-tissue swelling to assess the rare risk of forearm compartment syndrome[12].

Concomitant injuries

A concomitant fracture is seen in up to 39% of cases[5,7]. A retrospective study of 494 proximal radius fractures showed that 25% of the concomitant fractures were missed on the initial analysis of radiographs. In retrospect, 56% were visible, and 44% radiographically occult[7]. A high index of

suspicion of additional fractures is therefore required.

The most common concomitant injury is a fracture of the olecranon. Less common are ulnar metadiaphyseal fractures, ulnar fractures as part of a Monteggia fracture-dislocation and medial epicondyle fractures. Risk factors for concomitant fractures include joint effusion, young children, and complete or displaced proximal radius fractures[5,7]. In addition to concomitant fractures, other injury patterns can accompany a proximal radius fracture, such as elbow dislocation or acute longitudinal radioulnar disruption (ALRUD or Essex-Lopresti injury). In general, fractures in the pediatric patient can be easily missed due to the unique characteristics of the pediatric bone and varying clinical presentation, with patients not always being able to clearly communicate their symptoms[13]. Therefore, when assessing a child with a suspected fracture of the proximal radius, thorough examination of the wrist, shoulder and contralateral arm should be performed to exclude associated injuries.

IMAGING

Conventional radiographs are used for the diagnosis and grading of radial head and neck fractures in the pediatric patient. Anteroposterior and lateral views are made. In case of a high clinical suspicion of a fracture, such as a positive fat pad sign, but no fracture on standard radiographical views, an additional radial head-capitellum (Greenspan) view can be made to allow for easier visualization of the radial head [14]. Some studies have shown the effectiveness of the Greenspan view in identifying fractures which were occult on regular views, providing additional information in up to 21% of patients[14,15]. However, other studies dispute the added value of this view reporting only one additionally identified fracture in 32 and 125 patients[16,17].

A bilateral radiograph of the wrist can be made to exclude additional injuries such as an ALRUD injury. Nondisplaced radial neck fractures can be difficult to detect and are often occult on the initial radiograph. Fat pad signs may aid in diagnosing a nondisplaced fracture in combination with high clinical suspicion (Figure 1)[18]. However, since a part of the radial neck lies outside the joint capsule, joint effusion and fat pad signs may be absent in radial neck fractures. In these cases, a nondisplaced radial neck fracture is easily missed[7].

Imaging modalities other than plain radiographs play a less prominent role in the assessment of proximal radius fractures in children. Magnetic resonance imaging may be used to visualize the preossified elbow in young children but is not routinely indicated. In addition, magnetic resonance imaging may be useful in assessment of ligamentous integrity in case of elbow instability, dislocation, or secondary instability after successful treatment of the fracture[2,19]. Computed tomography may be used in planning operative fixation, specifically in cases of comminuted radial head fractures in older children and adolescents[2]. However, in the majority of cases plain radiographs are sufficient.

Determining fracture displacement

Angulation and translation of the proximal radius fracture are essential in the choice of treatment. There are several ways to determine these two measures. A simple way to determine angulation is to draw a line perpendicular to the articular surface of the radial head and a line through the center of the radial shaft, the angle is measured at the intersection of the lines (Figure 2A). Angulation should be measured using the radiograph that shows the greatest abnormality[2]. For the translation of the fracture, the percentage of the uncovered radial metaphysis is divided by the total width of the metaphysis. Alternatively, the distance in millimeters from the center of the proximal part to the center of the distal part of the radius can be measured (Figure 2B)[2].

Classification

Several classification systems of proximal radius fractures using conventional radiographs are available. Commonly used are the Judet classification, Metaizeau's modification of the Judet classification, and the O'Brien classification (Table 1, Figure 3)[20-22]. These classifications are useful for the choice of treatment.

TREATMENT AND OUTCOME

The treatment options for proximal radius fractures in the pediatric patient range from conservative measures, such as immobilization alone and closed reduction followed by immobilization, to more invasive options, including closed reduction and percutaneous pinning and open reduction with internal fixation. The choice of treatment depends on the degree of angulation and displacement of the fracture. Generally, an angulation of fewer than 30 degrees (O'Brien type I or Judet grade I or II) and translation of less than 50% or 3 millimeters (Metaizeau grade I or II) is accepted[2,3,23]. A higher degree of displacement is usually an indication for surgical treatment[3,23,24]. Studies comparing immobilization with percutaneous intervention and percutaneous with open treatment have shown that

Table 1 Classification systems

	Angulation, degrees	Translation
Judet		
I	Nondisplaced or horizontal shift	
II	< 30	
III	30-60	
IVa	60-80	
IVb	> 80	
Metaizeau's modification		
I	Non-displaced or horizontal shift	< 3 mm
II	< 30	< 50%
III	30-60	> 50%
IVa	60-80	> 100%
IVb	> 80	
V	Epiphyseal separation	
O'Brien		
Type I	< 30	
Type II	30-60	
Type III	> 60	



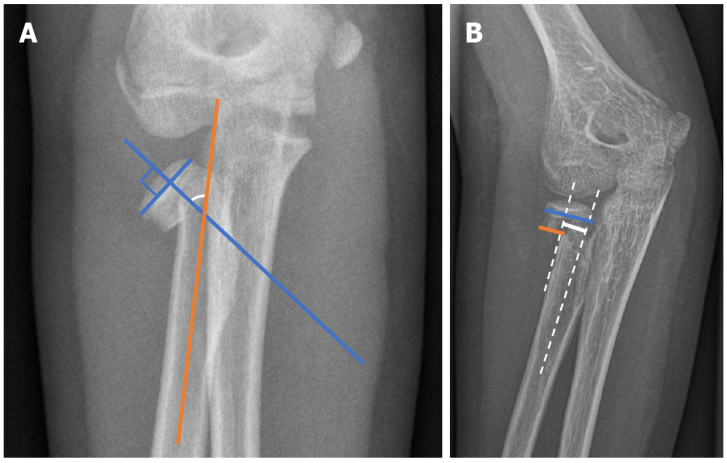
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Figure 1 Fat pad sign. Lateral radiograph of a 13-year-old boy, showing an anterior and posterior fat pad sign without visible fracture. A proximal radius fracture was identified using computed tomography.

a conservative approach leads to better outcomes in terms of patient-reported outcome scores, range of motion and fewer complications[3,4,25]. However, these results may be confounded by the fact that more severely displaced fractures are often treated more aggressively. Nonetheless, it is advised to initially attempt a conservative approach and follow a stepwise progression to more invasive options if the former fails to achieve an adequate and stable reduction (Figure 4).

Immobilization

The indication for non-surgical treatment is an isolated fracture with less than 30 degrees angulation and less than 50% translation, on the initial presentation or after closed reduction. In addition, some studies have shown superior results of non-surgical treatment in children younger than 10 years of age, suggesting that non-surgical treatment should be more liberally indicated for younger children[22,26-28]. The affected arm is splinted in a long-arm cast or pressure bandage for 1 wk, followed by range of motion exercises without loading. If reduction is required, the arm is immobilized for 2 wk to 4 wk



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Figure 2 Measurement of angulation and translation of the proximal radius fracture. A: Angulation measurement. Angulation of a proximal radius fracture is measured by drawing a line perpendicular to the surface of the radial head (blue line) and a line through the middle of the radial shaft (orange line). The angle is measured at the intersection of the two lines (white arc); B: Translation measurement. Translation of a proximal radius fracture is calculated by dividing the length the uncovered part of the metaphysis (orange line) by the total width of the proximal radius (blue line), multiplying by one hundred provides the percentage of translation. Alternatively, the distance from the middle of the proximal part to the middle of the distal part can be measured in millimeters (continuous white line).



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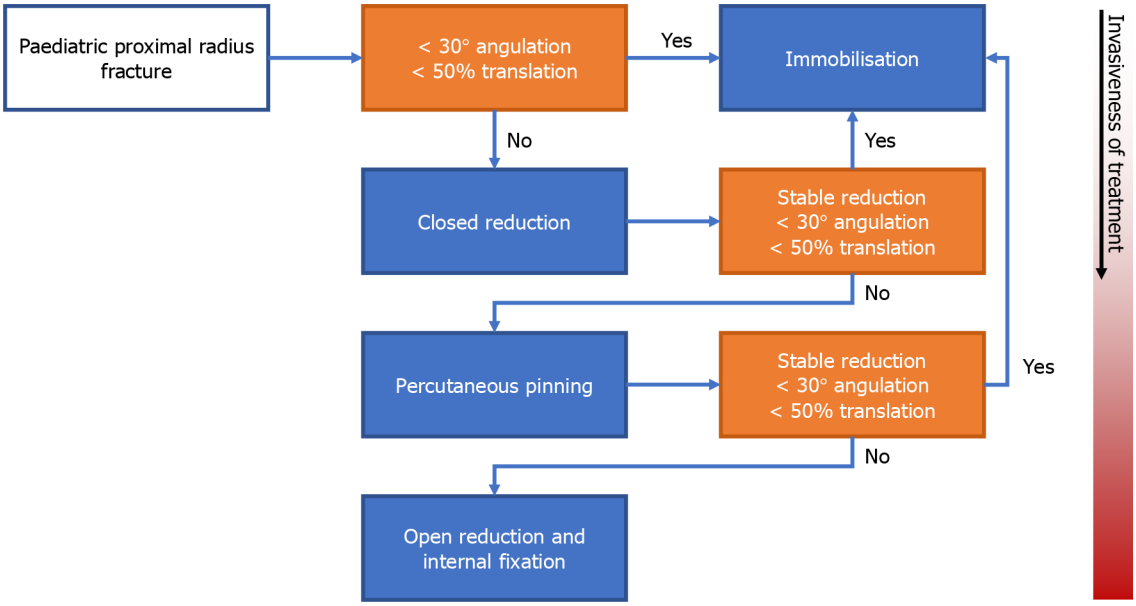
Figure 3 Anteroposterior radiograph of proximal radius fracture. A: Grade I fracture. Anteroposterior radiograph of a 5-year-old boy with a proximal radius fracture that is (nearly) nondisplaced. Judet grade I; Metaizeau grade I; O'Brien type I; B: Grade II fracture. Radiograph of a 9-year-old girl with a proximal radius fracture in 27 degrees of angulation and 17% translation. Judet grade II; Metaizeau grade II; O'Brien type I; C: Grade III fracture. Anteroposterior radiograph of a 10-year-old girl with a proximal radius fracture in 58 degrees of angulation and 55% translation. Judet grade III; Metaizeau grade III; O'Brien type II; D: Grade IV fracture. Anteroposterior radiograph of a 7-year-old girl with a proximal radius fracture in 87 degrees of angulation and 80% translation. Judet grade IVb; Metaizeau grade IVb; O'Brien type III.

depending on patient age and injury severity[29,30]. If there is no concomitant injury, the patient may return to full usage of the elbow after 4 wk[2,3]. Immobilization, with or without closed reduction, results in good to excellent outcomes in terms of range of motion and Mayo Elbow Performance Index in the majority of patients[3].

Closed reduction

In case fractures do not meet the criteria for direct immobilization, closed reduction under anesthesia is attempted. Various techniques have been described to reduce the proximal radius fracture[29,30]. (1) Patterson maneuver: With the elbow in extension and the forearm supinated, distal traction and varus force is applied while pressing directly over the radial head; (2) Israeli technique: With the elbow in flexion and the forearm supinated, pressure is applied directly over the radial head while pronating the forearm; (3) Neher-Torch technique: With the elbow in extension and the forearm supinated, two thumbs stabilize the radial head while distal traction, varus force and lateral pressure are applied. This technique requires at least two persons; and (4) Elastic bandage technique: An elastic bandage is tightly wrapped around the forearm starting at the wrist progressing proximally over the elbow. This may lead to a spontaneous reduction.

Overall success rate of closed reduction is approximately 25%, with higher success rates in lower Judet grade fractures[31]. A recent retrospective study of 70 children found that a longer time from injury to presentation and larger degree of angulation was associated with unsuccessful closed reduction; in only one of the 14 patients presenting more than 24 h after injury and none of the 10



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Figure 4 Treatment flowchart. Treatment flowchart that plots the stepwise progression from conservative to increasingly invasive treatment of pediatric proximal radius fractures. Starting from the left, orange boxes represent points of decision-making and blue boxes represent treatment options. Boxes placed lower in the chart represent more invasive procedures than those placed above.

patients with an angulation larger than 60 degrees the fracture could be successfully reduced[31].

If the fracture is successfully reduced, non-surgical treatment is sufficient. Otherwise, percutaneous pinning is the next step in the treatment ladder.

Percutaneous pinning

Besides the above-mentioned reduction maneuvers, the fracture can be reduced percutaneously in several ways. Kirschner wires can be used to position the fragment, either by placing the wire into the fragment and levering it into position (joystick technique) or by pushing the fragment with the blunt end of the wire. Kirschner wires can then be used to fixate the fragment (Figure 5A and B).

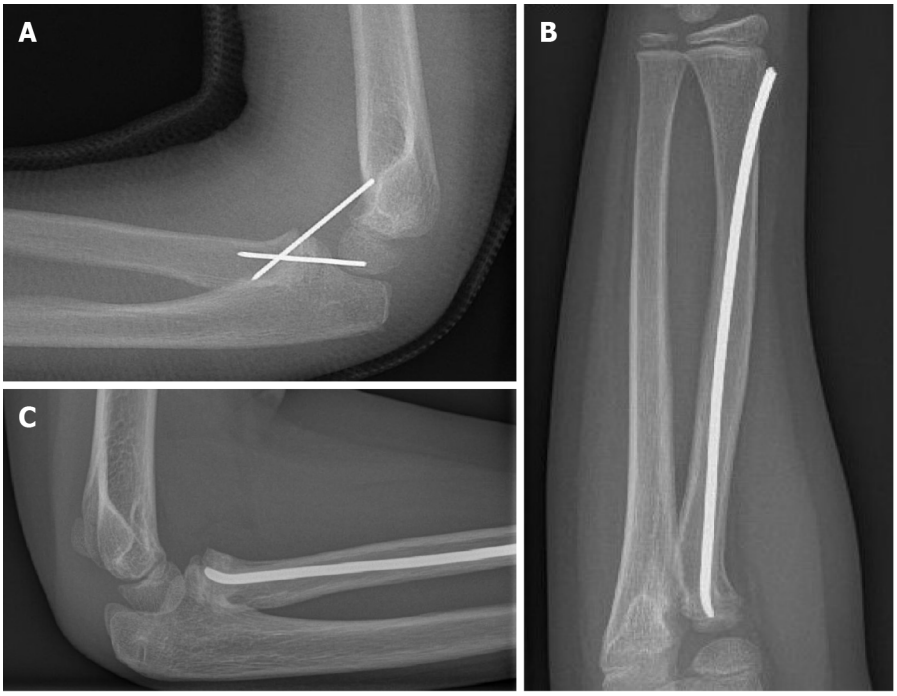
Alternatively, an elastic, flexible intramedullary nail can be used (Metaizeau technique). The nail is pre-bent and inserted at the distal radius through a standard radial styloid approach or a dorsal approach over Lister's tubercle. The nail is advanced in a retrograde fashion across the fracture site into the proximal fragment. The nail can be rotated to reduce the fragment and is left in place for permanent fixation (Figure 5C)[32]. Previous studies found no difference in functional and radiographic results between the two percutaneous techniques[28,33,34]. However, fluoroscopy and operating times are greater when using the Metaizeau technique[34].

Percutaneous fixation is generally performed under guidance of radiographic fluoroscopy. However, a recent retrospective study of 50 children showed the feasibility of percutaneous pinning under ultrasound guidance, reporting comparable outcomes between the two types of imaging guidance[35]. Using ultrasound may reduce the amount of radiation exposure in children with proximal radius fractures.

Following percutaneous fixation of a proximal radius fracture, the patient is placed into a long-arm cast for 4 wk, after which the Kirschner wires are removed and elbow range of motion exercises can be started. In case an intramedullary nail is used, it is removed after 3 mo to 6 mo[2,3,24]. If initial percutaneous fixation fails, there is controversy surrounding the choice for a second attempt at percutaneous fixation before continuing onto internal fixation. It is thought that multiple attempts may damage the blood supply to the radial head and increase the risk of complications. However, only one study has assessed this problem and found no association between multiple attempts and worse outcomes[28]. It is generally accepted to continue to the next step in the treatment ladder if a single attempt at percutaneous fixation is unsuccessful.

Open reduction and internal fixation

The indication for open reduction and internal fixation is a fracture with more than 30 degrees angulation or more than 50% translation, which is unstable and cannot be reduced adequately with the previously mentioned methods. In addition, in case of concomitant injuries that may result in instability, internal fixation can be indicated. A lateral approach through the Kocher or Kaplan interval is used. The forearm should be pronated to avoid the posterior interosseous nerve. The method of fixation varies greatly. Kirschner wires can be placed through the fracture to fixate the proximal fragment; titanium



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Figure 5 A fracture can be reduced percutaneously in several ways. A: Percutaneous Kirschner wire fixation. Lateral radiograph of a 7-year-old boy with a proximal radius fracture after percutaneous reduction and fixation using two Kirschner wires; B and C: Intramedullary nail: Anteroposterior radiograph of a 10-year-old girl with a proximal radius fracture that was reduced and fixated using a flexible intramedullary nail (Metaizeau technique) (B), Lateral radiograph of a 10-year-old girl with a proximal radius fracture that was reduced and fixated using a flexible intramedullary nail (Metaizeau technique) (C).

elastic nails can be placed in the radial shaft; or in some cases, screws are used to reattach the radial head[3,24]. If deemed necessary, the annular ligament can be repaired. Transcapitellar pin fixation has been used in the past but is no longer advised due to the tendency of these pins to break inside the joint, which may result in chondral damage of the capitellum. Fixation may not always be necessary after open reduction, and in rare cases, a stable situation is achieved with open reduction leaving the joint capsule intact. However, two studies have reported cases of non-union, synostosis and avascular necrosis after open reduction without fixation, arguing that open reduction should always be accompanied by adequate fixation[3,19].

Open reduction and internal fixation have been associated with a greater loss in range of motion and increased rates of osteonecrosis and synostosis compared to closed reduction techniques[3,25,36]. However, these results are controversial due to open reduction being more frequently used in fractures with a higher degree of displacement and more concomitant injuries. Worse outcomes have also been reported with increasing age, and better outcomes are achieved in children of 10 years or younger[3,8,27,28]. However, older children have been reported to sustain more severe fractures. Nonetheless, two studies have shown worse outcomes with increasing age while statistically correcting for the degree of fracture displacement[8,28]. Long-term results of pediatric proximal radius fractures are positive; a study of 24 patients treated conservatively or with open reduction and internal fixation with a mean follow-up of 19 years reported no complaints in 86% of patients, a mean decrease in flexion arc of 3 degrees compared to the uninjured population, and no osteoarthritis[37].

Intra-articular fractures

Intra-articular fractures are less common in skeletally immature children compared to skeletally mature adolescents (52 *vs* 7 per cent) and may be missed on radiographic imaging[38]. Recent case series have reported rapid radiocapitellar degeneration and progressive radial head subluxation in pediatric patients with an intra-articular radial head fracture[39,40]. This type of fracture should not be underestimated and should, in contrast to extra-articular fractures, be treated more aggressively.

COMPLICATIONS

Various complications have been reported after radial head or neck fractures in children. Overall, the complication rate increases with increasingly invasive treatment and is highest after open articular surgery[3]. General complications related to surgery or anesthesia, such as infection or postoperative bleeding, are not mentioned here. Common complications or complications with severe consequences

that are specific to radial head or neck fractures are discussed in descending order of severity.

Radio-ulnar synostosis

Radio-ulnar synostosis is a complication involving a bony or soft-tissue connection that is formed between the proximal radius and ulna during post-traumatic remodeling. It has a reported incidence of approximately 1% after radial head or neck fractures in children and occurs predominantly after open reduction or delayed treatment[3]. Synostosis is the most severe complication in terms of functional results and typically presents as an inability to rotate the forearm with an intact flexion arc. The diagnosis is confirmed on conventional radiographs or computed tomography. Treatment is surgical and involves excision of the synostosis. A common problem is the recurrence of the synostosis after excision, and a wide variety of additional techniques have been proposed to prevent this problem, including rotation osteotomy, the interposition of a silicone spacer, interposition of a free fat graft, interposition of a pedicled or free muscle flap, or nonsteroidal anti-inflammatory drugs. Due to the low incidence of post-traumatic radio-ulnar synostosis, the available evidence for all techniques is based on a handful of cases[41-47]. No conclusion can be drawn as to which technique is superior. Although pronation and supination motion is partly restored in most cases, the functional results of these procedures vary greatly, and a large proportion of patients have poor long-term outcomes[41-47]. Radio-ulnar synostosis is associated with open treatment of proximal radius fractures. Therefore, the incidence of synostosis is most effectively reduced by using minimally invasive techniques when possible[3,25,36]. Furthermore, it is the senior authors' practice to remove bone dust using gel or water and avoid interfering with the radio-ulnar space.

Avascular necrosis

Due to the main blood supply to the radial head entering through the metaphysis and running retrogradely to the radial head, it is vulnerable to disruption in the case of a radial neck fracture. This may result in osteonecrosis of the radial head. The reported incidence of avascular necrosis after proximal radius fractures in children is approximately 1%[3]. The occurrence of avascular necrosis is associated with a higher degree of fracture displacement and open treatment[3,48]. Patients with avascular necrosis present with a new and increasing pain at the elbow and restriction of movement. In addition, swelling is seen in some cases. Symptoms of post-traumatic necrosis can first occur several years after the initial injury[49]. The diagnosis is confirmed using conventional radiographs. Initial treatment is conservative with range of motion exercises and may provide relief in some cases. If severe symptoms persist, avascular necrosis can be treated surgically using bone grafting or radial head resection[3,49]. However, these interventions often do not provide sufficient pain relief or restore range of motion entirely and are associated with poor outcomes in the pediatric population[3,49]. Overall, the presence of avascular necrosis is associated with worse functional outcomes and restricted elbow motion at long-term follow-up[48,49].

Posterior interosseous nerve injury

The posterior interosseous nerve may be injured during the initial trauma or during surgery, resulting in transient or permanent nerve palsy. Iatrogenic injury of the posterior interosseous nerve is rare; a recent systematic review including 751 cases reported no cases of permanent iatrogenic nerve injury[3]. Risk of injury to the posterior interosseous nerve can be reduced by pronating the forearm during the (lateral) surgical approach. Transient neurological deficits in both the radial and ulnar nerves after treatment of proximal radius fractures are reported in approximately 1% of pediatric patients[3]. The typical clinical presentation of posterior interosseous nerve palsy includes limitations in finger and thumb extension together with radial deviation when extending the wrist, due to preserved function of the extensor carpi radialis longus and brevis. The posterior interosseous nerve does not have cutaneous branches, and there will be no loss of sensory function. Available follow-up data of proximal radius fracture-related posterior interosseous nerve palsies in children are limited. Case reports of adults generally show spontaneous recovery between 2 mo and 6 mo after injury, and operative intervention is rarely required[10,11,50,51].

Non-union

After treatment of a proximal radius fracture, non-union can occur. However, the incidence of non-union is low, with two studies reporting 0% and 0.7% non-union in children with a proximal radius fracture, respectively[27,28]. Patients may present with a decreased range of motion, mostly affecting supination. In addition, intermittent pain or functional complaints are reported in some cases, as well as valgus deformity[52]. The diagnosis is confirmed using conventional radiographs. The time between fracture and presentation for non-union varies greatly and is reported up to 8.5 years in rare cases[19]. Depending on the severity of the symptoms, a non-union can be treated conservatively with range of motion exercises. In case of severe symptoms, a non-union can be treated surgically with open reduction and internal fixation, with the option of bone grafting. In some cases, radial head resection is required [52]. Results of both conservative and operative treatment vary greatly. In general, improvement in complaints and range of motion is seen, but various remaining abnormalities are seen on follow-up

radiographs[19,52]. In case of radial head resection, improvement in range of motion often comes with complaints of instability[52]. However, the available evidence is limited and relies on a small case series.

Mal-union

If the fracture consolidates in a non-anatomical position, it is considered a mal-union. The reported incidence of mal-union is equally low, ranging from 0% to 4%[3,27,28]. Patients may present with elbow pain and restricted motion, which can occur up to decades after the initial injury in rare cases[53,54]. The diagnosis is made using conventional radiographs. Depending on the severity of the symptoms, a mal-union of the radial neck or head can be treated with corrective osteotomy or radial head resection [55]. Limited data are available on the results of surgical interventions in these patients. Case series have shown overall pain reduction after osteotomy, but contrasting results with regards to restoring range of motion[53,54,56]. Mal-union of the proximal radius should be distinguished from partial growth arrest or injury of the growth plate of the radius, resulting in a posttraumatic malformation of the radial head, most commonly an enlargement of the radial head and an incongruent proximal radioulnar joint[8,26].

Heterotopic ossification

Heterotopic ossification may occur in the soft-tissue surrounding the elbow after a proximal radius fracture. The incidence is approximately 2% after a proximal radius fracture in children[3]. Patients with heterotopic ossification may present with restricted motion, swelling of the joint, joint and muscle pain, or in some cases fever[57-59]. The severity of heterotopic ossification ranges from mild symptoms that resolve spontaneously to complete ankylosis. The presence of heterotopic ossification is confirmed on radiographs or computed tomography. The use of medications such as vitamin-K antagonists or nonsteroidal anti-inflammatory drugs have been suggested to prevent heterotopic ossification but are not routinely advised in children[60,61]. Treatment options for heterotopic ossification include range of motion exercises and excision of the ossification through arthroscopic or open surgery[57-59]. Limited data on the results of surgical excision of heterotopic ossification around the elbow in children are available, but the few reported cases show good results and no recurrence[57-59].

Physeal arrest or premature physeal closure

The damage caused to the growth plate by the fracture or consequential treatment may result in an arrest or premature closure of the physis, but it may also be the result of avascular necrosis. The incidence of premature physeal closure after a proximal radius fracture in children is approximately 1.5% but is not always reported, and a physeal arrest may be missed in the absence of symptoms[3]. Symptoms can include mild restriction of motion, pain, a clicking sensation, or a visible deformity such as cubitus valgus, but growth arrest can also be asymptomatic[62]. Closure of the physis or physeal arrest, with malformation of the radial head as a result, may be seen on conventional radiographs. Approximately 25% of growth in the radius occurs in the proximal physis[63]. Therefore, there is less remodeling potential than distally, but a lower chance of symptoms due to longitudinal deficiency. In most cases, physeal arrest or premature closure can be treated conservatively, with range of motion exercises. In case of severe symptoms, surgical treatment can be attempted using corrective osteotomy or bone lengthening procedures[64]. Limited data are available on the results of these interventions, and conflicting results are reported, with most treated children showing an improved range of motion, but worsened outcomes in a selection of cases[64].

Decreased range of motion

Elbow stiffness is the most common complication, reported in up to 31% of patients[27]. It is often caused by soft-tissue contraction and fibrous tissue formation, but can also be caused by bone overgrowth. It has been associated with injury severity, concomitant fractures and multiple attempts at closed and open reduction and has been correlated with a worse functional outcome[48]. Elbow stiffness is best prevented by early mobilization and adequate guidance during rehabilitation, preferably by a physiotherapist. If conservative treatment, including static progressive splinting, is unsuccessful and elbow motion is severely limited, the stiff elbow can be released arthroscopically or with open surgery. This generally results in improved range of motion, but rarely to the extent that it matches the unaffected side[65].

Radial head overgrowth

Post-traumatic osseous overgrowth of the radial head or neck is a common radiographic finding after fracture of the pediatric proximal radius, reported to occur in 18% to 37% of patients[66]. It is often asymptomatic but may result in restricted motion.

CONCLUSION

Radial head and neck fractures remain challenging injuries in the pediatric patient. Fractures are

classified based on the initial angulation and translation, which determine the type of treatment. With proper management, generally good to excellent results are achieved, and long-term sequelae are rare. However, severe complications such as synostosis, osteonecrosis or (partial) growth arrest do occur, especially after more invasive procedures. Complications such as stiffness and radial head overgrowth are more common but can generally be treated successfully with conservative measures. There is controversy in the literature regarding the treatment of older pediatric patients nearing skeletal maturity and whether they should be approached in a similar fashion as adult patients. Furthermore, apart from striving to use the least invasive treatment options, there is limited data available on prevention of specific complications. In addition, the rate of missed fractures and missed concomitant injuries is relatively high. Future research should focus on more accurate diagnosis, expanding the closed and percutaneous treatment options, and prevention of complications.

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REFERENCES

1 **Radomisli TE**, Rosen AL. Controversies regarding radial neck fractures in children. *Clin Orthop Relat Res* 1998; 30-39 [PMID: 9728157 DOI: 10.1097/00003086-199808000-00005]
2 **Nicholson LT**, Skaggs DL. Proximal Radius Fractures in Children. *J Am Acad Orthop Surg* 2019; **27**: e876-e886 [PMID: 30865025 DOI: 10.5435/JAAOS-D-18-00204]
3 **Kumar S**, Mishra A, Odak S, Dwyer J. Treatment principles, prognostic factors and controversies in radial neck fractures in children: A systematic review. *J Clin Orthop Trauma* 2020; **11**: S456-S463 [PMID: 32774012 DOI: 10.1016/j.jcot.2020.04.022]
4 **Landin LA**. Fracture patterns in children. Analysis of 8,682 fractures with special reference to incidence, etiology and secular changes in a Swedish urban population 1950-1979. *Acta Orthop Scand Suppl* 1983; **202**: 1-109 [PMID: 6574687 DOI: 10.3109/17453678309155630]
5 **DeFroda SF**, Hansen H, Gil JA, Hawari AH, Cruz AI Jr. Radiographic Evaluation of Common Pediatric Elbow Injuries. *Orthop Rev (Pavia)* 2017; **9**: 7030 [PMID: 28286625 DOI: 10.4081/or.2017.7030]
6 **Jacoby SM**, Herman MJ, Morrison WB, Osterman AL. Pediatric elbow trauma: an orthopaedic perspective on the importance of radiographic interpretation. *Semin Musculoskelet Radiol* 2007; **11**: 48-56 [PMID: 17665350 DOI: 10.1055/s-2007-984412]
7 **Degnan AJ**, Ho-Fung VM, Nguyen JC, Barrera CA, Lawrence JTR, Kaplan SL. Proximal radius fractures in children: evaluation of associated elbow fractures. *Pediatr Radiol* 2019; **49**: 1177-1184 [PMID: 31177320 DOI: 10.1007/s00247-019-04445-x]
8 **Tan BH**, Mahadev A. Radial neck fractures in children. *J Orthop Surg (Hong Kong)* 2011; **19**: 209-212 [PMID: 21857047 DOI: 10.1177/230949901101900216]
9 **Kim HH**, Gauguet JM. Pediatric Elbow Injuries. *Semin Ultrasound CT MR* 2018; **39**: 384-396 [PMID: 30070231 DOI: 10.1053/j.sult.2018.03.005]

10 **Stepanovich MT**, Hogan CJ. Posterior interosseous and ulnar nerve motor palsies after a minimally displaced radial neck fracture. *J Hand Surg Am* 2012; **37**: 1630-1633 [PMID: 22835587 DOI: 10.1016/j.jhsa.2012.05.028]
11 **Terra BB**, Sassine TJ, Lima GF, Rodrigues LM, Padua DV, Nadai A. Radial head fracture associated with posterior interosseous nerve injury. *Rev Bras Ortop* 2016; **51**: 725-729 [PMID: 28050547 DOI: 10.1016/j.rboe.2016.10.002]
12 **Lin JS**, Samora JB. Pediatric acute compartment syndrome: a systematic review and meta-analysis. *J Pediatr Orthop B* 2020; **29**: 90-96 [PMID: 30688754 DOI: 10.1097/BPB.0000000000000593]
13 **George MP**, Bixby S. Frequently Missed Fractures in Pediatric Trauma: A Pictorial Review of Plain Film Radiography. *Radiol Clin North Am* 2019; **57**: 843-855 [PMID: 31076036 DOI: 10.1016/j.rcl.2019.02.009]
14 **Greenspan A**, Norman A, Rosen H. Radial head-capitellum view in elbow trauma: clinical application and radiographic-anatomic correlation. *AJR Am J Roentgenol* 1984; **143**: 355-359 [PMID: 6611066 DOI: 10.2214/ajr.143.2.355]
15 **Grundy A**, Murphy G, Barker A, Guest P, Jack L. The value of the Radial Head-Capitellum view in radial head trauma. *Br J Radiol* 1985; **58**: 965-967 [PMID: 3916075 DOI: 10.1259/0007-1285-58-694-965]
16 **Manns RA**, Lee JR. Critical evaluation of the radial head-capitellum view in acute elbow with an effusion. *Clin Radiol* 1990; **42**: 433-436 [PMID: 2261724 DOI: 10.1016/S0009-9260(05)80901-8]
17 **Hall-Craggs MA**, Shorvon PJ, Chapman M. Assessment of the radial head-capitellum view and the dorsal fat-pad sign in acute elbow trauma. *AJR Am J Roentgenol* 1985; **145**: 607-609 [PMID: 3875263 DOI: 10.2214/ajr.145.3.607]
18 **Skaggs DL**, Mirzayan R. The posterior fat pad sign in association with occult fracture of the elbow in children. *J Bone Joint Surg Am* 1999; **81**: 1429-1433 [PMID: 10535592 DOI: 10.2106/00004623-199910000-00007]
19 **Waters PM**, Stewart SL. Radial neck fracture nonunion in children. *J Pediatr Orthop* 2001; **21**: 570-576 [PMID: 11521020 DOI: 10.1097/01241398-200109000-00003]
20 **Judet R**. Treatment of fractures of the femur neck by pedicled graft. *Acta Orthop Scand* 1962; **32**: 421-427 [PMID: 13957963 DOI: 10.3109/17453676208989601]
21 **O'Brien PI**. Injuries involving the proximal radial epiphysis. *Clin Orthop Relat Res* 1965; **41**: 51-58 [PMID: 5832738 DOI: 10.1097/00003086-196500410-00006]
22 **Metaizeau JP**, Lascombes P, Lemelle JL, Finlayson D, Prevot J. Reduction and fixation of displaced radial neck fractures by closed intramedullary pinning. *J Pediatr Orthop* 1993; **13**: 355-360 [PMID: 8496371 DOI: 10.1097/01241398-199305000-00015]
23 **Pring ME**. Pediatric radial neck fractures: when and how to fix. *J Pediatr Orthop* 2012; **32** Suppl 1: S14-S21 [PMID: 22588098 DOI: 10.1097/BPO.0B013e31824b251d]
24 **Watkins CJ**, Yeung CM, Rademacher E, Kramer DE. Percutaneous leverage technique for reduction of radial neck fractures in children: technical tips. *J Child Orthop* 2020; **14**: 118-124 [PMID: 32351624 DOI: 10.1302/1863-2548.14.190130]
25 **Dietzel M**, Scherer S, Esser M, Kirschner HJ, Fuchs J, Lieber J. Fractures of the proximal radius in children: management and results of 100 consecutive cases. *Arch Orthop Trauma Surg* 2021 [PMID: 33974141 DOI: 10.1007/s00402-021-03917-w]
26 **Vocke AK**, Von Laer L. Displaced fractures of the radial neck in children: long-term results and prognosis of conservative treatment. *J Pediatr Orthop B* 1998; **7**: 217-222 [PMID: 9702672 DOI: 10.1097/01202412-199807000-00007]
27 **Basmajian HG**, Choi PD, Huh K, Sankar WN, Wells L, Arkader A. Radial neck fractures in children: experience from two level-1 trauma centers. *J Pediatr Orthop B* 2014; **23**: 369-374 [PMID: 24811086 DOI: 10.1097/BPB.0000000000000057]
28 **Zimmerman RM**, Kalish LA, Hresko MT, Waters PM, Bae DS. Surgical management of pediatric radial neck fractures. *J Bone Joint Surg Am* 2013; **95**: 1825-1832 [PMID: 24132355 DOI: 10.2106/JBJS.L.01130]
29 **Augustithis GA**, Huntley JS. Closed reduction of paediatric radial neck fractures. *Ann R Coll Surg Engl* 2015; **97**: 316-317 [PMID: 26263944 DOI: 10.1308/rcsann.2015.97.4.316]
30 **Patterson R**. Treatment of displaced transverse fractures of the neck of the radius in children. *J Bone Jt Surg - Am Vol* 1934; **16**: 695-698
31 **Kong J**, Lewallen L, Elliott M, Jo C, McIntosh AL, Ho CA. Pediatric Radial Neck Fractures: Which Ones Can Be Successfully Closed Reduced in the Emergency Department? *J Pediatr Orthop* 2021; **41**: 17-22 [PMID: 33044259 DOI: 10.1097/BPO.0000000000001699]
32 **Métaizeau JP**. Reduction and osteosynthesis of radial neck fractures in children by centromedullary pinning. *Injury* 2005; **36** Suppl 1: A75-A77 [PMID: 15652940 DOI: 10.1016/j.injury.2004.12.016]
33 **Tarallo L**, Mugnai R, Fiacchi F, Capra F, Catani F. Management of displaced radial neck fractures in children: percutaneous pinning vs. elastic stable intramedullary nailing. *J Orthop Traumatol* 2013; **14**: 291-297 [PMID: 23843093 DOI: 10.1007/s10195-013-0252-0]
34 **Kalem M**, Şahin E, Kocaoğlu H, Başarır K, Kınık H. Comparison of two closed surgical techniques at isolated pediatric radial neck fractures. *Injury* 2018; **49**: 618-623 [PMID: 29395220 DOI: 10.1016/j.injury.2018.01.012]
35 **Su Y**, Jin C, Duan X, Wang J, Li K. Treatment of displaced radial neck fractures under ultrasonographic guidance in children. *Int Orthop* 2020; **44**: 2337-2342 [PMID: 32430548 DOI: 10.1007/s00264-020-04630-w]
36 **Hemmer J**, Happiette A, Muller F, Barbier D, Journeau P. Prognostic factors for intramedullary nailing in radial neck fracture in children. *Orthop Traumatol Surg Res* 2020; **106**: 1287-1291 [PMID: 32988780 DOI: 10.1016/j.otsr.2020.05.014]
37 **Malmvik J**, Herbertsson P, Olof Josefsson P, Hasserius R, Besjakov J, Karlsson MK. Fracture of the radial head and neck of Mason types II and III during growth: A 14-25 year follow-up. *J Pediatr Orthop Part B* 2003; **12**: 63-68 [DOI: 10.1097/01202412-200301000-00012]
38 **Leung AG**, Peterson HA. Fractures of the proximal radial head and neck in children with emphasis on those that involve the articular cartilage. *J Pediatr Orthop* 2000; **20**: 7-14 [PMID: 10641680 DOI: 10.1097/01241398-200001000-00003]
39 **Ekdahl M**, Baar A, Larraín C, López S, Flores S. Severe joint cartilage degeneration after minimally displaced fracture of proximal radius in children: a report of 2 cases. *JSES Int* 2020; **4**: 1006-1010 [PMID: 33345248 DOI: 10.1016/j.jseint.2020.08.017]
40 **Xu L**, Ye W. Radial neck fracture or Monteggia equivalent lesion: delayed radial head subluxation in an adolescent and

review of literature. *BMC Musculoskelet Disord* 2020; **21**: 282 [PMID: 32375718 DOI: 10.1186/s12891-020-03315-0]
41 **Jones ME**, Rider MA, Hughes J, Tonkin MA. The use of a proximally based posterior interosseous adipofascial flap to prevent recurrence of synostosis of the elbow joint and forearm. *J Hand Surg Eur Vol* 2007; **32**: 143-147 [PMID: 17134798 DOI: 10.1016/J.JHSB.2006.09.004]
42 **Green WT**, Mital MA. Congenital radio-ulnar synostosis: Surgical treatment. *J Bone Jt Surg - Ser A* 1979; **61**: 738-743 [DOI: 10.2106/00004623-197961050-00015]
43 **Proubasta IR**, Lluch A. Proximal radio-ulnar synostosis treated by interpositional silicone arthroplasty. A case report. *Int Orthop* 1995; **19**: 242-244 [PMID: 8557422 DOI: 10.1007/BF00185231]
44 **Yong-Hing K**, Tchang SP. Traumatic radio-ulnar synostosis treated by excision and a free fat transplant. A report of two cases. *J Bone Joint Surg Br* 1983; **65**: 433-435 [PMID: 6874714 DOI: 10.1302/0301-620X.65B4.6874714]
45 **Sugimoto M**, Masada K, Ohno H, Hosoya T. Treatment of traumatic radioulnar synostosis by excision, with interposition of a posterior interosseous island forearm flap. *J Hand Surg (British Eur Vol* 1996; **21**: 393-395 [DOI: 10.1016/S0266-7681(05)80213-X]
46 **Kanaya F**, Ibaraki K. Mobilization of a congenital proximal radioulnar synostosis with use of a free vascularized fascio-fat graft. *J Bone Joint Surg Am* 1998; **80**: 1186-1192 [PMID: 9730128 DOI: 10.2106/00004623-199808000-00012]
47 **Thurston AJ**, Spry NA. Post-traumatic radio-ulnar synostosis treated by surgical excision and adjunctive radiotherapy. *Aust N Z J Surg* 1993; **63**: 976-980 [PMID: 8285910 DOI: 10.1111/j.1445-2197.1993.tb01728.x]
48 **Falciglia F**, Giordano M, Aulisa AG, Di Lazzaro A, Guzzanti V. Radial neck fractures in children: results when open reduction is indicated. *J Pediatr Orthop* 2014; **34**: 756-762 [PMID: 25171679 DOI: 10.1097/BPO.0000000000000299]
49 **Young S**, Letts M, Jarvis J. Avascular necrosis of the radial head in children. *J Pediatr Orthop* 2000; **20**: 15-18 [PMID: 10641681 DOI: 10.1097/01241398-200001000-00004]
50 **Bulstra LF**, Schep NWL, van der Vlies CH. Posterior interosseous nerve palsy after closed proximal forearm fractures. *Trauma Case Rep* 2019; **23**: 100240 [PMID: 31497636 DOI: 10.1016/j.tcr.2019.100240]
51 **Daurka J**, Chen A, Akhtar K, Kamineni S. Tardy posterior interosseous nerve palsy associated with radial head fracture: a case report. *Cases J* 2009; **2**: 22 [PMID: 19128490 DOI: 10.1186/1757-1626-2-22]
52 **Fernandez Fernandez F**, Weiß B, Zwingmann J, Wirth T, Eberhardt O. Nonunion of the radial neck in children: a rare but severe complication after fractures of the radial neck. *Eur J Trauma Emerg Surg* 2021; **47**: 283-292 [PMID: 33660010 DOI: 10.1007/s00068-021-01604-4]
53 **Vandergugten S**, Troussel S, Lefebvre B. Radial Neck Osteotomy for Malunion of Radial Neck Fracture in Childhood. *Case Rep Orthop* 2015; **2015**: 871429 [PMID: 26347364 DOI: 10.1155/2015/871429]
54 **Ceroni D**, Campos J, Dahl-Farhoumand A, Holveck J, Kaelin A. Neck osteotomy for malunion of neglected radial neck fractures in children: a report of 2 cases. *J Pediatr Orthop* 2010; **30**: 649-654 [PMID: 20864847 DOI: 10.1097/BPO.0b013e3181ec95e0]
55 **Wegmann H**, Heider S, Novak M, Sperl M, Kraus T, Singer G, Till H. Outcome following excision of the radial head in children with open physes for impaired elbow motion. *J Shoulder Elbow Surg* 2019; **28**: 525-529 [PMID: 30502032 DOI: 10.1016/j.jse.2018.08.045]
56 **Weigelt L**, Fürnstahl P, Schweizer A. Computer-Assisted Corrective Osteotomy of Malunited Pediatric Radial Neck Fractures-Three-Dimensional Postoperative Accuracy and Clinical Outcome. *J Orthop Trauma* 2017; **31**: e436-e441 [PMID: 28742788 DOI: 10.1097/BOT.0000000000000970]
57 **Gaur A**, Sinclair M, Caruso E, Peretti G, Zaleske D. Heterotopic ossification around the elbow following burns in children: results after excision. *J Bone Joint Surg Am* 2003; **85**: 1538-1543 [PMID: 12925635 DOI: 10.2106/00004623-200308000-00016]
58 **Susnjar T**, Biocić M, Pogorelić Z. Traumatic heterotopic ossification of the elbow in children--a case report. *Acta Chir Belg* 2010; **110**: 246-249 [PMID: 20514847 DOI: 10.1080/00015458.2010.11680611]
59 **Kim BS**, Song KS, Bae KC, Lee SW, Um SH, Cho CH. Total Ankylosis by Heterotopic Ossification in an Adolescent Anterior Trans-olecranon Fracture Dislocation: A Case Report. *Clin Shoulder Elb* 2019; **22**: 154-158 [PMID: 33330213 DOI: 10.5397/cise.2019.22.3.154]
60 **Guillemin F**, Mainard D, Rolland H, Delagoutte JP. Antivitamin K prevents heterotopic ossification after hip arthroplasty in diffuse idiopathic skeletal hyperostosis. A retrospective study in 67 patients. *Acta Orthop Scand* 1995; **66**: 123-126 [PMID: 7740940 DOI: 10.3109/17453679508995504]
61 **Kan SL**, Yang B, Ning GZ, Chen LX, Li YL, Gao SJ, Chen XY, Sun JC, Feng SQ. Nonsteroidal Anti-inflammatory Drugs as Prophylaxis for Heterotopic Ossification after Total Hip Arthroplasty: A Systematic Review and Meta-Analysis. *Medicine (Baltimore)* 2015; **94**: e828 [PMID: 25950691 DOI: 10.1097/MD.0000000000000828]
62 **Gauger EM**, Casnovsky LL, Gauger EJ, Bohn DC, Van Heest AE. Acquired Upper Extremity Growth Arrest. *Orthopedics* 2017; **40**: e95-e103 [PMID: 27684080 DOI: 10.3928/01477447-20160926-07]
63 **Noonan KJ**, Price CT. Forearm and distal radius fractures in children. *J Am Acad Orthop Surg* 1998; **6**: 146-156 [PMID: 9689186 DOI: 10.5435/00124635-199805000-00002]
64 **Farr S**, Mindler G, Ganger R, Girsch W. Bone Lengthening in the Pediatric Upper Extremity. *J Bone Joint Surg Am* 2016; **98**: 1490-1503 [PMID: 27605694 DOI: 10.2106/JBJS.16.00007]
65 **Kodde IF**, van Rijn J, van den Bekerom MP, Eygendaal D. Surgical treatment of post-traumatic elbow stiffness: a systematic review. *J Shoulder Elbow Surg* 2013; **22**: 574-580 [PMID: 23375881 DOI: 10.1016/j.jse.2012.11.010]
66 **Vahvanen V**, Gripenberg L. Fracture of the radial neck in children. A long-term follow-up study of 43 cases. *Acta Orthop Scand* 1978; **49**: 32-38 [PMID: 654893 DOI: 10.3109/17453677809005720]

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ORIGINAL ARTICLE

Retrospective Cohort Study

Functional and radiological outcomes of different pin configuration for displaced pediatric supracondylar humeral fracture: A retrospective cohort study

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Abstract

BACKGROUND

The most widely accepted treatment for pediatric supracondylar humeral fracture is closed reduction and percutaneous pinning (CRPP). However, there is debate regarding the technique that is utilized, whether crossed or lateral pinning, and the number of pins used.

AIM

To compare the functional and radiological outcomes of lateral and cross pinning in the management of humeral supracondylar fracture.

METHODS

A retrospective analysis was performed on 101 patients who were surgically managed by either one of the CRPP techniques from 2015 to 2019. Several clinical parameters were taken into account, including pre- and post-intervention Baumann angle, as well as scores for pain, range of motion, function, and stability. Statistical analysis was performed to study the outcomes of the utilized techniques.

RESULTS

Amongst our study sample, which included 63 males and 38 females with a mean age of 5.87 years, about one-third of the patients underwent crossed pinning fixation configuration and the remaining two-thirds were managed by lateral pinning configuration. Similar results were obtained in the two groups with no

statistical difference regarding Mayo elbow performance scores (MEPS) and Baumann angle. The mean MEPS in the lateral and crossed pinning groups were 93.68 + 8.59 and 93.62 + 9.05, respectively. The mean Baumann angle was 72.5° + 6.46 in the lateral group and 72.3° + 4.70 in the crossed-pinning group (P = 0.878).

CONCLUSION

Both lateral pinning and crossed pinning fixation configuration for displaced pediatric supracondylar humeral fractures provide similar functional and radiological outcomes.

Key Words: Supracondylar fracture; Gartland; Pinning; Functional; Radiological

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Core Tip: Closed reduction and percutaneous pinning is the mainstay in the management of pediatric supracondylar fracture. It is still controversial what pin configuration should be used (lateral *vs* cross pinning), and how many pins should be used. Both lateral and cross pinning techniques provide adequate stability for the fracture with nearly similar radiological and functional outcomes.

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INTRODUCTION

A supracondylar humeral fracture happens through the thin part of the distal humerus above the growth plate level. These fractures are typical pediatric injuries, accounting for 60% of upper limb fractures and 13% of pediatric fractures. They are most commonly seen in children 5-7 years of age with no gender predilection[1-3].

These fractures may be complete or incomplete with varying degrees of severity. The Gartland classification system is a popular system for the evaluation and treatment of these fractures. It classifies them as type 1 - nondisplaced or minimally displaced, type 2 - displaced with intact posterior cortex, and type 3 - completely displaced without contact between fragments[3]. In addition, the modified Gartland classification is frequently used, describing one more type, type 4 - complete multidirectional displacement of fragments with periosteal disruption[4].

As for the management of these fractures, a trial of conservative management may be undertaken with type 1 fractures and minimally displaced type 2 fractures. This involves long arm casting with less than 90 degrees of elbow flexion[5].

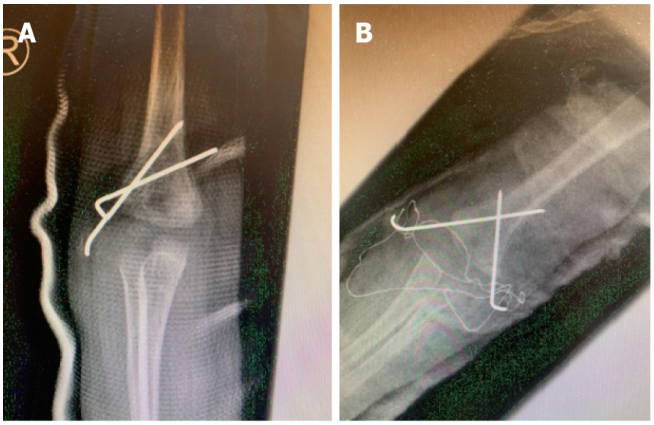
Operative management is almost always required in more severe types, including closed reduction and percutaneous pinning (CRPP). Pinning is performed retrogradely, using two pins for type 2 fractures and three pins for type 3 fractures. Rarely, open reduction with percutaneous pinning is needed in open fractures and in cases of failed closed reduction[6]. The most commonly reported postoperative complication is pin migration[7].

Despite reported complications of neurovascular injuries[8], it has been well documented in the previous literature that pediatric supracondylar humerus fractures generally have good outcomes. Elbow range of motion (ROM) and function are usually preserved, provided that adequate reduction is achieved through surgical intervention or casts application[9].

CRPP has two techniques: Lateral pinning technique (Figure 1A) and cross pinning technique (Figure 1B). Controversy persists between the two perspectives regarding which is better in terms of fixation stability and risk of developing complications.

Theoretically, crossed pinning is superior in providing biomechanical stability, yet this construct increases the risk of iatrogenic ulnar nerve injury due to the medial pin position. Conversely, lateral pinning may be less stable biomechanically but avoids ulnar nerve injury[10-12].

Therefore, this study aimed to study the difference in stability and functional outcomes between patients managed by lateral pinning and those managed by crossed pinning for displaced supracondylar fracture of the humerus. The null hypothesis was that there is no difference between the treatment groups.



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Figure 1 Postoperative AP view radiographs. A: Lateral pinning; B: Cross pinning.

In order to compare the two techniques, the well-validated Mayo elbow performance score (MEPS) was used as a standardized functional outcome measure[13,14]. Other measures with clinical-radiological value may be considered as well. These may include measurement of Baumann angle (Figure 2), carrying angle, the development of complications, and the necessity to re-operate.

MATERIALS AND METHODS

We conducted a single-blinded retrospective cohort study at the Department of Orthopedics of King Abdullah University Hospital (KAUH). Before conducting this study, ethical approval was obtained from the Institutional Review Board (IRB) committee of KAUH. This study reviewed a total of 101 cases of children with supracondylar humeral fractures that were presented to the emergency department of KAUH between 2015 and 2019. Multiple parameters were reviewed, including gender, age, and surgical intervention, as well as scores for pain, ROM, function, and stability. A convenience sampling method was used to obtain our sample.

Our inclusion criteria for the study involved any patient up to the age of 13 years who had a supracondylar humeral fracture and underwent closed reduction with percutaneous pinning within 24 h of the insult and with no neurological or vascular injury prior to the operation. The pinning was either lateral or crossed configuration with medial and lateral wires. Our exclusion criteria included patients who did not respond to our call, patients with bilateral fractures, patients with multiple surgeries in the same limb, and those who ever had a previous elbow fracture. This was to avoid the confounding effects of previous fractures and surgeries on our results. However, unknown confounders might still be present.

An orthopedic specialist reviewed the patients' radiographic images (Figure 3) and categorized them using the Gartland classification system. Then, surgery was performed and techniques were standardized in regards to pin location, pin size, stability, and positioning of the elbow. They were performed by a well-trained orthopedic surgeon.

Patients were scheduled for follow-up visits; the follow-up period was customized according to patient cases individually, with a timeframe ranging from 1 mo postoperatively to 1 year. They underwent pin removal and cast change and were inspected for symptoms and ROM. Radiographs were taken to guarantee proper healing and reduction (Figure 4).

All fractures were also assessed by altering their Baumann angle, which was measured both postoperatively and during the last follow-up in January-March 2020. Baumann angle refers to the angle between the long axis of the humeral shaft and the growth plate of the lateral condyle. A difference in the angle of more than 5 degrees between the two limbs was considered abnormal. All measurements were performed by a single calibrated examiner. The interclass correlation coefficient for the angle measurement was above 90%.

MEPS was used to assess functional limitations of the elbow on daily activities and administered during January-March 2020 *via* patient interviewing and physical examination in the clinic. Elbow function was measured across four domains: Pain (45 points), ROM (20 points), stability (10 points), and daily function (25 points). Clinical information from these four subscales was rated on a 100-point scale and categorized as follows: < 60, poor; 60-74, fair; 75-89, good; and 90-100, excellent[13,14].

All of our patients were eligible to participate in our study. Matching by age and gender was not performed due to the small number of patients in the crossed pinning group and the portability of introducing bias. Case selection bias was minimal because we applied strict inclusion and exclusion criteria, and the outcome of interest was clear for all categories. In addition, information bias was



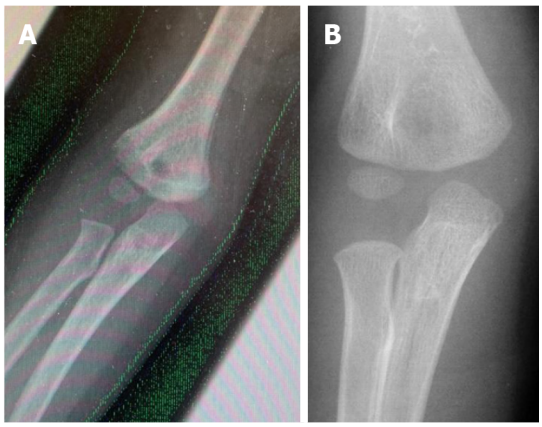
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Figure 2 Lateral radiograph demonstrating Baumann's angle (angle between the long axis of humeral shaft and growth plate of lateral humeral condyle).



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Figure 3 Pre-operative AP view radiograph.



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Figure 4 AP radiographs post pin removal. A: Lateral pinning B: Crossed pinning.

controlled by excluding all patients with missing information.

Data was entered and analyzed using IBM SPSS statistics version 23. We looked at MEPS, Gartland type, type of fixation, and Baumann angle. We classified the patients according to the technique used (crossed pinning *vs* lateral pinning); the lateral pinning group was further sub-classified into 2 pins *vs* 3 pins. Patients were also categorized according to Gartland type, MEPS score, and gender. Using the *t*-test, we measured if there was a difference in Baumann angle according to the type of fixation, and whether it was lateral pinning or crossed pinning. Using multiple linear regression, we measured the

factors that affect Baumann angle and MEPS. Using ANOVA, we measured if there was a difference between two lateral pins, three lateral pins, and crossed pinning groups in their effect on Baumann angle and MEPS. Results were considered significant at $P < 0.05$.

RESULTS

A total of 101 patients with supracondylar fractures were qualified to join our study. All patients responded and were included in the analysis. Of these patients, 63 (62.4%) were male, and 38 (37.6%) were female. The mean age of patients was 5.87 ± 1.5 years, with the youngest patient being 35 d of age and the eldest being 13.0 years of age.

We subdivided them by type of fixation into a cross pinning group with 28 patients (28.7%) and a lateral group with 72 patients (71.3%). Patients were further subdivided by Gartland type and MEPS (Table 1). As for Gartland type distribution, none had type I, 21 (20.8%) had type II, 43 (42.6%) had type III fractures, 28(27.7%) had type IV, and 9 (8.9%) had flexion type supracondylar fracture. The mean time for the last follow-up was 24.65 and 20.55 mo in the lateral pinning and cross pinning groups, respectively.

Regarding outcomes in the lateral pinning group, 62.5% of the patients had excellent outcomes, 36.1% had good outcomes, and 1.4% had fair outcomes. There were no reports of poor outcomes. Meanwhile, in the crossed pinning group, 62.1% of patients had excellent outcomes, 34.5% had good outcomes, and 3.4% had fair outcomes with no reports of poor outcomes.

There was no statistical difference in functional outcome according to MEPS ($P = 0.06$). The mean MEPS in the lateral pinning and crossed-pinning groups were 93.68 ± 8.6 and 93.62 ± 9.0, respectively. Multiple linear regression analysis was performed to determine the relationship between MEPS and different clinical parameters for functional outcomes. However, there was no statistical difference found in functional outcome regardless of gender ($P = 0.220$), fracture type ($P = 0.647$), and type of fixation ($P = 0.888$).

There was no statistical difference between the groups according to Baumann angle ($P = 0.878$). The means in the lateral pinning and crossed pinning groups were 72.5° ± 6.5 and 72.3° ± 4.7, respectively. Multiple linear regression analysis was also performed with Baumann angle with no result of statistical difference regardless of gender ($P = 0.115$), fracture type ($P = 0.949$), and type of fixation ($P = 0.995$).

We further subdivided the lateral group into 2 wires lateral (36 patients) and 3 wires lateral (36 patient) groups; there was no statistically significant difference between the three groups using one-way ANOVA according to MEPS ($P = 0.694$) and Baumann angle ($P = 0.115$).

DISCUSSION

The management of pediatric supracondylar humeral fractures includes non-operative and operative treatments. Fractures are further individualized based on the presentation (open or closed fracture), Gartland classification, the degree of the displacement, and the physician preference[5,7,10]. Regarding operative treatments, CRPP is the mainstay of treatment for displaced extension type supracondylar fracture. However, controversy regarding the optimal technique, whether lateral pinning or crossed pinning, remains under discussion[7,15,16].

In this study, we retrospectively evaluated 101 patients; some managed by crossed pinning (27.8%) and others by lateral pinning (72.1% [2 pins in 50% and 3 pins in the remaining 50%]). Supracondylar fracture incidence was higher in males, nearly 2 times more than in females. The mean age was 5.87, ranging from 35 d to 13 years, with a peak incidence of 5-7 years. This result is comparable to the series done by Patel *et al*[17], where they reported a peak incidence in the 6-8-year-age group with an average age of 7.48 years. Also, male predominance was noted in Patel *et al*[17], Wilkins *et al*[18], and Solak *et al*[19] series. Most clinical and radiological studies used Baumann angle, Flynn grade, and fracture complications to assess clinical outcomes[20]. In our study, we used the MEPS and Baumann angle for this purpose. There was no statistically significant difference between the treatment groups.

The loss of reduction in our study was 0%. In a recent meta-analysis done by Dekker *et al*[20] comparing the two techniques, the loss of reduction occurred in 11.6% of patients treated by crossed pinning and 12.4% of patients treated with lateral pins. Yet, there was no statistically significant difference between the two groups. In addition, there was no significant difference according to the Flynn criteria, ROM, and measures of radiographic outcome.

Patel *et al*[17] also used MEPS for comparing lateral and crossed pinning technique outcomes. For the crossed pinning group, they reported that 90% of the patients had excellent outcomes, 10% had good outcomes, and 0% had poor outcomes. Lateral pinning showed 83.33% excellent and 16.66% good outcomes with no reports of poor outcome. While in our study, 62.5% of the patients in the lateral pinning group had excellent outcomes, 36.1% had good outcomes, and 1.4% had fair outcomes with no poor outcomes. Crossed pinning showed 62.1% excellent outcomes, 34.5% good outcomes, and 3.4% fair outcomes. Both studies showed no statistically significant difference between the two treatment groups.

Table 1 Demographic characteristics

		Lateral group	Cross pin group
Male		43 (59.7%)	20 (69%)
Female		29 (40.3%)	9 (31%)
Extension type 2		15 (20.8%)	6 (20.7%)
Extension type 3		36 (50%)	7 (24.1%)
Extension type 4		15 (20.8%)	13 (44.8%)
Flexion type		6 (8.3%)	3 (10.3%)
Age mean		5.7920	6.0693
Age SD		3.17336	3.0422
MEPS mean		93.6806	93.6207
MEPS SD		8.59877	9.05307
MEPS	Poor	0 (0%)	0 (0%)
	Fair	1 (1.4%)	1 (3.4%)
	Good	26 (36.1%)	10 (34.5%)
	Excellent	45 (62.5%)	18 (62.1%)
Bumann angle mean		72.5139	72.3103
Bumann angle SD		6.46114	4.70640

SD: Standard deviation.

It could be that the difference in the percentages is due to the difference in the interpretation of the MEPS, as 15 points were considered a clinically negligible difference.

Several biomechanical studies demonstrated that crossed pinning is more stable than lateral pinning, especially on rotational testing and valgus and varus loading[21-23]. On the other hand, other studies reported no statistically significant differences radiologically and clinically between the two groups[15, 16]. Although crossed pins seem to provide more stabilization, their major disadvantage is the iatrogenic ulnar nerve injury. The studies estimated it to occur 3 to 5 times more than lateral pins alone [15,16,20]. Conversely, Chen *et al*[24] reported no significant difference in the biomechanical stability between divergent lateral pins and crossed pins in terms of resisting varus, internal rotation, and extension forces. Also, Hamdi *et al*[25] suggested that two or three divergent lateral pins provide optimal fracture stability. These studies support the concept that properly placed lateral pins provide adequate biomechanical stability.

The limitations of our study include it being a retrospective study, not a randomized prospective clinical trial. Another major limitation was the uneven number of cases in each group in addition to them only being followed for short intervals. Furthermore, we included patients with flexion type supracondylar fractures, and these patients may constitute a different population from those with the extension type. Moreover, we did not analyze or report complications. Thus, a randomized controlled trial involving larger samples and evenly distributed cases with long-term follow-up is warranted in future studies.

CONCLUSION

Within the limitations of our study, the two techniques for displaced pediatric supracondylar humeral fractures promote similar postoperative results. There is no significant difference between lateral and crossed pinning techniques regarding the functional and radiological outcomes.

ARTICLE HIGHLIGHTS

Research background

The most widely accepted treatment for pediatric supracondylar humeral fracture is closed reduction

and percutaneous pinning. However, there is debate regarding the technique that is utilized, whether crossed or lateral pinning, and the number of pins used.

Research motivation

To compare the functional and radiological outcomes of lateral and cross pinning in the management of humeral supracondylar fracture.

Research objectives

To compare the functional and radiological outcomes of lateral and cross pinning in the management of humeral supracondylar fracture.

Research methods

A retrospective analysis was performed on 101 patients who were surgically managed by either one of the CRPP techniques from 2015 to 2019. Several clinical parameters were taken into account, including pre- and post-intervention Baumann's angle, as well as scores for pain, range of motion, function, and stability. Statistical analyses were performed to study the outcomes of the utilized techniques.

Research results

Amongst our study sample, which included 63 males and 38 females with a mean age of 5.87 years, about one-third of the patients underwent crossed pinning fixation configuration and the remaining two-thirds were managed by lateral pinning configuration. Similar results were obtained in the two groups with no statistical difference regarding Mayo elbow performance scores (MEPS) and Baumann's angle. The mean MEPS in the lateral and crossed pinning groups were 93.68 + 8.59 and 93.62 + 9.05, respectively. The mean Baumann's angle was 72.5 + 6.46 in the lateral group and 72.3 + 4.70 in the cross-pinning group (P = 0.878).

Research conclusions

Both lateral pinning and crossed pinning fixation configuration for displaced pediatric supracondylar humeral fractures provide similar functional and radiological outcomes.

Research perspectives

A randomized controlled trial involving larger samples and evenly distributed cases with long-term follow-up is warranted in future studies.

FOOTNOTES

Author contributions: Radaideh AM, Rusan M, Mohaidat ZM, Sunallah AW, and Obeidat O designed the research; Radaideh AM, Rusan M, Mohaidat ZM, Sunallah AW, Obeidat O, Al-Nusair J, and Albustami IS performed the research; Obeidat O analyzed the data; Obeidat O, Al-Nusair J, and Albustami IS wrote the paper.

Institutional review board statement: This work was approved by the institutional review board (IRB) committee of King Abdullah University Hospital (KAUH).

Conflict-of-interest statement: Radaideh, Rusan, Obeidat, AL-Nusair, Albustami, Mohaidat and Sunallah declare that they have no conflict of interest.

Data sharing statement: The original anonymous dataset is available on request from the corresponding author at ahmadmr1970@yahoo.com.

STROBE statement: The authors have read the STROBE Statement—checklist of items, and the manuscript was prepared and revised according to the STROBE Statement—checklist of items.

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REFERENCES

1 **Al-Omari AA**, Rusan M, Obeidat O, Almomani Z, Albustami IS, Alrawashdeh MA. Spontaneous Full Recovery of High Radial Nerve Palsy Following Closed Reduction and Percutaneous Pinning of Gartland IV Supracondylar Fracture: A Case Report. *Am J Case Rep* 2021; **22**: e930277 [PMID: 33735158 DOI: 10.12659/AJCR.930277]
2 **Soon-Hyuck L**. Upper Extremity Fractures in Children-Prospective Epidemiological Study of Tertiary Medical Institutes. *J Korean Orth Assoc* 2007; 270-275 [DOI: 10.4055/jkoa.2007.42.2.270]
3 **Gartland JJ**. Management of supracondylar fractures of the humerus in children. *Surg Gynecol Obstet* 1959; **109**: 145-154 [PMID: 13675986]
4 **Leitch KK**, Kay RM, Femino JD, Tolo VT, Storer SK, Skaggs DL. Treatment of multidirectionally unstable supracondylar humeral fractures in children. A modified Gartland type-IV fracture. *J Bone Joint Surg Am* 2006; **88**: 980-985 [PMID: 16651572 DOI: 10.2106/JBJS.D.02956]
5 **Milbrandt TA**. Common elbow injuries in children: evaluation, treatment, and clinical outcomes. *Current Opinion in Orthopaedics* 2004; **15**: 286-294 [DOI: 10.1097/00001433-200408000-00017]
6 **Diesselhorst MM**, Deck JW, Davey JP. Compartment syndrome of the upper arm after closed reduction and percutaneous pinning of a supracondylar humerus fracture. *J Pediatr Orthop* 2014; **34**: e1-e4 [PMID: 23774207 DOI: 10.1097/BPO.0b013e3182933c69]
7 **Vuillermin C**, May C, Kasser J. Closed Reduction and Percutaneous Pinning of Pediatric Supracondylar Humeral Fractures. *JBJS Essent Surg Tech* 2018; **8**: e10 [PMID: 30233982 DOI: 10.2106/JBJS.ST.16.00011]
8 **Bashyal RK**, Chu JY, Schoenecker PL, Dobbs MB, Luhmann SJ, Gordon JE. Complications after pinning of supracondylar distal humerus fractures. *J Pediatr Orthop* 2009; **29**: 704-708 [PMID: 20104149 DOI: 10.1097/BPO.0b013e3181b768ac]
9 **Leiblein M**, Lustenberger T, Schulz AK, Schmitz-Rixen T, Marzi I. Neurovascular complications after supracondylar humerus fractures in children. *Trauma Case Rep* 2017; **8**: 16-19 [PMID: 29644308 DOI: 10.1016/j.tcr.2017.01.013]
10 **Isa AD**, Furey A, Stone C. Functional outcome of supracondylar elbow fractures in children: a 3- to 5-year follow-up. *Can J Surg* 2014; **57**: 241-246 [PMID: 25078928 DOI: 10.1503/cjs.019513]
11 **Brauer CA**, Lee BM, Bae DS, Waters PM, Kocher MS. A systematic review of medial and lateral entry pinning vs lateral entry pinning for supracondylar fractures of the humerus. *J Pediatr Orthop* 2007; **27**: 181-186 [DOI: 10.1097/bpo.0b013e3180316cf1]
12 **Babal JC**, Mehlman CT, Klein G. Nerve injuries associated with pediatric supracondylar humeral fractures: a meta-analysis. *J Pediatr Orthop* 2010; **30**: 253-263 [PMID: 20357592 DOI: 10.1097/BPO.0b013e3181d213a6]
13 **Cusick MC**, Bonnaig NS, Azar FM, Mauck BM, Smith RA, Throckmorton TW. Accuracy and reliability of the Mayo Elbow Performance Score. *J Hand Surg Am* 2014; **39**: 1146-1150 [PMID: 24656392 DOI: 10.1016/j.jhsa.2014.01.041]
14 **Longo UG**, Franceschi F, Loppini M, Maffulli N, Denaro V. Rating systems for evaluation of the elbow. *Br Med Bull* 2008; **87**: 131-161 [PMID: 18539627 DOI: 10.1093/bmb/ldn023]
15 **Prashant K**, Lakhotia D, Bhattacharyya TD, Mahanta AK, Ravoof A. A comparative study of two percutaneous pinning techniques (lateral vs medial-lateral) for Gartland type III pediatric supracondylar fracture of the humerus. *J Orthop Traumatol* 2016; **17**: 223-229 [PMID: 27312248 DOI: 10.1007/s10195-016-0410-2]
16 **Kocher M**, Kasser J, Waters P, Bae D, Snyder B, Hresko M et al Lateral Entry Compared with Medial and Lateral Entry Pin Fixation for Completely Displaced Supracondylar Humeral Fractures in Children. J Bone & Joint Surg 2007; 89: 706-712 [DOI: 10.2106/jbjs.f.00379]
17 **Patel N**, Patil P, Gaonkar K, Kulkarni H, Gupta K. A comparative study of outcomes of percutaneous crossed *vs* lateral divergent pinning in the treatment of displaced (grade - 3) supracondylar fractures of humerus in children. *J Evidence Based Med Healthcare* 2015; **2**: 789-798 [DOI: 10.18410/jebmh/2015/113]
18 **Wilkins K**. The Operative Management of Supracondylar Fractures. *Orthopedic Clinics of North America* 1990; **21**: 269-289 [DOI: 10.1016/s0030-5898(20)31545-5]
19 **Solak S**, Aydin E. Comparison of two percutaneous pinning methods for the treatment of the pediatric type III supracondylar humerus fractures. *J Pediatr Orthop B* 2003; **12**: 346-349 [PMID: 12973045 DOI: 10.1097/01.bpb.0000060288.16932.08]
20 **Dekker AE**, Krijnen P, Schipper IB. Results of crossed *vs* lateral entry K-wire fixation of displaced pediatric supracondylar humeral fractures: A systematic review and meta-analysis. *Injury* 2016; **47**: 2391-2398 [DOI: 10.1016/j.injury.2016.08.022]
21 **Zionts LE**, McKellop HA, Hathaway R. Torsional strength of pin configurations used to fix supracondylar fractures of the humerus in children. *J Bone Joint Surg Am* 1994; **76**: 253-256 [PMID: 8113261 DOI: 10.2106/00004623-199402000-00013]
22 **Lee SS**, Mahar AT, Miesen D, Newton PO. Displaced pediatric supracondylar humerus fractures: biomechanical analysis of percutaneous pinning techniques. *J Pediatr Orthop* 2002; **22**: 440-443 [PMID: 12131437]
23 **Feng C**, Guo Y, Zhu Z, Zhang J, Wang Y. Biomechanical analysis of supracondylar humerus fracture pinning for fractures with coronal lateral obliquity. *J Pediatr Orthop* 2012; **32**: 196-200 [PMID: 22327455 DOI: 10.1097/BPO.0b013e318242a99a]
24 **Chen T**, He C, Zheng T, Gan Y, Huang M, Zheng Y, et al. Stiffness of various pin configurations for pediatric

supracondylar humeral fracture. *J Pediatr Orthop* 2015; **24**: 389-399 [DOI: 10.1097/bpb.0000000000000196]

25 **Hamdi A**, Poitras P, Louati H, Dagenais S, Masquijo JJ, Kontio K. Biomechanical analysis of lateral pin placements for pediatric supracondylar humerus fractures. *J Pediatr Orthop* 2010; **30**: 135-139 [PMID: 20179560 DOI: 10.1097/BPO.0b013e3181cfcd14]

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ORIGINAL ARTICLE

Retrospective Study

Accuracy of shoulder joint injections with ultrasound guidance: Confirmed by magnetic resonance arthrography

Kosuke Kuratani, Makoto Tanaka, Hiroto Hanai, Kenji Hayashida

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Abstract

BACKGROUND

Intra-articular glenohumeral joint injections are essential procedures for treating various shoulder disorders. Fluoroscopy-guided injections have been extensively used; however, they pose a risk of radiation exposure and are expensive and time-consuming. Recently, it has been suggested that ultrasound-guided injections are accurate and cost effective procedures.

AIM

To evaluate the accuracy of ultrasound-guided glenohumeral injections using a posterior approach that is confirmed using magnetic resonance arthrography (MRA).

METHODS

The study included 179 shoulders of patients with recurrent anterior instability (150 patients; 103 and 76 right and left shoulders, respectively; 160 males and 19 females; average age = 20.5 years; age range: 14-63 years) who underwent MRA for preoperative diagnosis. They were injected with 12 mL lidocaine (1%) using the ultrasound-guided posterior approach and then underwent magnetic resonance imaging. Two shoulder surgeons, except for the injector, evaluated the transverse relaxation (T2)-weighted images of axial planes and classified the intra-articular condition of injected contrast into three groups based on one of the three

following scenarios: no leakage, injection into the glenohumeral joint without leakage; minor leakage, practical intra-articular injection with some leakage outside the posterior rotator cuffs; and major leakage, inaccurate injection with mass leakage without any contrast into the joint. The inter-rater reliability between two assessors was also evaluated by calculating Cohen's kappa coefficient. The learning curve was assessed regarding the inaccurate injection rate by analyzing Spearman's rank correlation coefficient.

RESULTS

Of the 179 injections, 163 shoulders (91.0%) had no leakage, 10 shoulders (5.6%) had minor leakage, and six shoulders (3.4%) had major leakage. In total, 173 shoulders (96.6%) were intra-articularly injected; thus, we could detect anterior labrum and capsular pathologies. Regarding the inter-rater reliability, the kappa coefficient was 0.925, indicating consistency in the evaluations by both examiners. Regression analysis of the inaccurate injection rate for assessingtechnical learning showed a logarithmic curve with a downward trend ($R^2 = 0.887$, $P < 0.001$). Three (50%) of the six inaccurate injections classified into "major leakage" were observed in the first 30 injections, indicating that the accurate injection showed a leaning effect.

CONCLUSION

Ultrasound-guided intra-articular glenohumeral injections using a posterior approach had high accuracy; however, injection accuracy depends on clinical experience.

Key Words: Shoulder injections; Glenohumeral injections; Ultrasound guidance; Magnetic resonance arthrography

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Core Tip: This is a retrospective study that has evaluated the accuracy of ultrasound-guided glenohumeral injection confirmed using magnetic resonance arthrography. In this study, 163 shoulders (91.0%) were accurately injected without leakage outside the glenohumeral joint. Ten shoulders (5.6%) had minor leakage. In total, 173 shoulders (96.6%) were intra-articularly injected. Ultrasound-guided intra-articular glenohumeral injection using a posterior approach is an accurate injection procedure.

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INTRODUCTION

Intra-articular glenohumeral joint injections are essential procedures for treating various shoulder disorders at clinical settings, such as frozen shoulder, osteoarthritis, and rheumatoid arthritis[1]. These injections are distinguished from subacromial injections commonly used for treating subacromial bursitis, rotator cuff tears, and impingement syndrome. Accurate intra-articular injections of drugs can provide good clinical outcomes and enhance patients' satisfaction with treatment. Furthermore, accurate intra-articular injections of lidocaine, commonly referred to as the lidocaine test, help develop accurate clinical diagnoses. Conversely, injections at erroneous locations may cause damage to nerves, vessels, muscles, or ligaments around the shoulder, and inaccurate injections of lidocaine may mislead the clinical assessment.

Various shoulder injection techniques have been used by orthopedic surgeons or radiologists in their efforts to perform arthrograms. These injection techniques include: (1) blind injections with structures that can be palpated from the body surface, such as the acromion and coracoid process; and (2) image-guided injections with fluoroscopic or ultrasonic guidance, using the anterior, posterior, or supraclavicular approach[2-5].

Conversely, magnetic resonance arthrography (MRA) is a valuable tool used for detecting rotator cuff tears or anterior shoulder instabilities associated with anterior labrum and capsular pathologies. Some studies have reported that MRA is superior to magnetic resonance imaging (MRI) and computed tomography arthrography (CTA) in detecting lesions associated with anterior shoulder instabilities[6, 7]. Precise imaging of these shoulder abnormalities can help plan operative procedures.

A fluoroscopy-guided shoulder injection has been extensively used in conjunction with MRA. This technique was first reported by Baert *et al* in 1933[8], while other studies have reported that the accuracy of fluoroscopy-guided shoulder injections is in the range of 62%-100%[9-11]. However, fluoroscopy-guided injections expose both the examiners and patients to radiation. When MRA is considered helpful for diagnosis, outsourcing the MRA examinations to special institutions is common. However, in Japan, only a few institutions offer MRA examinations because of the lack of dedicated radiologists who can conduct arthrograms. Accordingly, orthopedic surgeons themselves are often needed to perform intra-articular injections before MRI examinations. In these cases, fluoroscopy and MRI reservations are required that is cost-demanding and time-consuming. Therefore, at our institution, we typically perform ultrasonography-guided shoulder injections in conjunction with MRA. The ultrasonographic examinations can be performed before MRI. These procedures are not as time-consuming as the injections performed with fluoroscopy. Recently, ultrasonography has become a widely used diagnostic tool in the field of orthopedics because of its availability, safety, and high diagnostic potential. Particularly, the shoulder joint is one of the bodily areas for which ultrasonography is most useful. Ultrasonography can detect tendons, fluid around the biceps or subacromial bursa, and the contours of the glenohumeral joint clearly that it enables early detection of rotator cuff or intra-articular pathologies, such as tears and fractures[12]. Moreover, ultrasound-guided injections have been gaining attention due to their accessibilities and safety withoutradiation exposure and direct observation of the needle[13]. Although some reports have described the convenience of ultrasound-guided injections, no reports have evaluated its accuracy.

This study was designed to evaluate the accuracy of ultrasound-guided glenohumeral joint injections using a posterior approach confirmed using MRA.

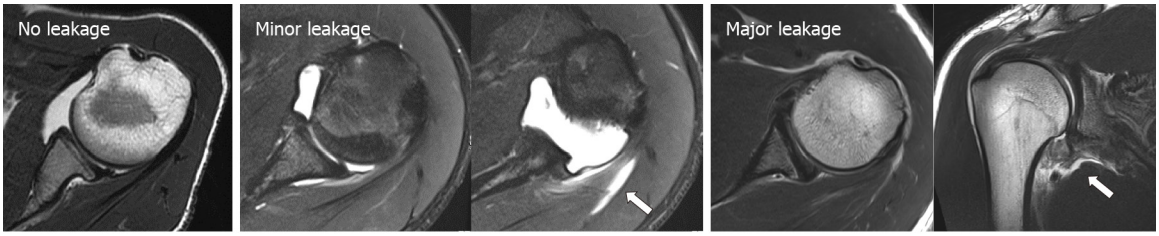
MATERIALS AND METHODS

We retrospectively reviewed the MRA images of patients with recurrent anterior shoulder instability. This study has been approved by the Internal Review Board of the corresponding author's affiliated institution. We excluded patients with rotator cuff tears and posterior shoulder instabilities and those who underwent surgeries. In total, 179 shoulders of 150 patients (including 103 right and 76 Left shoulders; 160 males and 19 females; average age of 20.5 years; age range, 14–63 years) were included in this study. Injections were performed with ultrasound guidance using the posterior approach, followed by MRI examinations (Magnetom Spectra 3T; Siemens Japan, Tokyo, Japan). Two shoulder surgeons, except for the injector, evaluated the transverse relaxation (T2)-weighted images of axial planes and classified the intra-articular condition of the injected contrast into three groups based on one of the three following scenarios. "No leakage" indicates injection into the glenohumeral joint without evidence of leakage. "Minor leakage" indicates intra-articular injections with some leakage outside the posterior rotator cuffs. "Major leakage" indicates inaccurate injection with severe/mass leakage without any contrast into the glenohumeral joint. Diagnosing joint pathologies in the last case was impossible (Figure 1). The chi-square test was used to compare the injection accuracy of the right and left shoulders. The inter-rater reliability between two assessors was evaluated by calculating Cohen's kappa coefficient. Moreover, the learning curve was assessed by determining the inaccuracy rate relative to the total cases. We defined inaccurate injection rate as the total number of "major leakage" divided by the total number of cases that was recorded every 10 cases and examined the correlation between the inaccurate injection rate and number of cases. This was analyzed using Spearman's rank correlation coefficient. All statistical analyses were performed using Statistical Package for the Social Sciences (version 26; IBM, NY, United States), and P values of less than 0.05 were used to denote statistical significance.

Injection technique

All injections were performed by an experienced surgeon (M.T.). The procedures were performed with the patients in the upright sitting position with their shoulders at the neutral rotation position. Ultrasound examinations were performed using a portable equipment (HI VISION Avius, HITACHI, Japan). The linear ultrasonic probe was operated within a variable frequency range (*i.e.*, 6–14 Hz) and was held horizontally and placed over the posterior aspect of the shoulder (Figure 2), allowing the detection of the glenohumeral joint space (Figure 3A). A 23-gage cathelin needle was inserted using an out-of-plane technique toward the gap between the humeral head and glenoid rim, and 12 mL lidocaine (1%) was administered. In the out-of-plane technique, observing the needle tip at all times during injection is difficult; however, the movement of the needle tip can be detected through the movement of soft tissues. Furthermore, as long as the needle does not deviate from the center of the ultrasound probe, the needle tip theoretically reaches the target in the glenohumeral joint. When the needle tip reaches the joint, the drug can be smoothly injected, and simultaneously, the flow of the fluid can be confirmed in the joint on the ultrasound image (Figure 3B and C).

MRI scans were obtained within 60 min after the injections.



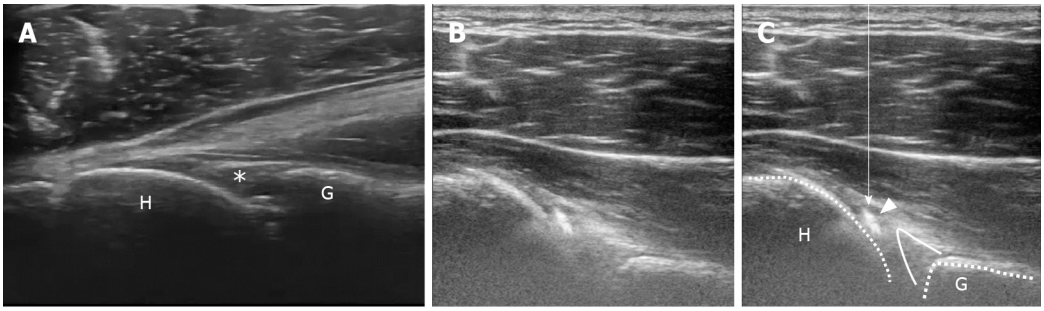
DOI: 10.5312/wjo.v13.i3.259 **Copyright** © The Author(s) 2022.

Figure 1 Classification of the transverse relaxation (T2)-weighted images of magnetic resonance arthrography into three groups. No leakage: Right shoulder injection into the glenohumeral joint without leakage; Minor leakage: Practical intra-articular right shoulder injection; however, another magnetic resonance arthrography image shows the presence of some leakage (white arrow) outside the posterior cuff; Major leakage: Inaccurate injection into the glenohumeral joint of the right shoulder with a noted severe/mass leakage (white arrow) surrounding the axillary area.



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Figure 2 The setting of the injection procedure. Glenohumeral injection performed by a shoulder surgeon using ultrasonic guidance. The patient sits upright with the shoulder at a neutral rotation position, and the ultrasonic probe is placed over the posterior part of the right shoulder.



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Figure 3 Identification of the glenohumeral joint and needle insertion point on a captured ultrasound image. A: The gap between the humeral head (H) and glenoid rim (G) is the target of this injection. The needle insertion point (asterisk) should be visualized more clearly; B: Ultrasonographic image during injection; C: Arrowhead shows the high echoic flow of the injection and arrow line indicates the assumed needle path.

RESULTS

No patient complained of poor physical conditions after the injections. Additionally, no neurological disturbances were observed. From the 179 injections, 163 (91.0%) were completely administered in the glenohumeral joint and were classified as "no leakage." Furthermore, intra-articular injection with some leakage out of the rotator cuffs was detected in 10 shoulders (5.6%), and these were classified as "minor leakage" (Table 1). We could detect anterior labrum and capsular pathologies in 96.6% (173/179 shoulders) of the tested cases. Six shoulders were classified as "major leakage." In these cases, the leakages were mostly observed around the axillary area. No significant differences in the accuracy were observed between the right and left shoulders. Regarding the inter-rater reliability, the kappa coefficient was 0.925, indicating consistency in the evaluations by both examiners. Regression analysis of the inaccurate injection rate showed that the curve was logarithmic with a downward trend ($R^2 = 0.887$; $P <$

Table 1 The accuracy of the injections

	No leakage	Minor leakage	Major leakage	Total
Right	94 (91.3%)	7 (6.8%)	2 (1.9%)	103
Left	69 (90.1%)	3 (3.9%)	4 (5.3%)	76
Total	163 (91.0%)	10 (5.6%)	6 (3.4%)	179

No leakage: Injection into the glenohumeral joint without any leakage; Minor leakage: Practical intra-articular right shoulder injection; however, another magnetic resonance arthrography image shows the presence of some leakage outside the posterior cuff; Major leakage: Inaccurate injection into the glenohumeral joint with a noted mass leakage. Right: Right shoulders; Left: Left shoulders.

0.001) (Figure 4). Three (50%) of the six inaccurate injections that were classified into "major leakage" were observed in the first 30 injections. This indicated that the accurate injection showed a leaning effect.

DISCUSSION

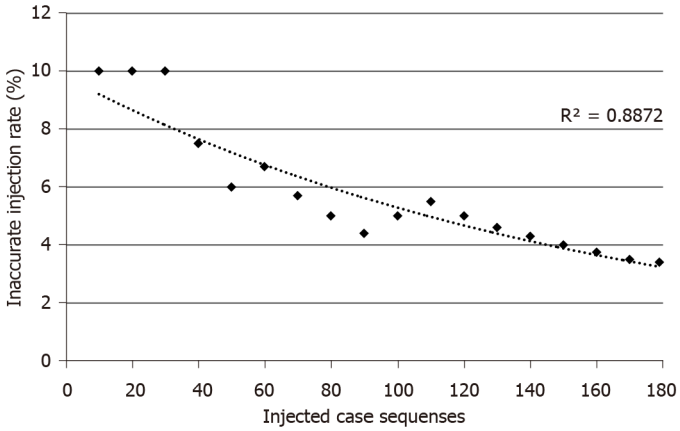
An intra-articular shoulder injection is an important technique for diagnosing and treating various shoulder disorders. However, it is reported: (1) that these injections are more difficult to perform than other joint injection types; and (2) that theaccuracy of injection into the glenohumeral joint is poor when performed without image guidance.

Some studies have reported about the accuracy and techniques of shoulder injection. Cunnington *et al* [2] have compared the accuracy of ultrasound-guided injections conducted by research fellows with that of blind (clinical examination-guided) injections conducted by rheumatology consultants for the shoulders, elbows, knees, and ankles and found that ultrasound-guided injections were significantly more accurate than blind injections. Moreover, they have reported that the accuracy of blind injections to the glenohumeral joint was only 40% (8/20 shoulders), which tended to be more difficult than other joint injections. Tobola *et al*[14] have reported on the technique and accuracy of blind injections using theanterior, posterior, and supraclavicular approaches implemented by different providers. As indicated, the anterior approach was the most accurate (22/34 shoulders, 64.7%) in shoulder cases, regardless of the experience of the clinicians who performed them. Patel *et al*[4] have evaluated the accuracy of the ultrasound-guided posterior approach on fresh cadaver shoulders and reported that the accuracy was 92.5% (37/40 shoulders) and showed no significant differences owing to the clinical experiences of the injectors. Most injection accuracy reports have been associated with the use of fluoroscopic images (acquired after the injection procedures) to confirm the intra-articular contrast. Sethi *et al* [15] performed injections using the blind approach with an accuracy of 26.8% with fluoroscopic confirmation. In this study, we evaluated the accuracy of intra-articular shoulder injections using the ultrasound-guided posterior approach in conjunction with MRA images acquired from 179 shoulders (150 patients) for the preoperative diagnosis of anterior shoulder instabilities.

There have been various reports of the accuracy of shoulder injections. However, no reports have neither evaluated injections into the shoulders of living patients nor assessed these using MRA images. In this study, intra-articular shoulder injections that can provide helpful information on labrum and capsular pathologies were performed on 173/179 shoulders (96.6%). The accuracy was equally good or better than those reported in previous cadaveric studies[4].

In current clinical settings, a fluoroscopy-guided injection technique is still extensively used when CTA or MRA is available. Dépelteau *et al*[9] have reported the accuracy of fluoroscopy-guided injections. In these, 59/65 shoulders (90.8%) were successfully injected on the first attempt, four shoulders (6.2%) on the second attempt, and one (1.5%) shoulder on the third attempt. A fluoroscopy-guided technique allows multiple punctures until accurate injection is achieved given that judging whether the contrast material has been injected into the joint during the injection is possible. Conversely, in an ultrasound-guided technique, only indirect information, such as the patient's pain or injector's sensation (*e.g.*, injection pressure), can determine whether the injection is accurate or not. Another disadvantage of an ultrasound-guided injection technique is that detecting the glenohumeral joint space in obese patients it could be difficult because of deep attenuation of ultrasound, unlike the fluoroscopy-guided injection. In such cases, passive movement of the upper arm during ultrasound examination could make detecting the joint space easier. Eventually, we could perform intra-articular injections into the glenohumeral joint with the same or higher accuracy than that reported previously in fluoroscopy-guided injections.

Ultrasound-guided injections have some benefits. They allow more accurate intra-articular injections based on the visualization of the needle's position. Additionally, the portability of the ultrasound equipment could allow the execution of the injections quickly in the examination room; thus, reserving a



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Figure 4 Learning curve. The inaccurate injection rate is the total number of "major leakage" divided by the total number of injected cases that was recorded every 10 cases. The learning curve is represented by the dotted curve. Spearman's rank correlation coefficient was analyzed ($R^2 = 0.887$, $P < 0.001$).

fluoroscopy room is not needed, and there is no risk of radiation exposure for both doctors and patients. Additionally, the ultrasound-guided injection technique is a simple procedure and is considered superior to fluoroscopy-guided injection techniques in terms of time and cost-effectiveness[16].

In this study, we performed injections using the ultrasound-guided out-of-plane technique; however, observing the needle path continually from the insertion point was more difficult than that using the in-plane technique. Therefore, fulfilling the aim of this injection is necessary, that is, the clear detection and visualization of the gap between the glenoid rim and humeral head achieved by holding the probe in a stable manner at the target position. Conversely, unlike the in-plane technique, in the out-of-plane technique, the injector does not need to change the hand sides that hold the ultrasound probe or the syringe, depending on the side the patient's shoulder. Correspondingly, we can always perform injections using the same procedure. In a blind injection technique, an anterior approach was reported to be the most accurate. In previous reports, fluoroscopy-guided injections had been performed using the anterior approach. This is because landmarks around the shoulder palpated from the anterior body surface, such as the acromion and coracoid process, can provide helpful indications for the injection. However, in an ultrasound-guided injection technique, a posterior approach may allow easier detection of the joint space, given that there are no structures on the posterior shoulder.

The study strengths are the patient size and the technique used to accurately evaluate the accuracy of intra-articular shoulder injections. This study represents the largest patient size among all available reports that targeted the accuracy of injection techniques. In previous reports, fluoroscopy images were used to evaluate the condition of the joint and the accuracy of the injection; however, MRA images could allow us to clearly evaluate intra-articular contrast and leakage outside the joint because identifying the location of the contrast material in a three-dimensional view is possible.

This study has some limitations. First, this study evaluated the accuracy of ultrasound-guided injections performed by a single shoulder surgeon. Whether inexperienced physicians, surgeons who do not specialize in shoulder surgeries, or trainee surgeons who specialize in shoulder surgeries could equally achieve accurate injection outcomes is unclear. Additional studies, including the participation of injectors with different experiences and comparisons with other image-guided techniques or approaches are needed. Second, this study has no control group with blind injections. MRA is an essential test for patients with anterior shoulder instability to detect capsular and labral pathologies. A control group could not be established because of the potential disadvantage to the patients if ultrasound guidance is not used.

Third, the subjects of this study were patients with anterior shoulder instabilities in a relatively young age. We have not assessed the accuracy of intra-articular injections for other shoulder disorders, such as osteoarthritis, rheumatoid arthritis, and frozen shoulders. An ultrasound-guided intra-articular injection could be more difficult for older patients owing to capsular contractures or the presence of osteophytes.

CONCLUSION

Ultrasound-guided intra-articular glenohumeral injections using the posterior approach were an accurate procedure. Of the 179 shoulders, 163 (91.0%) were accurately injected, and 173/179 injections were conducted intra-articularly and provided useful MRA images to detect abnormalities in the glenohumeral joint. We encourage using ultrasonic guidance during shoulder injections because it is a simple and cost effective procedure with acceptable accuracy.

ARTICLE HIGHLIGHTS

Research background

Intra-articular glenohumeral joint injections are essential procedures in a clinical setting of shoulder surgery. In general, a fluoroscopy-guided shoulder injection has been extensively used.

Research motivation

At our institution, we typically perform ultrasound-guided shoulder injections for magnetic resonance arthrography (MRA). The accuracy of ultrasound guided shoulder injection has not been reported.

Research objectives

To evaluate the accuracy of ultrasound-guided shoulder injections with MRA images.

Research methods

We reviewed the shoulder MRA images of patients with anterior shoulder instability and classified the intra-articular condition in three groups and calculated the injection accuracy.

Research results

From the total of 179 injections, 163 (91.0%) were completely administered in the glenohumeral joint. In addition, intra-articular injection with some leakage was detected in 10 shoulders (5.6%).

Research conclusions

The ultrasound-guided shoulder injection was shown to be a very accurate procedure.

Research perspectives

Further, it is necessary to evaluate whether this technique is effective even for inexperienced examiners.

FOOTNOTES

Author contributions: Kuratani K performed the research, contributed to the analysis and wrote the paper; Tanaka M designed and performed the research and supervised the report; Hanai H supervised the statistical analysis; Hayashida K designed the research and supervised the report.

Institutional review board statement: This research has been approved by the IRB of the corresponding author's affiliated institution.

Informed consent statement: Patients were not required to give informed consent to this study because the analysis used clinical data that were obtained after each patient agreed to treatment by written consent.

Conflict-of-interest statement: We have no financial relationships to disclose.

Data sharing statement: No additional data are available.

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P-Editor: Zhang H

REFERENCES

1 **Sun Y**, Zhang P, Liu S, Li H, Jiang J, Chen S, Chen J. Intra-articular Steroid Injection for Frozen Shoulder: A Systematic Review and Meta-analysis of Randomized Controlled Trials With Trial Sequential Analysis. *Am J Sports Med* 2017; **45**:

2171-2179 [PMID: 28298050 DOI: 10.1177/0363546516669944]
2 **Cunnington J**, Marshall N, Hide G, Bracewell C, Isaacs J, Platt P, Kane D. A randomized, double-blind, controlled study of ultrasound-guided corticosteroid injection into the joint of patients with inflammatory arthritis. *Arthritis Rheum* 2010; **62**: 1862-1869 [PMID: 20222114 DOI: 10.1002/art.27448]
3 **Aly AR**, Rajasekaran S, Ashworth N. Ultrasound-guided shoulder girdle injections are more accurate and more effective than landmark-guided injections: a systematic review and meta-analysis. *Br J Sports Med* 2015; **49**: 1042-1049 [PMID: 25403682 DOI: 10.1136/bjsports-2014-093573]
4 **Patel DN**, Nayyar S, Hasan S, Khatib O, Sidash S, Jazrawi LM. Comparison of ultrasound-guided *vs* blind glenohumeral injections: a cadaveric study. *J Shoulder Elbow Surg* 2012; **21**: 1664-1668 [PMID: 22445159 DOI: 10.1016/j.jse.2011.11.026]
5 **Koraman E**, Turkmen I, Uygur E, Poyanlı O. A Multisite Injection Is More Effective Than a Single Glenohumeral Injection of Corticosteroid in the Treatment of Primary Frozen Shoulder: A Randomized Controlled Trial. *Arthroscopy* 2021; **37**: 2031-2040 [PMID: 33581295 DOI: 10.1016/j.arthro.2021.01.069]
6 **Roy JS**, Braën C, Leblond J, Desmeules F, Dionne CE, MacDermid JC, Bureau NJ, Frémont P. Diagnostic accuracy of ultrasonography, MRI and MR arthrography in the characterisation of rotator cuff disorders: a systematic review and meta-analysis. *Br J Sports Med* 2015; **49**: 1316-1328 [PMID: 25677796 DOI: 10.1136/bjsports-2014-094148]
7 **Smith TO**, Drew BT, Toms AP. A meta-analysis of the diagnostic test accuracy of MRA and MRI for the detection of glenoid labral injury. *Arch Orthop Trauma Surg* 2012; **132**: 905-919 [PMID: 22395821 DOI: 10.1007/s00402-012-1493-8]
8 **Baert AL**. Imaging of the Shoulder, Techniques and Applications. Leuven: Springer Science & Business Media, 2003: 15-16
9 **Dépelteau H**, Bureau NJ, Cardinal E, Aubin B, Brassard P. Arthrography of the shoulder: a simple fluoroscopically guided approach for targeting the rotator cuff interval. *AJR Am J Roentgenol* 2004; **182**: 329-332 [PMID: 14736656 DOI: 10.2214/ajr.182.2.1820329]
10 **Gupton TB Jr**, Delgado J, Jaramillo D, Cahill AM, Chauvin NA. Comparative analysis of anterior and posterior contrast injection approaches for shoulder MR arthrograms in adolescents. *Pediatr Radiol* 2016; **46**: 1848-1855 [PMID: 27587064 DOI: 10.1007/s00247-016-3691-y]
11 **Rutten MJ**, Collins JM, Maresch BJ, Smeets JH, Janssen CM, Kiemeney LA, Jager GJ. Glenohumeral joint injection: a comparative study of ultrasound and fluoroscopically guided techniques before MR arthrography. *Eur Radiol* 2009; **19**: 722-730 [PMID: 18958474 DOI: 10.1007/s00330-008-1200-x]
12 **Blankstein A**. Ultrasound in the diagnosis of clinical orthopedics: The orthopedic stethoscope. *World J Orthop* 2011; **2**: 13-24 [PMID: 22474631 DOI: 10.5312/wjo.v2.i2.13]
13 **Royall NA**, Farrin E, Bahner DP, Stawicki SP. Ultrasound-assisted musculoskeletal procedures: A practical overview of current literature. *World J Orthop* 2011; **2**: 57-66 [PMID: 22474637 DOI: 10.5312/wjo.v2.i7]
14 **Tobola A**, Cook C, Cassas KJ, Hawkins RJ, Wienke JR, Tolan S, Kissenberth MJ. Accuracy of glenohumeral joint injections: comparing approach and experience of provider. *J Shoulder Elbow Surg* 2011; **20**: 1147-1154 [PMID: 21493103 DOI: 10.1016/j.jse.2010.12.021]
15 **Sethi PM**, Kingston S, Elattrache N. Accuracy of anterior intra-articular injection of the glenohumeral joint. *Arthroscopy* 2005; **21**: 77-80 [PMID: 15650670 DOI: 10.1016/j.arthro.2004.09.009]
16 **Gyftopoulos S**, Abballe V, Virk MS, Koo J, Gold HT, Subhas N. Comparison Between Image-Guided and Landmark-Based Glenohumeral Joint Injections for the Treatment of Adhesive Capsulitis: A Cost-Effectiveness Study. *AJR Am J Roentgenol* 2018; **210**: 1279-1287 [PMID: 29629805 DOI: 10.2214/AJR.17.19011]

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ORIGINAL ARTICLE

Retrospective Study

Comparative study of intertrochanteric fracture fixation using proximal femoral nail with and without distal interlocking screws

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Specialty type: Orthopedics

Provenance and peer review: Invited article; Externally peer reviewed.

Peer-review model: Single blind

Peer-review report's scientific quality classification

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Grade B (Very good): 0
Grade C (Good): C, C
Grade D (Fair): D
Grade E (Poor): 0

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Abstract

BACKGROUND

Intertrochanteric (IT) fracture is one of the most common fractures seen in an orthopaedic practice. Proximal femoral nailing (PFN) is a common modality of fixing IT femur fracture. We retrospectively studied whether a PFN with two proximal lag screws can be done without distal interlocking screws in the 31-A1 and 31-A2 fracture patterns according to the Arbeitsgemeinschaft für Osteosynthesefragen/Orthopaedic Trauma Association (AO/OTA) guidelines for IT femur fractures.

AIM

To compare the outcomes of IT fractures (AO/OTA 31-A1 and 31-A2) treated by PFN with and without distal interlocking screws.

METHODS

We carried out a retrospective study of 140 patients in a tertiary care centre who had AO/OTA type 31-A1 and 31-A2 IT fractures. We divided the patients into two groups, in which one of the groups received distal interlocking screws (group 1) and the other group did not (group 2). The subjects were followed up for a mean period of 14 mo and assessed for radiological union time, fracture site collapse, mechanical stability of implant, and complications associated with the PFN with distal interlocking and without distal interlocking. Then, the results were compared.

RESULTS

PFN without distal interlocking screws has several advantages and gives better results over PFN with distal interlocking screws in the AO/OTA 31-A2 fracture pattern. However, similar results were observed in both groups with the fracture pattern AO/OTA 31-A1. In patients with fracture pattern AO/OTA 31-A2 treated by PFN without distal interlocking screws, there were minimal proximal lock-related complications and no risk of distal interlock-related complications. The operative time, IITV radiation time and time to radiological union were reduced.

These patients also had better rotational alignment of the proximal femur, and the anatomy of the proximal femur was well maintained. It was also noted that in the cases where distal interlocking was performed, there was a gradual decrease in neck shaft angle, which led to varus collapse and failure of bone-implant construct in 21.40%.

CONCLUSION

In fracture pattern AO/OTA 31-A2, PFN without distal interlocking had better results and less complications than PFN with distal interlocking.

Key Words: Intertrochanteric fracture; Arbeitsgemeinschaft für Osteosynthesefra-gen/Orthopaedic Trauma Association 31-A1 and 31-A2; Proximal femoral nail; Distal interlocking screws; Without distal interlocking screws; Outcome

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Core Tip: There are few studies comparing clinical and radiological results of proximal femoral nail (PFN) with and without distal interlocking in fracture pattern 31-A1 and 31-A2 according to the Arbeitsgemeinschaft für Osteosynthesefragen/Orthopaedic Trauma Association guidelines. From this retrospective study, we conclude that in type 31-A1 intertrochanteric fractures use of long anatomical PFN with or without distal interlocking screws have similar results in terms of radiological union, postoperative proximal femur anatomy, and rotational alignment. In type 31-A2, the use of long anatomical PFN without distal interlocking screws gives better results and less proximal lock-related complications than PFN with distal interlocking screws.

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INTRODUCTION

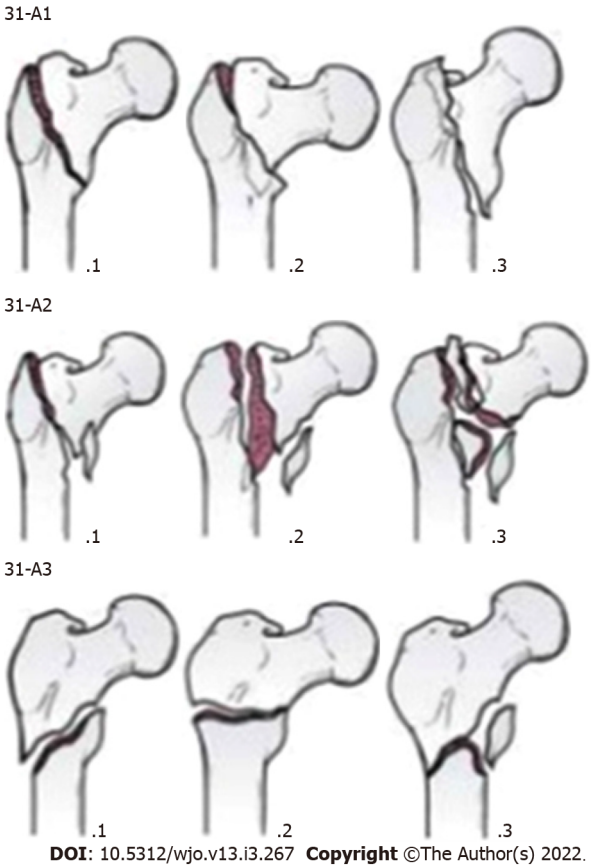
The incidence of fractures in the trochanteric area has risen with the increasing numbers of elderly persons with osteoporosis[1]. Intertrochanteric (IT) fracture is one of the most common fractures seen in orthopaedic practices, and proximal femoral nailing (PFN) has become a popular modality for its treatment. As per the Orthopaedic Trauma Association (OTA) classification system, these fractures are classified as Arbeitsgemeinschaft für Osteosynthesefragen (AO)/OTA 31-A and are further subdivided into groups A1, A2 and A3 (Figure 1). A1 fractures consist of two-part fractures, A2 fractures have multiple fragments, and A3 fractures include reverse oblique and transverse fracture patterns[2,3].

In 1996, for the treatment of unstable per-, intra- and subtrochanteric femur fractures the AO/Association for the Study of Internal Fixation designed the PFN as an intramedullary (IM) device [4]. It is routine practice to perform distal interlocking for fracture fixation while using PFN. Distal interlocking screws of the IM nail were made to avoid longitudinal or rotational instability as well as movement of distal tip of nail in cases of a broad canal for the IT fracture[5]. Nonetheless, drawback of the distal interlocking screw, like loosening, breaking and subsequent peripheral injures, and secondary femur fractures could not be ignored due to the minimal advantages gained[6].

The purpose of this study was to compare the outcomes of IT fractures (AO/OTA 31-A1 and 31-A2) treated by PFN with and without distal interlocking. We hypothesized that PFN without distal interlocking could be a dependable and acceptable option for IT fractures (AO/OTA 31-A1 and 31-A2).

MATERIALS AND METHODS

We conducted a retrospective study among 140 patients with AO/OTA 31-A1 and 31-A2 fractures treated with PFN at our institute from November 2016 to November 2019. The patients were divided into two equal groups, as follows: 70 patients treated with PFN with distal interlocking screws (group 1); and 70 patients treated without distal interlocking screws (group 2). The same chief surgeon performed the operations of all of the patients.



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Figure 1 Arbeitsgemeinschaft für Osteosynthesefragen/Orthopaedic Trauma Association classification of 31-A fractures. Arbeitsgemeinschaft für Osteosynthesefragen/Orthopaedic Trauma Association classification as follows: (1) A1: Simple two part, lateral cortex remains intact; (2) A2: Comminuted withpostero-medial fragment,lateral cortex remains intact; and (3) A3: line extend acrossboth medial and lateralcortices,include reverseobliques.

Inclusion criteria included AO/OTA 31-A1 and AO/OTA 31-A2 fracture pattern, age more than 20 years, no other injury or fracture, and those treated with long anatomical design PFN. Exclusion criteria included AO/OTA 31-A3 fracture pattern, age less than 20 years, patients lost to follow-up, patients having surgical site infection, and those treated with short PFN.

In our institute, standard preoperative workup included radiographic evaluation of the fracture type along with blood, medical and anaesthetic assessments. Postoperative protocol included intravenous antibiotics given for 48 h followed by oral antibiotics. On postoperative day 1 of surgery, bedside knee bending, static quadriceps exercises and ankle toe mobilisation exercises were started under supervision of a physical therapist. Regular stitch dressings were completed every third day, and stitches were removed between 12-14 d postoperatively. All patients were sent to the same rehabilitation program. Patients were followed up weekly for the first month after surgery. After that, they received follow-up care every 15 d for the next 2 mo and then monthly follow-up for 14 mo.

The patients were evaluated based on the following clinical and radiological parameters: (1) Fracture patterns according to the AO/OTA classification; (2) Duration of surgery (starting from skin incision to skin closure); (3) Time of IITV radiation exposure; (4) Time to radiological union; (5) Implant-related complications like backing-out of proximal screws from the lateral cortex of the femur, 'Z' effect, screw breakage, cut-through of implant from femoral head, breakage of distal interlocking screw, and breakage of nail; (6) Anatomy of the proximal femur (neck shaft angle of femur); (7) Level of the distal lock screw in relation to the nail in the anterior posterior (AP) view of the postoperative radiograph and radiograph after union were compared in group 1 and the downward migration of the nail in the IM canal in the AP view of the postoperative radiograph and radiograph after union were compared in group 2; and (8) Length and rotation of the limb after healing.

RESULTS

Out of 140 patients, the 70 patients in group 1 were treated with PFN with distal interlocking screws. Among these, 24 were male and 46 were female, and 32 patients had AO/OTA 31-A1 fracture pattern and 38 patients had AO/OTA 31-A2 fracture pattern. In group 2, 70 patients were treated with PFN without distal interlocking screws. Among these, 29 were male and 41 were female, and 28 patients had

Table 1 Distribution of participants according to groups, gender and fracture pattern according Arbeitsgemeinschaft für Osteosynthesefragen/Orthopaedic Trauma Association classification

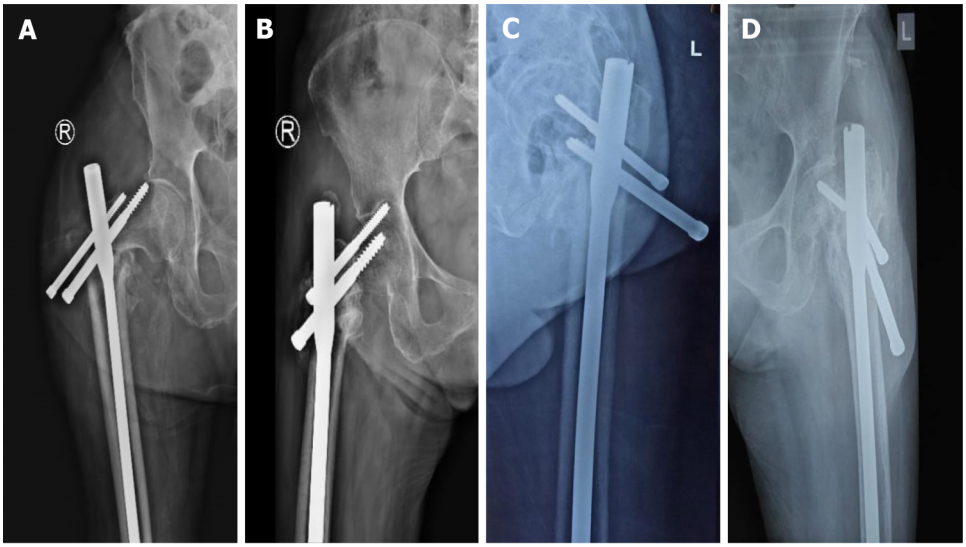
	Group-1 (with distal locking)	Group-2 (without distal locking)
Male	24	29
Female	46	41
Total patients	70	70
31-A1	32	28
31-A2	38	42

Table 2 Comparison of operative time and IITV radiation time amongst both groups

	Group-1	Group-2	*P* value
Average operative time	42 min	28 min	< 0.001
Average IITV radiation time	59 s	45 s	< 0.001

Table 3 Incidence of proximal lock related complications

	Group-1 (*n* = 70)		Group-2 (*n* = 70)	
	31A1 (*n* = 32)	31A2 (*n* = 38)	31A1 (*n* = 28)	31A1 (*n* = 42)
Proximal screw backout	01	08	00	04
Proximal screw breakage	00	01	00	00
Proximal screw cut out	00	02	00	00
Z effect	00	03	00	00



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Figure 2 Proximal lock-related complications. A: Proximal screw cut-out; B: Z-effect; C: Proximal screw back-out; D: Proximal screw breakage.

AO/OTA 31-A1 fracture pattern and 42 patients had AO/OTA 31-A2 fracture pattern. (Table 1)

Operative time and IITV radiation time

The average operation time in group 1 was 42 min, and IITV radiation time was 59 s. In group 2, the average operative time was 28 min ($P < 0.001$) and IITV radiation time was 45 s ($P < 0.001$). This suggests that there was a significant reduction in operative time and IITV radiation time in group 2. (Table 2)



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Figure 3 Distal screw breakage.

Proximal lock-related complications

As shown in Table 3, In group 1, 2 out of 70 (2.85%) patients had screw cut-out (Figure 2A), 3 out of 70 (4.28%) patients had Z-effect (Figure 2B), 9 out of 70 (12.85%) patients had a proximal screw back-out (average back-out = 14 mm) (also Figure 2C), and 1 out of 70 (1.42%) patients had proximal screw breakage (also Figure 2D). In group 2, 4 out of 70 (5.71%) patients had a proximal screw back-out (average back-out = 7 mm). There was no Z-effect, screw breakage or proximal screw cut-out.

Time for radiological union

Average time of union was 14-16 wk in both groups for patients having fracture pattern AO/OTA 31-A1. However, in fracture pattern AO/OTA 31-A2, the average union time was 16-18 wk in group 1 and 15-16 wk in group 2 ($P < 0.001$). There were 3 cases of non-union in group 1 and no cases of non-union in group 2.

Rotational alignment of the proximal femur

Compared to the opposite limb, there was an average of 5 degree external rotation difference in fracture pattern AO/OTA 31-A1 in both groups ($P = 0.66$). There was an average of 6 degrees more external rotation in group 1 with AO/OTA 31-A2 fracture pattern, and there was an average of 7 degrees more external rotation in group 2 with fracture pattern AO/OTA 31-A2 ($P = 0.08$). Malrotation of the operated limb was less than 10 degrees in all patients in both groups. This suggests that there was a negligible effect of distal interlocking on the rotational alignment of the limb for fracture patterns AO/OTA 31-A1 and AO/OTA 31-A2.

Anatomy of proximal femur

Varus rotation of the proximal femur was less than 5 degrees in both groups for all patients with AO/OTA 31-A1 ($P = 0.81$). In AO/OTA 31-A2, the mean neck shaft angle in group 1 was 117 degrees (114-125 degree), and the mean neck shaft angle in group 2 was 126 degrees (124-135 degree) ($P < 0.001$). This suggests that there was better control of the neck shaft angle where distal interlocking was not performed.

Downward migration of nail

We consider downward migration of the nail as a decrease in distance between the tip of the nail and the upper border of the intercondylar notch of the femur on the AP view of the radiograph. In group 2, 6 out of 70 patients had downward migration of the nail due to controlled collapse of the fracture site,

which averaged 5 ± 2 mm. Moreover, in 3 out of 70 patients in group 1, we observed that there was a change in position of the nail in relation to the distal dynamic interlocking screw. There was no downward migration of the nail in the patients in group 1 with static distal locking.

Distal lock-related complications

In group 1, we noted thigh pain over the distal locking site in 19 out of 70 (27.14%) patients, and 1 out of 70 patients had breakage of the distal lock due to downward migration of the nail resulting in auto-dynamization (Figure 3). No thigh pain was reported for any patient in group 2. In the postoperative period, 5 out of 70 patients in group 1 had knee joint effusion, and no patient had knee joint effusion in group 2.

Clinical evaluation

In group 1, 6 out of 70 patients had limb length discrepancy with mean shortening of 12 mm (6-18 mm), 10 out of 70 patients had implant impingement, and 5 out 70 patients had decreased range of movement. In group 2, there was an average of 10 mm of limb shortening (5-15 mm), 1 patient had implant impingement, and all patients had near to normal range of movement as compared to the opposite site.

DISCUSSION

IT femur fractures amount to almost half of total hip fractures caused by a low-energy injury, like a fall from standing height. These fragility hip fractures occur in a population with risk factors including elderly age, female sex, osteoporosis, history of trauma and gait problems[7]. IT fractures are not common in young age patients and require investigation; in this population, IT fractures are caused by high-energy injuries or from a pathological process. Thus, secondary injuries or malignancies must be ruled out[8]. Surgery is typically the recommended treatment as the morbidity and mortality associated with non-operative treatment has been high historically. Patients often have pre-existing comorbidities that dictate the ultimate outcome.

Diagnosis is confirmed by plain radiographs in the AP and lateral views. Traction with internal rotation radiograph view is helpful in assessing significant fracture displacement if the patient is able to tolerate. The antero-posterior and lateral X-ray views of the whole femur are required for long anatomical PFN fixation.

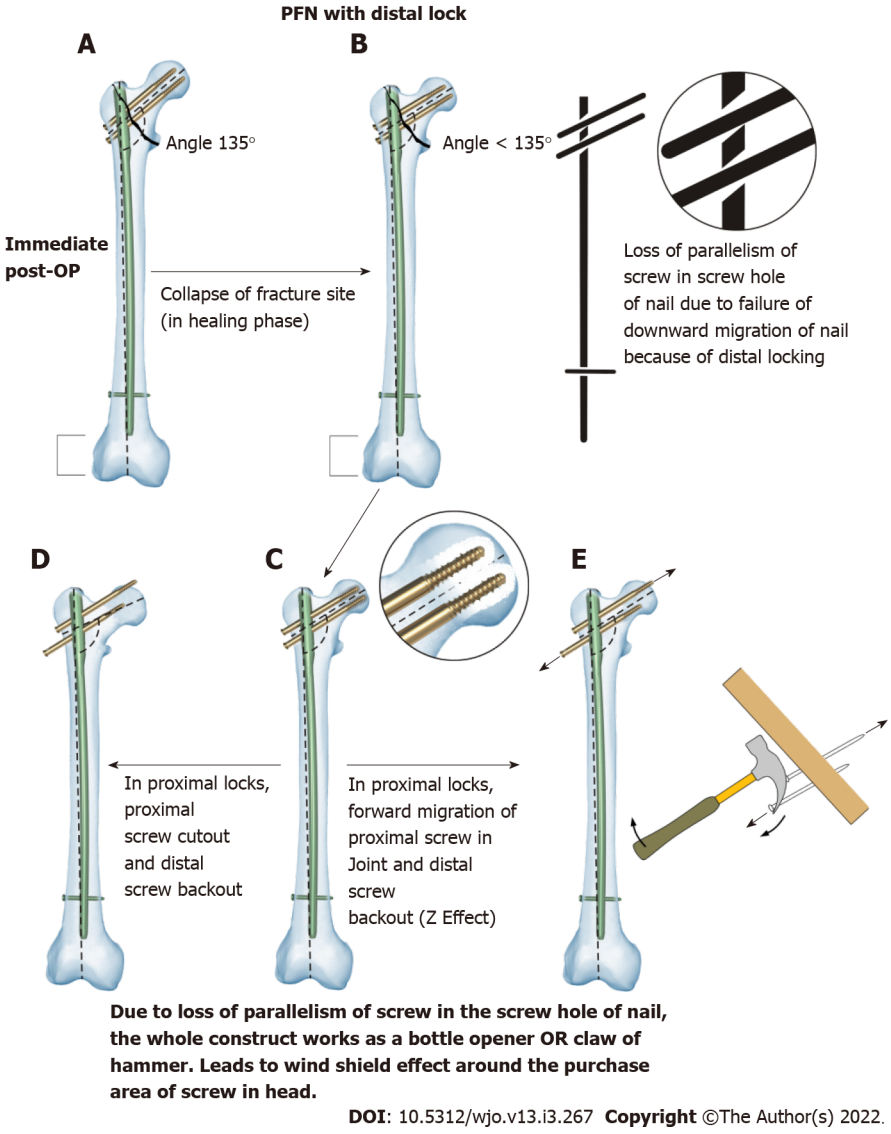
The treatment of proximal femoral fractures with sliding hip screw implants involving an extramedullary or an IM device is a universally accepted method of fixation[4]. In IM fixation there is minimal soft tissue dissection, less blood loss, a lower chance of infection, and fewer wound complications than extramedullary fixation, which has popularized PFN in IT fractures.

At present, PFN is a favourable minimally invasive technique for treating proximal femur fractures, especially where closed reduction is achievable. Nonetheless, proximal lag screw cut-out, Z-effect, reverse Z-effect, femur fracture at the tip of nail or at the site of distal screw insertion, thigh pain as a result of iliotibial tract irritation or cortical hypertrophy and difficulty in insertion of distal interlocking screw are among the probable complications that can occur[1].

There was no pre-established treatment protocol for choosing a long nail or short nail for femoral IT fractures. However, many surgeons are reluctant to use short nails based on the historic literature showing high fracture rates. They also believe that long nails will avoid diaphyseal stress risers and make peri-prosthetic fracture rates acceptable[9]. Short PFNs do not follow the anatomical curvature and the tip may impinge the endosteum of the anterior femoral cortex giving rise to anterior thigh pain. Long PFNs follow the anatomical shape of the femur and would not cause such a problem. At our institute, we have been using long anatomical PFNs. We routinely use long PFN with two proximal interlocks that maintain IT fracture reduction in good valgus position and provide excellent rotational control of the proximal fragment.

Hardware or fixation failure is not related to the type of nail, implant material or AO/OTA classification, but a neck shaft angle of < 125 degrees leads to a significant increase in fixation failure[10]. The influence of varusmal reduction for femur neck fractures and trochanteric fractures was described previously[11]. An increased varus reduction is associated with a higher cut-out rate after sliding hip screw fixation. An increased valgus reduction is beneficial for screw positioning resulting in stable fixation of the femoral head and neck[12]. Kashigar *et al*[13] showed a significant association between an increased varus reduction and cut-out for cephalo-medullary nailing. In addition to nail design, surgical method is also an important factor in determining the incidence of the above-mentioned complications.

Some personnel have supported the IM nailing without distal locking through their biomechanical studies. A biomechanical study done by Lacroix *et al*[14] comprised of 10 paired human cadaveric femurs and gave significant support that an added hole in the distal part of the IM nail could reduce the mean failure load in torsion by 36% because a stress raiser is a factor for peri-implant fracture.



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Figure 4 Typical case presentation of a patient treated with proximal femoral nail with distal interlocking screw. A: Immediate postoperative period; B: Downward migration of the nail because of distal locking; C: Windshield wiper effect around the purchase area of the screw in the head; D: Screw cut-through from the femoral head; E: Z-effect. PFN: Proximal femoral nailing; Post-OP: Postoperative period.

The pattern of the fracture had a significant effect on the distal interlocking of the nail. In stable IT fractures (31-A1 and 31-A2), the lateral cortex of the femur is unaffected. After anatomical reduction when the proximal locks are inserted from the lateral wall of the distal fracture part into the femoral head and the IM nail is matched well to the medullary canal, then varus deformity of the hip joint and rotational instability are controlled by the nail-proximal lock structure. In stable IT fractures, good cortical connection is established after acceptable reduction, and most of the compressive forces on the fracture site are borne by the bony cortex along the axis of neck of femur after surgery. Thus, performing distal interlocking of the nail was found to be unnecessary.

In unstable IT fractures (31-A3), the lateral cortex of the femur is fractured. This includes reverse oblique and transverse fracture patterns with particular anatomical and mechanical properties. Weight bearing on the affected limb gives rise to shearing movement at the fracture site that results in telescoping of the implant[15]. When IM nailing of this unstable fracture pattern was done without distal interlocking screws, neither longitudinal nor rotational stability was attained. Thus, this fracture is not fixed firmly without a distal interlocking screw. However, we concluded that distal interlocking screws are needed for unstable IT fractures (31-A3), particularly those with subtrochanteric extension of the fracture or those with wide IM canals.

Hardy *et al*[16] stated that use of two static locking screws during IM fixation of IT fractures is correlated with a higher rate of cortical hypertrophy, while the use of a dynamically locked nail significantly decreases the rate of this complication. On the basis of these findings, we discontinued the use of distal interlocking screws in AO/OTA 31-A1 and 31-A2 IT femur fractures.

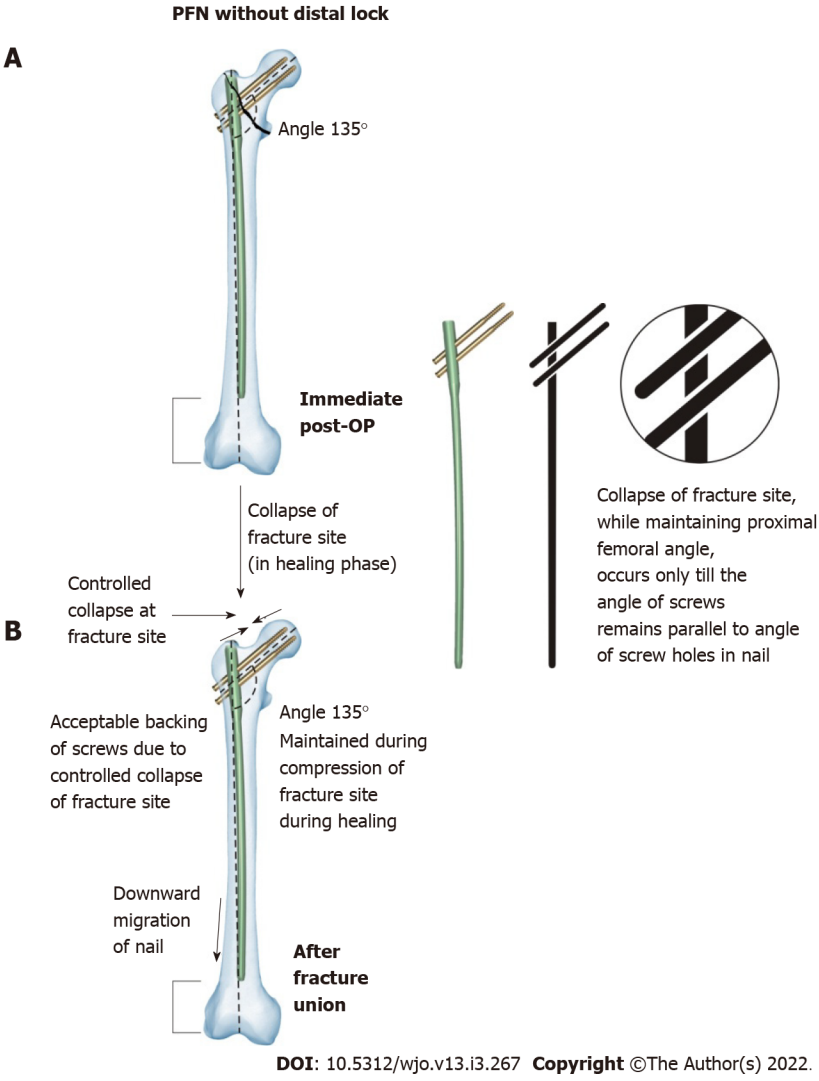
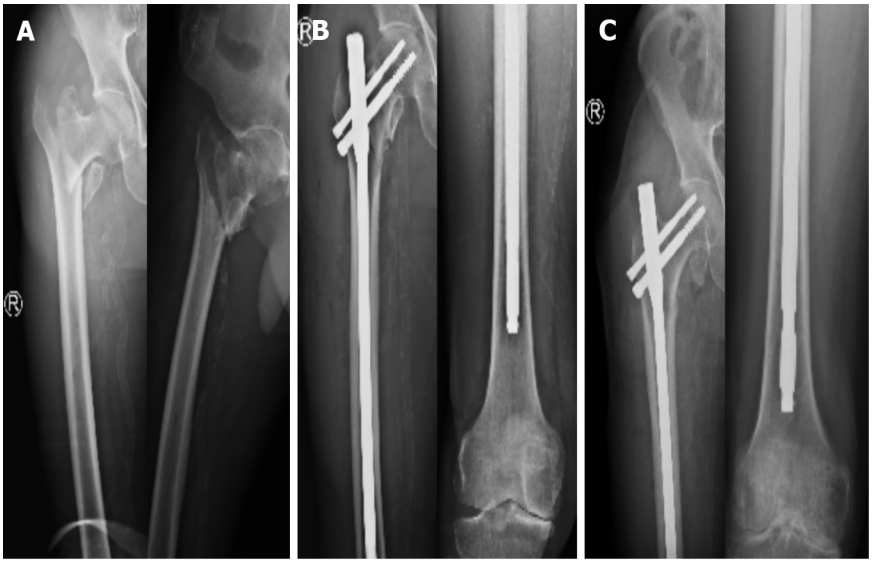


Figure 5 Typical case presentation of a patient treated with proximal femoral nail without distal interlocking screw. A: Immediate post-OP; B: After fracture union. PFN: Proximal femoral nailing; Post-OP: Postoperative period.

Figure 4 shows a typical case where PFN with distal locking was performed. In the immediate postoperative period (Figure 4A), the proximal femoral neck shaft angle was maintained. In the healing phase, there was collapse of the fracture site, but the proximal femoral neck shaft angle was not maintained. There was loss of parallelism of the screw in the screw hole of the nail due to failure of downward migration of the nail because of distal locking (Figure 4B). The whole construct works as a bottle opener or hammer claw, that leads to a windshield wiper effect around the purchase area of the screw in the head (Figure 4C) resulting in forward migration of the proximal lag screw and back-out of the distal lag screw. Due to this loss of parallelism, there can be screw back-out, screw cut-through from the femoral head (Figure 4D), Z-effect (Figure 4E), reverse Z-effect, and screw breakage.

Figure 5 shows a scenario where PFN with distal locking was not performed. It was observed during the postoperative period that the proximal femoral neck shaft angle was maintained. In the healing phase, controlled collapse of the fracture site occurred. During controlled collapse of the fracture site, the proximal neck shaft angle was maintained until the angle of the screws remained parallel to the screw holes in the nail. Parallelism of the screws in the screw holes was maintained due to downward migration of the nail in the canal during the healing phase. Also, there was acceptable backing-out of screws due to collapse of the fracture site.

Metaphyseal fractures heal by direct bone contact and creeping substitution. In comminuted IT femur fracture, controlled collapse at the fracture site is desirable for fracture union because of resorption and comminution at the fracture site. Therefore, in such situations, if there is a static implant bone construct, then there would be an increase in friction at the junction of the nail and screws (Figure 4). This would increase probability of Z-effect, reverse Z-effect, implant breakage, cut-through of screws and back-out of lag screws in the proximal femur. Whereas in cases where distal locking was not performed, the parallelism between the screw hole and screw will be maintained, and the controlled desired collapse with a maintained neck shaft angle would occur, which would increase the chances of fracture union



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Figure 6 Case of a 68-year-old female with right intertrochanteric fracture pattern Arbeitsgemeinschaft für Osteosynthesefragen/Orthopaedic Trauma Association 31-A2. A: Preoperative X-ray; B: Immediate postoperative X-ray; C: After union.

(Figure 5).

In PFN that is done without distal locking, it is desirable to keep the nail length up to the superior border of the patella. A nail with a length up to the intercondylar notch of the femur will not allow downward migration. Therefore, it is desirable to keep a nail short to allow downward migration of the nail with controlled collapse of the fracture.

In our study, it was noted that in the cases for which distal interlocking was performed, there was a gradual decrease in the neck shaft angle, which led to varus collapse and failure of bone implant construct in 21.40% of patients.

There was no significant difference in radiological union, postoperative rotational alignment and proximal femur anatomy between both groups with fracture pattern AO/OTA 31-A1, but the incidence of proximal lock-related complications was increased in group 1 patients with fracture pattern AO/OTA 31-A2 than in group 2 patients with fracture pattern AO/OTA 31-A2 (Table 3).

The limitations of our study were a short follow-up period and a small sample size. We also used only one type of long anatomically designed PFN with two proximal locks.

Case 1

A 68-year-old female patient sustained an IT femur fracture (AO/OTA 31-A2) on the right side (Figure 6A). A long anatomical PFN with two proximal screws without distal interlocking were used for the operation, as shown in immediate postoperative X-ray (Figure 6B). The X-ray image in Figure 6C showed a complete union at 12 mo with maintained neck shaft angle and distal downward migration of the nail, as compared to that in Figure 6B.

CONCLUSION

From this study, we concluded that in IT fractures AO/OTA type 31-A1, use of long anatomical PFN with or without distal interlocking screws gives similar results in terms of radiological union, postoperative proximal femur anatomy, and rotational alignment. However, in AO/OTA type 31-A2, use of long anatomical PFN without distal interlocking screws gave better results and less proximal lock-related complications than PFN with distal interlocking screws.

ARTICLE HIGHLIGHTS

Research background

There are few studies comparing clinical and radiological outcomes between proximal femoral nail (PFN) with or without distal interlocking screws in fracture pattern Arbeitsgemeinschaft für Osteosynthesefragen/Orthopaedic Trauma Association (AO/OTA) 31-A1 and 31-A2.

Research motivation

The motivation of this study was to assess the clinical and radiological outcomes of PFN with or without distal interlocking screws in fracture pattern AO/OTA 31-A1 and 31-A2, which were performed by the same chief surgeon.

Research objectives

The objective of this study was to compare the outcomes of intertrochanteric (IT) fractures (AO/OTA 31-A1 and 31-A2) treated by PFN with and without distal interlocking screws.

Research methods

We conducted a retrospective study of 140 patients having fracture pattern AO/OTA 31-A1 and 31-A2. We divided the patients into two groups based on distal interlocking. We evaluated patients based on clinical and radiological parameters like fracture type, duration of surgery and IITV radiation time, time for radiological union, proximal lock and distal lock-related complications, femoral neck shaft angle and length and rotation of limb after surgery.

Research results

There was no significant difference in radiological union, postoperative radiological alignment and proximal femur anatomy between patients with fracture pattern AO/OTA 31-A1 treated by PFN with or without distal interlocking. However, the incidence of proximal lock-related complications was higher in patients with fracture pattern AO/OTA 31-A2 treated by PFN with distal interlocking than in patients treated by PFN without distal interlocking.

Research conclusions

PFN without distal interlocking is a reliable and acceptable option for IT fracture types AO/OTA 31-A1 and 31-A2.

Research perspectives

A prospective study with long-term follow-up and a larger number of patients is necessary to draw a definitive conclusion.

FOOTNOTES

Author contributions: Lil NA, Makwana VR, Patel TD and Patel AR made substantial contributions to the study conception and design, to the acquisition, analysis and interpretation of data, and to the drafting of the article and making critical revisions related to important intellectual content of the manuscript; and all authors provided final approval of the version of the article to be published.

Institutional review board statement: This study was reviewed and approved by the NHL institutional review board (NHLIRB).

Informed consent statement: Patients were not required to give informed consent to the study because the analysis used anonymous clinical data that were obtained after each patient agreed to treatment by written consent.

Conflict-of-interest statement: The authors declare that they do not have any conflicts of interest.

Data sharing statement: No additional data are available.

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REFERENCES

1 **Ozkan K**, Unay K, Demircay C, Cakir M, Eceviz E. Distal unlocked proximal femoral intramedullary nailing for intertrochanteric femur fractures. *Int Orthop* 2009; **33**: 1397-1400 [PMID: 18956183 DOI: 10.1007/s00264-008-0673-1]

2 **Kregor PJ**, Obremskey WT, Kreder HJ, Swiontkowski MF; Evidence-Based Orthopaedic Trauma Working Group. Unstable pertrochanteric femoral fractures. *J Orthop Trauma* 2005; **19**: 63-66 [PMID: 15668589 DOI: 10.1097/00005131-200501000-00014]

3 **Schipper IB**, Steyerberg EW, Castelein RM, van der Heijden FH, den Hoed PT, Kerver AJ, van Vugt AB. Treatment of unstable trochanteric fractures. Randomised comparison of the gamma nail and the proximal femoral nail. *J Bone Joint Surg Br* 2004; **86**: 86-94 [PMID: 14765872]

4 **Boldin C**, Seibert FJ, Fankhauser F, Peicha G, Grechenig W, Szyszkowitz R. The proximal femoral nail (PFN)--a minimal invasive treatment of unstable proximal femoral fractures: a prospective study of 55 patients with a follow-up of 15 months. *ActaOrthopScand* 2003; **74**: 53-58 [PMID: 12635794 DOI: 10.1080/00016470310013662]

5 **Skála-Rosenbaum J**, Bartonícek J, Bartoska R. Is distal locking with IMHN necessary in every pertrochanteric fracture? *Int Orthop* 2010; **34**: 1041-1047 [PMID: 19882156 DOI: 10.1007/s00264-009-0874-2]

6 **Li X**, Zhang L, Hou Z, Meng Z, Chen W, Wang P, Zhang Y. Distal locked and unlocked nailing for perthrochanteric fractures--a prospective comparative randomized study. *Int Orthop* 2015; **39**: 1645-1652 [PMID: 25913263 DOI: 10.1007/s00264-015-2771-1]

7 **Grisso JA**, Kelsey JL, Strom BL, Chiu GY, Maislin G, O'Brien LA, Hoffman S, Kaplan F. Risk factors for falls as a cause of hip fracture in women. The Northeast Hip Fracture Study Group. *N Engl J Med* 1991; **324**: 1326-1331 [PMID: 2017229 DOI: 10.1056/NEJM199105093241905]

8 **Ahn J**, Bernstein J. Fractures in brief: intertrochanteric hip fractures. *ClinOrthopRelat Res* 2010; **468**: 1450-1452 [PMID: 20195807 DOI: 10.1007/s11999-010-1263-2]

9 **Li Z**, Liu Y, Liang Y, Zhao C, Zhang Y. Short versus long intramedullary nails for the treatment of intertrochanteric hip fractures in patients older than 65 years. *Int J Clin Exp Med* 2015; **8**: 6299-6302 [PMID: 26131244]

10 **Hoffmann MF**, Khoriaty JD, Sietsema DL, Jones CB. Outcome of intramedullary nailing treatment for intertrochanteric femoral fractures. *J OrthopSurg Res* 2019; **14**: 360 [PMID: 31718660 DOI: 10.1186/s13018-019-1431-3]

11 **Parker MJ**. Valgus reduction of trochanteric fractures. *Injury* 1993; **24**: 313-316 [PMID: 8349340 DOI: 10.1016/0020-1383(93)90053-9]

12 **Jung EY**, Oh IT, Shim SY, Yoon BH, Sung YB. The Effect of Valgus Reduction on the Position of the Blade of the Proximal Femoral Nail Antirotation in Intertrochanteric Hip Fractures. *ClinOrthopSurg* 2019; **11**: 36-42 [PMID: 30838106 DOI: 10.4055/cios.2019.11.1.36]

13 **Kashigar A**, Vincent A, Gunton MJ, Backstein D, Safir O, Kuzyk PR. Predictors of failure for cephalomedullary nailing of proximal femoral fractures. *Bone Joint J* 2014; **96-B**: 1029-1034 [PMID: 25086117 DOI: 10.1302/0301-620X.96B8.33644]

14 **Lacroix H**, Arwert H, Snijders CJ, Fontijne WP. Prevention of fracture at the distal locking site of the gamma nail. A biomechanical study. *J Bone Joint Surg Br* 1995; **77**: 274-276 [PMID: 7706346]

15 **Ozkan K**, Eceviz E, Unay K, Tasyikan L, Akman B, Eren A. Treatment of reverse oblique trochanteric femoral fractures with proximal femoral nail. *Int Orthop* 2011; **35**: 595-598 [PMID: 20349232 DOI: 10.1007/s00264-010-1002-z]

16 **Hardy DC**, Drossos K. Slotted intramedullary hip screw nails reduce proximal mechanical unloading. *ClinOrthopRelat Res* 2003; 176-184 [PMID: 12579017 DOI: 10.1097/01.blo.0000037444.23683.b2]

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ORIGINAL ARTICLE

Retrospective Study

Ilizarov bone transport combined with the Masquelet technique for bone defects of various etiologies (preliminary results)

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Abstract

BACKGROUND

The Ilizarov bone transport (IBT) and the Masquelet induced membrane technique (IMT) have specific merits and shortcomings, but numerous studies have shown their efficacy in the management of extensive long-bone defects of various etiologies, including congenital deficiencies. Combining their strong benefits seems a promising strategy to enhance bone regeneration and reduce the risk of refractures in the management of post-traumatic and congenital defects and nonunion that failed to respond to other treatments.

AIM

To combine IBT and IMT for the management of severe tibial defects and pseudarthrosis, and present preliminary results of this technological solution.

METHODS

Seven adults with post-traumatic tibial defects (subgroup A) and nine children (subgroup B) with congenital pseudarthrosis of the tibia (CPT) were treated with the combination of IMT and IBT after the failure of previous treatments. The mean number of previous surgeries was 2.0 ± 0.2 in subgroup A and 3.3 ± 0.7 in subgroup B. Step 1 included Ilizarov frame placement and spacer introduction into the defect to generate the induced membrane which remained in the interfragmental gap after spacer removal. Step 2 was an osteotomy and bone transport of the fragment through the tunnel in the induced membrane, its compression and docking for consolidation without grafting. The outcomes were retrospectively studied after a mean follow-up of 20.8 ± 2.7 mo in subgroup A and

25.3 ± 2.3 mo in subgroup B.

RESULTS

The "true defect" after resection was 13.3 ± 1.7% in subgroup A and 31.0 ± 3.0% in subgroup B relative to the contralateral limb. Upon completion of treatment, defects were filled by 75.4 ± 10.6% and 34.6 ± 4.2%, respectively. Total duration of external fixation was 397 ± 9.2 and 270.1 ± 16.3 d, including spacer retention time of 42.4 ± 4.5 and 55.8 ± 6.6 d, in subgroups A and B, respectively. Bone infection was not observed. Postoperative complications were several cases of pin-tract infection and regenerate deformity in both subgroups. Ischemic regeneration was observed in two cases of subgroup B. Complications were corrected during the course of treatment. Bone union was achieved in all patients of subgroup A and in seven patients of subgroup B. One non-united CPT case was further treated with the Ilizarov compression method only and achieved union. After a follow-up period of two to three years, refractures occurred in four cases of united CPT.

CONCLUSION

The combination of IMT and IBT provides good outcomes in post-traumatic tibial defects after previous treatment failure but external fixation is longer due to spacer retention. Refractures may occur in severe CPT.

Key Words: Ilizarov bone transport; Induced membrane technique; Post-traumatic tibial defect; Congenital pseudarthrosis of the tibia; Distraction osteogenesis; Regeneration

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Core Tip: This study presents preliminary outcomes and the protocol of a developed technology that includes phase 1 of the Masquelet technique for induced membrane generation and Ilizarov bone transport. The technology did not comprise bone grafting or skin flaps. It was used in 16 patients with post-traumatic tibial defects and congenital pseudarthrosis of the tibia (CPT), after multiple failed treatments. The results were rated as good in patients with post-traumatic tibial defects. Congenital cases showed similar rates of pseudarthrosis union as other means currently used for CPT. Refractures may be expected in severe types of CPT after multiple previous treatments

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INTRODUCTION

The challenges of long-bone defect management have increased in contemporary orthopedic practice due to the severity of high-energy trauma and its complications[1]. These defects can lead to a multi-stage, long and costly treatment. The Ilizarov method of bone transport (IBT) and the Masquelet induced membrane technique (IMT) have been used in a great variety of challenging clinical situations including post-traumatic bone loss, infected nonunion, tumor resection, and congenital deficiency, such as congenital pseudarthrosis of the tibia (CPT)[2-4]. Both techniques have specific merits and shortcomings, but numerous studies have shown their efficacy in the management of extensive long-bone defects of various etiologies, including congenital defects[2-5].

The IBT has been praised for high union rates and its biological aspect of growing authentic bone tissue to close bone defects[5-7]. Its followers believe that it is an ideal type of non-free bone grafting by which a vascularized autologous osteotomized bone fragment is transported gradually in the interfragmental gap within the soft tissue envelope to grow the missing bone part of a required length and shape [2,6-8]. The Ilizarov system has been criticized due to complications such as pin-tract infection, pain, possible joint contractures, risk of ischemic regeneration in compromised soft-tissues around a large defect and impaired quality of life due to the long time needed to provide treatment tasks and new bone remodeling[9]. The IMT is also based on the biological tissues of the induced membrane (IM) and autologous bone grafting, and utilizes internal or external fixation[10,11]. It is not devoid of characteristic complications either, being a staged treatment that takes months to complete bone remodeling. However, it provides a better quality of life, especially if pathology is located in the upper limb and

femur[3,10].

Recent available studies have reported mostly good final outcomes of both procedures[6,7,10,11]. A study that compared the IBT (37 sources) and the IMT (41 sources) did not find statistical differences and reliable advantages between them in regard to consolidation, infection risks and failures that ended with amputation[12]. However, the study found that IBT patients had a higher rate of refractures. This may be associated with the fact that bone regeneration in large defects requires a longer time for remodeling and needs supportive internal fixation[8]. Nevertheless, several reviews and clinical studies doubt the superiority of IMT over IBT for long-bone defects in the lower extremity and point out that bone consolidation time may be unpredictable while non-weight bearing is prolonged in IMT[13,14]. High rates of infection and even amputation were reported for tibial defects after open fractures treated with IMT[14]. On the contrary, IBT allows weight-bearing from the first days. It is primarily used in patients with an infected tibia and rarely results in amputation[2,5]. In pediatrics, IMT has been frequently used for cancer surgery reconstructions[4]. Congenital anomalies, including CPT, may be treated with both options[4,15,16].

The importance of improving bone regeneration in the management of large bone defects and CPT is a very relevant issue due to treatment failures that diminish bone potential for regeneration. Management of CPT may take years in a growing child due to frequent recurrences and has a negative impact on the child's development. Therefore, a combination of the biological merits of IBT and IMT seemed to us a promising strategy in the management of cases with a history of failed attempts and impaired regeneration potential. Following use of the combined technique in an experimental canine model[17], we aimed to conduct clinical studies on the use of this new technological solution that integrates the IMT and IBT techniques for treating non-viable tibial defects of post-traumatic (PTD) etiology and CPT to improve bone regeneration at the docking site, bone consolidation and reduce the refracture rate.

MATERIALS AND METHODS

We retrospectively studied the treatment course and outcomes in a case series that included seven PTD patients (subgroup A) and nine CPT cases (subgroup B) managed using the combination of IMT and IBT. The patients were treated at the same specialized department in our orthopedic center by one team of surgeons in 2014–2019.

Tibial defects in subgroup A were caused by falls from a height, injuries at production sites and traffic accidents (Table 1). Time since injury was from one to 12 years (mean, 3.7 ± 0.9 years) and all subjects were adults (six males and one female with a mean age of 38.5 ± 4.1 years). Six cases had a history of infection and one had delayed wound healing. Patients' inclusion criteria in subgroup A were bone defects of post-traumatic origin after several failed previous treatments, with a disease history of one year or more, and non-viable types of nonunion (hypotrophic, torsion-wedge, defect-pseudarthrosis). Patients with active infection or hematogenous osteomyelitis were excluded. Subgroup B included nine children with a mean age of 6.1 ± 0.9 years and severe CPT types (Paley types 4 a-c)[15], mostly due to neurofibromatosis type I, who had had numerous failed interventions to unite pseudarthrosis and had no active infection (Table 2). Mean preoperative data of both subgroups are given in Table 3.

Surgical protocol

Step 1: Ilizarov frame mounting + spacer implantation. The Ilizarov frame was constructed of three ring supports with three wires in the proximal and distal rings and two wires in the middle ring at the level of the tibial diaphysis. Fibular osteotomy was performed in order to eliminate segment deformities. For pseudarthrosis resection, an anterior approach to the tibia was used. In subgroup A, the resection started from the level of the endplate and extended to the margin with the bleeding bone. The "blood dew" sign indicated an adequate level of resection. In subgroup B, the pseudarthrosis zone along with the surrounding pathologically altered periosteum was resected. After resection, the limb was fixed with the Ilizarov frame in a neutral position according to the tension of soft tissues with the correct anatomical axis of the segment. Next, the defect size was measured. A pre-shaped spacer was prepared from methyl methacrylate cement by molding in a syringe. Its diameter corresponded to the bone diameter of the specific patient, coinciding with the level of the cortical plates, or going beyond the cortices by 2-3 mm. The spacer was placed into the defect gap after being hardened and was fixed in the gap by applying compression with the Ilizarov frame. One dose of vancomycin was added to the spacer material for infection prevention in subgroup A. Wounds were closed in the regular manner. We used only the first phase of the IMT procedure.

Step 2: Osteotomy for bone fragment transport. The spacer was accessed through the previous incision. Careful handling was required to maximize preservation of the induced membrane. Upon removal of the spacer, the induced membrane that enveloped it remained in the interfragmental gap and the wound was sutured. In the frame being unchanged, a mainly proximal osteotomy for bone transport was performed. The distal fragment was osteotomized in PTD-case 5 (Table 1); osteotomy was

Table 1 Demographic, clinical and outcome data of subgroup A patients treated with a combined technology Masquelet induced membrane technique + Ilizarov bone transport

Patient	Age (yr), Gender	Mechanism of injury/Type the fracture	Disease duration (yr)	Type (number) of previous surgeries	Type of nonunion/Infection	Shortening/Bone defect (cm)	Joint Function before surgery	Regenerate/nonunion consolidation completeness	Nonunion consolidation (mo)	Postoperative complication (Paley classification)	Follow-up (mo)	Residual limb length discrepancy (cm)	Further surgery
PTD-1	51, F	MVA, OF	1	EF (1)	TW; Delayed wound healing	3/3	Knee and ankle stiffness	+/+	11	Pin-tract infection Regenerate deformity; Deep vein thrombosis	17	2	-
PTD-2	50, M	MVA, OF	4	Plate (1); EF (1)	HN; History of infection	3/5	Ankle ankyloses	+/+	10	Regenerate deformity	24	5	Rejected further surgery
PTD-3	48, M	IF, OF	3	Plate (1); EF (1)	HN; History of infection	0/3	Ankle stiffness	+/+	7	Pin-tract infection	12	-	-
PTD-4	18, M	IF, OF	3	Plate (2); EF (2)	HN; History of infection	6/3	Ankle ankyloses	+/+	11	Knee joint stiffness	36	6	3-cm lengthening
PTD-5	21, M	IF; OF	1	EF (2)	HN	0/4	Full function	+/+	5	Regenerate deformity	24	-	-
PTD-6	39, M	CT; CF	12	Plate (1); EF (1)	HN; History of infection	1/3	Ankle stiffness	+/+	7	Pin-tract infection	12	-	-
PTD-7	43, M	CT	2	Plate (1)	HN; History of infection	0/4	Ankle stiffness	+/+	8	-	n/a	-	N/A

PTD: Post-traumatic defect; F: Female; M: Male; MVA: Motor vehicle accident; IF: Isolated fracture; CT: Catatrauma; OF: Open fracture; CF: Closed fracture; EF: External fixation; TW: Torsion-wedge nonunion; HN: Hypotrophic nonunion; DP: Defect-pseudarthrosis; N/A: Not available.

performed at two levels in CPT-case 7 (Table 2). Distraction was initiated from day 5 to 7 at a rate of 1 mm/d produced with 4 increments. Condition of the regeneration was checked radiographically every ten days. In low optical density of the regenerate or its deformity, the rate of distraction was adjusted or reduced to 2 or 3 increments, a quarter of a mm each. The transported bone fragment ran in the membrane without technical problems. Distraction was carried out until close docking of the fragments. Upon docking, supportive compression of 1 mm was provided once every two weeks in the consolidation phase. Autologous grafting was not added.

Postoperative care and radiographic checks followed the standards of the Ilizarov method. Radiographic evidence of bony union, external fixation time, defect filling rate and complications were assessed. The primary outcome measure was radiographic bone union. Secondary outcomes were correction of limb length discrepancy and deformities.

Table 2 Demographic, clinical and outcome data of subgroup B patients treated with a combined technology Masquelet induced membrane technique + Ilizarov bone transport

Patient	Age (yr), Gender	Neurofibromatosis	Type (number) of previous surgeries	Paley CPT Type	Shortening/Bone defect (cm)	Joint Function	Regenerate/nonunion consolidation completeness	Consolidation time (mo)	Complications (Paley classification)	Follow-up (mo)	Residual limb length discrepancy (cm)	Recurrence/Further surgery
CPT-1	4, M	I type	-	4C	5/3	Full	+/+	7	Regenerate deformity	24	3	Refracture
CPT -2	3, M	-	EF (1); Nail (1)	4C	5/2	Ankle stiffness	+/+	9	Pin-tract infection	36	3	Refracture
CPT -3	15, F	I type	More than 10 including EF, Nail	4A	15/3	Ankle stiffness	+/+	10	Pin-tract infection	12	12	
CPT -4	5, M	I type	-	4B	3/1.5	Full	+/-	7.5	Pin-tract infection	24	3	Ilizarov monofocal compression
CPT -5	8, F	I type	Plate (1); Nail (2); EF (4)	4B	10/3	Ankle ankylosis	+/+	9	-	36	12	Twice Ilizarov lengthening by 6 cm
CPT -6	4, M	I type	EF (1); Autograft (1)	4C	5/1.5	Full	-/-	8	Ischemic regenerate	24	6	Bone defect, rejected further treatment
CPT -7	6, F	-	EF and allograft (2)	4A	5/5	Full	+/+	13.5	Ischemic regenerate	12	5	-
CPT -8	6, F	-	Plate (1); Nail (2); EF (4)	4B	4/3	Full	+/+	7	Pin-tract infection	24	2	Refracture
CPT -9	4, F	-	Plate (1); Nail (2); EF (4)	4A	2/2	Ankle stiffness	+/+	8	-	36	2	Refracture

CPT: Congenital pseudarthrosis of the tibia; F: Female; M: Male; EF: External fixation.

Thin fragments of the biomembrane formed around the cement spacer were harvested prior to bone transport for histological examination in all patients. The material was collected intraoperatively at step 2.

All adult patients and the children's parents gave informed consent for surgical treatment and inclusion in the study. The study was approved by the ethics board of our institution.

The subgroups had different etiologies of the defects and belonged to different age groups. Thus, we did not aim to compare them. The statistical method included calculation of mean values and their deviations using Microsoft Excel 2019. Moreover, the sample size of subgroups was small; therefore, only descriptive statistics were used.

Table 3 Main mean values of preoperative and postoperative data by combined use of Masquelet induced membrane technique + Ilizarov bone transport

Parameter	Subgroup A	Subgroup B
Number of previous surgeries per patient	2.0 ± 0.2	3.3 ± 0.7
LLD at admission (cm)	3.5 ± 0.5	6.0 ± 1.0
Defect size (cm)	3.6 ± 0.3	2.7 ± 0.3
True defect (LLD + bone gap) after debridement relative to the contralateral limb (%)	13.3 ± 1.7	31.0 ± 3.0
Time of spacer retention (d)	42.4 ± 4.5	55.8 ± 6.6
Duration of distraction (d)	43.0 ± 4.2	31.9 ± 4.2
Distraction regenerate size (cm)	3.1 ± 0.2	2.6 ± 0.2
Completeness of defect filling (%)	75.4 ± 10.6	34.6 ± 4.2
External fixation index per cm	143.5 ± 13.2	117.8 ± 8.5
Duration of total external fixation, including spacer retention time (d)	397.0 ± 15.3	270.1 ± 16.3
Mean follow-up time (mo)	20.8 ± 2.7	25.3 ± 2.3

LLD: Limb length discrepancy.

RESULTS

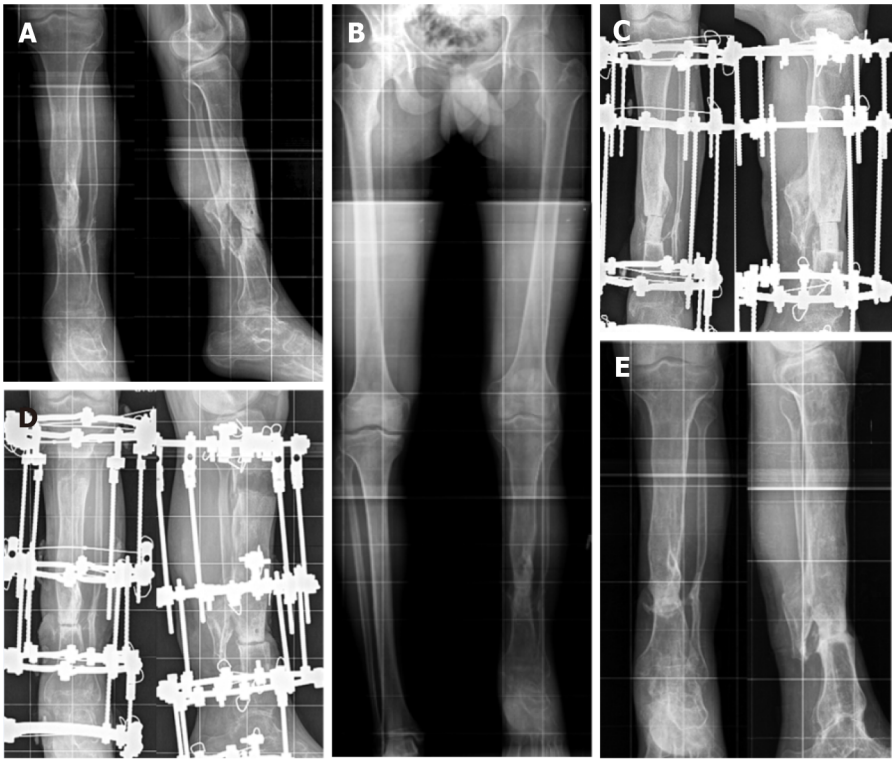
Table 1 and Table 2 present the main preoperative and treatment parameters along with outcomes of the combined technique of IMT + IBT in all patients. The mean values of the main measures are shown in Table 3. Bone union was achieved in all patients of subgroup A (Figure 1) and in seven patients of subgroup B (Figure 2). Total duration of external fixation was 397.0 ± 15.3 and 270.1 ± 16.3 d, including spacer retention time of 42.4 ± 4.5 and 55.8 ± 6.6 d, in subgroups A and B, respectively. One non-united CPT case was further treated with the Ilizarov compression method only and achieved union. Another failed CPT case was lost. After a follow-up period of one to three years, there were no refractures in subgroup A. Refractures occurred in four cases of CPT due to severe disease (mostly Paley CPT type 4 C) and multiple previous treatments. Cases CPT-8 and CPT-9 had seven previous surgeries each.

Bone transport in the membrane ran smoothly. Postoperative complications included several cases of pin-tract infection and regenerate deformity in both subgroups. Insufficient ischemic regeneration was observed in two cases of subgroup B. Bone regenerate deformity and pin-tract infection were resolved during the course of treatment. The regenerate zone was perforated with wires and supportive compression was performed with the same frame in ischemic hourglass-shaped regeneration for its stimulation. We prefer delayed lengthening to finally correct the length in non-viable nonunion, after bone consolidation has been secured. Thus, we subsequently performed this in two patients of subgroup A who applied for length compensation. Further treatment reduced limb length discrepancy from 12 to 6 cm in CPT-case 5 with two procedures.

Subgroup A patients could walk with crutches after frame removal gradually increasing weight-bearing. Subgroup B patients were recommended to use crutches for one month and then leg braces for one year.

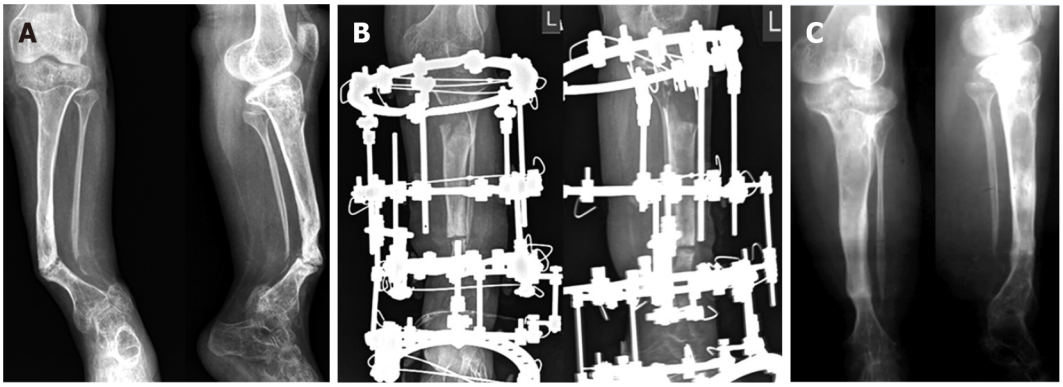
DISCUSSION

Several surgeries are often required to manage extensive segmental bone loss after multiple failures or severe congenital deficiency. They may result in prolonged recovery times, poor outcomes, and even amputation as a complex of mechanical issues and biological factors should be utilized for reconstruction[1,2]. IBT has established itself as an efficient tool for long bone defect management, including patients with infections, especially in the tibia[5-9]. It is able to resolve the problematic triad of bone loss, soft-tissue compromise and bone infection. The IMT has recently been used for extensive defects in any long-bone segment[3,4,18]. According to several authors, the advantage of IMT over IBT lies in the fact that the consolidation time does not depend on the bone defect size as it is filled with autologous graft material[3,11]. Nevertheless, extensive defects need a lot of bone graft substance, especially in the lower extremities[18]. Alternately, the distraction procedure, being a part of IBT, is able to supply new regenerated bone substance[2].



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Figure 1 Post-traumatic defect case 4 (Table 1). A: Preoperative radiographs of the right tibia capturing the adjacent joints showing a hypotrophic nonunion of the tibia; B: Preoperative telemetry compensated by a sole elevation 6-cm left leg discrepancy; C: Spacer fills the defect; D: Closed docking of the fragments and the regenerate of satisfactory optical density and zonal structure; E: Bone callus at the fragments docking and the regenerate with signs of its remodeling and cortical plates at 6-mo follow-up.



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Figure 2 Congenital pseudarthrosis of the tibia case 3 (Table 2). A: Preoperative radiographs of the left tibia capturing the adjacent joints showing valgus and antecurvatum at the pseudarthrosis level, extended sclerosis of fragments ends; B: Completion of distraction and defect filling at the time of docking between the ends without signs of ossification; C: Continuous distraction regenerate and consistent bone callus at the docking site at 1-year follow-up.

We assumed that defect filling would provide a particularly favorable environment for bone regeneration and the reparative process with the combined use of IMT and IBT. After extraction of a spacer there is a tunnel in the interfragmental gap the walls of which are formed by the induced membrane which was found to be a type of neoperiosteum[16,19]. Apart from a favorable mechanical effect, the combined conditions could provide a biological effect of the induced membrane on osteogenesis. It was shown that multiple microvessels of the biomembrane penetrate into the regenerate zone and promote the inflow of low differentiated pluripotent cells[16]. The cells of the membrane basal layer and perivascular osteopontin-positive cells that possess osteogenic differentiation ability contribute to the formation of a low mineralized bone matrix on the surface of the spacer. This could cause an osteoinductive effect on the pluripotent cells in the region of the compression regenerate formed at the docking site. According to the reported findings, the osteoinductive membrane is adequately vascularized and produces growth factors (vascular endothelial growth factor, transforming

growth factor-beta 1) and bone morphogenetic protein-2 that play a role in regeneration and may prevent lysis[19]. It is also assumed that the biomembrane features antimicrobial activity related to the synthesis of antioxidants which are secreted locally along with growth factors[20]. Another mechanism of the supposed bacteriostatic effect is the presence of local peptides in the membrane which are able to inhibit secretion of the bacterial biofilm[16]. There were no foci of infection in the biomembrane fragments harvested at step 2 of our procedure in all cases. In addition, none of the patients developed infection.

The results of the subgroups in our series could not be compared due to different etiologies and the pathogenesis of nonunion. For this reason, the outcomes were presented separately. Despite the absence of active infection, we chose the primary task to achieve radical debridement in order to prevent possible infection. In subgroup A, the spacer's role was also to sanitize the site of previous infection. The absence of infection recurrence is attributed equally to the impact of radical debridement and that of the vascularized membrane. The interval between the first operation and the osteotomy was a period of infection control that was based on the results of bacteriological tests for selection of antibiotic therapy. The spacer maintained the shape of the defect gap to exclude soft tissues invagination into the defect.

We also promoted osteogenesis at bone fragments docking. As the role of the periosteum in CPT pathogenesis has already been proven, we expected that the neoperiosteum-like nature of the induced membrane would have an effect on bone union and regeneration in the CPT subgroup. The induced membrane was supposed to supply blood to the area with a new vascular network, thereby excluding osteolysis. However, the results in subgroup B were similar to other current techniques used for this pathology[15].

The removal of the spacer presupposes repeated trauma to the skin and soft tissues in the pseudarthrosis zone. However, if we draw a parallel, classical bone transport involves an open co-aptation for fragments docking. According to the protocol for our combined technique, docking was performed in a closed way by compression at the junction of the fragments without grafting. The known approach to create the maximum "bone mass" in the area of pseudoarthrosis was implemented by the technique[15]. Therefore, to add autologous bone grafting or internal fixation to the described combination seemed to us extremely invasive. However, open docking and a graft were used in an earlier study of infected tibial defects treated with a similar technology[21]. Thus, there could be options to synergistically widen the integrated approach.

Consolidation of nonunion was achieved in all the defects of post-traumatic etiology but it should be noted that the IM effect was not strong enough for CPT consolidation and did not help to eliminate refractures in the long term. The refracture rate was comparable with the literature data on the use of other methods, including the Ilizarov method used separately[15].

The management of CPT has been much discussed recently and there is plenty of clinical research with variable results[15,22-30]. The superiority of one of the techniques for reconstruction in CPT has not yet been confirmed. The latest clinical studies predominantly describe patients where the Ilizarov method is the main component of CPT management in conjunction with intramedullary nailing and bone grafting[22-25]. The combined technique of the Ilizarov external fixation, stabilization with an intramedullary rod and corticocancellous bone autograft yields a statistically significant reduction in the number of refractures compared with standalone fixation methods. It was stated that the four methods of CPT treatment might achieve primary union of about 50% without refracture and this was attributed to the biological nature of CPT[15]. Improved union rates in IMT assisted by the Ilizarov external fixator and grafting for previously failed CPT treatment were reported[26].

However, regardless of the primary bone fusion rates, most of the authors state that the probability of long-term bone union retention remains unpredictable due to biological factors of the disease characterized by low osteogenic potential. Therefore, methods to enhance this potential have been identified such as wrapping, grafting, crossunion of the tibia and fibula, and application of several biological agents to promote osteogenesis[27-30]. Our technology might also be used.

The combination of technologies to treat orthopedic pathology is largely associated with the need to obtain a faster and a more efficient result in the most severe cases. Apart from our previous study[16], we found only three case reports that used the combined principles of IMT and IBT with satisfactory outcomes, although not quite the same as our technology[21,31,32]. The limitation of our series is the small sample of patients with two different etiologies of defects and various clinical situations, but all severe cases. Our preliminary results suggest that the etiological factor plays a significant role in the use of this combined technique. Both subgroups had impaired bone regeneration potential due to multiple previous failures and a worsened condition of the tibia, but undoubtedly this was greater in subgroup B.

We did not complete limb length compensation in our patients due to the severity of their tibial defects and pseudarthrosis. The primary goal was bone union. Of course, residual limb length discrepancy is the factor affecting the final result in post-traumatic cases. We recommend IBT for defects less than 12 cm, and free vascularized fibula or transverse Ilizarov transport of the fibular fragment for bigger defects[2]. Due to the fact that IBT is able to realize the potential of human bone regeneration for anatomical and functional restoration in large long-bone defects with minimal trauma, it is extensively used after the failure of other established methods of treatment or infection. The arguments against it as a primary treatment option are the complexity of the Ilizarov apparatus mounting and its size, the

number of adjustments, pin-tract infection, multi-stage and long treatment course that needs a lot of compliance both from the patient and the surgeon. Although IMT seems simple, it is not so easy to complete successfully in severe cases[33]. Finally, it is worth noting the significant disadvantage of the combined approach which is an increase in the duration of total external fixation[21]. Due to these facts, the integration is a more complex procedure. Its effects, modification or failures should be studied further.

CONCLUSION

The combination of IMT and IBT may provide good outcomes in post-traumatic tibial defects after previous treatment failures, although the external fixation is longer due to spacer retention time. This combination might also be used for severe types of CPT despite possible refractures.

ARTICLE HIGHLIGHTS

Research background

The challenges of long-bone defect management have increased in contemporary orthopedic practice due to the severity of high-energy trauma and its complications. They lead to a multi-stage, long and costly treatment. The Ilizarov method of bone transport (IBT) and the Masquelet induced membrane technique (IMT) have been used in a great variety of challenging clinical situations including post-traumatic bone loss, infected nonunion, tumor resection, and congenital pseudarthrosis of the tibia (CPT).

Research motivation

The importance of improving bone regeneration in the management of large bone defects and CPT is a very relevant issue due to treatment failures that diminish bone potential for regeneration. Therefore, a combination of the biological merits of IBT and IMT seemed a promising strategy for the management of cases with a history of failed attempts and impaired regeneration potential.

Research objectives

We aimed to conduct clinical studies on the use of a new technological solution that integrates the IMT and IBT techniques for treating non-viable tibial defects of post-traumatic (PTD) etiology and CPT to improve bone regeneration at the docking site, bone consolidation and reduce refracture rate.

Research methods

We retrospectively studied the treatment course and outcomes in a case series that included seven PTD patients (subgroup A) and nine CPT cases (subgroup B) managed by the combined technology of IMT and IBT. Adult patients in subgroup A had bone defects of post-traumatic origin after several previous treatments failed and non-viable types of nonunion (hypotrophic, torsion-wedge, defect-pseudarthrosis). Subgroup B included nine children with a mean age of 6.1 ± 0.9 years with severe CPT types who had numerous failed interventions to unite pseudarthrosis. Step 1 included Ilizarov frame placement and spacer introduction into the resected defect to generate the induced membrane which remained in the interfragmental gap after spacer removal. Step 2 was an osteotomy and bone transport of the fragment through the tunnel in the induced membrane, its compression and closed docking for consolidation without grafting. Upon docking, supportive compression of 1 mm was provided once every two weeks in the consolidation phase. Postoperative care and radiographic checks followed the standards of the Ilizarov method. Radiographic evidence of bony union, external fixation time, defect filling rate and complications were assessed. The primary outcome measure was radiographic bone union. Secondary outcomes were correction of limb length discrepancy and deformities. The outcomes were retrospectively studied after a mean follow-up period of 20.8 ± 2.7 mo in subgroup A and 25.3 ± 2.3 mo in subgroup B.

Research results

Upon completion of treatment, defects were filled by 75.4 ± 10.6% and 34.6 ± 4.2%, in subgroups A and B, respectively. Total duration of external fixation was 397 ± 9.2 and 270.1 ± 16.3 d, including spacer retention time of 42.4 ± 4.5 and 55.8 ± 6.6 d, respectively. Bone infection was not observed. Postoperative complications included several cases of pin-tract infection and regenerate deformity in both subgroups. Ischemic regeneration was observed in two cases of subgroup B. Complications were corrected during the course of treatment. Bone union was achieved in all patients of subgroup A and in seven patients of subgroup B. One non-united CPT case was further treated with the Ilizarov compression method only and achieved union. After a follow-up period of two to three years, refractures occurred in four cases of

united CPT.

Research conclusions

The combination of IMT and IBT may provide good outcomes in post-traumatic tibial defects after previous treatment failures, although the external fixation is longer due to spacer retention time. This combination might also be used for severe types of CPT, despite the fact that refractures may occur.

Research perspectives

There are ways to further investigate the adjuncts to our protocol such as grafting at the docking site and intramedullary nailing, especially in severe CPT.

FOOTNOTES

Author contributions: All authors contributed to the conception and design, drafting of the manuscript, analysis and interpretation of data, and critical revision of the manuscript; Malkova TA and Kolchin SN contributed to the acquisition of literature data; Kolchin SN performed statistical analysis. Borzunov DY, Kolchin SN, Mokhovikov DS performed the interventions in the cases included into this study.

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REFERENCES

1 **Hoogervorst LA**, Hart MJ, Simpson PM, Kimmel LA, Oppy A, Edwards ER, Gabbe BJ. Outcomes of severe lower limb injury with Mangled Extremity Severity Score ≥ 7. *Bone Joint J* 2021; **103-B**: 769-774 [PMID: 33789468 DOI: 10.1302/0301-620X.103B4.BJJ-2020-1647.R1]
2 **Borzunov DY**, Kolchin SN, Malkova TA. Role of the Ilizarov non-free bone plasty in the management of long bone defects and nonunion: Problems solved and unsolved. *World J Orthop* 2020; **11**: 304-318 [PMID: 32572367 DOI: 10.5312/wjo.v11.i6.304]
3 **Masquelet AC**, Kishi T, Benko PE. Very long-term results of post-traumatic bone defect reconstruction by the induced membrane technique. *Orthop Traumatol Surg Res* 2019; **105**: 159-166 [PMID: 30639175 DOI: 10.1016/j.otsr.2018.11.012]
4 **Gouron R**. Surgical technique and indications of the induced membrane procedure in children. *Orthop Traumatol Surg Res* 2016; **102**: S133-S139 [PMID: 26774902 DOI: 10.1016/j.otsr.2015.06.027]
5 **El-Alfy BS**. Unhappy triad in limb reconstruction: Management by Ilizarov method. *World J Orthop* 2017; **8**: 42-48 [PMID: 28144578 DOI: 10.5312/wjo.v8.i1.42]
6 **Catagni MA**, Azzam W, Guerreschi F, Lovisetti L, Poli P, Khan MS, Di Giacomo LM. Trifocal versus bifocal bone transport in treatment of long segmental tibial bone defects. *Bone Joint J* 2019; **101-B**: 162-169 [PMID: 30700126 DOI: 10.1302/0301-620X.101B2.BJJ-2018-0340.R2]
7 **Li R**, Zhu G, Chen C, Chen Y, Ren G. Bone Transport for Treatment of Traumatic Composite Tibial Bone and Soft Tissue Defects: Any Specific Needs besides the Ilizarov Technique? *Biomed Res Int* 2020; **2020**: 2716547 [PMID: 32185197 DOI: 10.1155/2020/2716547]
8 **Bernstein M**, Fragomen AT, Sabharwal S, Barclay J, Rozbruch SR. Does Integrated Fixation Provide Benefit in the Reconstruction of Posttraumatic Tibial Bone Defects? *Clin Orthop Relat Res* 2015; **473**: 3143-3153 [PMID: 25940337

DOI: 10.1007/s11999-015-4326-6]
9 **Liu Y**, Yushan M, Liu Z, Liu J, Ma C, Yusufu A. Complications of bone transport technique using the Ilizarov method in the lower extremity: a retrospective analysis of 282 consecutive cases over 10 years. *BMC Musculoskelet Disord* 2020; **21**: 354 [PMID: 32505174 DOI: 10.1186/s12891-020-03335-w]
10 **Ayouba G**, Lemonne F, Kombate NK, Bakriga B, Yaovi Edem J, André-Pierre Max U. Interest of nailing associated with the Masquelet technique in reconstruction of bone defect. *J Orthop* 2020; **20**: 228-231 [PMID: 32055148 DOI: 10.1016/j.jor.2019.12.014]
11 **Gupta G**, Ahmad S, Mohd Zahid, Khan AH, Sherwani MK, Khan AQ. Management of traumatic tibial diaphyseal bone defect by "induced-membrane technique". *Indian J Orthop* 2016; **50**: 290-296 [PMID: 27293290 DOI: 10.4103/0019-5413.181780]
12 **Mi M**, Papakostidis C, Wu X, Giannoudis PV. Mixed results with the Masquelet technique: A fact or a myth? *Injury* 2020; **51**: 132-135 [PMID: 31883866 DOI: 10.1016/j.injury.2019.12.032]
13 **Morelli I**, Drago L, George DA, Gallazzi E, Scarponi S, Romanò CL. Masquelet technique: myth or reality? *Injury* 2016; **47** Suppl 6: S68-S76 [PMID: 28040090 DOI: 10.1016/S0020-1383(16)30842-7]
14 **Morris R**, Hossain M, Evans A, Pallister I. Induced membrane technique for treating tibial defects gives mixed results. *Bone Joint J* 2017; **99-B**: 680-685 [PMID: 28455479 DOI: 10.1302/0301-620X.99B5.BJJ-2016-0694.R2]
15 **Paley D**. Congenital pseudarthrosis of the tibia: biological and biomechanical considerations to achieve union and prevent refracture. *J Child Orthop* 2019; **13**: 120-133 [PMID: 30996736 DOI: 10.1302/1863-2548.13.180147]
16 **Borzunov DY**, Gorbach EN, Mokhovikov DS, Kolchin SN. Combined bone plasty interventions for rehabilitation of patients with congenital pseudarthrosis of the tibia. *Genij Ortopedii* 2019; **25**: 304-311 [DOI: 10.18019/1028-4427-2019-25-3-304-311]
17 **Mokhovikov DS**, Stupina TA, Varsegova TN, Diuriagina OV, Emanov AA, Borzunov DYu. Histomorphometric characteristics of the tibialis anterior muscle and the peroneal nerve in experimental repair of post-resection tibial defect using the Ilizarov external fixation and the Masquelet technique. *Genij Ortopedii* 2020; **26**: 216-221 [DOI: 10.18019/1028-4427-2020-26-2-216-221]
18 **Piacentini F**, Ceglia MJ, Bettini L, Bianco S, Buzzi R, Campanacci DA. Induced membrane technique using enriched bone grafts for treatment of posttraumatic segmental long bone defects. *J Orthop Traumatol* 2019; **20**: 13 [PMID: 30859333 DOI: 10.1186/s10195-019-0522-6]
19 **Wang X**, Wei F, Luo F, Huang K, Xie Z. Induction of granulation tissue for the secretion of growth factors and the promotion of bone defect repair. *J Orthop Surg Res* 2015; **10**: 147 [PMID: 26381122 DOI: 10.1186/s13018-015-0287-4]
20 **Roukoz S**, El Khoury G, Saghbini E, Saliba I, Khazzaka A, Rizkallah M. Does the induced membrane have antibacterial properties? *Int Orthop* 2020; **44**: 391-398 [PMID: 31796993 DOI: 10.1007/s00264-019-04453-4]
21 **Marais LC**, Ferreira N. Bone transport through an induced membrane in the management of tibial bone defects resulting from chronic osteomyelitis. *Strategies Trauma Limb Reconstr* 2015; **10**: 27-33 [PMID: 25840909 DOI: 10.1007/s11751-015-0221-7]
22 **El-Rosasy MA**. Congenital pseudarthrosis of the tibia: the outcome of a pathology-oriented classification system and treatment protocol. *J Pediatr Orthop B* 2020; **29**: 337-347 [PMID: 31503102 DOI: 10.1097/BPB.0000000000000660]
23 **Kocaoğlu M**, Eralp L, Bilen FE, Civan M. Congenital pseudarthrosis of the tibia: Results of circular external fixation treatment with intramedullary rodding and periosteal grafting technique. *Acta Orthop Traumatol Turc* 2020; **54**: 245-254 [PMID: 32442122 DOI: 10.5152/j.aott.2020.03.26]
24 **Kesireddy N**, Kheireldin RK, Lu A, Cooper J, Liu J, Ebraheim NA. Current treatment of congenital pseudarthrosis of the tibia: a systematic review and meta-analysis. *J Pediatr Orthop B* 2018; **27**: 541-550 [PMID: 29878977 DOI: 10.1097/BPB.0000000000000524]
25 **Yan A**, Mei HB, Liu K, Wu JY, Tang J, Zhu GH, Ye WH. Wrapping grafting for congenital pseudarthrosis of the tibia: A preliminary report. *Medicine (Baltimore)* 2017; **96**: e8835 [PMID: 29310362 DOI: 10.1097/MD.0000000000008835]
26 **Meselhy MA**, Elhammady AS, Singer MS. Outcome of Induced Membrane Technique in Treatment of failed previously operated Congenital Pseudarthrosis of the Tibia. *Orthop Traumatol Surg Res* 2020; **106**: 813-818 [PMID: 32249159 DOI: 10.1016/j.otsr.2019.11.033]
27 **Vaidya SV**, Aroojis A, Mehta R, Agashe MV, Dhawale A, Bansal AV, Sarathy K. Short Term Results of a New Comprehensive Protocol for the Management of Congenital Pseudarthrosis of the Tibia. *Indian J Orthop* 2019; **53**: 736-744 [PMID: 31673175 DOI: 10.4103/ortho.IJOrtho_155_19]
28 **Liu Y**, Yang G, Liu K, Wu J, Zhu G, Tang J, Zheng Y, Mei H. Combined surgery with 3-in-1 osteosynthesis in congenital pseudarthrosis of the tibia with intact fibula. *Orphanet J Rare Dis* 2020; **15**: 62 [PMID: 32122367 DOI: 10.1186/s13023-020-1330-z]
29 **Memeo A**, Verdoni F, Minoli CF, Voto A, D'Amato RD, Formiconi F, Priano D, Montanari L, Panuccio E. Effectiveness of bone marrow aspirate concentrate (BMAC) as adjuvant therapy in the surgical treatment of congenital pseudoarthrosis of the tibia: a retrospective comparative study. *J Biol Regul Homeost Agents* 2020; **34**: 431-440. Congress of the Italian Orthopaedic Research Society [PMID: 33261306]
30 **Richards BS**, Anderson TD. rhBMP-2 and Intramedullary Fixation in Congenital Pseudarthrosis of the Tibia. *J Pediatr Orthop* 2018; **38**: 230-238 [PMID: 27261960 DOI: 10.1097/BPO.0000000000000789]
31 **Uzel AP**, Lemonne F, Casoli V. Tibial segmental bone defect reconstruction by Ilizarov type bone transport in an induced membrane. *Orthop Traumatol Surg Res* 2010; **96**: 194-198 [PMID: 20417920 DOI: 10.1016/j.rcot.2010.02.001]
32 **Mitrofanov AI**, Al Delamy OK, Al Harris MS. Repair of tibial bone defects with fibular fragment and the induced membrane technique. *Genij Ortopedii* 2019; **25**: 239-242 [DOI: 10.18019/1028-4427-2019-25-2-239-242]
33 **Mathieu L**, Potier L, Ndiaye R, Choufani C, Mbaye E, Niang CD. Challenges of the induced-membrane technique in the reconstruction of traumatic tibial defect with limited resources : a cohort study. *Acta Orthop Belg* 2020; **86**: 606-613 [PMID: 33861906]

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ORIGINAL ARTICLE

Retrospective Study

Diagnostic role of Xpert-MTB RIF assay in osteoarticular tuberculosis: A retrospective study

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Abstract

BACKGROUND

Osteoarticular tuberculosis (OATB) is a severe form of extrapulmonary tuberculosis (TB), which causes notable morbidity and warrants a high index of suspicion for prompt management. The diagnosis of OATB poses a challenge, because of the difficulty of collecting the samples and, secondarily, the paucibacillary nature of lesion, which gives poor sensitivity and reproducibility, with long turnaround time of routine/conventional laboratory tests and the requirement for invasive procedures and expertise. The Xpert MTB/RIF assay has been approved by the World Health Organization as a rapid diagnostic tool for diagnosing pulmonary and extrapulmonary TB.

AIM

To emphasize the diagnostic efficiency of gene Xpert for OATB in suspected patients in a tertiary care hospital of Eastern India.

METHODS

This retrospective study was conducted in the Department of Microbiology and Orthopaedics by analyzing the data of the gene Xpert assay over a 3-year duration from January 2018 to February 2021. Demographic and clinical data were recorded. The diagnostic efficiency of gene Xpert was evaluated against the composite reference standard (CRS).

RESULTS

A total of 37 cases fell into positive, probable, and possible categories of osteoarticular TB out of 112 patients included in the study by CRS; gene Xpert result was positive in 35 out of the 37 different CRS categorized cases. Of the 112 cases, culture was put in 40 cases, and, of these cultures, 5 cases showed the growth of MTB. Of these, 4 cases were included in the 35 cases diagnosed by gene Xpert.

Smear microscopy was positive in 6 out of 37 CRS categorized cases. When compared with CRS, the sensitivity of gene Xpert assay, culture, and smear was found to be 94.6%, 13.5%, and 16.2%, respectively, while specificity in all the three types of tests was 100%. When kappa statistics were applied, the percentage of agreement gene Xpert, culture, and microscopy with CRS was found to be 95%, 20%, and 22.6%, respectively. Follow-up of the gene Xpert positive patients after getting anti-tubercular treatment revealed improved conditions.

CONCLUSION

Gene Xpert could detect 31 extra cases with a low and very low mycobacterial load that were missed by the routine culture methods. Hence, more samples should be processed for molecular diagnostic methods like gene Xpert along with other conventional methods for the validation of the molecular test prospectively for the timely diagnosis of osteoarticular TB.

Key Words: Tuberculosis; Extrapulmonary; Osteoarticular; Gene Xpert assay; Composite reference standard

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Core Tip: Osteoarticular tuberculosis (OATB) is a severe form of extrapulmonary tuberculosis (TB) that needs prompt management. However, there is difficulty in collecting samples and, secondarily, the paucibacillary nature of the lesion gives poor sensitivity and reproducibility, often with long turnaround time of the routine conventional laboratory tests. Xpert MTB RIF assay has been approved by the World Health Organization for rapid diagnosis of pulmonary/extrapulmonary TB. This study aims to find the diagnostic efficiency of gene Xpert for OATB in suspected patients. We found sensitivity of gene Xpert assay, culture, and smear when compared with CRS to be 94.6%, 13.5%, and 16.2%, respectively, while specificity in all the three types of tests was 100%. The kappa percentage of agreement for gene Xpert, culture, and microscopy were found to be 95%, 20%, and 22.6%, respectively. Follow-up of the gene Xpert positive patients after getting anti-tubercular treatment revealed improvement of their conditions. We conclude that gene Xpert has higher sensitivity than other conventional tests for the timely diagnosis of OATB.

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INTRODUCTION

Tuberculosis (TB) is among the top ten causes of mortality worldwide. In 2019, an estimated 10.0 million (range, 8.9–11.0 million) were affected with TB globally, of which 1.2 million died, including 208000 human immunodeficiency viruses (HIV)-positive patients[1]. Most people who developed TB in 2019 belonged to the World Health Organization (WHO) regions of South-East Asia (44%). India topped the list of eight high burden TB countries contributing to almost 26% of the global TB cases[1].

Primarily, it is a disease of the lower respiratory tract, but it can involve other organs with multitudinous presentations. It can be classified as pulmonary TB and extrapulmonary TB (EPTB), with the latter contributing to approximately 14% of all the reported TB cases[2]. Osteoarticular TB (OATB) is a form of EPTB that comprises 1%-4.3% of total tuberculosis cases and 10%-15% of all EPTB cases[3,4]. Osteoarticular involvement usually results from paucibacillary hematological dissemination and fixation of a colony of mycobacteria inside the active bone marrow. OATB can cause notable morbidity, and a high index of suspicion is required for prompt diagnosis to avoid unwanted sequelae[5,6]. OATB remains a significant problem worldwide, leading to severe deformities and functional disability due to difficulty in diagnosis and delay in the initiation of specific treatment. Moreover, India is an endemic focus of TB, where most orthopedic surgeons continue to practice diagnosing OATB solely on clinical and radiological findings and initiating empirical anti-TB treatment (ATT)[5-7]. This is partly attributed to the challenges faced in collecting the samples from the appropriate site (which at times are difficult anatomically) and the paucibacillary nature of lesion, causing poor sensitivity reproducibility and long turnaround time of the routine conventional laboratory tests and the requirement for invasive procedures and expertise[8]. Hence, there is a need for a molecular diagnostic test with a short turnaround time to diagnose OATB rapidly.

In 2010, the WHO recommended using Xpert MTB/RIF assay (Xpert) in pulmonary TB cases for concurrent diagnosis and rifampicin resistance of TB bacilli. WHO also contemplated the same for EPTB in the year 2013[9,10]. The automated Xpert MTB/RIF (Cepheid, Sunnyvale, CA, United States) assay is based on hemi-nested real-time polymerase chain reaction principle for the concurrent detection of MTB complex and RIF resistance[11]. The present study aims to estimate the efficacy of the gene Xpert assay for the precise diagnosis of OATB.

MATERIALS AND METHODS

This is a retrospective study conducted jointly by the Department of Microbiology and Orthopaedics at a tertiary center in eastern India. The study was conducted by analyzing the data of the gene Xpert assay and follow-up data of patients spread over a 3-year duration from January 2018 to February 2021. Clinical specimens of 112 OATB TB cases were received for diagnosis of TB by the Gene-Xpert-MTB-Rif assay. A part of the sample was processed according to the standard protocol of gene Xpert and subjected to the assay[11]. Tissue samples were cut into small pieces followed by crushing, mixing with buffer, and then vortexing for homogenization. Samples were then incubated for 15 min or more till the tissue was dissolved and centrifuged at 3000 rpm; the supernatant was used for the assay. Synovial fluid and pus samples were also processed according to standard protocol. Cartridges were put inside the device for extraction of DNA and simultaneous amplification of *rpoB* gene (192bp) and generation results[11]; the remaining part of the samples was subjected for smear microscopy by Ziehl–Neelsen stain. Forty samples were subjected to culture. The demographic details and part of involvement were retrieved from files in the medical records. A follow-up telephonic survey of the health status survey, including compliance to ATT, using short form survey-12 free online calculator was performed by one of the researchers (Jain M)[12].

Composite reference standard (CRS) was taken into account to evaluate the diagnostic efficacy of the different test methods used in the study. According to CRS, patients were categorized into four groups: (1) confirmed OATB cases (culture-positive); (2) probable OATB cases (culture-negative but gene Xpert positive, and the patient responded well to anti-TB therapy); (3) possible OATB cases (condition improved after getting anti-TB therapy and had radiographic findings consistent with OATB but lack of bacteriological evidence); and (4) non-TB (culture and all other tests for TB were negative, and the patient improved without getting any anti-TB treatment)[13-15].

The data were entered into a Microsoft Office Excel sheet. The sensitivity, specificity, positive predictive value, and negative predictive value were calculated to evaluate the diagnostic performance of gene Xpert assay and microscopy against the culture method. Kappa statistics was applied to derive the percentage of agreement between gene Xpert and culture.

RESULTS

Synovial fluid was the most common sample (86/112) received in the laboratory. The other samples included tissues of the intervertebral disc and bone fragments (n = 11/112) and aspirated pus (n = 25/112). All 112 samples were subjected to smear microscopy and CBNAAT by gene Xpert MTB-Rif assay, and 40 samples were put on culture. According to CRS, 5 cases were confirmed to have OATB; of the 35 gene Xpert positive cases, 31 belonged to the probable OATB category, and 1 showed improvement after getting ATT despite being culture. Gene Xpert negative belonged to possible OATB category. Of the 112 samples, 35 samples were positive for MTB complex by gene Xpert. Smear microscopy was positive in 6 cases; all of these were detected by gene Xpert and culture was positive in 5 cases; of these, 4 were also positive by gene Xpert (Table 1).

The study population aged between 10-60 years. However, most of the cases (27.0%) confirmed OATB belonged to age group 21-30 years (Table 2). The positivity rate was equal for gender (male: female = 51.4%: 48.6% (Table 2). The spine was the most common confirmed site involved, followed by the knee, as shown in Table 3. The duration of the illness in the confirmed cases varied from 1-12 mo. All the cases were human immunodeficiency virus-negative.

Of the 35 gene Xpert confirmed cases, smear microscopy was positive only in 6 cases where MTB was detected in the range of low; in the remaining 29 cases, the detection of MTB was very low. None of the cases were resistant to rifampicin. Of the 35 cases, 18 cases could be followed up with clinical outcome and treated with ATT, and these 18 cases responded to standard combination ATT (Table 1).

Sensitivity of Xpert assay, culture, and smear, when compared with CRS, was found to be 94.6%, 13.5%, and 16.2%, respectively; specificity in all three types of the test was found to be 100%. When kappa statistics were applied, the percentage of agreement among Gene Xpert, culture, and microscopy with that of CRS was found to be 95.0%, 20.0%, and 22.5%, respectively (Table 3).

Table 1 Categorization of cases according to composite reference standard

Cases	Smear microscopy	Culture	Gene Xpert	ATT course (in mo)	Outcome (SF-12)		CRS category
					PCS-12	MCS-12	
Case No. 1	Negative	No growth	Positive	12	48.76	55.50	Probable OATB case
Case No. 2	Negative	Positive	Positive	Lost to follow-up			Confirmed OATB case
Case No. 3	Negative	No growth	Positive	15	46.03	56.9	Probable OATB case
Case No. 4	Negative	No growth	Positive	Lost to follow-up			Probable OATB case
Case No. 5	Negative	No growth	Positive	Lost to follow-up			Probable OATB case
Case No. 6	Positive	No growth	Positive	Lost to follow-up			Probable OATB case
Case No. 7	Negative	No growth	Positive	24	56.57	60.75	Probable OATB case
Case No. 8	Negative	No growth	Positive	24	46.03	56.9	Probable OATB case
Case No. 9	Negative	No growth	Positive	6	48.60	33.57	Probable OATB case
Case No. 10	Positive	No growth	Positive	Lost to follow-up			Probable OATB case
Case No. 11	Negative	No growth	Positive	Lost to follow-up			Probable OATB case
Case No. 12	Negative	No growth	Positive	Lost to follow-up			Probable OATB case
Case No. 13	Negative	No growth	Positive	Lost to follow-up			Probable OATB case
Case No. 14	Positive	No growth	Positive	Lost to follow-up			Probable OATB case
Case No. 15	Positive	Contamination	Positive	Lost to follow-up			Probable OATB case
Case No. 16	Negative	Contamination	Positive	Lost to follow-up			Probable OATB case
Case No. 17	Negative	No growth	Positive	6	56.57	60.75	Probable OATB case
Case No. 18	Negative	No growth	Positive	Lost to follow-up			Probable OATB case
Case No. 19	Negative	No growth	Positive	6	52.23	56.51	Probable OATB case
Case No. 20	Negative	No growth	Positive	21	52.23	56.51	Probable OATB case
Case No. 21	Negative	No growth	Positive	15	52.23	53.63	Probable OATB case
Case No. 22	Positive	Contamination	Positive	12	56.57	60.75	Probable OATB case
Case No. 23	Negative	No growth	Positive	15	48.60	33.57	Probable OATB case
Case No. 24	Negative	No growth	Positive	Lost to follow-up			Probable OATB case
Case No. 25	Positive	Positive	Positive	Lost to follow-up			Confirmed OATB case
Case No. 26	Negative	No growth	Positive	12	51.81	48.67	Probable OATB case
Case No. 27	Negative	Positive	Positive	12	48.76	55.50	Confirmed OATB case
Case No. 28	Negative	No growth	Positive	6	56.57	60.75	Probable OATB case
Case No. 29	Negative	No growth	Positive	Lost to follow-up			Probable OATB case
Case No. 30	Negative	No growth	Positive	12	51.81	48.67	Probable OATB case
Case No. 31	Negative	No growth	Positive	Lost to follow-up			Probable OATB case
Case No. 32	Negative	No growth	Positive	12	40.76	40.94	Probable OATB case
Case No. 33	Negative	No growth	Positive	Lost to follow-up			Probable OATB case
Case No. 34	Negative	Positive	Positive	2	28.93	40.32	Confirmed OATB case
Case No. 35	Negative	No growth	Positive	1.5	28.93	40.32	Probable OATB case
Case No. 36	Negative	Positive	Negative	12	48.76	55.50	Confirmed OATB case
Case No. 37	Negative	No growth	Negative	1.5	28.93	40.32	Possible OATB case

CRS: Composite reference standard; ATT: Anti-tuberculosis treatment; OATB: Osteoarticular tuberculosis; SF-12: Short form survey-12; PCS-12: Physical composite scale-12; MCS-12: Mental health composite scale-12.

Table 2 Demographic and clinical distribution of composite reference standard positive, probable and possible osteoarticular tuberculosis cases, *n* (%)

Characteristics		Cases (*n* = 37)
Age group (yr)	0 - 10	1 (2.7)
	11 - 20	5 (13.6)
	21 – 30	10 (27.0)
	31 - 40	6 (16.2)
	41- 50	6 (16.2)
	51 - 60	6 (16.2)
	> 60	3 (8.1)
Sex	Male	19 (51.4)
	Female	18 (48.6)
Site if OATB	Knee	8 (21.6)
	Spine	20 (54.1)
	Elbow	1 (2.7)
	Wrist	1 (2.7)
	Psoas abscess	7 (18.9)

OATB: Osteoarticular tuberculosis.

Table 3 Performance assay and statistical analysis of gene Xpert, culture and, smear microscopy against composite reference standard (*n* = 40)

Methods	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Kappa statistics (% agreement)
Gene Xpert	94.6	100.0	94.6	100.0	95.0
Culture	13.5	100.0	13.5	100.0	20.0
Smear microscopy	16.2	100.0	16.2	100.0	22.5

PPV: Positive predictive value; NPV: Negative predictive value.

DISCUSSION

OATB remains a nuisance as the provenance of functional disability, which could lead to severe deformities and cause lifetime stigma. Therefore, making an early diagnosis and treatment is imperative to avoid unacceptable consequences. India is one of the high burden TB countries where many orthopedic surgeons diagnose OATB by relying on clinical and radiological findings and start ATT empirically[5].

The incidence of OATB ranges from 1.0%-4.3% of all TB cases and comprises 5-15% of all EPTB[5,14-16]. In a study by Gogia *et al*[5], 16 cases out of 120 were diagnosed with OATB over 3 years. However, Muangchan *et al*[7] reported 99 cases of OATB during a 2 year period, which seems to be quite a high number. In the present study, 37 cases were proven of the 112 cases (33.03%) to have OATB after a retrospective analysis of 3 years of data, similar to the study by Yoon *et al*[16].

Enache *et al*[8], in their study on EPTB, found that two-third of patients were older than 40 years. In some other studies, the median age was reported in the higher range of 50-60 years[9,13]. However, in our study, maximum cases belonged to the younger age group; the highest was in the 21-30 age group (27.0%). Female predominance was observed in some studies[7,16], and in others, the maximum cases were males[5,8]. In our study, it was almost equally distributed. Clinically, pain is the most common

symptom[7], which was the finding in our study also.

The spinal area was the most common (54.1%) site affected in our study, followed by knee joint and psoas abscess (21.6% and 18.9%, respectively), which is in concordance with several other studies with a preponderance of spinal involvement[3,17].

Yoon *et al*[16], in their study, observed that there are limited diagnostic options for EPTB, which led them to analyze retrospectively the different spectrums of EPTB regarding clinical patterns, underlying diseases, and diagnostic methods. Synovial fluid or any drained purulent fluid from the suspected lesion site can be examined for acid-fast bacteria (AFB) in cases of OATB. A direct smear of the sample can show positivity for AFB in as low as 27% of cases[17]. Six out of 35 gene Xpert confirmed cases in our study were AFB positive. Low positivity in OATB may be due to the paucibacillary nature of the lesion[18]. Culture on various specimens like a biopsy, cold abscess, or synovial fluid is considered the standard gold method for diagnosis[17]. A lower range of culture positivity has been observed in different studies, such as 11.2% and 19.2 % by Yoong *et al*[16] and Muangchan *et al*[7]. However, a higher positivity (63%) was seen in the review article by Haider *et al*[17].

In our study, we also found a lower culture positivity rate (13.7%) in samples subjected for culture, which could be due to a less amount of such samples, as the maximum amount was subjected for gene Xpert. The long turnaround time and the possibilities of contamination were the major disadvantages of the conventional culture technique. Similarly, the microscopy method also has the drawback of lack of reproducibility and low reliability, particularly in EPTB cases with a low bacterial load[18-20]. Molecular tests like gene Xpert, on the other hand, have the advantage of short turnaround time, which can help the physician determine the correct management of cases[21]. In the present study, the sensitivity, specificity, and percentage of agreement compared with CRS of gene Xpert were similar (94.6%, 100%, and 95%, respectively)[22]. These results may be because fewer samples were put in culture, and the statistical analysis was made using those small proportions of samples; in addition, the sample size was also less. Despite the statistical values, it cannot be ignored that the gene Xpert could detect 31 extra cases with low and very low bacterial load, which were missed by the culture methods. All the cases detected by gene Xpert were sensitive to rifampicin, and the clinical outcome was favorable.

Since this is a retrospective study and not all samples were processed for culture, accurate analysis of all the samples could not be done, which is the limitation of our study. Moreover, clinical data were retrieved from the database, and some patients were lost to follow-up; if the follow-up data of all the patients had been included in the present study, then the utility of the molecular methods could have been more established.

CONCLUSION

Hence, to conclude, conventional diagnostic methods such as smear are done everywhere for mycobacterium TB diagnosis, but this test is negative in most orthopedic cases. Therefore, more samples should be processed using molecular diagnostic methods like gene Xpert along with other conventional methods in order to validate the molecular test prospectively for the timely diagnosis of OATB. When more cases can be diagnosed early and treatment initiated at the right time, the likelihood of cure is greater and the severe consequences of the disease can be prevented.

ARTICLE HIGHLIGHTS

Research background

Tuberculosis (TB) is among the top ten causes of mortality worldwide. In 2019, an estimated 10.0 million were affected with TB globally, of which 1.2 million died. India topped the list of eight high burden TB countries, which contribute to almost 26% of the global TB cases. Osteoarticular tuberculosis (OATB) is a form of extrapulmonary TB that comprises 1.0%-4.3% of total tuberculosis cases and 10%-15% of all extrapulmonary TB cases. OATB remains a significant problem worldwide, leading to severe deformities and functional disability due to difficulty in diagnosis and delay in the initiation of specific treatment. Moreover, India is an endemic focus of TB, where most orthopedic surgeons continue to practice diagnosing OATB solely on clinical and radiological findings and initiating empirical anti-TB treatment.

Research motivation

There is a need for a molecular diagnostic test with a short turnaround time to diagnose OATB rapidly. In 2010, the World Health Organization recommended using Xpert MTB/RIF assay in pulmonary TB cases for concurrent diagnosis and rifampicin resistance of TB bacilli.

Research objectives
The objective is to estimate the efficacy of gene Xpert assay for the precise diagnosis of OATB.

Research methods
This retrospective study was conducted by analyzing the data of the gene Xpert assay over a 3-year period. The diagnostic efficiency of gene Xpert was evaluated against the composite reference standard.

Research results
A total of 37 cases fell into positive, probable, and possible categories of OATB out of 112 patients included in the study by composite reference standard; gene Xpert result was positive in 35 out of the 37 different composite reference standard categorized cases. Follow-up of the gene Xpert positive patients after getting anti-tubercular treatment revealed improved conditions.

Research conclusions
Conventional diagnostic methods such as smear are done everywhere for mycobacterium TB diagnosis, which is negative in most orthopedic cases.

Research perspectives
More samples should be processed for molecular diagnostic methods like gene Xpert along with other conventional methods for the validation of the molecular test prospectively for the timely diagnosis of osteoarticular TB.

FOOTNOTES

Author contributions: Mohanty M and Mishra B conceived the idea; Jain M created the proposal and Mishra B received the clearance; Mohanty M and Puthiyapura LK collected the data; Jain M and Mohanty M wrote the paper; Mishra B and Puthiyapura LK revised the manuscript for important intellectual content; All authors have read and agreed to the content of the manuscript.

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REFERENCES

1 **World Health Organization**. Global tuberculosis report 2020. Available from: https://www.who.int/publications-detail-redirect/9789240013131
2 **Chen Y**, Wu P, Fu L, Liu YH, Zhang Y, Zhao Y. Multicentre evaluation of Xpert MTB/RIF assay in detecting urinary tract tuberculosis with urine samples. *Sci Rep* 2019; **9**: 11053 [PMID: 31363115 DOI: 10.1038/s41598-019-47358-3]
3 **Jutte PC**, van Loenhout-Rooyackers JH, Borgdorff MW, van Horn JR. Increase of bone and joint tuberculosis in The Netherlands. *J Bone Joint Surg Br* 2004; **86**: 901-904 [PMID: 15330034 DOI: 10.1302/0301-620x.86b6.14844]
4 **Sharma SK**, Mohan A. Extrapulmonary tuberculosis. *Indian J Med Res* 2004; **120**: 316-353 [PMID: 15520485]
5 **Gogia KK**, Gupta S. Osteoarticular Tuberculosis - A Study Associated with Socio Demographic Factors. *Ann Int Med Den*

Res 2016; **2**: OR012-OR017

6 **Procopie I**, Popescu EL, Huplea V, Pleșea RM, Ghelase ȘM, Stoica GA, Mureșan RF, Onțică V, Pleșea IE, Anușca DN. Osteoraticular Tuberculosis-Brief Review of Clinical Morphological and Therapeutic Profiles. *Curr Health Sci J* 2017; **43**: 171-190 [PMID: 30595874 DOI: 10.12865/CHSJ.43.03.01]

7 **Muangchan C**, Nilganuwong S. The study of clinical manifestation of osteoarticular tuberculosis in Siriraj Hospital, Thailand. *J Med Assoc Thai* 2009; **92** Suppl 2: S101-S109 [PMID: 19562993]

8 **Enache SD**, Pleșea IE, Anușca D, Zaharia B, Pop OT. Osteoarticular tuberculosis--a ten years case review. *Rom J Morphol Embryol* 2005; **46**: 67-72 [PMID: 16286988]

9 **World Health Organization**. WHO endorses new rapid tuberculosis test. Geneva: World Health Organization, 2010

10 **Walmsley S**. ACP Journal Club: review: Xpert MTB/RIF assay detects extrapulmonary TB in lymph nodes and CSF, but not pleural fluid. *Ann Intern Med* 2015; **162**: JC11 [PMID: 25686186 DOI: 10.7326/ACPJC-2015-162-4-011]

11 **World Health Organization**. Automated real-time nucleic acid amplifiation technology for rapid and simultaneous detection of tuberculosis and rifampicin resistance: Xpert MTB/RIF assay for the diagnosis of pulmonary and extrapulmonary TB in adults and children. Geneva: World Health Organization, 2013

12 **Huo T**, Guo Y, Shenkman E, Muller K. Assessing the reliability of the short form 12 (SF-12) health survey in adults with mental health conditions: a report from the wellness incentive and navigation (WIN) study. *Health Qual Life Outcomes* 2018; **16**: 34 [PMID: 29439718 DOI: 10.1186/s12955-018-0858-2]

13 **National Institute of Health and Care Excellence**. NICE guidelines for the diagnosis of TB 2011. Available from: http://www.nice.org.uk/guidance/cg117/chapter/guidance

14 **Gu Y**, Wang G, Dong W, Li Y, Ma Y, Shang Y, Qin S, Huang H. Xpert MTB/RIF and GenoType MTBDRplus assays for the rapid diagnosis of bone and joint tuberculosis. *Int J Infect Dis* 2015; **36**: 27-30 [PMID: 26004172 DOI: 10.1016/j.ijid.2015.05.014]

15 **Sharma SK**, Kohli M, Chaubey J, Yadav RN, Sharma R, Singh BK, Sreenivas V, Sharma A, Bhatia R, Jain D, Seenu V, Dhar A, Soneja M. Evaluation of Xpert MTB/RIF assay performance in diagnosing extrapulmonary tuberculosis among adults in a tertiary care centre in India. *Eur Respir J* 2014; **44**: 1090-1093 [PMID: 25063241 DOI: 10.1183/09031936.00059014]

16 **Yoon HJ**, Song YG, Park WI, Choi JP, Chang KH, Kim JM. Clinical manifestations and diagnosis of extrapulmonary tuberculosis. *Yonsei Med J* 2004; **45**: 453-461 [PMID: 15227732 DOI: 10.3349/ymj.2004.45.3.453]

17 **Haider ALM**. Bones and Joints Tuberculosis. *BMB* 2007; **29**: 1-9

18 **Wares F**, Balasubramanian R, Mohan A, Sharma SK. Extrapulmonary Tuberculosis: Management and Control. In: Agarwal SP, Chauhan LS, editors. Tuberculosis Control in India. Directorate General of Health Services/Ministry of Health and Family Welfare, 2005: 95-114

19 **Caviedes L**, Lee TS, Gilman RH, Sheen P, Spellman E, Lee EH, Berg DE, Montenegro-James S. Rapid, efficient detection and drug susceptibility testing of Mycobacterium tuberculosis in sputum by microscopic observation of broth cultures. The Tuberculosis Working Group in Peru. *J Clin Microbiol* 2000; **38**: 1203-1208 [PMID: 10699023 DOI: 10.1128/JCM.38.3.1203-1208.2000]

20 **Arockiaraj J**, Michael JS, Amritanand R, David KS, Krishnan V. The role of Xpert MTB/RIF assay in the diagnosis of tubercular spondylodiscitis. *Eur Spine J* 2017; **26**: 3162-3169 [PMID: 28391384 DOI: 10.1007/s00586-017-5076-9]

21 **World Health Organization**. Checklist of prerequisites to country implementation of Xpert MTB/RIF and key action points at country level. Geneva: World Health Organization, 2011

22 **Li Y**, Jia W, Lei G, Zhao D, Wang G, Qin S. Diagnostic efficiency of Xpert MTB/RIF assay for osteoarticular tuberculosis in patients with inflammatory arthritis in China. *PLoS One* 2018; **13**: e0198600 [PMID: 29856840 DOI: 10.1371/journal.pone.0198600]

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ORIGINAL ARTICLE

Prospective Study

Plate *vs* reverse shoulder arthroplasty for proximal humeral fractures: The psychological health influence the choice of device?

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Abstract

BACKGROUND

Proximal humeral fractures represent the third most common observed osteoporotic fracture; the treatment in three and four-part proximal humeral fractures in patients over 65 years is still controversial. Among the treatments described in literature, open reduction and internal fixation (O.R.I.F) and reverse shoulder arthroplasty (RSA) are gaining an increasing popularity.

AIM

To investigate the correct treatment for three and four-part proximal humeral fractures according to psychological aspects.

METHODS

It was conducted a prospective study with a series of 63 patients treated with O.R.I.F. (group A) and with RSA (group B) for three and four-part proximal humeral fractures according to Neer classification system. A conservative treatment group, as control, was finally introduced. One independent observer performed clinical and a psychological evaluation at one (T0), six (T1) and twelve months (T2) postoperatively. The Constant's score and The Disabilities of the

Arm, Shoulder and Hand (DASH score) were used for clinical evaluation, while General Anxiety Disorder-7 (GAD-7) and Caregiver Strain Scale (CSS) were used for psychological evaluation.

RESULTS

At one month follow up in group A the mean values were DASH score 50.8, Constant score 36.1, GAD-7 score 5.4, CSS 5.0. For the group B, the average values at T0 were: DASH score 54.6, Constant score 32.0; GAD-7 score 6.4, CSS 6.2. At six months in group A the average values were DASH score 42.1, Constant score 47.3, GAD-7 score 4.3, CSS 3.9. For the group B, the average values at T1 were: DASH score 39.1, Constant score 43.2, GAD-7 score 5.7, CSS 5.5. At twelve months in the group A, the mean values were DASH score 32.8, Constant score 60.0, GAD-7 score 3.2, CSS 3.1. For the group B shown these mean values: DASH score 33.6, Constant score 52.9, GAD-7 score 4.3, CSS 4.5. We demonstrated a better clinical and psychological outcome at T2 in the group treated with osteosynthesis compared to the group treated with arthroplasty (Constant $P = 0.049$, GAD-7 $P = 0.012$ and CSS $P = 0.005$). A better clinical and psychological outcome emerged in control group at T2 comparing with surgical group (DASH score $P = 0.014$, Constant score $P < 0.001$, GAD-7 $P = 0.002$ and CSS $P = 0.001$).

CONCLUSION

Both open osteosynthesis and reverse shoulder arthroplasty are valid treatments for proximal humeral fractures. According to the best osteosynthesis results the authors suggested to perform a psychological analysis for each patient in order to choose the appropriate treatment.

Key Words: Proximal humerus fractures; Open reduction and fixation; Reverse shoulder arthroplasty; Psychological health; General Anxiety Disorder-7 scale; Caregiver Strain scale

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Core Tip: This was a prospective study with 63 patients seeking to evaluate how psychological factors can influence the choice of device for proximal humeral fractures.

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INTRODUCTION

Proximal humeral fractures account for 6%-8% of all fractures and around 85% occurs in patients over 50 years old[1]. Most patients sustaining these fractures are women above the age of 60. These fractures represent the third most common observed osteoporotic fracture in elderly patients, after wrist and hip fractures[2-4], with an incidence of 82 per 100000 person-years. It has been suggested that the overall fracture rate is increasing along with the increase in the elderly population[5,6]. Furthermore, a Finnish study estimated the incidence of fall-related proximal humerus fractures has tripled since 1970[7]. The Neer classification, based on the number of bone fragments, is used for the therapeutic decision[8]. This remains the most commonly used classification, but additional systems have been described more recently, giving other useful indications to surgeon for type of surgery to adopt. About 80% of the proximal humeral fractures is nondisplaced or minimally displaced, therefore in these cases the treatment is conservative. In the remaining 20% of cases, the surgical strategy probably is the first option, although conservative treatment is chosen by some surgeons[9]. In relation to different factors, such as age, daily activity, and fracture pattern, operative treatment options include: synthesis and joint replacement[10-13]. Many studies compared the clinical and radiological outcomes of three and four-part proximal humeral fractures in patients over 65 years old treated with open reduction and internal fixation (O.R.I.F.) and joint replacement. Giardella *et al*[14], in their retrospective study enrolling patients over 65 years old, reported better clinical and functional results in patients treated with reverse shoulder arthroplasty (R.S.A.) respect to O.R.I.F, confirming that R.S.A. is the best treatment in proximal humeral fractures in elderly patients, especially in case of a rotator cuff tear or degeneration.

The aim of our study was to compare O.R.I.F. with R.S.A. in terms of clinical and psychological outcomes of three- and four-part proximal humeral fractures in patients older than 65 years evaluating

whether post-operative psychological symptoms may influence the clinical results after surgery.

MATERIALS AND METHODS

The Authors conducted a prospective observational study with a sequential recruitment of subjects affected by proximal humeral fractures, which was approved by the local Ethics Committee (No. 6809). The study was also registered on ClinicalTrials.gov, Protocol Registration and Result System (NCT04821180).

At the University Hospital of Bari, 63 patients who had undergone shoulder surgery between January 2016 and January 2019 were enrolled.

The inclusion criterion for enrollment was: (1) three and four-part proximal humeral fractures according to Neer classification system; (2) patients seventy years or older; and (3) shoulder surgery within one week after trauma.

The exclusion criteria were: (1) exposed fractures; (2) pathological fractures; (3) proximal humerus fractures with metaphyseal or diaphyseal extension; (4) contraindications to surgery associated with organ dysfunctions or with coagulopathy, allergy or hypersensitivity to the orthopedic implants; (5) patients who were unable to attend the different follow-ups; and (6) patients with psychiatric disorders.

We assumed that all enrolled patients suffered cuff tear arthropathy based on biological and anagraphic age.

All patients were properly informed of the nature of the study and they signed an informed consent document according to the Declaration of Helsinki.

The study group was stratified according to age class (class 1: 70-74 years; class 2: 75-79 years; class 3: 80-85 years) and gender differences (Table 1).

All patients were then divided into two groups according to the choice of surgery treatment: Group A: O.R.I.F. by angle-stable plate PHILOS (PHLPSYNTHES®, Oberdorf, Switzerland) (Figure 1A); and Group B: reverse total shoulder arthroplasty by Modular Shoulder Replacement SMR (LIMA® Corporate, San Benedetto del Friuli, Italy) (Figure 1B).

All patients were treated by the same surgical team with more than five years of experience in upper limb surgery.

The type of treatment was due to rotator cuff status, and shoulder clinical history.

We introduced a control group (Group C), made up of patients with the same characteristics of the study groups, but treated conservatively.

One independent observer performed clinical [Constant score and Disabilities of the Arm, Shoulder and Hand (DASH) score[15,16]] evaluation at one-month (T0), six months (T1) and at one year (T2) post operatively for each groups.

Furthermore the Clinical Psychology Service of our University Hospital performed a psychological evaluation (General Anxiety Disorder-7 scale and Caregiver Strain scale[17,18]) at the same follow-ups for each groups.

The Constant score determines the shoulder functionality and a higher score is indicative of high functional outcomes. The DASH score analyzes individual ability to perform certain activities and a higher score is indicative of worse functional outcomes.

The General Anxiety disorder 7 scale and the Caregiver Strain scale are two screening psychological tools used to define the level of stress. A higher score is indicative of poor outcomes.

In each case we evaluated the antero-posterior, lateral and transthoracic humerus X-rays at the T0, T1 and T2.

Statistical analysis

All data were collected electronically and were analyzed using R version 3.5.2 (released on 2018-12-20). In order to account for non-normality (Shapiro-Wilk test), continuous variables were reported as median and interquartile range (IQR) and compared (univariable analysis) through Wilcoxon rank sum test. Categorical variables were reported as absolute and relative frequencies. A multivariable linear regression model was then fitted for each score and time in order to evaluate the effect of PI intervention compared to O.R.I.F. intervention ("beta" coefficients) adjusted for age and sex. Linearity of dependent variable and normality and homoscedasticity of residuals were checked for each model through a test of significance. Statistical significance "alpha" was fixed to 0.05. The primary endpoint examined was psychological outcomes of proximal humeral fractures using General Anxiety disorder 7 scale. The secondary endpoint was clinical and shoulder functionality using Constant score. In addition, the Caregiver Strain scale and DASH score were used to complete psychological and clinical outcomes.

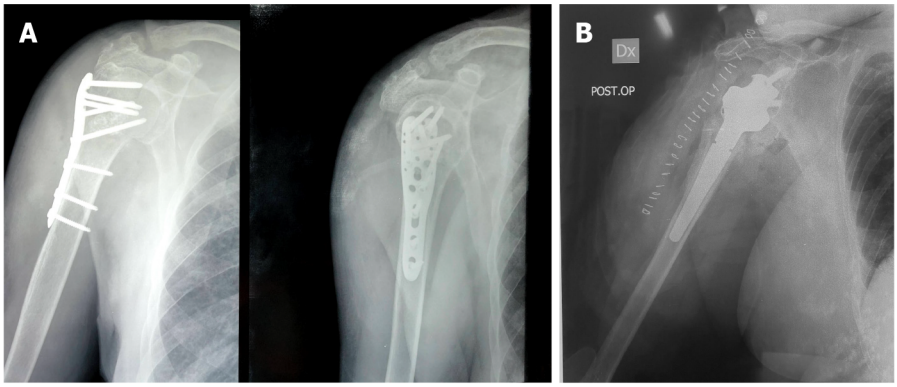
RESULTS

The study group was made up of sixty-three patients, 5 males (7.9%) and 58 females (92.1%). The

Table 1 The range value of variables analyzed for the study group

Age (yr)	Female	Men
CLASS 1 (70-74)	30	1
CLASS 2 (75-80)	15	3
CLASS 3 (80-85)	13	1
Total	58	5

CLASS: Age class.



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Figure 1 X-rays images of a patient. A: Post-operative X-rays of a patient treated with open reduction and internal fixation for three-parts proximal humeral fractures; B: Post-operative X-rays of a patient treated with reverse shoulder arthroplasty for three-parts proximal humeral fractures.

average age was 76.0 (4.0) years, range 70-82. Median (IQR) age was 76.0 (4.0) years.

In 70% of cases the right limb was involved and in 65.1% of cases (41 of 63 cases) were three-part proximal humeral fractures (Table 2).

The analysis showed a prevalence of the four-part proximal humeral fracture in the class 3 age group whilst the three-part proximal humeral fracture in the class 2 (Table 3).

Domestic accident was responsible for 70% of cases whilst road traffic accident was the commonest mechanism in 30% of cases.

The 48.2% (31) of patients were treated by angle stable plate PHILOS (PHLP-SYNTHES®, Oberdorf, Switzerland) with O.R.I.F. (group A) while the 50.8% (32) of patients were treated by reverse total shoulder arthroplasty SMR (LIMA®Corporate, San Benedetto del Friuli, Italy) (group B). The Control group, 32 patients, was treated conservatively.

For the group A, the average values at T0 were: DASH score 50.8 (range 44-62), Constant score 36.1 (range 22-49) (Table 4); as regards the psychological test, the average values at T0 were: General Anxiety Disorder-7 scale 5.4 (range 2-9), Caregiver Strain Scale 5.0 (range 2-9) (Table 4).

For the group B, the average values at T0 were: DASH score 54.6 (range 28-65), Constant score 32.0 (range 23-53) (Table 4); as regards the psychological test, the average values at T0 were: General Anxiety Disorder-7 scale 6.4 (range 3-9), Caregiver Strain Scale 6.2 (range 2-9) (Table 4).

For the group A, the average values at T1 were: DASH score 42.1 (range 32-58), Constant score 47.3 (range 25-63) (Table 5); as regards the psychological test, the average values at T1 were: General Anxiety Disorder-7 scale 4.3 (range 1-8), Caregiver Strain Scale 3.9 (range 1-8) (Table 5).

For the group B, the average values at T1 were: DASH score 39.1 (range 21-60), Constant score 43.2 (range 28-65) (Table 5); as regards the psychological test, the average values at T1 were: General Anxiety Disorder-7 scale 5.7 (range 3-9), Caregiver Strain Scale 5.5 (range 2-9) (Table 5).

At T2 in the group A, the mean values were: DASH score 32.8 (range 16-60), Constant score 60.0 (range 30-80) (Table 6); as regards the psychological test, the average values at T2 were: General Anxiety Disorder-7 scale 3.2 (range 1-7), Caregiver Strain Scale 3.1 (range 1-7) (Table 6).

At T2 the group B shown these mean values: DASH score 33.6 (range 17-55), Constant score 52.9 (range 35-79) (Table 6); as regards the psychological test, the average values at T2 were General Anxiety Disorder-7 scale 4.3 (range 1-7), Caregiver Strain Scale 4.5 (range 1-8) (Table 6).

At T0 median (IQR) DASH score was 53.0 (11.0), Constant score was 34.0 (10.5), General Anxiety Disorder-7 scale was 6.0 (2.0) and Caregiver Strain Scale was 6.0 (3.0).

Table 2 Analysis of the fracture pattern

	Total	Three-part fractures	Four-part fractures
Number	63	41	22

Table 3 Analysis of distribution considering age class and fracture personality

	Age class (yr)		
Neer classification	70-75	75-80	80-90
Three-part fractures	10	27	4
Four-part fractures	5	7	10

Table 4 Postoperative clinical and psychological mean values at T0 follow-up

	Group A	Group B
DASH	50.8	54.6
CONSTANT	36.1	32.0
GAD-7	5.4	6.4
CSS	5.0	6.2

DASH: The Disabilities of the Arm, Shoulder and Hand score; CONSTANT: The Constant score; GAD-7: General Anxiety Disorder-7; CSS: Caregiver Strain Scale.

Table 5 Description of clinical and psychological scores at T1 follow-up

	Group A	Group B
DASH	42.1	39.1
CONSTANT	47.3	43.2
GAD-7	4.3	5.7
CSS	3.9	5.5

DASH: The Disabilities of the Arm, Shoulder and Hand score; CONSTANT: The Constant score; GAD-7: General Anxiety Disorder-7; CSS: Caregiver Strain Scale.

Table 6 Analysis of clinical and psychological scores at T2 follow-up

	Group A	Group B
DASH	32.8	33.6
CONSTANT	60.0	52.9
GAD-7	3.2	4.3
CSS	3.1	4.5

DASH: The Disabilities of the Arm, Shoulder and Hand score; CONSTANT: The Constant score; GAD-7: General Anxiety Disorder-7; CSS: Caregiver Strain Scale.

At T1 median (IQR) DASH score was 38.0 (12.0), Constant score was 44.0 (11.5), General Anxiety Disorder-7 scale was 5.0 (2.5) and Caregiver Strain Scale was 5.0 (3.0).

At T2 median (IQR) DASH score was 32.0 (13.5), Constant score was 55.0 (20.0), General Anxiety Disorder-7 scale was 4.0 (2.5) and Caregiver Strain Scale was 4.0 (3.0).

For the group C, the mean values are reported separately (Table 7).

The univariable analysis (Table 8) showed a significant difference between the two treatment groups for Dash score at T0 (O.R.I.F. *vs* PI, median 50.0 *vs* 57.5, $P = 0.002$), Constant at T0 (O.R.I.F. *vs* PI, median 38.0 *vs* 31.5, $P = 0.008$), GAD-7 at T0 (O.R.I.F. *vs* PI, median 5.0 *vs* 6.0, $P = 0.015$), CSS at T0 (O.R.I.F. *vs* PI, median 5.0 *vs* 6.5, $P = 0.008$), GAD-7 at T1 (O.R.I.F. *vs* PI, median 4.0 *vs* 6.0, $P = 0.002$), CSS at T1 (O.R.I.F. *vs* PI, median 4.0 *vs* 6.0, $P = 0.001$), Constant at T2 (O.R.I.F. *vs* PI, median 60.0 *vs* 51.0, $P = 0.049$), GAD-7 at T2 (O.R.I.F. *vs* PI, median 3.0 *vs* 4.0, $P = 0.012$) and CSS at T2 (O.R.I.F. *vs* PI, median 3.0 *vs* 4.0, $P = 0.005$).

A second univariable analysis (Table 9) between conservative and surgical treatment (using values of the two treatments) was made to enhance the relevance of the study. We reported no statistical difference at T0 regarding clinical and psychological outcomes. On the contrary, conservative treatment has shown to have better clinical and psychological outcomes, although not statistically significant at T1 and statistically significant at T2.

We did not observe complications in the study and control group.

DISCUSSION

Three- and four-part fractures account for 21% to 23% of proximal humerus fractures[19,20], are usually treated surgically by O.R.I.F. in younger patients and by arthroplasty in the elderly[21,22].

Many risk factors patient-related such as osteoporosis, degenerative joint disease of the shoulder, rotator cuff dysfunctions, comorbidities and non-modified risk factors such as gender and age class may influence the choice of treatment[23,24].

In accordance with the literature, we reported a gender differences and age class stratification in favor of female and first class which was most represented (Table 1, Table 3)[25,26].

Due to the poor outcomes associated with conventional anatomic replacement of the humeral head, an extended use of the reverse shoulder arthroplasty has emerged in the literature, linked to good results as both a primary procedure and as a secondary procedure for failed open reductions[27-29].

Until now all the studies described in the literature comparing open reduction and osteosynthesis with reverse shoulder arthroplasty as surgical options of treatment for three and four-part proximal humeral fractures in patients over 65 years old, used clinical and radiological methods of evaluation[30-33].

Our study is the first in literature that compares the psychological and functional results in order to underline the importance of each one or both for the pre-operative planning.

In our study, the Authors reported a tendency to the improvement of functional outcomes for the two groups. As regards the DASH and the Constant score, the Authors reported good results in both groups from T0 to T2 by analyzing the average value of Table 4, Table 5, and Table 6.

The univariable analysis (Table 8) showed a significant difference between the two treatment groups in favor of Group A as regards DASH score at T0 (O.R.I.F. *vs* PI, median 50.0 *vs* 57.5, $P = 0.002$) and Constant at T0 (O.R.I.F. *vs* PI, median 38.0 *vs* 31.5, $P = 0.008$).

The Authors linked these results to reach more confidence with the plate respect to the prosthesis. Furthermore, we did not report any statistically significance difference between the two groups at T1 ($P = 0.256$; $P = 0.110$).

The univariable analysis (Table 8) did not show a statistically significant difference between the two treatment groups for DASH score at T2 (O.R.I.F. *vs* PI, median 30.0 *vs* 32.0, $P = 0.587$); as regard the Constant score at T2 (O.R.I.F. *vs* PI, median 60.0 *vs* 51.0, $P = 0.049$), there emerged a statistically significant difference in favor of group A who obtained better results but these were very near to the significance limit.

According to the literature, the functional results of the two surgical options (O.R.I.F. *vs* reverse prosthesis) overlapped at 1 year post operatively[34].

As regards the psychological evaluation, the Authors observed a tendency to the improvement for both groups from T0 to T2 according to Table 4, Table 5, and Table 6.

By better analysis, the Authors highlighted an improvement of psychological evaluation for the group A at T0.

Analyzing GAD-7 at T0 (O.R.I.F. *vs* PI, median 5.0 *vs* 6.0, $P = 0.015$) and CSS at T0 (O.R.I.F. *vs* PI, median 5.0 *vs* 6.5, $P = 0.008$), the Authors reported the superiority in terms of results for the group A respect to the group B according to Table 8.

The statistical evaluation was significant for both tests in the group A and also at T1 and at T2 as reported in the Table 8 analyzing GAD-7 at T1 (O.R.I.F. *vs* PI, median 4.0 *vs* 6.0, $P = 0.002$), CSS at T1 (O.R.I.F. *vs* PI, median 4.0 *vs* 6.0, $P = 0.001$), GAD-7 at T2 (O.R.I.F. *vs* PI, median 3.0 *vs* 4.0, $P = 0.012$) and CSS at T2 (O.R.I.F. *vs* PI, median 3.0 *vs* 4.0, $P = 0.005$).

Patients underwent primary reverse shoulder arthroplasty (group B) showed in each postoperative follow-ups a generalized anxiety disorder and a greater irritability then patients underwent osteosynthesis (group A).

Table 7 Group C clinical and psychological mean values at three different follow-ups

	DASH	CONSTANT	GAD-7	CSS
T0	51.1	33.2	5.9	5.7
T1	38.8	46.9	4.9	4.5
T2	29.9	65.5	3.1	3.0

DASH: The Disabilities of the Arm, Shoulder and Hand score; CONSTANT: The Constant score, GAD-7: General Anxiety Disorder-7; CSS: Caregiver Strain Scale.

Table 8 Score distribution between treatment open reduction and internal fixation and PI

	TO			T1			T2		
	O.R.I.F. (*n* = 31)	RSA (*n* = 32)	*P* value	O.R.I.F. (*n* = 31)	RSA (*n* = 32)	*P* value	O.R.I.F. (*n* = 31)	RSA (*n* = 32)	*P* value
DASH	50.0 (7.5)	57.5 (7.0)	**0.002**	45.0 (12.5)	36.5 (12.3)	0.256	30.0 (24.0)	32.0 (5.5)	0.587
CONSTANT	38.0 (7.5)	31.5 (6.0)	**0.008**	48.0 (19.0)	42.0 (7.3)	0.110	60.0 (31.0)	51.0 (5.8)	**0.049**
GAD-7	5.0 (2.5)	6.0 (2.3)	**0.015**	4.0 (2.5)	6.0 (2.0)	**0.002**	3.0 (3.0)	4.0 (1.3)	**0.012**
CSS	5.0 (2.0)	6.5 (2.3)	**0.008**	4.0 (2.5)	6.0 (1.3)	**0.001**	3.0 (2.5)	4.0 (2.3)	**0.005**

Data are median (Interquartile range). *P* values are from Wilcoxon rank sum test. O.R.I.F: Open reduction and internal fixation; RSA: Reverse shoulder arthroplasty; DASH: The Disabilities of the Arm, Shoulder and Hand score; CONSTANT: The Constant score, GAD-7: General Anxiety Disorder-7; CSS: Caregiver Strain Scale.

Table 9 Comparison between surgical and conservative treatment

n = 32	T0	*P* value	T1	*P* value	T2	*P* value
DASH	53 (44.5)	0.344	39 (35)	0.421	30 (26)	0.014
CONSTANT	32 (30)	0.223	48.5 (42)	0.063	65.5 (60)	< 0.001
GAD-7	6 (5)	0.827	5 (3.3)	0.548	3 (2)	0.002
CSS	6 (5)	0.481	5 (3)	0.090	3 (2)	0.001

Data are median (Interquartile range) of conservative group. *P* values are from Wilcoxon rank sum test. DASH: The Disabilities of the Arm, Shoulder and Hand score; CONSTANT: The Constant score, GAD-7: General Anxiety Disorder-7; CSS: Caregiver Strain Scale.

We revealed a residual fear during shoulder movement in patients underwent primary reverse shoulder arthroplasty, unlike the group of patients which have done osteosynthesis, who seemed more confident and secure in shoulder movements.

The authors linked these results for group B to the anxiety about loosening of humeral head. In fact, the patients underwent osteosynthesis, showed better results in terms of anxiety due to the idea to preserve their humeral head. The perception of own humeral head could play a role in the genesis of anxiety.

Moreover, the comparison between the surgical (group A and B) and the conservative group (group C) revealed better clinical and functional results at 12 mo for the group C. In fact, with mean values of 3.1 and 3.0 for the GAD-7 and CSS scales respectively, the group C showed less anxiety and fear at T2 notwithstanding at 12 mo no statistically differences were found. These results are consistent with a previous study that underlined the importance of conservative treatment which remains a valid option mainly in the three-part proximal humeral fractures in selected cases with good functional results and low complications[9].

This study has some limitations: the number of participants is limited to 63; the maximum follow-up achieved was 12 mo; the device for open reduction and internal fixation used was a single type of angle stable plate with specific surgical technique.

CONCLUSION

The aim of our study was to compare open osteosynthesis and reverse shoulder arthroplasty in the three and four-part proximal humeral fractures, in terms of functional and psychological scores at one, six months and at one year follow-ups in order to underline the importance of each one or both of them for the pre-operative planning.

Based on the results obtained, we highlighted the best results for group A in terms of psychological results respect to group B.

For this reason, we suggest to evaluate before surgical choice not only anatomical parameters but also patient psychological profile, always evaluating the possibility of a hypothetical conservative treatment.

The strong point of our study is the type of the study in fact it is a prospective observational comparative study.

Instead, the weak point is the lack of psychological evaluation for each patient enrolled before the surgery.

Due to the pain after the trauma, the Authors did not administer the psychological evaluation because it may be influenced negatively.

According to recent data of bibliography, we confirm the efficacy at 1 year of the osteosynthesis and shoulder arthroplasty in terms of functional evaluation.

As pointed out by the Authors, it is very important to perform a psychological analysis of each patient, in order to identify correctly the patient and to reserve the shoulder arthroplasty for a very limit case in which the bone stock is very poor.

ARTICLE HIGHLIGHTS

Research background

Patient affected by fractures is evaluated only from a surgical point of view. Psychological aspect is very often underestimated.

Research motivation

More studies are needed in literature, to evaluate before surgical choice not only anatomical parameters but also patient psychological profile.

Research objectives

The aim of our study was to compare open reduction and internal fixation with joint replacement in terms of clinical and psychological outcomes of three- and four- part proximal humeral fractures in patients older than 65 years evaluating whether post-operative psychological symptoms may influence the clinical results after surgery.

Research methods

An observational prospective single-center study with 12 mo follow-up was performed with a sequential recruitment of subjects affected by proximal humeral fractures treated with open reduction and internal fixation and joint replacement. A conservative treatment group, as control, was introduced.

Research results

Patients underwent primary reverse shoulder arthroplasty showed in each postoperative follow-ups a generalized anxiety disorder and a greater irritability then patients underwent osteosynthesis.

Research conclusions

Patient psychological profile should be evaluated by the surgeon before surgery for the choice of surgical devices.

Research perspectives

Future investigations are needed to confirm the role of the psychological profile in the field of orthopedic surgical treatment. In addition, long- term analysis needs to clarify if differences in outcomes are really related to the patient's mental state.

FOOTNOTES

Author contributions: Maccagnano G drafted the manuscript, and assisted with data analysis; Solarino G participated in design and oversight of the study; Pesce V drafted the manuscript, and assisted with data analysis; Vicenti G participated in study design and performed statistical analysis; Nappi VS participated in design of the study, and

was involved with data collection; Coviello M was involved with data collection, and assisted with data analysis; Giannico OV participated in study design and performed statistical analysis; Notarnicola A participated in design of the study; Moretti B participated in design and oversight of the study.

Institutional review board statement: The authors conducted a prospective observational study with a sequential recruitment of subjects affected by proximal humeral fractures, which was approved by the local Ethics Committee (No. 6809).

Clinical trial registration statement: The study was also registered on ClinicalTrials.gov, Protocol Registration and Result System (PRS) (NCT04821180).

Informed consent statement: All patients were properly informed of the nature of the study and they signed an informed consent document according to the Declaration of Helsinki.

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REFERENCES

1 **Court-Brown CM**, Caesar B. Epidemiology of adult fractures: A review. *Injury* 2006; **37**: 691-697 [PMID: 16814787 DOI: 10.1016/j.injury.2006.04.130]
2 **Lauritzen JB**, Schwarz P, Lund B, McNair P, Transbøl I. Changing incidence and residual lifetime risk of common osteoporosis-related fractures. *Osteoporos Int* 1993; **3**: 127-132 [PMID: 8481588 DOI: 10.1007/BF01623273]
3 **Seeley DG**, Browner WS, Nevitt MC, Genant HK, Scott JC, Cummings SR. Which fractures are associated with low appendicular bone mass in elderly women? *Ann Intern Med* 1991; **115**: 837-842 [PMID: 1952469 DOI: 10.7326/0003-4819-115-11-837]
4 **Launonen AP**, Lepola V, Saranko A, Flinkkilä T, Laitinen M, Mattila VM. Epidemiology of proximal humerus fractures. *Arch Osteoporos* 2015; **10**: 209 [PMID: 25675881 DOI: 10.1007/s11657-015-0209-4]
5 **van Staa TP**, Dennison EM, Leufkens HG, Cooper C. Epidemiology of fractures in England and Wales. *Bone* 2001; **29**: 517-522 [PMID: 11728921 DOI: 10.1016/s8756-3282(01)00614-7]
6 **Hagino H**, Yamamoto K, Ohshiro H, Nakamura T, Kishimoto H, Nose T. Changing incidence of hip, distal radius, and proximal humerus fractures in Tottori Prefecture, Japan. *Bone* 1999; **24**: 265-270 [PMID: 10071921 DOI: 10.1016/s8756-3282(98)00175-6]
7 **Palvanen M**, Kannus P, Niemi S, Parkkari J. Update in the epidemiology of proximal humeral fractures. *Clin Orthop Relat Res* 2006; **442**: 87-92 [PMID: 16394745 DOI: 10.1097/01.blo.0000194672.79634.78]
8 **Neer CS 2nd**. Displaced proximal humeral fractures. I. Classification and evaluation. *J Bone Joint Surg Am* 1970; **52**: 1077-1089 [PMID: 5455339]
9 **Soler-Peiro M**, García-Martínez L, Aguilella L, Perez-Bermejo M. Conservative treatment of 3-part and 4-part proximal humeral fractures: a systematic review. *J Orthop Surg Res* 2020; **15**: 347 [PMID: 32831119 DOI: 10.1186/s13018-020-01880-7]
10 **Beks RB**, Ochen Y, Frima H, Smeeing DPJ, van der Meijden O, Timmers TK, van der Velde D, van Heijl M, Leenen LPH, Groenwold RHH, Houwert RM. Operative versus nonoperative treatment of proximal humeral fractures: a systematic review, meta-analysis, and comparison of observational studies and randomized controlled trials. *J Shoulder Elbow Surg* 2018; **27**: 1526-1534 [PMID: 29735376 DOI: 10.1016/j.jse.2018.03.009]

11 **Robinson CM**, Page RS, Hill RM, Sanders DL, Court-Brown CM, Wakefield AE. Primary hemiarthroplasty for treatment of proximal humeral fractures. *J Bone Joint Surg Am* 2003; **85**: 1215-1223 [PMID: 12851345 DOI: 10.2106/00004623-200307000-00006]

12 **Solberg BD**, Moon CN, Franco DP, Paiement GD. Surgical treatment of three and four-part proximal humeral fractures. *J Bone Joint Surg Am* 2009; **91**: 1689-1697 [PMID: 19571092 DOI: 10.2106/JBJS.H.00133]

13 **de Kruijf M**, Vroemen JP, de Leur K, van der Voort EA, Vos DI, Van der Laan L. Proximal fractures of the humerus in patients older than 75 years of age: should we consider operative treatment? *J Orthop Traumatol* 2014; **15**: 111-115 [PMID: 24233865 DOI: 10.1007/s10195-013-0273-8]

14 **Giardella A**, Ascione F, Mocchi M, Berlusconi M, Romano AM, Oliva F, Maradei L. Reverse total shoulder versus angular stable plate treatment for proximal humeral fractures in over 65 years old patients. *Muscles Ligaments Tendons J* 2017; **7**: 271-278 [PMID: 29264338 DOI: 10.11138/mltj/2017.7.2.271]

15 **Constant RC**. Age related recovery of shoulder function after injury. Thesis, Univ Coll. 1986.

16 **Hudak PL**, Amadio PC, Bombardier C. Development of an upper extremity outcome measure: the DASH (disabilities of the arm, shoulder and hand) [corrected]. The Upper Extremity Collaborative Group (UECG). *Am J Ind Med* 1996; **29**: 602-608 [PMID: 8773720 DOI: 10.1002/(SICI)1097-0274(199606)29:6<602::AID-AJIM4>3.0.CO;2-L]

17 **Sadak T**, Korpak A, Wright JD, Lee MK, Noel M, Buckwalter K, Borson S. Psychometric Evaluation of Kingston Caregiver Stress Scale. *Clin Gerontol* 2017; **40**: 268-280 [PMID: 28459351 DOI: 10.1080/07317115.2017.1313349]

18 **Spitzer RL**, Kroenke K, Williams JB, Löwe B. A brief measure for assessing generalized anxiety disorder: the GAD-7. *Arch Intern Med* 2006; **166**: 1092-1097 [PMID: 16717171 DOI: 10.1001/archinte.166.10.1092]

19 **Tamai K**, Ishige N, Kuroda S, Ohno W, Itoh H, Hashiguchi H, Iizawa N, Mikasa M. Four-segment classification of proximal humeral fractures revisited: a multicenter study on 509 cases. *J Shoulder Elbow Surg* 2009; **18**: 845-850 [PMID: 19297201 DOI: 10.1016/j.jse.2009.01.018]

20 **Schumaier A**, Grawe B. Proximal Humerus Fractures: Evaluation and Management in the Elderly Patient. *Geriatr Orthop Surg Rehabil* 2018; **9**: 2151458517750516 [PMID: 29399372 DOI: 10.1177/2151458517750516]

21 **Boileau P**, Pennington SD, Alami G. Proximal humeral fractures in younger patients: fixation techniques and arthroplasty. *J Shoulder Elbow Surg* 2011; **20**: S47-S60 [PMID: 21281922 DOI: 10.1016/j.jse.2010.12.006]

22 **Gregory TM**, Vandenbussche E, Augereau B. Surgical treatment of three and four-part proximal humeral fractures. *Orthop Traumatol Surg Res* 2013; **99**: S197-S207 [PMID: 23333125 DOI: 10.1016/j.otsr.2012.12.006]

23 **Murray IR**, Amin AK, White TO, Robinson CM. Proximal humeral fractures: current concepts in classification, treatment and outcomes. *J Bone Joint Surg Br* 2011; **93**: 1-11 [PMID: 21196536 DOI: 10.1302/0301-620X.93B1.25702]

24 **Murena L**, Canton G, Ratti C, Hoxhaj B, Giraldi G, Surace MF, Grassi FA. Indications and results of osteosynthesis for proximal humerus fragility fractures in elderly patients. *Orthop Rev (Pavia)* 2020; **12**: 8559 [PMID: 32391138 DOI: 10.4081/or.2020.8559]

25 **de Oliveira AP**, Mestieri MC, Pontin JC. Epidemiological Profile of Patients with Proximal Humerus Fracture Treated at Hospital São Paulo, Brazil. *Acta Ortop Bras* 2015; **23**: 271-274 [PMID: 26981037 DOI: 10.1590/1413-785220152305143730]

26 **Iglesias-Rodríguez S**, Domínguez-Prado DM, García-Reza A, Fernández-Fernández D, Pérez-Alfonso E, García-Piñeiro J, Castro-Menéndez M. Epidemiology of proximal humerus fractures. *J Orthop Surg Res* 2021; **16**: 402 [PMID: 34158100 DOI: 10.1186/s13018-021-02551-x]

27 **Grassi FA**, Murena L, Valli F, Alberio R. Six-year experience with the Delta III reverse shoulder prosthesis. *J Orthop Surg (Hong Kong)* 2009; **17**: 151-156 [PMID: 19721141 DOI: 10.1177/230949900901700205]

28 **Klein M**, Juschka M, Hinkenjann B, Scherger B, Ostermann PA. Treatment of comminuted fractures of the proximal humerus in elderly patients with the Delta III reverse shoulder prosthesis. *J Orthop Trauma* 2008; **22**: 698-704 [PMID: 18978545 DOI: 10.1097/BOT.0b013e31818afe40]

29 **Grassi FA**, Zorzolo I. Reverse shoulder arthroplasty without subscapularis repair for the treatment of proximal humeral fractures in the elderly. *Musculoskelet Surg* 2014; **98** Suppl 1: 5-13 [PMID: 24659198 DOI: 10.1007/s12306-014-0321-4]

30 **Ross M**, Hope B, Stokes A, Peters SE, McLeod I, Duke PF. Reverse shoulder arthroplasty for the treatment of three-part and four-part proximal humeral fractures in the elderly. *J Shoulder Elbow Surg* 2015; **24**: 215-222 [PMID: 25168347 DOI: 10.1016/j.jse.2014.05.022]

31 **Mata-Fink A**, Meinke M, Jones C, Kim B, Bell JE. Reverse shoulder arthroplasty for treatment of proximal humeral fractures in older adults: a systematic review. *J Shoulder Elbow Surg* 2013; **22**: 1737-1748 [PMID: 24246529 DOI: 10.1016/j.jse.2013.08.021]

32 **Rosas S**, Law TY, Kurowicki J, Formaini N, Kalandiak SP, Levy JC. Trends in surgical management of proximal humeral fractures in the Medicare population: a nationwide study of records from 2009 to 2012. *J Shoulder Elbow Surg* 2016; **25**: 608-613 [PMID: 26475637 DOI: 10.1016/j.jse.2015.08.011]

33 **Fjalestad T**, Iversen P, Hole MØ, Smedsrud M, Madsen JE. Clinical investigation for displaced proximal humeral fractures in the elderly: a randomized study of two surgical treatments: reverse total prosthetic replacement versus angular stable plate Philos (The DELPHI-trial). *BMC Musculoskelet Disord* 2014; **15**: 323 [PMID: 25261913 DOI: 10.1186/1471-2474-15-323]

34 **Ockert B**, Biermann N, Haasters F, Mutschler W, Braunstein V. [Reverse shoulder arthroplasty for primary fracture treatment. Displaced three and four part fractures of the proximal humerus in the elderly patient]. *Unfallchirurg* 2013; **116**: 684-690 [PMID: 23934531 DOI: 10.1007/s00113-013-2410-5]

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SYSTEMATIC REVIEWS

Impact of enhanced recovery pathways on safety and efficacy of hip and knee arthroplasty: A systematic review and meta-analysis

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Abstract

BACKGROUND

Over the past decades, clinical pathways (CPs) for hip and knee arthroplasty have been strongly and continuously evolved based on scientific evidence and innovation.

AIM

The present systematic review, including meta-analysis, aimed to compare the safety and efficacy of enhanced recovery pathways (ERP) with regular pathways for patients with hip and/or knee arthroplasty.

METHODS

A literature search in healthcare databases (Embase, PubMed, Cochrane Library, CINAHL, and Web of Science) was conducted from inception up to June 2018. Relevant randomized controlled trials as well as observational studies comparing ERP, based on novel evidence, with regular or standard pathways, prescribing care as usual for hip and/or knee arthroplasty, were included. The effect of both CPs was assessed for (serious) adverse events [(S)AEs], readmission rate, length of hospital stay (LoS), clinician-derived clinical outcomes, patient reported outcome

measures (PROMs), and financial benefits. If possible, a meta-analysis was performed. In case of considerable heterogeneity among studies, a qualitative analysis was performed.

RESULTS

Forty studies were eligible for data extraction, 34 in meta-analysis and 40 in qualitative analysis. The total sample size consisted of more than 2 million patients undergoing hip or knee arthroplasty, with a mean age of 66 years and with 60% of females. The methodological quality of the included studies ranged from average to good. The ERP had lower (S)AEs [relative risk (RR): 0.9, 95% confidence interval (CI): 0.8-1] and readmission rates (RR: 0.8, 95%CI: 0.7-1), and reduced LoS [median days 6.5 (0.3-9.5)], and showed similar or improved outcomes for functional recovery and PROMs compared to regular pathways. The analyses for readmission presented a statistically significant difference in the enhanced recovery pathway in favor of knee arthroplasties (P = 0.01). ERP were reported to be cost effective, and the cost reduction varied largely between studies (€109 and $20573). The overall outcomes of all studies reported using Grading of Recommendation, Assessment, Development and Evaluation, presented moderate or high quality of evidence.

CONCLUSION

This study showed that implementation of ERP resulted in improved clinical and patient related outcomes compared to regular pathways in hip and knee arthroplasty, with a potential reduction of costs.

Key Words: Hip arthroplasty; Knee arthroplasty; Joint arthroplasty; Clinical pathway; Enhanced recovery pathway; Systematic review; Meta-analysis

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Core Tip: Enhanced recovery pathways for hip and knee arthroplasty help the patient and the multidisciplinary team to achieve the best possible results. Based on the results presented, it may help health care providers to make informed decisions regarding the optimization of currently used regular pathways. We strongly recommend orthopedic surgeons worldwide to keep up-to-date with the latest literature and to optimize their regular pathway with the latest evidence. This study involves an extensive literature search for care pathways for hip and knee arthroplasty, and the effects on multiple outcomes have been analyzed in terms of (serious) adverse events, readmissions, length of hospital stay, functional recovery, patient reported outcome measures, and costs.

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INTRODUCTION

The numbers of hip and knee arthroplasties performed worldwide are growing as a result of the increased incidence of osteoarthritis[1-5]. With the increasing life expectancy, hip and knee osteoarthritis will become a significant health issue in the upcoming years[6] and thereby arthroplasty surgeries will increasingly be performed. Clinical pathways (CPs) have been introduced to improve the quality of hip and knee arthroplasty, by optimizing recovery, minimizing variation in care, and reducing costs[7,8]. Due to scientific advancement, innovation, and novel technologies, CPs for hip and knee arthroplasty are continuously being changed. The enhanced recovery pathways (ERP) are based on novel evidence, while regular pathways are not necessarily based on the latest evidence. Because the optimizations in CPs are accomplished with an increase in costs, time, and resources[9], but might also be able to reduce costs in the long term[10], it is essential to gain knowledge on the actual benefits of the ERP. Therefore, we included all ERP studies for hip and knee arthroplasty and investigated the impact of the optimization process. This study, as far as we know, is the most extensive systematic review (SR) and meta-analysis on CPs for hip and knee arthroplasty.

The purpose of this SR and meta-analysis was to investigate the effect of *enhanced recovery pathways* compared to *regular pathways* for total hip arthroplasty (THA), total knee arthroplasty (TKA), and/or unicompartmental knee arthroplasty (UKA) on (serious) adverse events [(S)AEs], readmission rate,

length of hospital stay (LoS), clinician-derived clinical outcomes (*e.g.*, Knee- and Hip Society Scores), patient reported outcome measures (PROMs), and costs. This present SR and meta-analysis is complementary to previous reviews[1,11-18].

MATERIALS AND METHODS

A review protocol was developed according to the Preferred Items for Reporting Systematic Reviews and Meta-Analysis (PRISMA-P) statement[19] and registered in PROSPERO, the International Prospective Register of Systematic Reviews, in September 2016 (CRD42016040210).

Literature search

A systematic literature search in five key healthcare databases was conducted (MH). Embase.com, PubMed, Wiley/Cochrane Library, Clarivate Analytics/Web of Science, and Ebsco/CINAHL were searched from inception until June 10, 2018. Three trial registers were searched to identify ongoing unpublished trials, including the World Health Organization portal, ClinicalTrials.gov, and PROSPERO. The first terms used, including all synonyms, were 'knee arthroplasty' or 'hip arthroplasty' combined with 'clinical pathways' or 'enhanced recovery' or 'ambulatory care' or 'outpatients'. There was no restriction on language or publication type or date.

Eligibility criteria

Randomized controlled trials (RCTs) and observational studies written in English, comparing within the studies ERP with the foregoing regular pathway, including patients 18 years or older undergoing THA, TKA, and/or UKA, were included. At least one of the following outcomes needed to be evaluated for inclusion for one of the arthroplasties: (S)AEs, readmission rate, LoS, functional recovery, PROMs, and costs. Descriptive articles (*e.g.*, historical articles) and studies investigating patients who underwent revision, fracture, or bilateral arthroplasty were excluded.

Study selection

The results of the literature search were collated and de-duplicated in RefWorks[20]. All articles were screened on title and abstract independently by two reviewers (MH and MS). After retrieving and examining the full text of all potentially relevant articles, both reviewers indicated independently if the study should be included. Disagreements regarding study inclusion were resolved by consensus between the two reviewers.

One reviewer (MH) extracted and added data into Review Manager (RevMan)[21] and the other (MS) verified the accuracy of the data; disagreements were resolved by discussion and if no agreement was reached, by the involvement of a third reviewer (BS).

Clinical pathways

We divided the CPs into ERP and regular pathways. It is challenging to get consensus on a definition for ERP[32], because of the different concepts of care under different health care systems. CPs with rapid or enhanced recovery, fast-track, day care, or outpatient surgery, including novel experimental evidence, are an updated version of the regular pathway and were defined as ERP. These pathways are continually evolving, aiming to improve the standard of care. Several factors may streamline these ERP, during the pre-, peri-, and/or post-operative stage. We used the definitions as stated by Galbraith *et al* [11] for the specific elements of ERP. The regular pathways, maintaining the standard or non-optimized program and containing the previous evidence, prescribe care as usual. The regular pathways were considered to be the initial procedures. A pragmatic approach was chosen to distinguish between regular and enhanced. Results between ERP and regular pathways were compared for (S)AEs, LoS, functional recovery, PROMs, and costs.

Outcomes

The following data were extracted systematically from the included papers by both reviewers (MH and MS): Author, publication year, study design, procedure, clinical pathways, number of participants, patients' characteristics, country, and outcomes. We determined AEs as patient events and wound disorders, surgical and/or prosthesis related[3]. SAEs were reported as undesired medical events, not necessarily associated with the treatment[22]. Classification as AE or SAE was analyzed together as one outcome measure in (S)AE. Readmission rate was registered as the number of readmissions related to the hip or knee surgery. LoS was evaluated as time in days between hospital admission and discharge. Clinical outcomes were assessed in terms of functional recovery and with the use of PROMs. Costs included only intramural hospital costs and were reported in the monetary unit of the study.

Risk of bias

For all included studies, a risk-of-bias (RoB) table was used to identify potential sources of bias with the

use of the Cochrane Collaboration tool[23] or the ROBINS-I tool[24] for RCTs and non-randomized studies, respectively. Two authors (MH and MS) independently assessed the RoB. The outcomes of all studies were reported using Grading of Recommendation, Assessment, Development and Evaluation (GRADE)[25].

Statistical analysis

Outcomes were summarized using RevMan 5.3[21]. We extracted all data used from the original studies. To quantify the statistical heterogeneity in the studies, the I^2 value was used. Only if studies were sufficiently clinically, methodologically, and statistically homogenous, the data were pooled in a meta-analysis. In case of considerable heterogeneity (> 75%), a qualitative analysis was performed[23] and outcomes between included studies were described. In the situation where one of the sensitivity analyses showed no considerable heterogeneity (< 75%), a meta-analysis was performed on this outcome. For the meta-analysis, we used a random effects model and report relative risk (RR) with 95% confidence interval (CI). We present the results within forest plots, subdivided for type of arthroplasty (THA, TKA, and/or UKA). If no distinction between the different arthroplasties was possible, analysis for the combined group were included as a subgroup (THA and/or TKA and/or UKA). In a sensitivity analysis, we also combined (S)AE with a follow-up time of 30 d or more and readmission rate as one combined outcome, as they are interrelated in clinical practice. Studies for (S)AE with a follow-up time of 30 d or more were analyzed because of their clinical relevance. P value ≤ 0.05 was considered statistically significant.

RESULTS

The full search strategies can be found in the Supplementary material (Databases and search strings). This systematic search identified 7901 references. The literature search and selection process are shown in Figure 1. After removal of duplicates, 4502 references remained for screening on title and abstract. Of these, 106 full-text articles were assessed for eligibility. No additional records were identified by checking reference lists. Eventually, 40 studies were included[3,7,26-63]. A summary of the characteristics of these studies is given in Table 1.

We included five RCTs[7,28,30,35,38], six prospective cohort studies[31,33,37,41,50,52], thirteen retrospective cohort studies[36,42-44,46,51,53,54,57-59,62,63], five observational cohort studies[27,34,45,47,60], four case control studies[3,48,49,56], four comparative studies with prospective[32,61] and retrospective designs for the standard CPs[39,55], and one each prospective pilot study[26], prospective follow-up study[29], and propensity score matched study[40]. Nine articles studied THA[26,29,38,41,50,52,54,60,63], nineteen studied TKA[3,7,30-33,36,37,39,42,44,48,49,51,55,58,59,61,62], six studied UKA[3,43,45,48,55,56], and eleven studied both hip and knee arthroplasty[27,28,34,35,40,43,46,47,53,56,57]. Of the included studies, which were published between 1999 and 2018, eighteen were conducted in the United States[26,30,31,36,38,40,42-46,51,53-55,59,60,63], five in the Netherlands[3,27,48,50,56], three each in the United Kingdom[34,37,41], Germany[7,32,33], and Canada[35,49,61], two in Spain[29,57], and one each in Australia[28], Malaysia[39], Italy[58], New Zealand[47], Denmark[52], and Finland[62]. The setting varied from a hospital[3,26,27,34,41,47,48,50,56,57,60-62] to a medical[36,40,42,43-46,53,54,59] or orthopedic center[7,35,37,38,51,52,55,58,63], a tertiary[28,30,49] or a university hospital[29,32,33,39], or a single institution[31].

The total sample size consisted of 2223534 patients undergoing hip or knee arthroplasty; 997765 patients were treated according to ERP compared with 1225769 patients with regular pathways (Table 1). Overall, more female patients were included (60.1%). Of 5095 (0.2%) patients, sex was not reported. The mean age was 65.1 years for patients with ERP and 66.5 years for those with regular pathways. The mean body mass index was similar for both CPs (30 kg/m^2). In ERP, 25 studies applied enhanced elements during the pre-operative phases, mostly for education[27,32-36,41,47,50,52,57,61,62], 19 applied during the peri-operative phase, *e.g.*, for pre-medication or neuraxial-regional anesthesia[3,26,34-37,41,47,50,57,58,60], and 35 during the postoperative phase, mostly for the rehabilitation program or early discharge home[3,7,26,27,29,31,32,35,36,38,40,42-49,51,54,55,57,59-61]. An overview of the pre-, peri-, and postoperative management during ERP is listed in Table 2.

Risk of bias

The methodological quality is presented in a RoB summary (Figures 2 and 4) and as percentages (Figures 3 and 5) for the RCTs and non-randomized studies, respectively. Blinding of participants and personnel was not possible because of the content of the CPs. Selection bias was unclear in three RCTs (60%) and blinding of outcome in two RCTs (40%). Five non-randomized studies were of high quality with a low RoB, whereas three were of low-quality with a serious RoB. All low-quality studies had bias due to confounding. A serious or critical bias in the selection of the reported results was found in the majority of studies (71%). In 31% of the studies, the outcome could have been influenced by knowledge of the applied CPs. Five studies reported missing data (14%), and four had bias due to selection of participants (11%). Overall, the methodological quality of the included studies ranged from average to

Table 1 Characteristics of the included studies, patient demographics, ERP versus regular pathways, and outcome

Author/year	Procedure	Study design	Country/setting	ERP/regular pathway	Number participants ERP/regular pathway	Participants characteristics ERP/regular pathway	Outcome
Arshi *et al*[42]; 2017	TKA	Retrospective cohort	United States; Humana subset of the pearl-diver patient record database	Outpatient/inpatient	*n* = 133.342; 4.391/128.951	Age: (70-74), modus 65-69; Men-women: (1.560-2.831)/(46.805-82.146)	LoS, (S)AE
Auyong *et al* [36]; 2015	TKA	Retrospective cohort	United States; Medical center	Updated ERAS/ERAS	*n* = 252; 126/126	Age: 66.02 (10.02)/68.44 (9.98); Men-women: (44-82)/(41-85); BMI: 31.88 (7.629)/31.3 (6.562)	LoS, (S)AE, functional recovery, PROMs, readmission
Basques *et al* [43]; 2017	THA; TKA	Retrospective matched cohort	United States; NSQIP database	Same day/inpatient	*n* = 177.818, 1.236/176.582; THA: *n* = 63.360, 368/368; TKA: *n* = 110.410, 608/608; UKA: *n* = 4.048, 260/260	Age: Most between 65-74; Men-women: (46.6%-53.4%)/(39.8%-60.2%); BMI: Most between 25-29.9	LoS, (S)AE, readmission
Bertin *et al*[26]; 2005	THA	Pilot study, retrospectively chosen control group	United States; Hospital	Outpatient/existing protocol	*n* = 20; 10/10	Age: 62/63; Men-women: (6-4)/(5-5); BMI: 30.024/29.64	LoS, (S)AE, costs
Bovonratwet *et al*[44]; 2017	TKA	Retrospective cohort	United States; NSQIP database	Outpatient/inpatient	*n* = 112.922; 642/112.280	Age: 64/67; Men-women: (265-377)/(41.821-70.459); BMI: 32/33	LoS, (S)AE, readmission
Bovonratwet *et al*[45]; 2017	UKA	Cohort	United States; NSQIP database	Outpatient/inpatient	*n* = 5880; 568/5312	Age: 62.9/63.7; Men-women: (284-284)/(2501-2811); BMI: 31.5/31.6	LoS, (S)AE, readmission
Brunenberg *et al* [27]; 2005	THA; TKA	Before-after trial	Netherlands; University hospital	Joint recovery programme/usual care	*n* = 160; THA: *n* = 98, 48/50; TKA: *n* = 62, 30/32	Age: 64.4 (28-87); THA: Age 63.38 (11.48)/ 65.4 (13.04), Men-women% (35.4-64.6)/(24-76); TKA: Age 64.9(9.43)/63.94 (12.6), Men-women % (33.3-66.7)/(31.3-68.7)	LoS, functional recovery; PROMs; costs
Castorina *et al* [58]; 2017	TKA	Retrospective observational cohort study	Italy; Orthopedics traumatology and rehabilitation unit	Fast track/traditional group	*n* = 132; 95/37	Age: 71.1 (7.77)/74.62 (± 6.42)	Functional recovery; (S)AE
Courtney *et al* [46]; 2017	THA; TKA	Retrospective cohort	United States; NSQIP database	Outpatient/inpatient	*n* = 169.406; 1220/168.186	Age: 63.1/65.9; Men-women: (539-681)/(67.687-100.499); BMI: 32.1/31.7	LoS, (S)AE, readmission
Courtney *et al* [59]; 2018	TKA	Retrospective cohort	United States; NSQIP database	Outpatient/short stay/LOS ≥ 2 d	*n* = 49.136; 365/3033/45.738		LoS, (S)AE, readmission
den Hertog *et al* [7]; 2012	TKA	Randomized prospective study	Germany; Hospital	Fast-track group/standard care re-habilitation	*n* = 147 (ITT), 74/73; *n* = 140 (PP), 71/69	Age: 66.58 (8.21)/68.25 (7.91); Men-women: (23-51)/(20-53); BMI: 31.17 (5.82)/30.38 (6.05)	LoS, (S)AE, functional recovery, PROMs
Dowsey *et al* [28]; 1999	THA; TKA	Prospective randomized controlled study	Australia; Tertiary hospital	Clinical pathway/control	*n* = 163; 92/71	Age: 64.2/68.2; Men-women: 56/107	LoS, (S)AE, functional recovery, readmission
Featherall *et al* [60]; 2018	THA	Cohort	United States; Clinic	Full protocol/transition cohort/Pre-protocol	*n* = 6090; 2081/2009/2000	Age: 63.77 (11.72)/64.09 (12.04)/64.03 (12.09); Men-women: (1033-1048)/(983-1026)/(960-1040); BMI: 30.13 (6.17)/ 29.93 (6.19)/ 30.09 (6.38)	LoS, (S)AE, cost

Gauthier-Kwan *et al*[61]; 2018	TKA	Prospective comparative cohort	Canada; Hospital	Outpatient/inpatient	*n* = 86; 43/43	Age: 62.5 (50.4-75), 62.5 (51.2-74); Men-women: (29-14)/(22-21); BMI: 28.6 (23.7-35.8)/30.4 (23.5-41.6)	LoS, (S)AE, readmission, functional outcome, PROMs
Gooch *et al*[35]; 2012	THA; TKA	RCT	Canada; Bone and Joint Health Institute	New clinical pathway/standard care	*n* = 1570, 1066 (THA: 615; TKA: 451)/504 (THA: 278; TKA: 226)	Age: 69 (11.1)/69 (10.4); Men-women%: (39.6-60.4)/(40.1-59.9); BMI: 29.5 (5.6)/29.4 (5.4)	(S)AE, functional recovery, PROMs
Goyal *et al*[38]; 2017	THA	Prospective randomized study	United States; Two reconstruction centres	Outpatient/inpatient	*n* = 220; 112/108	Age: 59.8 (8.5) (59.3) (27-74)/60.2 (8.9) (61) (34-74); Men-women: (59-53)/(58-50); BMI: 27.6 (4.1) (27.1) (18-38.4)/ 28.3 (4.7) (27.7) (18.4-39.9)	LoS, (S)AE, readmission, functional recovery, PROMs
Gwynne-Jones *et al*[47]; 2017	THA; TKA	Matched cohort study	New Zealand; Hospital	Post ERAS/pre ERAS	*n* = 1035, 528/507; THA: 318/314; TKA: 210/193	THA: Age 68.3 (11.8)/66.8 (11.8), Men-women (146-172)/(146-168); TKA: Age 70.4 (8.9)/69.8 (9.0), Men-women: 107-103/83-110	LoS, (S)AE, readmission, PROMs
Ho *et al*[30]; 2007	TKA	Randomized controlled trial; retrospective cost analysis	United States; Tertiary teaching hospital	Critical pathway/no uniform CP	*n* = 90; 3 cohorts: 30/30/30	Age: 66/67/68; Men-women: (14-16)/(14-16)/(14-16); Weight: 89/91/88	LoS, (S)AE, costs
Hoorntje *et al*[48]; 2017	UKA	Case control study	Netherlands; Hospital	Outpatient/fast-track	*n* = 40; 20/20	Age: 62.2 (5.5)/63.8 (7.5); Men-women: (10-10)/(7-13); BMI: 27.8 (3.7)/30.5 (7.0)	LoS, PROMs
Huang *et al*[49]; 2017	TKA	Prospective case control study	Canada; Tertiary academic medical centre	Same day discharge/inpatient	*n* = 40; 20/20	Age: 58.5 (5.6)/61.5 (5.9); Men-women: (14-6)/(14-6); BMI: 29.0 (3.7)/30.6 (5.3)	LoS, (S)AE, readmission, cost
Ismail A *et al*[39]; 2016	TKA	Non-randomized control trial	Malaysia; University hospital	CP/control	*n* = 152; 73/79	Age: 66.1/64.7	LoS, (S)AE, readmission
Jimenez Muñoz *et al*[29]; 2006	THA	Prospective follow-up study	Spain; University general hospital	After CP/prior CP	*n* = 487; 384/98; 309/75	Not present	LoS, (S)AE
Klapwijk *et al*[50]; 2017	THA	Prospective cohort	Netherlands; Hospital	Outpatient/inpatient	*n* = 94; 42/52	Age: 61 (41-78)/68 (48-82); Men-women: (17-25)/(21-31); BMI: 29 (20-35) /26 (18-39)	LoS, (S)AE, functional recovery, PROMs
Klingenstein *et al*[51]; 2017	TKA	Retrospective cohort	United States; Joint replacement centre	Short stay/traditional stay	*n* = 2287; 1502/785	Age: 71.7 (5.4)/73.3 (6.1); Men-women%: (39-61)/(25-75); BMI ≥ 30 (%): 50/57	LoS, (S)AE, readmission
Kolisek *et al*[31]; 2009	TKA	Prospective matched cohort	United States; Hospital	Outpatient/conventional inpatient stay	*n* = 128; 64/64	Age: 55 (42-64)/55 (42-63); Men-women: (40-24)/(40-24); BMI: 30.8 (24.3-38)/30.8(24.2-37.8)	LoS, (S)AE, functional recovery, PROMs, readmission
Kort *et al*[3]; 2017	UKA	Case control study	Netherlands; Hospital	Outpatient/rapid recovery	*n* = 40; 20/20	Age: 60.5 (5.65)/61.2 (5.15); Men-women: (13-7)/(11-9); BMI: 29.1 (3.85)/27.7 (3.27)	LoS, (S)AE, readmission, PROMs
Larsen *et al*[52]; 2017	THA	Observational cohort	Denmark; Orthopedic clinic	Day case (< 12 h)/standard 2-d	*n* = 56; 20/36	Age: 64.6; Men-women: 15-5; BMI: 28.8 (23.8-33.7)	LoS, (S)AE, readmission, PROMs
Lovecchio *et al*[40]; 2016	THA; TKA	Propensity score matched study	United States; NSQIP database	Outpatient/fast-track inpatients	*n* = 1968, 492/1476; THA/TKA: (183-585)/(309-891)	Age: Most between 60 to 69; Men-women: (217-275)/(664-812); BMI between 25-30	LoS, (S)AE, readmission
Maempel *et al*	THA	Prospective cohort	United Kingdom; Hospital	ERP/traditional rehabilitation	*n* = 1161; 550/611	Age: 64 (18-94)/66 (23-90); Men-women: (212-	LoS, (S)AE,

[41]; 2016						338)/(242-369); BMI: 30 (7)/29 (7)	functional recovery, PROMs
Maempel *et al* [37]; 2015	TKA	Non-randomized prospective cohort	United Kingdom; Arthroplasty clinic	ERP/traditional rehabilitation	*n* = 165; 84/81	Age: 69.8 (8.9)/70.1 (10.5); Men-women: (42-42)/(37-44); BMI: 32.4 (22.6-46.6)/31.8 (20.5-41.9)	LoS, (S)AE, functional recovery
Malviya *et al* [34]; 2011	THA; TKA	Observational study	United Kingdom; Hospital	ERP/traditional pathway	*n* = 4500; 1500 (THA: 630; TKA: 870)/3000 (THA: 1368; TKA: 1632)	Age: 68/69; Men-women: (711-789)/(1482-1518)	LoS, (S)AE, readmission
Nelson *et al*[54]; 2017	THA	Retrospective cohort, data prospectively collected	United States; NSQIP database	Outpatient/inpatient	*n* = 63.844; 420/63.424	Age: 62/65; Men-women: (222-198)/(28.587-34.833); BMI most between 25-30	LoS, (S)AE, readmission
Pamilo *et al*[62]; 2018	TKA	Retrospective cohort	Finland; Finnish Hospital Discharge Register	Fast-track CP/non-fast-track	*n* = 4256, 2310/1946; Hospital A: 624/437	Age and sex: No statistically significant difference between CP's	LoS, (S)AE, readmission
Renkawitz *et al* [32]; 2010	TKA	Prospective parallel group design	Germany; Orthopaedic university medical centre	Optimized accelerated CP/standard CP	*n* = 143; 67/76	Age: 67 (9)/68.1 (11.1); Men-women: (14-53)/(23-53); BMI: 31.4 (5.1)/30.7 (5.6)	LoS, (S)AE, readmission, functional recovery
Richter *et al*[55]; 2017	UKA	Retrospective chart review	United States; Surgical outpatient center	Outpatient/inpatient	*n* = 22; 12/10	Age: 67.2 (9.2)/64.5 (9.8); Men-women: (7-5)/(8-2); BMI: 28.7 (5.1)/25.8 (8.1)	LoS, (S)AE, readmission, cost
Schotanus *et al* [69]; 2017	TKA; UKA	Case control study	Netherlands; Hospital	Outpatient/ERP	*n* = 361; 94/267	Age: 63.4 (8.0)/68.4 (9.0); Men-women: (49-45)/(94-173); BMI: 28.25 (3.68)/29.49 (5.05)	LoS, PROMs
Toy *et al*[63]; 2018	THA	Retrospective cohort	United States; Ambulatory surgery centers	Later outpatient pathway/initial outpatient pathway	*n* = 145; 72/73	Age: 55 (27-70); Men-women: 76-49; BMI: 29.7 (19.6-43)	LoS, (S)AE, readmission
Wilche *et al*[57]; 2017	THA; TKA	Retrospective review	Spain; Hospital	Fast-track recovery/conventional recovery	*n* = 200; THA: 50/50; TKA: 50/50	Age: 69.24 (9.64)/73.07 (8.33); Men-women: (40-60)/(40-60)	LoS, (S)AE, readmission, cost

Age in years, mean ± SD (median) (range); Weight in kg. BMI: Body mass index; NSQIP: National Surgical Quality Improvement Program; THA: Total hip arthroplasty; TKA: Total knee arthroplasty; CP: Clinical pathway; UKA: Unicompartmental knee arthroplasty; Los: Length of hospital stay; (S)AE: (Serious) adverse events; PROMS: Patient reported outcome measures; ERP: Enhanced recovery pathways; ERAS: Enhanced Recovery After Orthopedic Surgery; RCT: Randomized controlled trial.

good.

Heterogeneity

The studies varied clinically (*e.g.*, patient characteristics and CPs) and methodologically. Different measurement tools were used, and outcome measures were reported in different ways across studies. Therefore, a meta-analysis was only feasible with studies that used the same measurement tools. For this study, data for the sensitivity analyses were pooled for (S)AEs and readmission rate. A qualitative analysis was performed for the results of LoS, functional recovery, PROMs, and costs.

(S)AEs and readmission rate

Thirty-five studies examined AEs, SAEs, or both[3,7,26,28-32,34-47,49-52,54,55,57-63] and twenty four examined readmission rate[3,28,31,32,34,36,38,39,40,43-47,49,51-52,54,55,57,59,61-63]. The follow-up time

Table 2 Pre-, peri-, and post-operative management during enhanced recovery pathways

Author	Year	ERP			Preoperative					Peri-operative							Post-operative				
		Pre-operative	Peri-operative	Post-operative	Education	Outpatient consultation	Discharge planning	Physiotherapy	Pre-assessment outpatient clinic	Day of surgery admission	Premedication	Optimal hydration	Neuraxial-regional anaesthesia	Multimodal blood loss reduction	+/- peri articular injection	Avoid surgical drains	Multimodal analgesia regimen	Day of surgery mobilisation	Venous thromboembolic prophylaxis	Rehabilitation programme	Early discharge home
Arshi *et al*[42]	2017			X																	X
Auyong *et al*[36]	2015	X	X	X	X						X		X				X	X			X
Basques *et al*[43]	2017			X																	X
Bertin *et al*[26]	2005	X	X	X				X			X		X							X	X
Bovonra-twet *et al*[44]	2017			X																	X
Bovonra-twet *et al*[45]	2017			X																	X
Brunenberg *et al*[27]	2005	X		X	X				X											X	
Castorina *et al*[58]	2017	X	X	X									X				X				
Courtney *et al*[46]	2017			X																	X
Courtney *et al*[59]	2018			X																	X
den Hertog *et al*[7]	2012	X		X														X		X	X
Dowsey *et al*[28]	1999		X	X																	

Feathe-rall *et al*[60]	2018	**X**	**X**	**X**					X						X		X			X	
Gau-thier-Kwan *et al*[61]	2018	**X**	**X**	**X**	X						X		X				X			X	X
Gooch *et al*[35]	2012	**X**	**X**	**X**	X	X	X	X			X		X					X		X	
Goyal *et al*[38]	2017			**X**													X				X
Gwynne-Jones *et al*[47]	2017	**X**	**X**	**X**	X					X	X		X	X				X		X	
Ho *et al* [30]	2007	**X**	**X**																		
Hoorn-tje *et al*[48]	2017	**X**	**X**	**X**								X								X	X
Huang *et al*[49]	2017	**X**	**X**	**X**		X				X					X					X	
Ismail A *et al*[39]	2016																				
Jimenez Muñoz *et al*[29]	2006			**X**																X	X
Klapwi-jk *et al*[50]	2017	**X**	**X**	**X**	X						X		X			X		X			
Klingen-stein *et al*[51]	2017			**X**																	X
Kolisek *et al*[31]	2009	**X**		**X**														X		X	X
Kort *et al*[3]	2017	**X**	**X**	**X**			X	X		X	X									X	X
Krumm-enauer *et al*[33]	2011	**X**		**X**	X	X														X	
Larsen *et al*[52]	2017	**X**		**X**	X													X			

Lovecchio *et al*[40]	2016			**X**																		X
Maempel *et al*[41]	2016	**X**	**X**	**X**	X	X	X	X						X				X				
Maempel *et al*[37]	2015	**X**	**X**	**X**		X					X			X				X				
Malviya *et al*[34]	2011	**X**	**X**	**X**	X				X			X		X				X				
Molloy *et al*[53]	2017																					
Nelson *et al*[54]	2017			**X**																		X
Pamilo *et al*[62]	2018	**X**			X	X																
Renkawitz *et al*[32]	2010	**X**	**X**	**X**	X	X			X									X		X		
Richter *et al*[55]	2017			**X**																		X
Schotanus *et al*[69]	2017	**X**	**X**	**X**			X				X							X				
Toy *et al* [63]	2018	**X**				X																
Wilches *et al*[57]	2017	**X**	**X**	**X**	X				X			X	X	X	X			X		X		

ERP: Enhanced recovery pathways.

varied from 8 d up to 24 mo postoperatively.

In the ERP, there were less (S)AEs (RR: 0.9; 95%CI: 0.8-1) and a lower readmission rate (RR: 0.8; 95%CI: 0.7-1) when compared to the regular pathways. The analyses for overall (S)AEs resulted in considerable heterogeneity (I^2 = 83%, P = 0.2). Studies of (S)AEs with a follow-up time of 30 d or more yielded a RR of 0.9 (95%CI: 0.8-1), with substantial heterogeneity (I^2 = 74%, P = 0.3) (Figures 6 and 7). Only the THA subgroup showed heterogeneity (I^2 = 89%, P = 0.7) while the TKA (I^2 = 21%, P = 0.2) and the combined groups (THA and TKA; I^2 = 47%, P = 0.1) were homogeneous.

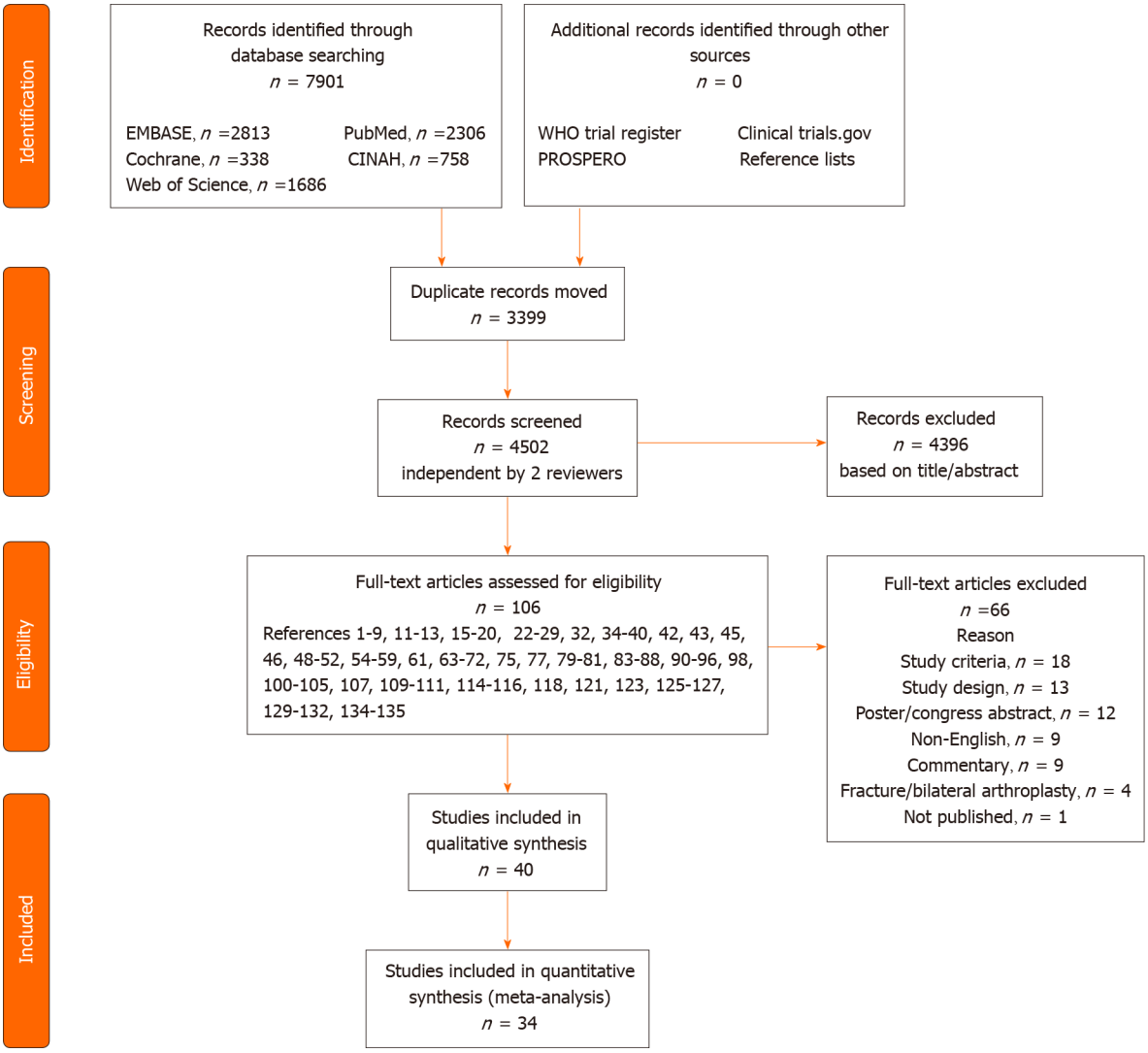


Figure 1 Flow diagram of the literature search and selection procedure. WHO: World Health Organization.

The analyses for readmission rate were homogenous (I^2 = 48%, P = 0.2). The readmission rate in ERP was statistically significant different in favor of the knee arthroplasties without heterogeneity (TKA: I^2 = 15%, P = 0.01; UKA: I^2 = 0%, P = 0.01). The plots for readmission rate for THA, TKA, UKA, and the combined subgroups (THA and TKA) are shown in Figures 8 and 9.

Sensitivity analyses of (S)AEs together with readmission rate resulted in a RR of 0.9 (95%CI: 0.7-1) with substantial heterogeneity (I^2 = 84%, P = 0.1). According to GRADE, there was moderate quality of evidence for (S)AE and readmission rate (Table 3).

Length of hospital stay

Thirty-eight studies described LoS[3,7,26-34,36-57,59-63]. A reduced LoS was found in all ERPs, of which 20 studies reported a statistically significant reduction ranging between 0.5-10.1, 3.2-10.0, 2.8-7.1, and 2.6 d for the THA[29,41,50,52,60,63], TKA[7,30,32,36,37,39,62], the combined outcome of THA and TKA[27,28,34,47,53,57], and UKA[3], respectively. The overall median LoS reduced up to 6.5 d. For regular pathways, the median values were between 0.5 and 16 d and the mean values were between 1.5 to 19.5 d. All the analyzed arthroplasties showed high heterogeneity for LoS (> I^2 = 98%). The GRADE table shows high evidence for LoS (Table 3).

Clinician-derived outcome and PROMs

Functional recovery was assessed in 13 studies for THA[38,41,50], TKA[7,31,32,36,37,58,61], and the combined subgroup THA and TKA[27,28,35], respectively. The Harris Hip Score, Range of Motion, and scores from the American Knee Society were mostly reported. Four articles studied THA[38,41,50,52], six studied TKA[7,31,33,36,56,61], and three each studied UKA[3,48,56] and both THA and TKA[27,35,47] regarding the PROMs, using similar measurement types. The Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) questionnaire, EuroQual, Oxford Knee Score, and pain scales were mostly used as PROMs.

Table 3 Grading of Recommendation, Assessment, Development and Evaluation evidence profile: Enhanced recovery pathways compared to regular pathways for hip and knee arthroplasty

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	(S)AE	Control	Relative (95%CI)	Absolute		
Functional recovery (follow-up 24 mo)												
12	Randomised trials	No serious risk of bias	Serious[1]	No serious indirectness	No serious imprecision	None	0/2289 (0%)	0/1802 (0%) 0%	Not pooled	Not pooled Not pooled	Moderate	Important
PROMs (follow-up 24 mo; Better indicated by lower values)												
15	Randomised trials	No serious risk of bias	Serious[2]	No serious indirectness	No serious imprecision	None	2966	2388	-	Not pooled	Moderate	Important
LoS (follow-up 24 mo; Better indicated by lower values)												
38	Randomised trials	No serious risk of bias	No serious inconsistency	No serious indirectness	No serious imprecision	None	997447	1573895	-	MD 2.45 lower (3.42 to 1.48 lower)	High	Important
(S)AEs												
34	Randomised trials	No serious risk of bias	No serious inconsistency	Serious[3]	No serious imprecision	None	2103/18344 (11.5%)	83989/540864 (15.5%) 11.7%	RR 0.91 (0.78 to 1.06)	14 fewer per 1000 (from 34 fewer to 9 more) 11 fewer per 1000 (from 26 fewer to 7 more)	Moderate	Important
Readmission (follow-up 24 mo)												
23	Randomised trials	No serious risk of bias	No serious inconsistency	No serious indirectness	Serious[4]	None	273/9846 (2.8%)	8360/406167 (2.1%) 2.7%	RR 0.83 (0.65 to 1.07)	3 fewer per 1000 (from 7 fewer to 1 more) 5 fewer per 1000 (from 9 fewer to 2 more)	Moderate	Important

[1]Different outcomes for functional recovery: HHS [with/without range of motion (ROM), pain], American Knee Society Score, ROM.
[2]Different patient reported outcome measures: SF-36, WOMAC, KATZ.
[3]No clear distinction between adverse event (AE) and serious AE.
[4]Wide confidence interval.
(S)AE: (Serious) adverse event; CI: Confidence interval; PROMS: Patient reported outcome measures; LoS: Length of hospital stay; RR: Relative risk.

The follow-up time differed from the first postoperative day up to 24 mo postoperatively. In view of the clinician-derived outcomes and PROMs, the results in the ERP were similar or improved for THA [41,50,52], TKA[31-33,58,61], UKA[48], and the combined group THA and TKA[27], or were statistically significant better than those in the regular pathways for TKA[7,36,56], UKA[3], and the combined group THA and TKA[35,47]. Moderate quality for functional recovery and PROMs is presented in GRADE (Table 3).

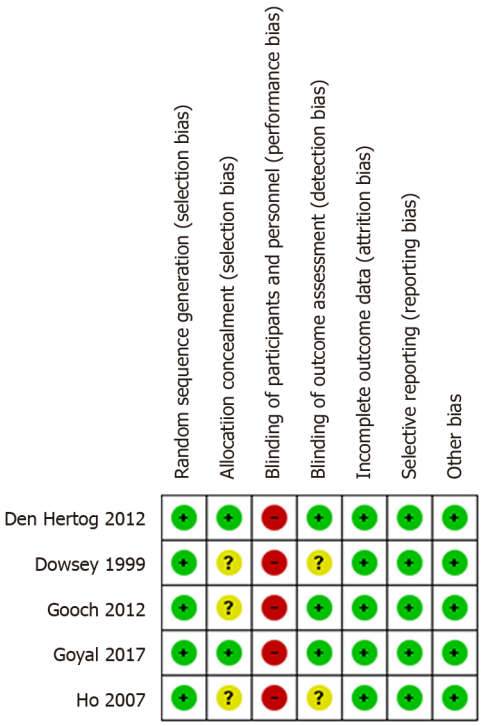


Figure 2 Cochrane risk of bias summary of the randomized controlled trials. Review authors' judgements about each risk of bias item. Low RoB (green + symbol), high RoB (red - symbol), or unclear RoB (yellow - symbol) is shown.

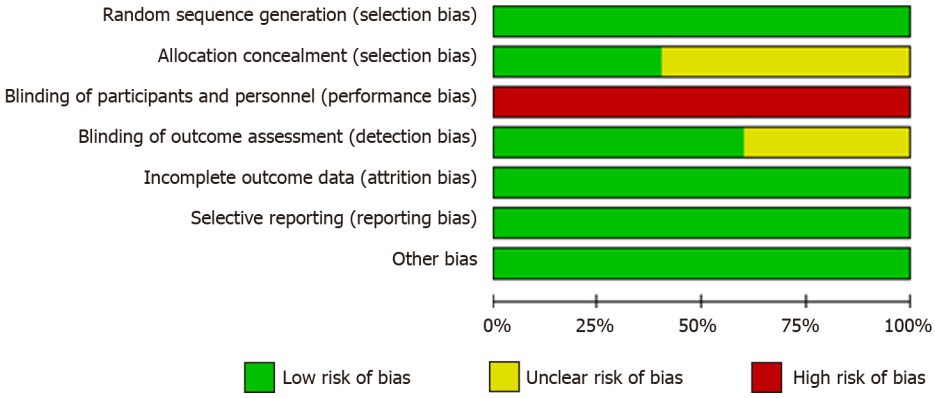


Figure 3 Cochrane RoB graph: Review authors' judgements about each risk of bias item presented as percentages across all included randomized studies.

Costs

Nine observational studies analyzed costs[26,27,30,33,49,53,55,57,60]. The reduction in LoS resulted in statistically significant cost savings for THA in an ERP compared to the regular pathways[26]. Preadmission, physical therapy, and home care charges resulted in a saving for the combined group (THA and TKA) per patient[27] and reduced hospital costs after TKA[30]. Hospital costs were reduced significantly in patients operated for knee arthroplasty in an ERP because of the reduction in room costs, fewer laboratory tests, used medications, physical therapy, and meal costs[30,49,55]. The cost reduction per patient for knee arthroplasty was in favor of the ERP[27,30,33,49,55,57], with a range between €109 and $20573. The cost savings per patient for hip arthroplasty was also higher for the ERP[26,27,57,60] with a range between €581 and $2500. The ERP resulted in a statistically significant economic saving for both knee and hip arthroplasty[49,55,57,60] without affecting complication rate[34], functional improvement, and satisfaction of the patient operated after THA or UKA[26,55]. The individual cost/benefit relation was inferior only in one TKA study[33].

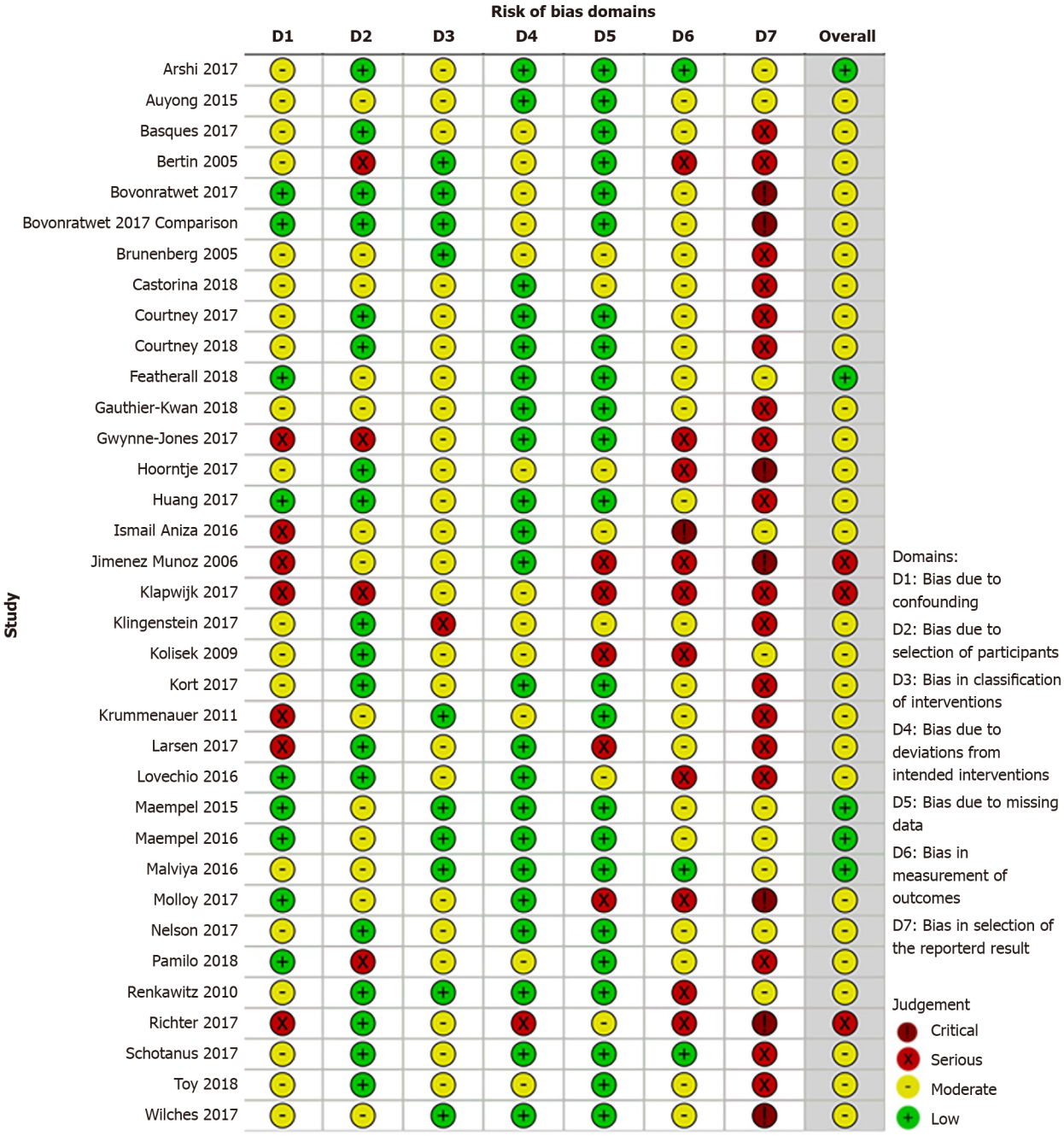


Figure 4 ROBINS-I bias assessment of the non-randomized studies. Review authors' judgements about each risk of bias domain.

DISCUSSION

The most important findings of the present SR and meta-analysis were that the use of ERP yielded similar or improved outcomes for patients with hip and/or knee arthroplasty. In the ERP, there were less (S)AEs and a lower readmission rate when compared to the regular pathways. The readmission rate in the ERP was statistically significant different in favor of the knee arthroplasties without heterogeneity. There were improved results for clinician-derived outcomes and PROMs, reduced LoS, and saved costs compared to regular pathways.

Multiple enhancements can be taken during the pre-, peri-, or post-operative program, to upgrade a regular pathway to enhanced, with respect to local situations. Continuously looking for improvements is important for successful hip and/or knee CPs.

Explanation of findings

The overall methodological quality varied due to the inclusion of five RCTs and 35 observational studies. The studies were heterogeneous regarding patient populations, hospital resources and procedures, multi-disciplinary teams, surgical and anesthetic techniques, practice variation, and follow-up times. Most of the heterogeneity was probably due to methodological differences between the

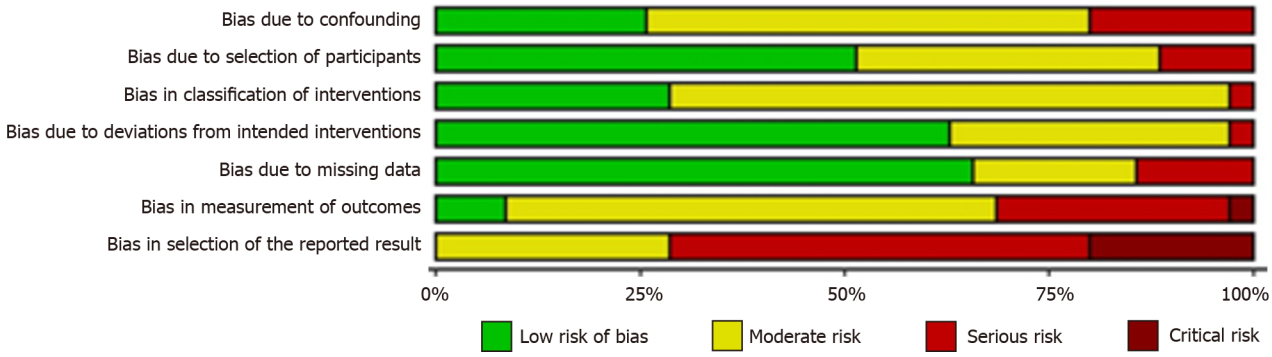


Figure 5 ROBINS-I weighted summary plot.

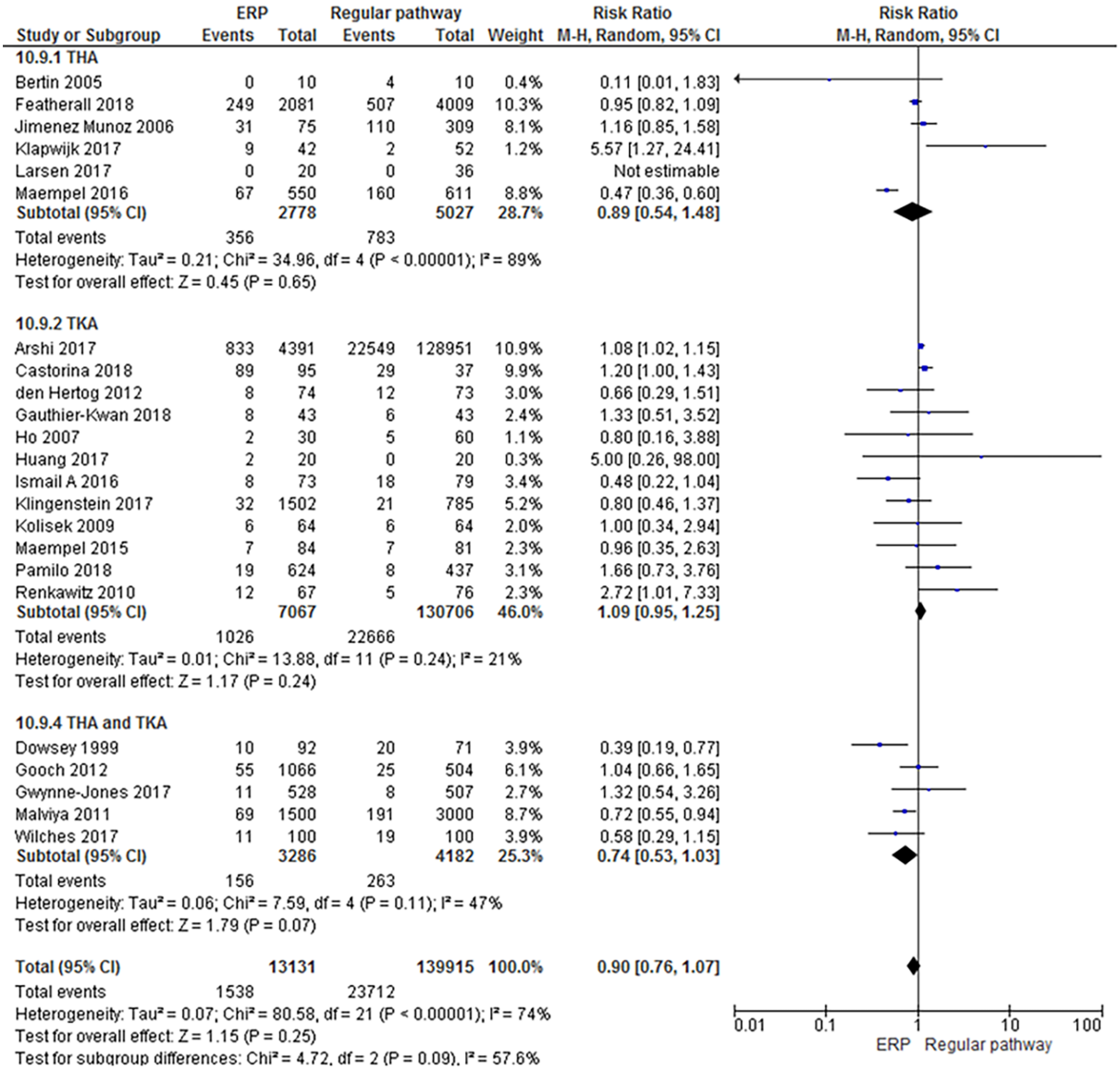


Figure 6 Forest plot with relative risk for each study and pooled relative risk with 95% confidence interval for (serious) adverse events with a follow-up time of 30 d or more for enhanced recovery pathways *vs* regular pathways for hip and knee arthroplasty. THA: Total hip arthroplasty; TKA: Total knee arthroplasty; CI: Confidence interval; ERP: Enhanced recovery pathways.

included studies. The included studies were published throughout the past 20 years, the view of hospital stays after an operation and discharge criteria have been changed over time. And, the obtained data came from different healthcare systems from different countries, from retrospective studies or from national registries. Nevertheless, even within all this practical and methodological variation, the

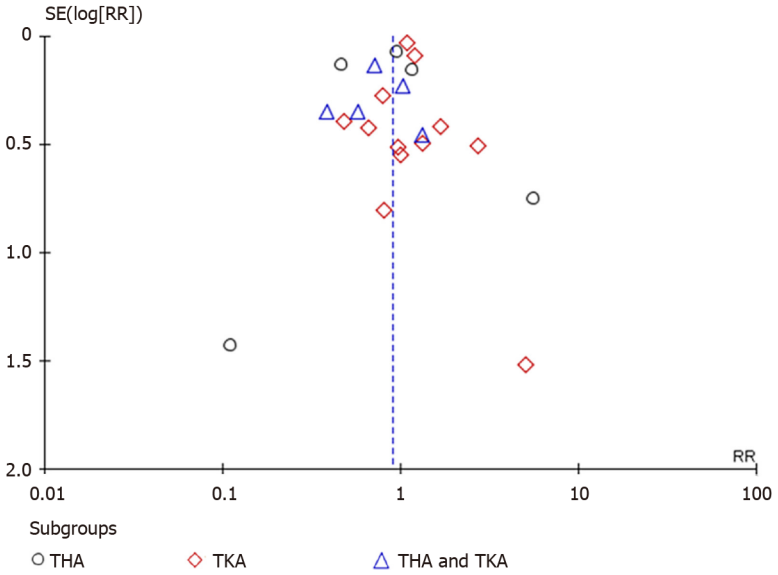


Figure 7 Funnel plot for the studies with described (serious) adverse events with a follow-up time of 30 d or more. THA: Total hip arthroplasty; TKA: Total knee arthroplasty; RR: Risk ratio.

outcomes indicated a positive effect in favor of ERP.

The results of the meta-analysis demonstrated less (S)AEs in patients following the ERP, with fewer readmissions compared to the regular pathways (P = 0.25). Substantial heterogeneity was present when AE and SAE were analyzed together and separately for the different arthroplasties (THA, TKA, and both combined). This heterogeneity was probably due to the lack of definition in primary studies. Also, not all studies made a distinction between AE and SAE. For further investigation, consensus on terminology is recommended. Compared to our findings, another study found statistically significant fewer complications for the ERP compared to the regular pathway[18]. Because of the relative high risk of postoperative complications, careful patient selection for outpatient joint arthroplasty is crucial to obtain successful outcomes[42,44-46,54,63].

All studies showed a reduction in LoS after implementing ERP. In half of these studies, this reduction was statistically significant, which is in line with previous SRs[13,17,18]. LoS can be influenced by preoperative patient education and patient expectations[11,27,28,31,36,37,41,48,57,62,64,65], training in home-based rehabilitation settings[3], and a positive influence from relatives[28,52,53]. The discharge also influenced LoS from the hospital to a rehabilitation center or a center with care facilities instead of discharge to the home environment[28,32,33,47,50]. The reduction of LoS allowed more joint replacements without additional bed capacity and could therefore have a potential positive economic effect[34].

Implementation of CPs for hip and knee arthroplasty were associated with similar or improved outcome for clinician-derived outcome and PROMs. These outcomes represent the best subjective measurement of clinical outcome[66]. However, there is no single best outcome measurement tool after arthroplasty. Besides the positive results of PROMs, various scores are not capturing changes due to a lack of power as averse to a lack of change, *e.g.*, floor and ceiling effects[67]. It could therefore be that further improvement in one of the CPs was not detected. In order to characterize the objective changes in physical activity after arthroplasty in detail, activity monitoring can be used to capture changes over time and to detect potential objective differences[68,69].

This study indicated that patients in the ERP had a substantial reduction in hospital costs, mainly explained by the shorter stay. With a hip arthroplasty incidence of 468000, national cost savings of CP implementation would amount to greater than $1.2 billion annually in costs from a payer perspective in the United States[60]. For joint arthroplasty, the mean hospital cost from 2002-2013 increased about 50%, as a result of rising total joint arthroplasties and prices of implants[53]. Long waiting lists and the contribution to health expenditure growth since joint replacement are expensive interventions, and the increasing economic burden on public healthcare providers should also be taken into account[1,70]. Besides, the improvement of CPs is accomplished with investment in training, knowledge, and adjustments to daily practice for the surgeon, nurse, and physiotherapist[3,58,71]. Establishing the real cost and saving obtained by a CP can be complicated. Savings also depend on charge systems and reimbursement[55,57].

Strengths and limitations

Some limitations should be noted. Due to methodological as well as statistical heterogeneity, a meta-analysis could not be performed for most outcomes. In most of these studies, a high RoB was present,

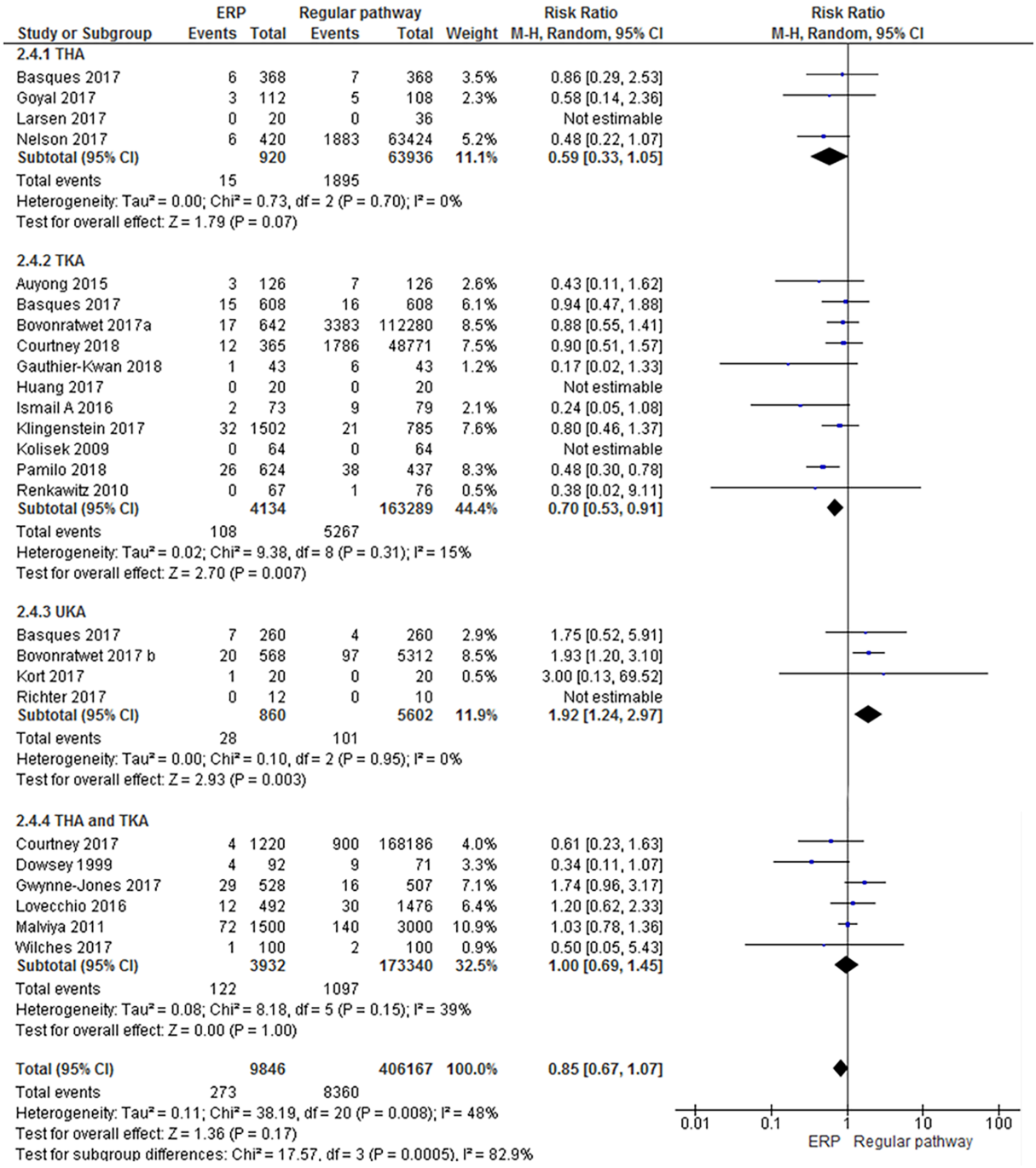


Figure 8 Forest plot with relative risk for each study and pooled relative risk with 95% confidence interval for readmission for enhanced recovery pathways *vs* regular pathways. THA: Total hip arthroplasty; TKA: Total knee arthroplasty; CI: Confidence interval; ERP: Enhanced recovery pathways.

which could have overestimated our results. Selection bias occurred due to the lack of randomization. Performance bias was present because the staff and patients were not blinded to the CP strategy. Clinical bias during data collection was possible because data from large databases were used. Reporting bias is a problem in primary studies because of the selective reporting of outcomes.

Due to the high heterogeneity, it was only possible to perform a meta-analysis for (S)AEs and readmission rate for the different arthroplasties. Although a cut-off I^2 value of 75% has been chosen beforehand, we also present results that exceed this limit, to indicate the trend, *e.g.*, (S)AEs with a follow-up of 30 d or more in the THA (I^2 = 89%, P = 0.7).

The lack of a clear definition for regular pathways and ERP makes it difficult to pool results and compare between large groups of studies. By pointing out the enhanced aspects, we tried to solve this limitation as much as possible.

The strengths of this review include an extensive literature strategy. All included studies compared outcomes from an enhanced recovery pathway with a regular pathway. Data from a large population of

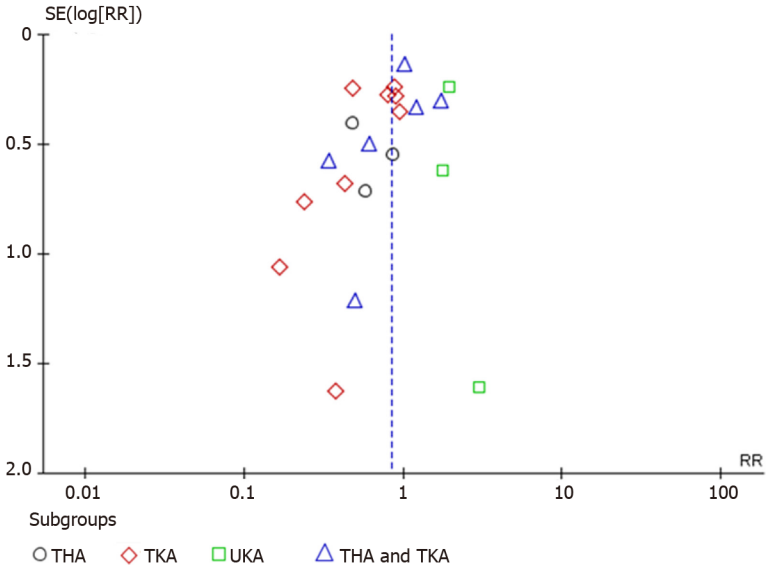


Figure 9 Funnel plot for the studies with described readmission. THA: Total hip arthroplasty; TKA: Total knee arthroplasty; UKA: Unicompartmental knee arthroplasty; RR: Risk ratio.

over 2 million patients were analyzed, including both hip and/or knee arthroplasty, with different follow-up times and outcome measures. Even, an update with the recent literature will provide comparable insights to continuously updating CPs to achieve the most optimal results for patients, professionals, and organizations.

CONCLUSION

Based on the present SR and meta-analysis, it can be concluded that ERPs for hip and/or knee arthroplasty can result in less SAEs with reduced readmission rate and length of stay, and similar or improved clinical outcomes and PROMs with financial benefits, when compared to regular pathways.

ARTICLE HIGHLIGHTS

Research background

Over the past 20 years, clinical pathways (CPs) for total knee and hip arthroplasty have been evolved and optimized. Based on novel evidence and new standards, at this moment we can safely discharge patients on the day of surgery. Whereas in the past, 2-wk bed rest was the standard.

Research motivation

A clinical pathway is a stochastic process that needs to be updated with the latest evidence so the hospital, orthopedic surgeon, and other staff involved in this multidisciplinary approach will be satisfied, with financial benefits for the hospital and improved outcome for the patients. Although, these days in modern medicine, orthopedic surgeons, nurses and hospital staff still needs to be convinced by these optimized CPs. For this reason, we did this systematic review and meta-analysis.

Research objectives

The aim of the present review was to compare the effect of enhanced recovery pathways with regular pathways for adult patients with elective hip and/or knee arthroplasty for (serious) adverse events [(S)AEs], readmission rate, length of hospital stay (LoS), clinician-derived clinical outcomes, patient reported outcome measures (PROMs), and costs.

Research methods

A systematic literature search was conducted in EMBASE, PubMed, Cochrane Library, Web of Science, and CINAHL. All relevant studies were considered for analysis based on the defined eligibility criteria. For the included studies, the risk of bias was assessed. Data for sensitivity analysis were pooled for (S)AE and readmission. A qualitative analysis was performed for the results of LoS, clinician-derived outcome, PROMs, and costs.

Research results

A total of 40 studies were included, 34 in meta-analysis and 40 in qualitative analysis, with data of more than 2 million patients. The meta-analysis presented less (S)AEs in patients following the enhanced recovery pathways (ERP), with fewer readmissions when compared to the regular pathways. The readmission rate was statistically different in favor for the knee arthroplasties without heterogeneity. A reduced LoS was found in all ERP, and in half of these studies, this reduction was statistically significant. The implementation of CPs for hip and knee arthroplasty was associated with similar or improved outcome for clinician-derived outcome and PROMs. ERP were reported to be cost effective. The overall outcomes of all studies reported using Grading of Recommendation, Assessment, Development and Evaluation, presented moderate or high quality of evidence.

Research conclusions

The implementation of ERP for hip and/or knee arthroplasty results in improved clinical and patient related outcomes with financial benefits, compared to regular pathways.

Research perspectives

Based on the results presented, we recommend orthopedic surgeons worldwide, to keep optimizing their standard pathway with the latest evidence. This paper highlights the importance that regular pathways for hip and knee arthroplasty continuously need to be updated according to the latest scientific evidence, which can result in improved clinical outcomes with satisfied patients and financial benefits for patients, healthcare organizations, and hospital management. In this context, high-quality care for hip and/or knee arthroplasty can be achieved.

FOOTNOTES

Author contributions: Heymans MJ designed the study, gathered and analyzed the data, wrote the initial draft of the manuscript, and managed the study; Kort NP is initiator of pathway optimization; Snoeker BA ensured the accuracy of the data; Schotanus MG conceived the study, analyzed the data, and wrote the manuscript; Kort NP, Snoeker BA, and Schotanus MG revised the manuscript; and all authors read and approved the final manuscript.

Conflict-of-interest statement: One author (Kort NP) is a paid consultant for Stryker and Zimmer-Biomet. The other authors declare that they have no conflicts of interest to disclose.

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REFERENCES

1 **Barbieri A**, Vanhaecht K, Van Herck P, Sermeus W, Faggiano F, Marchisio S, Panella M. Effects of clinical pathways in the joint replacement: a meta-analysis. *BMC Med* 2009; **7**: 32 [PMID: 19570193 DOI: 10.1186/1741-7015-7-32]
2 **Jansen E**, Brienza S, Gierasimowicz-Fontana A, Matos C, Reynders-Frederix-Dobre C, HateM SM. [Rehabilitation after total knee arthroplasty of hip and knee]. *Rev Med Brux* 2015; **36**: 313-320 [PMID: 26591319]
3 **Kort NP**, Bemelmans YFL, Schotanus MGM. Outpatient surgery for unicompartmental knee arthroplasty is effective and safe. *Knee Surg Sports Traumatol Arthrosc* 2017; **25**: 2659-2667 [PMID: 26130425 DOI: 10.1007/s00167-015-3680-y]
4 **Singh JA**. Epidemiology of knee and hip arthroplasty: a systematic review. *Open Orthop J* 2011; **5**: 80-85 [PMID: 21584277 DOI: 10.2174/1874325001105010080]
5 **Xu H**, He ML, Xiao ZM, Cao Y. Hip resurfacing vs traditional total hip arthroplasty for osteoarthritis and other non-traumatic diseases of the hip. *Cochrane Database Syst Rev* 2013; **12** [DOI: 10.1002/14651858.CD010851]

6 **OECD**. Health at a Glance 2017 OECD Indicators. [cited 2 February 2021]. Available from: https://www.oecd.org/social/health-at-a-glance-19991312.htm

7 **den Hertog A**, Gliesche K, Timm J, Mühlbauer B, Zebrowski S. Pathway-controlled fast-track rehabilitation after total knee arthroplasty: a randomized prospective clinical study evaluating the recovery pattern, drug consumption, and length of stay. *Arch Orthop Trauma Surg* 2012; **132**: 1153-1163 [PMID: 22643801 DOI: 10.1007/s00402-012-1528-1]

8 **Mabrey JD**, Toohey JS, Armstrong DA, Lavery L, Wammack LA. Clinical pathway management of total knee arthroplasty. *Clin Orthop Relat Res* 1997; 125-133 [PMID: 9418629]

9 **Vehmeijer SBW**, Husted H, Kehlet H. Outpatient total hip and knee arthroplasty. *Acta Orthop* 2018; **89**: 141-144 [PMID: 29202644 DOI: 10.1080/17453674.2017.1410958]

10 **Larsen K**, Hansen TB, Thomsen PB, Christiansen T, Søballe K. Cost-effectiveness of accelerated perioperative care and rehabilitation after total hip and knee arthroplasty. *J Bone Joint Surg Am* 2009; **91**: 761-772 [PMID: 19339559 DOI: 10.2106/JBJS.G.01472]

11 **Galbraith AS**, McGloughlin E, Cashman J. Enhanced recovery protocols in total joint arthroplasty: a review of the literature and their implementation. *Ir J Med Sci* 2018; **187**: 97-109 [PMID: 28623570 DOI: 10.1007/s11845-017-1641-9]

12 **Hoffmann JD**, Kusnezov NA, Dunn JC, Zarkadis NJ, Goodman GP, Berger RA. The Shift to Same-Day Outpatient Joint Arthroplasty: A Systematic Review. *J Arthroplasty* 2018; **33**: 1265-1274 [PMID: 29224990 DOI: 10.1016/j.arth.2017.11.027]

13 **Kim S**, Losina E, Solomon DH, Wright J, Katz JN. Effectiveness of clinical pathways for total knee and total hip arthroplasty: literature review. *J Arthroplasty* 2003; **18**: 69-74 [PMID: 12555186 DOI: 10.1054/arth.2003.50030]

14 **Lovett-Carter D**, Sayeed Z, Abaab L, Pallekonda V, Mihalko W, Saleh KJ. Impact of Outpatient Total Joint Replacement on Postoperative Outcomes. *Orthop Clin North Am* 2018; **49**: 35-44 [PMID: 29145982 DOI: 10.1016/j.ocl.2017.08.006]

15 **Murphy J**, Pritchard MG, Cheng LY, Janarthanan R, Leal J. Cost-effectiveness of enhanced recovery in hip and knee replacement: a systematic review protocol. *BMJ Open* 2018; **8**: e019740 [PMID: 29540418 DOI: 10.1136/bmjopen-2017-019740]

16 **Pollock M**, Somerville L, Firth A, Lanting B. Outpatient Total Hip Arthroplasty, Total Knee Arthroplasty, and Unicompartmental Knee Arthroplasty: A Systematic Review of the Literature. *JBJS Rev* 2016; **4** [PMID: 28060788 DOI: 10.2106/JBJS.RVW.16.00002]

17 **Van Herck P**, Vanhaecht K, Deneckere S, Bellemans J, Panella M, Barbieri A, Sermeus W. Key interventions and outcomes in joint arthroplasty clinical pathways: a systematic review. *J Eval Clin Pract* 2010; **16**: 39-49 [PMID: 20367814 DOI: 10.1111/j.1365-2753.2008.01111.x]

18 **Zhu S**, Qian W, Jiang C, Ye C, Chen X. Enhanced recovery after surgery for hip and knee arthroplasty: a systematic review and meta-analysis. *Postgrad Med J* 2017; **93**: 736-742 [PMID: 28751437 DOI: 10.1136/postgradmedj-2017-134991]

19 **Shamseer L**, Moher D, Clarke M, Ghersi D, Liberati A, Petticrew M, Shekelle P, Stewart LA; PRISMA-P Group. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015: elaboration and explanation. *BMJ* 2015; **350**: g7647 [PMID: 25555855 DOI: 10.1136/bmj.g7647]

20 RefWorks-COS P. L. ProQuest LLC. RefWorks. Ann Arbour: ProQuest LLC 2001

21 **RTC Collaboration**. Review Manager (RevMan) Version 5.3 2014

22 **Centrale Commissie Mensgebonden Onderzoek**, CCMO. [cited 2 February 2021]. Available from: https://www.ccmo.nl

23 **Higgins JP**, Green S. Cochrane handbook for systematic reviews of interventions. United States: John Wiley & Sons, 2011

24 **Sterne JA**, Hernán MA, Reeves BC, Savović J, Berkman ND, Viswanathan M, Henry D, Altman DG, Ansari MT, Boutron I, Carpenter JR, Chan AW, Churchill R, Deeks JJ, Hróbjartsson A, Kirkham J, Jüni P, Loke YK, Pigott TD, Ramsay CR, Regidor D, Rothstein HR, Sandhu L, Santaguida PL, Schünemann HJ, Shea B, Shrier I, Tugwell P, Turner L, Valentine JC, Waddington H, Waters E, Wells GA, Whiting PF, Higgins JP. ROBINS-I: a tool for assessing risk of bias in non-randomised studies of interventions. *BMJ* 2016; **355**: i4919 [PMID: 27733354 DOI: 10.1136/bmj.i4919]

25 **Higgins JPT**, Thomas J, Chandler J, Cumpston M, Li TJ, Page MJ, Welch VA. Cochrane handbook for systematic reviews of interventions. In: Schünemann HJ, Oxman AD, Vist GE, Higgins JP, Deeks PG. Interpreting results and drawing conclusions. Oxford: Cochrane Collaboration, 2011 [DOI: 10.1002/9781119536604.ch15]

26 **Bertin KC**. Minimally invasive outpatient total hip arthroplasty: a financial analysis. *Clin Orthop Relat Res* 2005; 154-163 [PMID: 15930933 DOI: 10.1097/01.blo.0000157173.22995.cf]

27 **Brunenberg DE**, van Steyn MJ, Sluimer JC, Bekebrede LL, Bulstra SK, Joore MA. Joint recovery programme versus usual care: an economic evaluation of a clinical pathway for joint replacement surgery. *Med Care* 2005; **43**: 1018-1026 [PMID: 16166871 DOI: 10.1097/01.mlr.0000178266.75744.35]

28 **Dowsey MM**, Kilgour ML, Santamaria NM, Choong PF. Clinical pathways in hip and knee arthroplasty: a prospective randomised controlled study. *Med J Aust* 1999; **170**: 59-62 [PMID: 10026684 DOI: 10.5694/j.1326-5377.1999.tb126882.x]

29 **Jimenez Muñoz AB**, Duran Garcia ME, Rodriguez Perez MP, Sanjurjo M, Vigil MD, Vaquero J. Clinical pathway for hip arthroplasty six years after introduction. *Int J Health Care Qual Assur Inc Leadersh Health Serv* 2006; **19**: 237-245 [PMID: 16875102 DOI: 10.1108/09526860610661455]

30 **Ho DM**, Huo MH. Are critical pathways and implant standardization programs effective in reducing costs in total knee replacement operations? *J Am Coll Surg* 2007; **205**: 97-100 [PMID: 17617338 DOI: 10.1016/j.jamcollsurg.2007.03.009]

31 **Kolisek FR**, McGrath MS, Jessup NM, Monesmith EA, Mont MA. Comparison of outpatient versus inpatient total knee arthroplasty. *Clin Orthop Relat Res* 2009; **467**: 1438-1442 [PMID: 19224306 DOI: 10.1007/s11999-009-0730-0]

32 **Renkawitz T**, Rieder T, Handel M, Koller M, Drescher J, Bonnlaender G, Grifka J. Comparison of two accelerated clinical pathways--after total knee replacement how fast can we really go? *Clin Rehabil* 2010; **24**: 230-239 [PMID: 20156984 DOI: 10.1177/0269215509353267]

33 **Krummenauer F**, Guenther KP, Kirschner S. Cost effectiveness of total knee arthroplasty from a health care providers' perspective before and after introduction of an interdisciplinary clinical pathway--is investment always improvement? *BMC Health Serv Res* 2011; **11**: 338 [PMID: 22168149 DOI: 10.1186/1472-6963-11-338]

34 **Malviya A**, Martin K, Harper I, Muller SD, Emmerson KP, Partington PF, Reed MR. Enhanced recovery program for hip

and knee replacement reduces death rate. *Acta Orthop* 2011; **82**: 577-581 [PMID: 21895500 DOI: 10.3109/17453674.2011.618911]

35 **Gooch K**, Marshall DA, Faris PD, Khong H, Wasylak T, Pearce T, Johnston DW, Arnett G, Hibbert J, Beaupre LA, Zernicke RF, Frank C. Comparative effectiveness of alternative clinical pathways for primary hip and knee joint replacement patients: a pragmatic randomized, controlled trial. *Osteoarthritis Cartilage* 2012; **20**: 1086-1094 [PMID: 22796513 DOI: 10.1016/j.joca.2012.06.017]

36 **Auyong DB**, Allen CJ, Pahang JA, Clabeaux JJ, MacDonald KM, Hanson NA. Reduced Length of Hospitalization in Primary Total Knee Arthroplasty Patients Using an Updated Enhanced Recovery After Orthopedic Surgery (ERAS) Pathway. *J Arthroplasty* 2015; **30**: 1705-1709 [PMID: 26024988 DOI: 10.1016/j.arth.2015.05.007]

37 **Maempel JF**, Walmsley PJ. Enhanced recovery programmes can reduce length of stay after total knee replacement without sacrificing functional outcome at one year. *Ann R Coll Surg Engl* 2015; **97**: 563-567 [PMID: 26462116 DOI: 10.1308/rcsann.2015.0016]

38 **Goyal N**, Chen AF, Padgett SE, Tan TL, Kheir MM, Hopper RH Jr, Hamilton WG, Hozack WJ. Otto Aufranc Award: A Multicenter, Randomized Study of Outpatient versus Inpatient Total Hip Arthroplasty. *Clin Orthop Relat Res* 2017; **475**: 364-372 [PMID: 27287858 DOI: 10.1007/s11999-016-4915-z]

39 **Ismail A**, Sulong S, Zafar A, Junid, Syed Mohamed Al-Junid Syed, Wan Norlida I, Maskon O, Husyairi H, Ismail S, Nor Hamdan Y, Faizal Amri H. Implementation of clinical pathways in Malaysia: Can clinical pathways improve the quality of care? *Int Med J* 2016; **23**: 47-50

40 **Lovecchio F**, Alvi H, Sahota S, Beal M, Manning D. Is Outpatient Arthroplasty as Safe as Fast-Track Inpatient Arthroplasty? *J Arthroplasty* 2016; **31**: 197-201 [PMID: 27378634 DOI: 10.1016/j.arth.2016.05.037]

41 **Maempel JF**, Clement ND, Ballantyne JA, Dunstan E. Enhanced recovery programmes after total hip arthroplasty can result in reduced length of hospital stay without compromising functional outcome. *Bone Joint J* 2016; **98-B**: 475-482 [PMID: 27037429 DOI: 10.1302/0301-620X.98B4.36243]

42 **Arshi A**, Leong NL, D'Oro A, Wang C, Buser Z, Wang JC, Jones KJ, Petrigliano FA, SooHoo NF. Outpatient Total Knee Arthroplasty Is Associated with Higher Risk of Perioperative Complications. *J Bone Joint Surg Am* 2017; **99**: 1978-1986 [PMID: 29206787 DOI: 10.2106/JBJS.16.01332]

43 **Basques BA**, Tetreault MW, Della Valle CJ. Same-Day Discharge Compared with Inpatient Hospitalization Following Hip and Knee Arthroplasty. *J Bone Joint Surg Am* 2017; **99**: 1969-1977 [PMID: 29206786 DOI: 10.2106/JBJS.16.00739]

44 **Bovonratwet P**, Ondeck NT, Nelson SJ, Cui JJ, Webb ML, Grauer JN. Comparison of Outpatient vs Inpatient Total Knee Arthroplasty: An ACS-NSQIP Analysis. *J Arthroplasty* 2017; **32**: 1773-1778 [PMID: 28237215 DOI: 10.1016/j.arth.2017.01.043]

45 **Bovonratwet P**, Ondeck NT, Tyagi V, Nelson SJ, Rubin LE, Grauer JN. Outpatient and Inpatient Unicompartmental Knee Arthroplasty Procedures Have Similar Short-Term Complication Profiles. *J Arthroplasty* 2017; **32**: 2935-2940 [PMID: 28602533 DOI: 10.1016/j.arth.2017.05.018]

46 **Courtney PM**, Boniello AJ, Berger RA. Complications Following Outpatient Total Joint Arthroplasty: An Analysis of a National Database. *J Arthroplasty* 2017; **32**: 1426-1430 [PMID: 28034481 DOI: 10.1016/j.arth.2016.11.055]

47 **Gwynne-Jones DP**, Martin G, Crane C. Enhanced Recovery After Surgery for Hip and Knee Replacements. *Orthop Nurs* 2017; **36**: 203-210 [PMID: 28538534 DOI: 10.1097/NOR.0000000000000351]

48 **Hoorntje A**, Koenraadt KLM, Boevé MG, van Geenen RCI. Outpatient unicompartmental knee arthroplasty: who is afraid of outpatient surgery? *Knee Surg Sports Traumatol Arthrosc* 2017; **25**: 759-766 [PMID: 28229182 DOI: 10.1007/s00167-017-4440-y]

49 **Huang A**, Ryu JJ, Dervin G. Cost savings of outpatient versus standard inpatient total knee arthroplasty. *Can J Surg* 2017; **60**: 57-62 [PMID: 28234591 DOI: 10.1503/cjs.002516]

50 **Klapwijk LC**, Mathijssen NM, Van Egmond JC, Verbeek BM, Vehmeijer SB. The first 6 weeks of recovery after primary total hip arthroplasty with fast track. *Acta Orthop* 2017; **88**: 140-144 [PMID: 28079428 DOI: 10.1080/17453674.2016.1274865]

51 **Klingenstein GG**, Schoifet SD, Jain RK, Reid JJ, Porat MD, Otegbeye MK. Rapid Discharge to Home After Total Knee Arthroplasty Is Safe in Eligible Medicare Patients. *J Arthroplasty* 2017; **32**: 3308-3313 [PMID: 28754579 DOI: 10.1016/j.arth.2017.06.034]

52 **Larsen JR**, Skovgaard B, Prynø T, Bendikas L, Mikkelsen LR, Laursen M, Høybye MT, Mikkelsen S, Jørgensen LB. Feasibility of day-case total hip arthroplasty: a single-centre observational study. *Hip Int* 2017; **27**: 60-65 [PMID: 27791240 DOI: 10.5301/hipint.5000421]

53 **Molloy IB**, Martin BI, Moschetti WE, Jevsevar DS. Effects of the Length of Stay on the Cost of Total Knee and Total Hip Arthroplasty from 2002 to 2013. *J Bone Joint Surg Am* 2017; **99**: 402-407 [PMID: 28244911 DOI: 10.2106/JBJS.16.00019]

54 **Nelson SJ**, Webb ML, Lukasiewicz AM, Varthi AG, Samuel AM, Grauer JN. Is Outpatient Total Hip Arthroplasty Safe? *J Arthroplasty* 2017; **32**: 1439-1442 [PMID: 28065622 DOI: 10.1016/j.arth.2016.11.053]

55 **Richter DL**, Diduch DR. Cost Comparison of Outpatient Versus Inpatient Unicompartmental Knee Arthroplasty. *Orthop J Sports Med* 2017; **5**: 2325967117694352 [PMID: 28451601 DOI: 10.1177/2325967117694352]

56 **Schotanus M**, Bemelmans Y, Kort N. Improved Health-Related Quality of Life after Knee Arthroplasty Following an Outpatient Surgery Pathway: an Observational Comparative Case Study. *J Clin Trials* 2017; **7** [DOI: 10.4172/2167-0870.1000327]

57 **Wilches C**, Sulbarán JD, Fernández JE, Gisbert JM, Bausili JM, Pelfort X. Fast-track recovery technique applied to primary total hip and knee replacement surgery. Analysis of costs and complications. *Rev Esp Cir Ortop Traumatol* 2017; **61**: 111-116 [PMID: 28073671 DOI: 10.1016/j.recot.2016.10.002]

58 **Castorina S**, Guglielmino C, Castrogiovanni P, Szychlinska MA, Ioppolo F, Massimino P, Leonardi P, Maci C, Iannuzzi M, Di Giunta A, Musumeci G. Clinical evidence of traditional *vs* fast track recovery methodologies after total arthroplasty for osteoarthritic knee treatment. A retrospective observational study. *Muscles Ligaments Tendons J* 2017; **7**: 504-513 [PMID: 29387645 DOI: 10.11138/mltj/2017.7.3.504]

59 **Courtney PM**, Froimson MI, Meneghini RM, Lee GC, Della Valle CJ. Can Total Knee Arthroplasty Be Performed Safely

as an Outpatient in the Medicare Population? *J Arthroplasty* 2018; **33**: S28-S31 [PMID: 29395721 DOI: 10.1016/j.arth.2018.01.003]

60 **Featherall J**, Brigati DP, Faour M, Messner W, Higuera CA. Implementation of a Total Hip Arthroplasty Care Pathway at a High-Volume Health System: Effect on Length of Stay, Discharge Disposition, and 90-Day Complications. *J Arthroplasty* 2018; **33**: 1675-1680 [PMID: 29478678 DOI: 10.1016/j.arth.2018.01.038]

61 **Gauthier-Kwan OY**, Dobransky JS, Dervin GF. Quality of Recovery, Postdischarge Hospital Utilization, and 2-Year Functional Outcomes After an Outpatient Total Knee Arthroplasty Program. *J Arthroplasty* 2018; **33**: 2159-2164.e1 [PMID: 29506929 DOI: 10.1016/j.arth.2018.01.058]

62 **Pamilo KJ**, Torkki P, Peltola M, Pesola M, Remes V, Paloneva J. Fast-tracking for total knee replacement reduces use of institutional care without compromising quality. *Acta Orthop* 2018; **89**: 184-189 [PMID: 29160123 DOI: 10.1080/17453674.2017.1399643]

63 **Toy PC**, Fournier MN, Throckmorton TW, Mihalko WM. Low Rates of Adverse Events Following Ambulatory Outpatient Total Hip Arthroplasty at a Free-Standing Surgery Center. *J Arthroplasty* 2018; **33**: 46-50 [PMID: 28927566 DOI: 10.1016/j.arth.2017.08.026]

64 **Feng JE**, Novikov D, Anoushiravani AA, Schwarzkopf R. Total knee arthroplasty: improving outcomes with a multidisciplinary approach. *J Multidiscip Healthc* 2018; **11**: 63-73 [PMID: 29416347 DOI: 10.2147/JMDH.S140550]

65 **Lazic S**, Boughton O, Kellett CF, Kader DF, Villet L, Rivière C. Day-case surgery for total hip and knee replacement: How safe and effective is it? *EFORT Open Rev* 2018; **3**: 130-135 [PMID: 29780620 DOI: 10.1302/2058-5241.3.170031]

66 **Rolfson O**, Malchau H. The use of patient-reported outcomes after routine arthroplasty: beyond the whys and ifs. *Bone Joint J* 2015; **97-B**: 578-581 [PMID: 25922448 DOI: 10.1302/0301-620X.97B5.35356]

67 **Giesinger K**, Hamilton DF, Jost B, Holzner B, Giesinger JM. Comparative responsiveness of outcome measures for total knee arthroplasty. *Osteoarthritis Cartilage* 2014; **22**: 184-189 [PMID: 24262431 DOI: 10.1016/j.joca.2013.11.001]

68 **Bolink SA**, Grimm B, Heyligers IC. Patient-reported outcome measures vs inertial performance-based outcome measures: A prospective study in patients undergoing primary total knee arthroplasty. *Knee* 2015; **22**: 618-623 [DOI: 10.1016/j.knee.2015.04.002]

69 **Schotanus MGM**, Bemelmans YFL, Grimm B, Heyligers IC, Kort NP. Physical activity after outpatient surgery and enhanced recovery for total knee arthroplasty. *Knee Surg Sports Traumatol Arthrosc* 2017; **25**: 3366-3371 [PMID: 27492381 DOI: 10.1007/s00167-016-4256-1]

70 **Kurtz SM**, Ong KL, Schmier J, Mowat F, Saleh K, Dybvik E, Kärrholm J, Garellick G, Havelin LI, Furnes O, Malchau H, Lau E. Future clinical and economic impact of revision total hip and knee arthroplasty. *J Bone Joint Surg Am* 2007; **89** Suppl 3: 144-151 [PMID: 17908880 DOI: 10.2106/JBJS.G.00587]

71 **Kehlet H**, Thienpont E. Fast-track knee arthroplasty -- status and future challenges. *Knee* 2013; **20** Suppl 1: S29-S33 [PMID: 24034592 DOI: 10.1016/S0968-0160(13)70006-1]

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SYSTEMATIC REVIEWS

Surgical treatment of femoral deformities in polyostotic fibrous dysplasia and McCune-Albright syndrome: A literature review

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Abstract

BACKGROUND

Surgical correction of femoral deformities in polyostotic fibrous dysplasia (PFD) or McCune-Albright syndrome (MAS), such as coxa vara or shepherd's crook deformity, is a challenge.

AIM

To evaluate the treatment of patients with femoral deformities caused by PDF or MAS treated by osteotomies and stabilized with different methods, by analyzing the most relevant studies on the topic.

METHODS

A literature search was performed in Medline database (PubMed). Articles were screened for patients affected by PFD or MAS surgically managed by osteotomies and stabilized with different methods.

RESULTS

The initial search produced 184 studies, with 15 fulfilling the eligibility criteria of our study. Selected articles (1987-2019) included 111 patients overall (136 femurs).

CONCLUSION

Based on our results, the preferred method to stabilize corrective osteotomies is intramedullary nailing with neck cross pinning. When the deformity is limited to the proximal part of the femur, a screw or blade plate may be used, although there is a high risk of fracture below the plate. When the femur is entirely involved, a two-stage procedure may be considered.

Key Words: Polyostotic fibrous dysplasia; McCune-Albright syndrome; Coxa vara; Shepherd's crook deformity; Femoral osteotomy; Intramedullary nailing

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Core Tip: Polyostotic fibrous dysplasia and McCune-Albright syndrome commonly affect the femur, causing deformities and fractures. The proximal third of the femur represents the site where the most difficult to treat deformities are located, such as coxa vara and shepherd's crook deformity. Surgical correction is difficult, since the fibrodysplastic bone is much weaker and more vascularized compared to normal bone and, in the most severe forms, the medullary canal is absent. The best device to stabilize corrective osteotomies seems to be the cervico-diaphyseal intramedullary nail, but the surgical technique may be difficult, because of the absence of the medullary canal and the high risk of bleeding.

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INTRODUCTION

Fibrous dysplasia of bone is an uncommon hereditary genetic skeletal disorder, characterized by the replacement of the bone marrow organ with a tissue formed by pre-osteogenic fibroblast-like cells and trabeculae of immature bone. The disease is due to a sporadic, congenital mutation that causes an increased synthesis of the G protein, a factor stimulating the mitosis of pre-osteoblastic cells, with the consequence that only some pre-osteoblastic cells reach a more mature stage. These immature pre-osteoblastic cells form thin bone trabeculae with structural anomalies and poor mineralization, causing bone fragility with possible deformities and fractures[1-3]. The disease was first defined as polyostotic fibrous dysplasia (PFD) by Lichtenstein in 1938, and subsequently Lichtenstein and Jaffe in 1942 described the clinical, radiographic, and histological aspects of the disease[3]. There are monostotic and polyostotic forms (PFD) that may be associated with cafè-au-lait skin spots and hyperfunctioning endocrine disorders in the McCune-Albright syndrome (MAS) or with intramuscular myxomas in the Mazabraud's syndrome. In MAS, the most frequent endocrinopathies including precocious puberty, hyperthyroidism, growth hormone excess, rickets, and osteomalacia amongst others[4]. PFD and MAS commonly affect the femur and tibia, causing deformities and fractures; however, other bones including the spine and the craniofacial bones may also be affected[4-6]. The proximal third of the femur represents the site where the most difficult deformities that require surgical correction are located, such as coxa vara and shepherd's crook deformity, sometimes associated with deformities of the diaphysis or of the distal part of the femur. A classification of femoral deformities has recently been proposed[7]. Surgical correction of femoral deformities in patients with PFD or MAS is a challenge, since the fibrodysplastic bone is much weaker and more vascularized than the normal bone and, in the most severe form, the medullary canal is completely absent. To stabilize corrective osteotomies performed in PFD, a cervico-diaphyseal interlocking intramedullary nail may be preferred, because failures are very likely to occur with either screw or blade plates. However, in some deformities, such as isolated coxa vara, screw or blade plate remain the most appropriate devices for stabilizing corrective valgus osteotomy[8-10]. Curettage and bone grafting, both with allograft and autograft, have been commonly used in PFD. However, this treatment usually fails, since no retention of any graft material has been observed over time, as reported in long-term follow-up studies[11,12].

The aim of our study was to analyze a series of papers published from 1987 to 2019, to identify the correct indications for surgical treatment of femoral deformities in patients with PDF, the effectiveness over time of the different corrective osteotomies performed, and finally the best devices to better stabilize the fibrodysplastic bone.

MATERIALS AND METHODS

Inclusion and exclusion criteria were formulated according to the population, intervention, comparator, outcome (PICO) method and are summarized in Table 1[13].

Search strategy and sources of information: authors of this review (GG, AC, LN, FDM, PF) performed a literature search about the topic by querying Medline database, Scopus and Web of Science (WOS). Studies were located by searching the database *via* Pubmed, Scopus and WOS. The search strategy covers PICO and was performed independently by each author on March 2021. Keywords and Medical Subject Headings (MeSH) terms were identified by a preliminary search and selected by discussion. The

Table 1 Inclusion and exclusion criteria (population, intervention, comparator, outcome)

	Inclusion criteria	Exclusion criteria
Population	(1) Patients affected by polyostotic fibrous dysplasia or MAS; and (2) Patients affected by femoral deformities	(1) Patients affected by monostotic fibrous dysplasia; (2) Patients affected by PFD or MAS originally treated for fractures or impending fractures; (3) Patients affected by other kind of dysplastic pathologies as fibrocartilaginous dysplasia; and (4) Patients treated for deformities caused by PFD but not affecting femur
Intervention	(1) Osteotomies; and (2) Internal fixation by intramedullary nailing	(1) External fixation only; (2) Bone grafting or transplantations techniques only; and (3) Other surgical techniques
Comparison group	Internal fixation by peripheral plate	Not applicable
Outcome	Studies reporting clinical, radiographic evaluation	Not applicable
Time	Studies published from any date to 2021	Not applicable
Study type	(1) Cohort studies; (2) Case-control studies; and (3) Randomized control trials	(1) Letters; and (2) Case reports
Language	English	Other languages

MAS: McCune-Albright syndrome; PFD: Polyostotic fibrous dysplasia.

search was conducted using the following keywords and their synonyms, assembled in various combination to obtain most pertinent articles: PFD, fibrous dysplasia, MAS, femoral deformities, intramedullary nailing, surgical treatment, surgical procedure. The following is the list of all of the terms used and the Boolean operators used to combine them: (("Fibrous Dysplasia of Bone" [Mesh] OR "Fibrous Dysplasia, Polyostotic" [Mesh] OR "Fibrous Dysplasia, Monostotic" [Mesh] OR "Mc CUNE-ALBRIGHT SYNDROME" [Title/Abstract]) AND (("Surgical Procedures, Operative" [Mesh] OR "surgical" [Title/Abstract]) OR (((("fracture fixation, intramedullary" [MeSH Terms] OR ("fracture" [All Fields] AND "fixation" [All Fields] AND "intramedullary" [All Fields]) OR "intramedullary fracture fixation" [All Fields] OR ("intramedullary" [All Fields] AND "nailing" [All Fields]) OR "intramedullary nailing" [All Fields])))) OR "intramedullary" [All Fields] OR "nailing" [All Fields])) AND ("femur" [Title/Abstract] OR "femoral" [Title/Abstract] OR "Femur" [Mesh])) OR ((("surgical procedures, operative" [MeSH Terms] OR ("surgical" [All Fields] AND "procedures" [All Fields] AND "operative" [All Fields]) OR "operative surgical procedures" [All Fields] OR ("surgical" [All Fields] AND "treatment" [All Fields]) OR "surgical treatment" [All Fields]) OR ((((("fracture fixation, intramedullary" [MeSH Terms] OR ("fracture" [All Fields] AND "fixation" [All Fields] AND "intramedullary" [All Fields]) OR "intramedullary fracture fixation" [All Fields] OR ("intramedullary" [All Fields] AND "nailing" [All Fields]) OR "intramedullary nailing" [All Fields])))) OR "intramedullary" [All Fields] OR "nailing" [All Fields])) AND ("femur" [All Fields] OR "femoral" [All Fields] OR "femur" [MeSH Terms] OR "femur" [All Fields] OR "femoral" [All Fields]) AND ("abnormalities" [MeSH Subheading] OR "abnormalities" [All Fields] OR "deformities" [All Fields] OR "congenital abnormalities" [MeSH Terms] OR ("congenital" [All Fields] AND "abnormalities" [All Fields]) OR "congenital abnormalities" [All Fields] OR "deformity" [All Fields] OR "deform" [All Fields] OR "deformabilities" [All Fields] OR "deformability" [All Fields] OR "deformable" [All Fields] OR "deformably" [All Fields] OR "deformation"[All Fields] OR "deformational" [All Fields] OR "deformations" [All Fields] OR "deformative" [All Fields] OR "deformed" [All Fields] OR "deforming" [All Fields] OR "deforms" [All Fields]) AND ("fibrous dysplasia, polyostotic" [MeSH Terms] OR ("fibrous" [All Fields] AND "dysplasia" [All Fields] AND "polyostotic" [All Fields]) OR "polyostotic fibrous dysplasia"[All Fields] OR ("polyostotic"[All Fields] AND "fibrous" [All Fields] AND "dysplasia" [All Fields]))) OR ((("surgical procedures, operative" [MeSH Terms] OR ("surgical" [All Fields] AND "procedures" [All Fields] AND "operative" [All Fields]) OR "operative surgical procedures" [All Fields] OR ("surgical" [All Fields] AND "treatment" [All Fields]) OR "surgical treatment" [All Fields])) OR ((((("fracture fixation, intramedullary" [MeSH Terms] OR ("fracture" [All Fields] AND "fixation" [All Fields] AND "intramedullary" [All Fields]) OR "intramedullary fracture fixation" [All Fields] OR ("intramedullary" [All Fields] AND "nailing" [All Fields]) OR "intramedullary nailing" [All Fields])))) OR "intramedullary" [All Fields] OR "nailing" [All Fields]) AND ("femur" [All Fields] OR "femoral" [All Fields] OR "femur" [MeSH Terms] OR "femur" [All Fields] OR "femoral" [All Fields]) AND ("fibrous dysplasia, polyostotic" [MeSH Terms] OR ("fibrous"[All Fields] AND "dysplasia" [All Fields] AND "polyostotic" [All Fields]) OR "polyostotic fibrous dysplasia" [All Fields] OR ("polyostotic" [All Fields] AND "fibrous" [All Fields] AND "dysplasia" [All Fields]))).

No publication date filter was applied to select articles and review articles. Language restriction was applied to identify only English articles. In addition, a manual search was performed of the references cited in the studies included.

The reviewers (GG, AC, LN, FDM, PF) retrieved the data and independently analyzed each selected study; instances of disagreement were resolved by the senior investigator (PF).

The articles were screened for the presence of the following inclusion criteria: patients affected by PFD or MAS; patients affected by femoral deformities (coxa vara, shepherd's crook deformity, *etc.*); patients surgically treated by corrective osteotomies and internal fixation; studies providing an adequate level of evidence, including retrospective studies; availability of full text. The studies were excluded if they provided information regarding: patients affected by monostotic fibrous dysplasia or affected by different dysplastic pathologies as fibrocartilaginous dysplasia; patients affected by PFD but originally treated for fractures; patients treated for deformities caused by fibrous dysplasia that did not affect the femur; and patients treated exclusively with external fixation or bone grafting or transplantation techniques.

Figure 1 shows the flowchart for study selection.

RESULTS

The initial search produced 146 studies from the Medline database, 28 studies from Scopus and 10 from WOS, for a total of 184 papers. After a first screening, we eliminated 21 duplicates. Of the remaining 163 studies, after a detailed evaluation based on inclusion and exclusion criteria, articles were screened and only 14 studies fulfilled the eligibility criteria of our study. The other studies were excluded for the following reasons: 4 included monostotic forms, 5 included fractures or impending fractures, 27 included different type of dysplasia or other pathologies, 6 included deformities not affecting femur, one included patients treated by external fixation, 7 included patients treated by curettage and bone grafting, 14 included patients non surgically treated, 20 included patients treated with other surgical techniques, 26 studies were case reports, and 39 articles were published in a different language other than in English. After screening the references by reading the full-text studies included, we added one more article. In conclusion, a total of 15 articles were enrolled in the present review (Table 2).

All of the selected articles were published from 1987 to 2019 and included 111 patients overall (136 femurs). Table 2 presents a list of the studies, summarizing the number of patients and femurs, type of deformity, age at surgery, surgical technique performed, length of follow-up, results and conclusions.

DISCUSSION

The femur is the most common skeletal segment affected in PFD with a high incidence of severe deformities, especially of the proximal part of the bone, which may cause a progressive and disabling condition[2]. The most frequent deformities are represented by coxa vara and shepherd's crook deformity that, in severe cases, may be associated[3]. Treatment of these deformities is challenging; surgery based on curettage and bone grafting are usually inadequate in symptomatic lesions of the femur, especially in polyostotic form and skeletally immature patients. This treatment generally fails with a high percentage of relapses of the deformity and requires internal fixation in order to achieve satisfactory result[12].

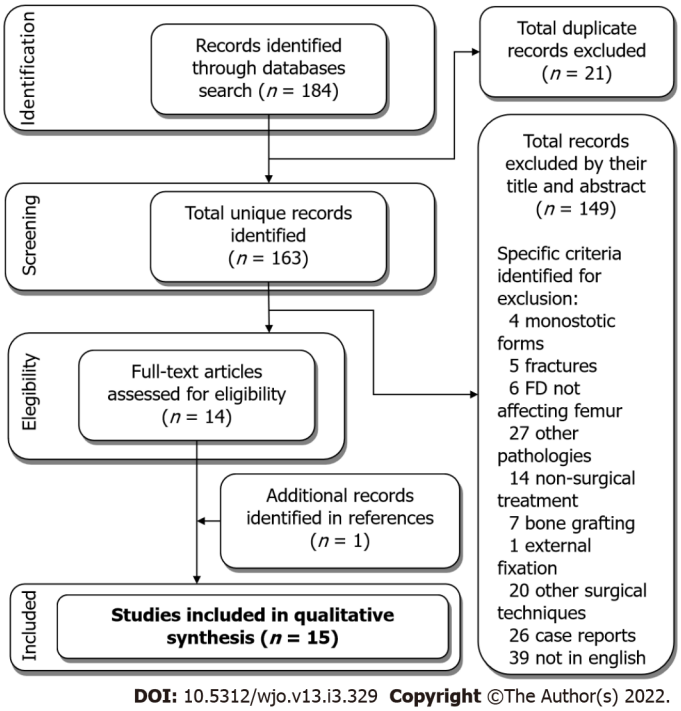
Freeman *et al*[14] first reported the results obtained in a series of four patients affected by PFD (six femurs) treated by multiple osteotomies and fixation using a Zickel intramedullary nail. The authors concluded that in complex deformities of the femur, Zickel nail applied after multiple corrective osteotomies, provides a good control of the deformity, and allows the patients to return to normal activities. In fact, this cervico-diaphyseal device gives a good stabilization of the entire skeletal segment including the femoral neck through the screw inserted into the femoral head. The same authors stated that internal fixation with peripheral plate avoids prolonged immobilization, but a progression of the deformity often occurs, with a high risk of fracture below the plate. Ten years later, some authors[15] reported a long term-follow-up study on eight patients (7 PFD and 1 MAS) with an average age at diagnosis of 8.4 years and an average follow-up of 19.5 years. Of these patients, only two were operated on at 7 years and 5 years of age respectively, by valgus osteotomy for coxa vara, twice in one case. However, in both children the deformity continued to progress until puberty. Over 80% of patients younger than 18 years, treated by curettage and bone grafting, have an unsatisfactory result[12]. In the subsequent decade, other authors[16-19] reported the results of treatment of four series of patients affected by femoral deformities caused by PFD or MAS, with 24 patients overall (9 PFD and 15 MAS) with 37 femurs involved. The authors performed one or multiple femoral osteotomies stabilized with an intramedullary rigid nail. In some cases, curettage and bone grafting and cryosurgery or medical treatment with bisphosphonates was used in concomitance. Most of the patients were surgically treated in adolescence and followed up at least 2 years after surgery. Better results were obtained using a cervico-diaphyseal nail that Freeman *et al*[14] had proposed many years earlier, which allows a good stabilization of the femoral neck that in PFD represents an anatomical site where the bone is particularly weak. In fact, some of these authors[18], using an elongating intramedullary rod, without stabilization of the femoral neck in a younger series of patients, observed at follow-up, a progressive coxa vara in

Table 2 Summary of literature data on surgical treatment of femoral deformities in polyostotic fibrous dysplasia and McCune-Albright syndrome

Ref.	Patients (femurs)	Type of deformities	Mean age at surgery	Surgical treatment	Length of follow-up	Results	Complications	Conclusions
Freeman *et al*[14], 1987	4 (6)	Complex	14.5 yr	Multiple osteotomies and fixation with Zickel nail	2.8 yr	Patients return to normal activities	Intraoperative fracture (1), Respiratory distress syndrome (1), Delayed union (1)	Definitive control of deformities and recurrent fracture
Ozaki *et al* [15], 1996	8 (11)	Coxa vara, Shepherd's crook deformity	6 yr	Valgus osteotomy in 2 cases + curettage and bone grafting	19.5 yr	Deformities continue to progress until puberty	None	The lesions stop progressing after puberty, with the change in activity of pathologic tissue from childhood to adult life
Keijser *et al* [16], 2001	7 (10)	Complex	14.5 yr	Several corrective osteotomies + curettage, cryosurgery and grafting with definitive I.M. fixation	6 yr	Progression of the deformities in patients with MAS	None	Functional outcomes of extended lesions are satisfactory although some lesions need multiple procedures
Ippolito *et al*[17], 2002	7 (10)	Complex	17 yr	Single or multiple osteotomies and fixation with UFN nail with spiral blade	2 yr	All patients were painless and able to walk, one with brace and another with crutches	Delayed union (1)	Provide mechanical support to the weak and fragile dysplastic bone through intramedullary nailing
O'Sullivan *et al*[18], 2002	5 (10)	Complex	8.6 yr	Elongating intramedullary rods + biphosphonates	> 2 yr	Improvement of quality of life, decreasing pain and fracture rate and improving walking ability	None	Elongating rod without stabilization of the femoral neck is effective but doesn't prevent coxa vara
Jung *et al* [19], 2006	5 (7)	Shepherd's crook deformity	24 yr	Multiple osteotomies and I.M. nailing with neck cross pinning	2.5 yr	All patients were able to return to normal activities of daily living	Loosening of the distal locking screw (1)	Good correction of progressing shepherd's crook deformity and prevention of recurrences and fractures
Yang *et al* [20], 2010	7 (8)	Coxa vara, Shepherd's crook deformity	22.7 yr	Valgus osteotomy, curettage, massive allograft and I.M. nailing with neck cross pinning	6.2 yr	Correction of coxa vara from 75° to 120°. No progression of deformity	None	The device represents the first choice of internal fixation, improving limb function and preventing fractures. Good incorporation of allografts
Li *et al* [21], 2013	12 (12)	Coxa vara, Shepherd's crook deformity	14.3 yr	Valgus osteotomy stabilized by DHS plate	1.5 to 10.6 yr	Correction of coxa vara from 89° to 129°	Fracture below the plate (1)	Restore the neck-shaft angle and the mechanical alignment of the femur and improve function
Kushare *et al*[22], 2014	5 (5)	Coxa vara, Shepherd's crook deformity	21.6 yr	Valgus osteotomy stabilized with different devices (plate, I.M. nail, E.F.)	2.2 yr	Satisfactory in 3 patients and unsatisfactory in 2 for persistent pain	Loosening of External Fixator (1)	I.M. implants with neck cross pinning are the preferable method of stabilizing osteotomies in shepherd's crook deformities
Ippolito *et al*[23], 2015	11 (12)	Complex	14 yr	Two stages: (1) Valgus osteotomy for correction of coxa vara and hip plate; and (2) Definitive fixation by I.M. nail with spiral blade	4.5 yr	Neck-shaft angle and shepherd's crook deformities were fully corrected	Cut out of the spiral blade (2), Plate's screw loosening (1), Fracture below the plate (1)	Restore femoral alignment, pain relief and gait improvement, avoiding complications related to peripheral plates
Benedetti *et al*	5 (8)	Complex	6 yr	Valgus osteotomy	3 yr	Correction of	Nail breaking	Proximal humeral nail

[24], 2015				stabilized by I.M. nail with spiral blade		deformities in all cases. Loss of coxa vara correction in 2 cases. Nail breakage in one case	below the spiral blade (1)	connected to a spiral blade may represent a useful device to fix deformities in PFD in young children
Hefti *et al* [25], 2017	13 (15)	Shepherd's crook deformity	14.5 yr	Corrective osteotomy stabilized by a custom made retrograde intramedullary nail	4.5 yr	Most patients were pain free. All patients but one were able to walk, 3 of them with crutches	Nail breaking (1), Screw penetration into the acetabulum (1), Proximal screw migration (1)	This new operative method corrects and stabilizes severe difficult deformities. The operation is technical demanding requiring a careful ability to manage significant blood loss
Majoor *et al*[27], 2018	6 (6)	Shepherd's crook deformity	15.7 yr	Corrective osteotomy stabilized by angle blade plate or I.M. nail (1 case), plus grafting in 3 cases	11.2 yr	No significant change of the femoral neck shaft angle	Fractures of the distal part of the plate (2)	PDF deformities can be adequately and safety treated with angled blade plates. Based on literature review, they propose an individu-alized patient-tailored approach
Fang *et al* [26], 2018	6 (6)	Shepherd's crook or complex deformity	25.8 yr	Corrective osteotomy stabilized with I.M. nail (PFNA) plus curettage and grafting	3 yr	All patients except one had satisfactory functional and radiologic results	Cut out of the spiral blade (1)	Internal fixation with I.M. nail plus curettage and bone grafting is recommended for treating large lesions with deformity
Wan *et al* [28], 2019	10 (10)	Shepherd's crook deformity	31.2 yr	Corrective osteotomy stabilized by DHS plate or I.M. nail (3 cases) plus PMMA augmentation in 5 cases	2.8 yr	Correction of coxa vara from 88.1° to 128.5°. Longer operating times and greater blood loss in I.M. nailing	Wound superficial infection (1)	3D printing osteotomy templates facilitate the correction of shepherd's crook deformity. DHS plus PMMA yields excellent results

DHS: Dynamic hip screw; I.M.: Intramedullary; MAS: McCune-Albright syndrome; PFD: Polyostotic fibrous dysplasia; PMMA: Polymethyl methacrylate.



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Figure 1 Flow diagram of the search process.

half of their patients. The main intraoperative technical problems reported in these studies were the difficulty to ream a new medullary canal through the fibrodysplastic bone and the considerable amount of blood loss. Some authors[16] were forced to stop surgery for the massive bleeding observed during exposure of the proximal femur. From 2010 to 2015, we selected five studies on the surgical treatment of PFD or MAS femoral deformities in five corresponding series of patients with coxa vara and shepherd's crook deformity[20-24]. Some authors[20] suggested correcting the deformity by valgus osteotomy or medial displacement valgus osteotomy and stabilizing it by an intramedullary nail with neck cross pinning associated to curettage and massive impaction allograft. They reported a series of 7 patients with PFD (8 femurs) in adolescent or adult age, followed up 6.2 years after surgery, obtaining a mean correction of the coxa vara from 75° to 120°. By contrast, other authors[21] suggested to stabilize the corrective valgus osteotomy by a dynamic hip screw-plate without grafting. They reported a series of 12 patients with PFD (12 femurs), of average age similar to the previous study, and a length of follow-up from 1.5 years to 10.6 years, with an improvement of the neck-shaft angle from 89° to 129°. One of these patients had a fracture below the plate and he was reoperated, stabilizing the femur by an intramedullary nail with a neck cross screw. To avoid this complication, the remaining authors[22-24] preferred to stabilize the corrective osteotomy by a cervico-diaphyseal intramedullary nail. Other possible devices are not recommended, such as the external fixator used by Kushare *et al*[22] that reported a failure of treatment for an early loosening of the hardware which had to be removed. The same authors reported that the additional procedures as curettage and bone grafting using autograft, allograft or calcium sulfate are questionable, because none of their patients had complete radiographic resolution of the fibrodysplastic lesion[22]. Ippolito *et al*[23] first proposed to treat these complex femoral lesions by a two-stage surgical treatment: The first stage was performed by correction of the coxa vara and fixation with a hip plate, while the second stage, by correction of a shepherd's crook deformity and a definitive fixation with a cervicodiaphyseal nail connected to a spiral blade. The second stage procedure was performed as soon as the valgus osteotomy had healed. The authors reported a series of 11 patients (12 femurs) with a mean age of 14 years, followed up after an average of 4.5 years after the second stage procedure. They concluded that the proposed treatment restored a satisfactory femoral alignment with pain relief and gait improvement, avoiding all the complications related to the peripheral plate. The same authors in another study[24] which involved 5 children (8 femora), aged from 4 years to 7 years, proposed to use intramedullary nailing also in young patients, using a custom-modified adult humeral nail 7-mm thick with a spiral blade. They concluded that this device may represent a useful method of treatment in fixing femoral deformities in young children with PFD.

Regarding the most recent literature, two studies[25,26] recommended stabilizing the corrective osteotomy of the classic shepherd's crook deformity using an intramedullary nail, while two other studies[27,28], suggested an angle blade plate or a dynamic hip screw plate, adding bone graft or polymethyl methacrylate. Of the first two papers (overall 19 patients, 21 femurs), Hefti *et al*[25], introduced a new type of custom made retrograde intramedullary nail, reporting 15 operated femurs followed up 4.5 years after surgery, with satisfactory results, although the surgical technique is demanding with significant blood loss. By contrast, the other two studies reported a total of 16 patients (16 femurs), in which the deformities were stabilized with plates; 10 patients were followed up after more than 10 years. They concluded that all the corrections obtained were stable over time, although in two cases, a fracture of the distal part of the plate occurred. Wan *et al*[28], underlined that using the plate instead of the intramedullary nail reduced operation time and blood loss.

According to our review, we believe that isolated coxa vara should be corrected by an osteotomy and stabilized with a peripheral plate, while isolated shepherd's crook deformity should be treated by multiple osteotomies and stabilized by a cervicodiaphyseal intramedullary nail. Complex deformities in which coxa vara is associated to shepherd's crook deformity should be treated by two staged procedures.

The main strength of this review is the topic, as PFD and MAS are uncommon disease that, especially when they are presented in severe form, are difficult to manage. The main limitation lies in the papers included in the review, as they are all retrospective studies without a control group. Further studies are needed to address points that remain controversial in the treatment this disease.

CONCLUSION

In conclusion, we believe, in accordance with the majority of the authors, that correction of coxa vara and shepherd's crook deformity as well as the other deformities of the femur when it is entirely involved, remains a demanding procedure and, especially in severe cases, more than one operation is necessary. Intramedullary nailing is often preferred to stabilize osteotomies performed in fibrodysplastic bone, while peripheral plating remains the device of choice to stabilize osteotomies performed for coxa vara. The use of cancellous or cortical bone graft in addition to corrective osteotomy is still controversial. Significant blood loss represents a surgical problem, which must be kept in mind during the operation by the surgeon and the anesthesiologist, especially in patients affected by MAS with complex deformities. High X-ray exposure for both the patient and surgeon must also be considered.

ARTICLE HIGHLIGHTS

Research background

Surgical correction of femoral deformities in polyostotic fibrous dysplasia (PFD) or McCune-Albright syndrome (MAS), such as coxa vara or shepherd's crook deformity, is a challenge. Different surgical fixation devices have been described in the past.

Research motivation

No common consensus on the optimal surgical treatment for this pathology among orthopedic surgeons is present.

Research objectives

The aim of our study was to identify the correct indications for surgical treatment of femoral deformities in patients with PDF and MAS, the effectiveness over time of the different corrective osteotomies performed and the best devices to better stabilize the fibrodysplastic bone.

Research methods

A review of English language literature from 1987 until now was performed following the population, intervention, comparator, outcome guidelines.

Research results

Fifteen articles were included for qualitative synthesis in the study after the initial screening resulted in 184 papers.

Research conclusions

Correction of coxa vara and shepherd's crook deformity remains a demanding procedure and, especially in severe cases, more than one operation is necessary. Intramedullary nailing is often preferred to stabilize osteotomies performed in fibrodysplastic bone, while peripheral plating remains the device of choice to stabilize osteotomies performed for coxa vara.

Research perspectives

High-quality prospective randomized clinical trials are needed.

FOOTNOTES

Author contributions: Gorgolini G and Farsetti P designed the study and contributed to manuscript preparation and editing; Caterini A, De Maio F, and Efremov K equally contributed to data analysis and manuscript preparation; Nicotra L contributed to data collection and manuscript preparation.

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REFERENCES

1 **Bianco P**, Kuznetsov SA, Riminucci M, Fisher LW, Spiegel AM, Robey PG. Reproduction of human fibrous dysplasia of bone in immunocompromised mice by transplanted mosaics of normal and Gsalpha-mutated skeletal progenitor cells. *J Clin Invest* 1998; **101**: 1737-1744 [PMID: 9541505 DOI: 10.1172/JCI2361]

2 **Hart ES**, Kelly MH, Brillante B, Chen CC, Ziran N, Lee JS, Feuillan P, Leet AI, Kushner H, Robey PG, Collins MT. Onset, progression, and plateau of skeletal lesions in fibrous dysplasia and the relationship to functional outcome. *J Bone Miner Res* 2007; **22**: 1468-1474 [PMID: 17501668 DOI: 10.1359/jbmr.070511]

3 **Javaid MK**, Boyce A, Appelman-Dijkstra N, Ong J, Defabianis P, Offiah A, Arundel P, Shaw N, Pos VD, Underhil A, Portero D, Heral L, Heegaard AM, Masi L, Monsell F, Stanton R, Dijkstra PDS, Brandi ML, Chapurlat R, Hamdy NAT, Collins MT. Best practice management guidelines for fibrous dysplasia/McCune-Albright syndrome: a consensus statement from the FD/MAS international consortium. *Orphanet J Rare Dis* 2019; **14**: 139 [PMID: 31196103 DOI: 10.1186/s13023-019-1102-9]

4 **Leet AI**, Collins MT. Current approach to fibrous dysplasia of bone and McCune-Albright syndrome. *J Child Orthop* 2007; **1**: 3-17 [PMID: 19308500 DOI: 10.1007/s11832-007-0006-8]

5 **Bunnell WP**. The natural history of idiopathic scoliosis before skeletal maturity. *Spine (Phila Pa 1976)* 1986; **11**: 773-776 [PMID: 3810290 DOI: 10.1097/00007632-198610000-00003]

6 **Eachempati P**, Aggarwal H, Shenoy V, Baliga M. Multidisciplinary approach for management of a patient with fibrous dysplasia of maxilla. *BMJ Case Rep* 2015; **2015** [PMID: 26245286 DOI: 10.1136/bcr-2015-210330]

7 **Zhang X**, Chen C, Duan H, Tu C. Radiographic classification and treatment of fibrous dysplasia of the proximal femur: 227 femurs with a mean follow-up of 6 years. *J Orthop Surg Res* 2015; **10**: 171 [PMID: 26567848 DOI: 10.1186/s13018-015-0313-6]

8 **Saglik Y**, Atalar H, Yildiz Y, Basarir K, Erekul S. Management of fibrous dysplasia. A report on 36 cases. *Acta Orthop Belg* 2007; **73**: 96-101 [PMID: 17441665]

9 **Stanton RP**, Ippolito E, Springfield D, Lindaman L, Wientroub S, Leet A. The surgical management of fibrous dysplasia of bone. *Orphanet J Rare Dis* 2012; **7** Suppl 1: S1 [PMID: 22640754 DOI: 10.1186/1750-1172-7-S1-S1]

10 **Chen F**, Wei Y, Xia J, Wu J, Wang S, Huang G, Chen J, Shi J. Double-level osteotomy and one-stage reconstruction with long intramedullary femoral nail to correct a severe proximal and diaphyseal femur deformity in a patient with polyostotic fibrous dysplasia: case report and literatures review. *Int J Clin Exp Med* 2015; **8**: 14188-14195 [PMID: 26550394]

11 **Leet AI**, Boyce AM, Ibrahim KA, Wientroub S, Kushner H, Collins MT. Bone-Grafting in Polyostotic Fibrous Dysplasia. *J Bone Joint Surg Am* 2016; **98**: 211-219 [PMID: 26842411 DOI: 10.2106/JBJS.O.00547]

12 **Stephenson RB**, London MD, Hankin FM, Kaufer H. Fibrous dysplasia. An analysis of options for treatment. *J Bone Joint Surg Am* 1987; **69**: 400-409 [PMID: 3546323]

13 **Riva JJ**, Malik KM, Burnie SJ, Endicott AR, Busse JW. What is your research question? *J Can Chiropr Assoc* 2012; **56**: 167-171 [PMID: 22997465]

14 **Freeman BH**, Bray EW 3rd, Meyer LC. Multiple osteotomies with Zickel nail fixation for polyostotic fibrous dysplasia involving the proximal part of the femur. *J Bone Joint Surg Am* 1987; **69**: 691-698 [PMID: 3597469]

15 **Ozaki T**, Sugihara M, Nakatsuka Y, Kawai A, Inoue H. Polyostotic fibrous dysplasia. A long-term follow up of 8 patients. *Int Orthop* 1996; **20**: 227-232 [PMID: 8872545 DOI: 10.1007/s002640050069]

16 **Keijser LC**, Van Tienen TG, Schreuder HW, Lemmens JA, Pruszczynski M, Veth RP. Fibrous dysplasia of bone: management and outcome of 20 cases. *J Surg Oncol* 2001; **76**: 157-66; discussion 167 [PMID: 11276018 DOI: 10.1002/jso.1028]

17 **Ippolito E**, Caterini R, Farsetti P, Potenza V. Surgical treatment of fibrous dysplasia of bone in McCune-Albright syndrome. *J Pediatr Endocrinol Metab* 2002; **15** Suppl 3: 939-944 [PMID: 12199353]

18 **O'Sullivan M**, Zacharin M. Intramedullary rodding and bisphosphonate treatment of polyostotic fibrous dysplasia associated with the McCune-Albright syndrome. *J Pediatr Orthop* 2002; **22**: 255-260 [PMID: 11856942]

19 **Jung ST**, Chung JY, Seo HY, Bae BH, Lim KY. Multiple osteotomies and intramedullary nailing with neck cross-pinning for shepherd's crook deformity in polyostotic fibrous dysplasia: 7 femurs with a minimum of 2 years follow-up. *Acta Orthop* 2006; **77**: 469-473 [PMID: 16819687 DOI: 10.1080/17453670610046415]

20 **Yang L**, Jing Y, Hong D, Chong-Qi T. Valgus osteotomy combined with intramedullary nail for Shepherd's crook deformity in fibrous dysplasia: 14 femurs with a minimum of 4 years follow-up. *Arch Orthop Trauma Surg* 2010; **130**: 497-502 [PMID: 19629503 DOI: 10.1007/s00402-009-0943-4]

21 **Li W**, Huang X, Ye Z, Yang D, Tao H, Lin N, Yang Z. Valgus osteotomy in combination with dynamic hip screw fixation for fibrous dysplasia with shepherd's crook deformity. *Arch Orthop Trauma Surg* 2013; **133**: 147-152 [PMID: 23161149 DOI: 10.1007/s00402-012-1633-1]

22 **Kushare IV**, Colo D, Bakhshi H, Dormans JP. Fibrous dysplasia of the proximal femur: surgical management options and outcomes. *J Child Orthop* 2014; **8**: 505-511 [PMID: 25409925 DOI: 10.1007/s11832-014-0625-9]

23 **Ippolito E**, Farsetti P, Valentini MB, Potenza V. Two-stage surgical treatment of complex femoral deformities with severe coxa vara in polyostotic fibrous dysplasia. *J Bone Joint Surg Am* 2015; **97**: 119-125 [DOI: 10.2106/JBJS.N.00230]

24 **Benedetti Valentini M**, Ippolito E, Catellani F, Farsetti P. Internal fixation after fracture or osteotomy of the femur in young children with polyostotic fibrous dysplasia. *J Pediatr Orthop B* 2015; **24**: 291-295 [PMID: 25932827 DOI: 10.1097/BPB.0000000000000192]

25 **Hefti F**, Donnan L, Krieg AH. Treatment of shepherd's crook deformity in patients with polyostotic fibrous dysplasia using a new type of custom made retrograde intramedullary nail: a technical note. *J Child Orthop* 2017; **11**: 64-70 [PMID: 28439311 DOI: 10.1302/1863-2548.11.170002]

26 **Fang X**, Liu H, Lang Y, Xiong Y, Duan H. Fibrous dysplasia of bone: Surgical management options and outcomes of 22 cases. *Mol Clin Oncol* 2018; **9**: 98-103 [PMID: 29977545 DOI: 10.3892/mco.2018.1636]

27 **Majoor BCJ**, Leithner A, van de Sande MAJ, Appelman-Dijkstra NM, Hamdy NAT, Dijkstra PDS. Individualized

approach to the surgical management of fibrous dysplasia of the proximal femur. *Orphanet J Rare Dis* 2018; **13**: 72 [PMID: 29720212 DOI: 10.1186/s13023-018-0805-7]

28 **Wan J**, Zhang C, Liu YP, He HB. Surgical treatment for shepherd's crook deformity in fibrous dysplasia: There is no best, only better. *Int Orthop* 2019; **43**: 719-726 [PMID: 30083845 DOI: 10.1007/s00264-018-4074-9]



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REVIEW

Antibiotic-free antimicrobial poly (methyl methacrylate) bone cements: A state-of-the-art review

Gladius Lewis

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Abstract

Prosthetic joint infection (PJI) is the most serious complication following total joint arthroplasty, this being because it is associated with, among other things, high morbidity and low quality of life, is difficult to prevent, and is very challenging to treat/manage. The many shortcomings of antibiotic-loaded poly (methyl methacrylate) (PMMA) bone cement (ALBC) as an agent for preventing and treating/managing PJI are well-known. One is that microorganisms responsible for most PJI cases, such as methicillin-resistant *S. aureus*, have developed or are developing resistance to gentamicin sulfate, which is the antibiotic in the vast majority of approved ALBC brands. This has led to many research efforts to develop cements that do not contain gentamicin (or, for that matter, any antibiotic) but demonstrate excellent antimicrobial efficacy. There is a sizeable body of literature on these so-called "antibiotic-free antimicrobial" PMMA bone cements (AFAMBCs). The present work is a comprehensive and critical review of this body. In addition to summaries of key trends in results of characterization studies of AFAMBCs, the attractive features and shortcomings of the literature are highlighted. Shortcomings provide motivation for future work, with some ideas being formulation of a new generation of AFAMBCs by, example, adding a nanostructured material and/or an extract from a natural product to the powder and/or liquid of the basis cement, respectively.

Key Words: Periprosthetic joint infection; Poly (methyl methacrylate) bone cement; Antibiotic-loaded poly (methyl methacrylate) bone cement bone cement; Antibiotic-free antimicrobial poly (methyl methacrylate) bone cement bone cement

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Core Tip: Although antibiotic-loaded poly (methyl methacrylate) (PMMA) bone cements are widely used both as prophylactic agent and in the treatment/management of prosthetic joint infection, there is dissatisfaction about the material. A new generation of antibiotic-free antimicrobial PMMA bone cements (AFAMBCs) is emerging. The present review is a critical appraisal of the literature on AFAMBCs, highlighting its strengths, shortcomings, and possible areas for future studies. The conclusion is that state-of-the-art on AFAMBC formulations is such that it is premature to comment on the potential of any of the formulations for clinical application.

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INTRODUCTION

Regardless of the patient group, periprosthetic joint infection (PJI) is a relatively rare occurrence; for example, 2 years after total hip arthroplasty (THA) and total knee arthroplasty (TKA), the cumulative incidence rate is on the order of between 0.5% and 0.8% and about 1.0% of cases, respectively[1,2]. Nonetheless, PJI is recognized as being the most challenging of complications of total joint arthroplasties (TJAs) (to the point of intractability) because of the associated risk for revision of the implant, increase in mortality, increase in morbidity, decrease in quality of life of the patient, and increased direct and indirect costs[3,4]. As such, PJI has been the subject of myriad studies, the bulk of which has been devoted to four aspects, these being identification and stratification of patient- and surgery-based risk factors, diagnosis, prevention, and treatment/management[4]. Among risk factors, the significant roles of morbid obesity (body mass index greater than 40 kg/m^2), young age (< 50 years) of the patient, preoperative use of opioids by the patient, and prolonged surgery time (> 2 h) are recognized even though the supporting clinical evidence ranges from limited to moderate[5-8]. With respect to diagnosis, an assortment of methods is in current clinical use, such as ^{18}F-labeled fluorodeoxyglucose-positron emission tomography (FDG-PET)[9], and measurement of synovial fluid biomarkers, notably, alpha-defensin[10], or under investigation, among which are measurement of temporal change in D-dimer level in conjunction with serum erythrocyte sedimentation rate and C-reactive protein level[11], use of monocyte/lymphocyte ratio, neutrophil/lymphocyte ratio, platelet/lymphocyte ratio (PLR), and platelet/mean platelet volume ratio (PVR), in conjunction with other hematologic and aspirate markers [12], and landmark-guided hip aspiration[13]. To date, a gold standard has not emerged. The most widely used prevention method is anchoring the implant in a bed of antibiotic-loaded poly(methyl methacrylate) bone cement (ALBC)[4]. As for treatment/management, the two common approaches are: (1) Surgical debridement (debridement followed by intravenous or highly bioavailable oral delivery of antimicrobial medication specific to the microorganism found in the case (medical therapy) and retention of the implant (DAIR)[14,15]); and (2) Resection arthroplasty using two-stage exchange[16,17] (although, in recent years, in some countries, enthusiasm is being shown for one-stage exchange[18,19] followed by medical therapy[4,16]). In either option, it is common to fix the exchanged implant to the contiguous bone in an ALBC bed[16].

While an ALBC has a number of attractive features, chief among which are ease of preparation in the operating room and low intrinsic toxicity, it has its share of shortcomings and concerns. One shortcoming is its lack of bioactivity[20,21]. Another is the fact that the bacterial species that are responsible for PJI, most commonly, *S. aureus* and *S. epidermidis*[22], are becoming resistant to gentamicin sulfate, which is the antibiotic in the vast majority of ALBC brands approved by national regulatory bodies, such as the US Food and Drug Administration (the method of mixing of the antibiotic with the cement powder is proprietary) and physician-directed ALBC formulations (mixing of antibiotic and cement powder is carried out in the operating room)[4,23]. A third shortcoming is that the release profile of the antibiotic is sub-optimal, being characterized by 1) an initial short high release rate (zone lasts, typically, < 2 d), followed by a significant reduction in release rate, culminating in exhaustion of release after, typically, 20-30 d and 2) cumulative release of only, typically, between about 0.3% and about 13% of the loaded antibiotic[24,25]. Additionally, there is a lack of consensus that even with risk-stratified usage in primary TJA, the current generation of ALBCs is efficacious and cost-effective[26-36]. As for concerns about ALBC, there are long-standing ones, such as potential deleterious effect on mechanical properties of basis cement[37], and ones that have only recently been raised, such as an increase in immunological factors (specifically, soluble interleukin-6 and C-reactive protein) in patients in which there is a gentamicin-loaded cement implant, suggesting that unknown immunomodulatory pathways may be altered by an ALBC[38].

The aforementioned observations highlight the need for novel methods for reducing the risk for PJI whether ALBC is used as a prophylactic agent in primary THAs and TKAs (as is common practice in a number of countries, such as Norway, and limited use in others, such as United States) or during the second stage of a two-stage exchange arthroplasty (as is common practice in the United States[39]). This need has served as the driver for the large amount of research attention that has been given to this field. These efforts may be grouped into four approaches: application of an antimicrobial coating to part(s) of implant component(s), such as the proximal zone of the femoral stem of a THA[4,40-45]; use of ALBCs in which a relatively new antibiotic/antibacterial compound (for example, daptomycin[46] or a second-generation lipophosphonoxin[47]) is added to the cement powder; modification of the surface of the implant (for example, incorporation of an antibiotic-releasing polymer into the surface of a joint implant [48] and use of a nanofabrication method to create biomimetically-inspired nanostructures on an implant surface[49]); and proposed use of antibiotic-free antimicrobial PMMA bone cements (AFAMBCs)[50-68]. The focus of the present review is AFAMBCs, which have been the subject of many studies on their formulation and characterization[50-68]. However, to date, only one review of this body of literature has been published[69] but it has two shortcomings. First, only about half of that review was devoted to AFAMBCs, with the balance being on aspects such as PMMA bone cement and orthopaedic infections in general and details of the classification, diagnosis, and treatment of PJI. Second, some of the literature studies reviewed were not appropriate to bone cement use in TJAs; for example, the subject of the studies was cement for beads, blocks, and spacers for the treatment of severely contaminated open tibial fractures[70], bone reconstruction[71,72], cement used for stabilizing/augmenting fractured osteoporotic vertebral body fractures (for example, *via* vertebroplasty or balloon kyphoplasty)[73], and antibacterial coatings[74].

The present work focuses exclusively on the literature on AFAMBCs for long-term load-bearing TJA applications (as such, it excludes its use in spacers and blocks), giving a comprehensive and critical review of this body of knowledge by not only summarizing key results (with special emphasis on evaluations of antimicrobial efficacy and cytotoxicity) but, also, highlighting attractive features and shortcomings of literature studies. The latter feature should point to opportunities for future research in the field. This review should inform discussion of the potential for use of AFAMBCs to replace ALBCs.

LITERATURE STUDIES

Antimicrobial activity

The activity of a bone cement, in which the powder additive comprised NanoSilver particles (silver particles, of size 5-50 nm and porosity 85%-90%) (loading between 0% and 1%), when tested against a clinical isolate of MRSE showed loading dependency, with increased loading of the additive leading to increased activity; specifically, cement having a loading of 1% of the additive producing complete inhibition of proliferation of the bacterial strain. As a reference, uninhibited proliferation of the strain occurred when an approved ALBC brand (that contained 2% gentamicin) was used[50]. This same comparative trend was found when 1% NanoSilver-loaded cement was compared with the approved ALBC brand when a clinical isolate of *S. epidermidis* was used[50].

Chitosan (CS) nanoparticles (CS-NPs) (diameter: 220 ± 3 nm) were prepared using the ionic gelation method and quaternary ammonium chitosan (QCS) was synthesized by the method presented by Huh *et al*[75] QCS NPs (mean diameter: 284 ± 2 nm) were obtained from QCS in the same manner as was done for CS-NPs. Two approved plain ALBC brands and two approved ALBC brands were used as negative and positive control cements, respectively. Two sets of experimental AFAMBCs were formulated, one by adding CS-NPs to the cement powder and the other by adding QCS-NPs to the cement powder[51]. Against both *S. aureus* and *S. epidermidis*, each of the AFAMBCs showed significant improvement in antimicrobial activity compared to a control cement, but with QCS-NP-loaded cement showing significantly higher activity than the CS-NP-loaded cement[51]. These results were attributed to the fact that the NPs provide a high surface charge density for interacting with and disrupting bacterial cell membranes[51].

An experimental AFAMBC was obtained by mixing a monomer of quaternized ethylene glycol dimethacrylate piperazine octyl ammonium iodide (QAMA) into the liquid of an approved plain ALBC brand (10, 15, and 20 wt/wt%) (designated PMMA-10QAMA, PMMA-15QAMA, and PMMA-20QAMA cements, respectively)[52]. While *Escherichia coli* (*E. coli*) was retained on the surface of plain cement specimens, there was no evidence of retention and aggregation on experimental AFAMBC specimens. The antimicrobial action displayed by the AFAMBCs was attributed to the presence of QAMA, a polymerizable monomer that has an irreversibly bound component[52].

Using a novel synthesis route, Ag nanoparticles (AgNPs) with very well controlled geometrical properties and stability were obtained and, then, these particles were capped with tiopronin (TIOP), an agent that allows binding of other compounds to the nanoparticles[54]. These nanoparticles (AgNPs-TIOP) were added to the powder of a plain PMMA bone cement (0.1%, 0.5%, and 1.0%)[54]. Against gram-positive methicillin-resistant *S. aureus* (MRSA), the difference in growth rate of the bacterial strain when specimens of the experimental AFAMBC (1% of mean diameter 11 nm Ag-TIOP nanoparticles)

and those of a control cement (no Ag nanoparticles) were used was not significant but the lag time (directly related to resistance to growth of the bacterial strain) of the AFAMBC was approximately 12 times longer than that the control cement specimens were used, indicating the better antimicrobial performance of the former cement[54]. Although the exact mechanism responsible for the antimicrobial activity of Ag nanoparticles has not been established, many explanations have been put forward. Examples are uptake of free Ag ions followed by disruption of the production of an energy storage molecule (adenosine triphosphate (ATP)) and replication of DNA[76]; inactivation of the bacterial cell (cell membrane and enzymes) by the Ag ions interfering with enzymes that interact with sulfur in the protein chains and/or generating reactive oxygen species[54], which kill the cells; and Ag ions causing separation of paired strands of DNA in the bacteria[77].

A bioactive glass (SiO_2-Na_2O-CaO-P_2O_5-B_2O_3-Al_2O_3-Ag_2O) was produced by melting the reactants in a Pt crucible at 1450 °C, then quenching the melt in water to obtain a frit that was milled and sieved to yield glass powder (SBAG powder) (grain size < 20 mm)[55]. An experimental AFAMBC was obtained by mechanically mixing SBAG powder with the powder of an approved plain cement brand (loading: 30% and 50%), with two brands being used as control, one classified as low-viscosity (LV) and the other high-viscosity. Against *S. aureus*, a small drop in both proliferation and adhesion were observed when an AFAMBC rather than a control cement was used, with the same trends being seen in the values of the McFarland Index[55]. In an inhibition halo test, as expected, the size of the halo zone when AFAMBC specimens were used decreased with length of time of contact of the specimens with the agar substrate but, importantly, at the end of the 2nd day, the inhibition zone measured between approximately 1.0 and approximately 1.5 mm, indicating that the antibacterial capability of the cements is good[78,79]. The antimicrobial activity of a bioactive glass has been attributed to an increase of aqueous pH and osmolarity in the *in vivo* zone that surrounds the glass, which accompanies the dissolution of the glass [80], and deposition of glass debris on the surface of the bacteria[81].

Organic nanoparticles containing propylparaben were prepared by fast simultaneous removal of solvents and water from a volatile oil-in-water microemulsion composed of polypylparaben, *n*-butyl acetate, iso-propyl alcohol, sodium dodecyl sulfate (SDS), polyvinylpyrrolidone (PVP), and water, resulting in a fine powder composed of propylparaben nanoparticles (16 wt/wt%), SDS (45 wt/wt%), and PVP (39 wt/wt%)[56]. An AFAMBC was formulated by adding this fine powder to the powder of an experimental plain bone cement formulation (0.1%, 0.5%, 1%, 2%, 5%, and 7%). Overall, against a given bacterial strain (*S. aureus*, MRSA, or *S. epidermidis*), the duration of the lag phase increased but the growth rate (GR) decreased with increase in concentration of nanoparticles in the AFAMBC[56]. These trends suggest that the antimicrobial effect of the AFAMBC is a consequence of the conjoint reduction of viable microbial population and the viable cells not exhibiting the same phenotype of the cells in contact with the nanoparticles[56].

A modified Tollens method that involved reduction of $AgNO_3$ to metal Ag by use of a glucose was used to synthesize Ag nanoparticles (AgNPs), which were then capped with oleic acid (OA) (Ag NPs-OA)[57]. These Ag NPs-OA were loaded into the powder of a plain PMMA bone cement (0.01, 0.05, and 0.10%)[57]. Against *S. aureus*, the mean duration of the lag phase (l) and the growth rate (GR) was between 5 and 6 times longer and between 2 and 3 lower on specimens of AFAMBC (0.05% AgNPs) compared to the corresponding values for plain cement (control cement) specimens, with the trend being the same when MRSA was used[57]. However, when *S. epidermidis* was used, the ratio for either l or GR was much smaller (approximately 1.4)[57].

An AFAMBC was formulated by mixing commercially-available Ag nanoparticles (diameter: 30-50 nm), which had been surface-functionalized with polyvinylpyrrolidone (0.2 wt/wt%) to aid dispersion and minimize agglomeration of the particles, into the liquid of an approved plain cement brand or an approved ALBC brand (loading ratio: 0.25%, 0.50%, and 1.0%, relative to mass of its powder) using an ultrasonic homogenizer with a solid Ti tip[58]. Using a modified Kirby-Bauer disk diffusion assay, it was found that against each of the bacterial strains used (commercially-available *S. aureus* and *S. epidermidis* and 4 clinical isolates obtained from patients with active PJIs (2 *S. aureus* and 2 *S. epidermidi* s)), none of the AFAMBCs demonstrated antimicrobial activity (that is, there was a large area of bacterial colony growth) while the positive control (an approved ALBC brand; antibiotic: gentamicin) exhibited large zones of inhibition (about 18-39 mm)[58]. Similar trends were found in the results of studies in which time-kill assays against planktonic bacteria were performed[58]. However, results of bacterial adhesion tests showed that each of the AFAMBCs significantly reduced biofilm formation relative to the plain cement[58]. These results suggest that while the AFAMBCs have no antimicrobial activity against planktonic bacteria, they have good potential for use in cases where prevention of bacterial adhesion is needed (for example, in primary TJAs)[58]. It is to be noted that: (1) Many of the bacteria commonly involved in PJI, such as *S. aureus*, produce a biofilm, which is a community of microorganisms embedded in an organic polymer that mainly is composed of polysaccharides, proteins, extracellular DNA and lipids, that adheres to an implant surface[82]; (2) A biofilm allows planktonic cells to change their mode of growth to the sessile form[82]; and (3) It is expected that a biofilm will protect the dividing bacteria from the action of an AFAMBC[82,83].

An experimental AFAMBC was formulated by adding a first-generation quaternary ammonium dendrimer of tripropylene glycol diacrylate (TPGDA G-1) to the liquid of a commercially-available plain bone cement (5, 10, 15, or 20 wt/wt%)[59]. Against a commercially-available *S. aureus* strain, the mean

antimicrobial efficiencies of 5TPGDA cement and 10TPGDA cement were 45% and 100%, respectively, compared to a negligible amount for the plain cement counterpart[59]. The antimicrobial action of the quaternary ammonium dendrimer was attributed to it breaking the wall and membrane of the microorganism[59].

A bioactive glass (SiO_2-Na_2O-CaO-P_2O_5-B_2O_3-Al_2O_3) was produced by melting the reactants in a Pt crucible at 1450 °C for 1 h, then quenching the melt in water to obtain a frit that was milled and sieved to yield glass powder (SBA2 powder) (grain size < 20 mm)[60]. This powder was then subjected to an optimized ion-exchange process in aqueous solution of $AgNO_3$, after which the silver-doped powder was dried in air at 60 °C (Ag-SBA2 powder). The experimental AFAMBC was obtained by mechanically mixing 30 wt% of Ag-SBA2 powder with the powder of an approved plain cement brand (Ag-SBA2 cement), with three approved plain PMMA cement brands being used as controls. Against a commercially-available stock of *S. aureus*, 1) a significant drop in both proliferation and adhesion were observed when the AFAMBC rather than a control cement was used, trends that were also seen in the values of the McFarland Index; and 2) in an inhibition halo test (Kirby-Bauer test), the size of the halo zone when AFAMBC specimens were used was between approximately 2.5 and approximately 3.0 mm[60].

An AFAMBC was formulated by mixing commercially-available gold nanoparticles (Au NPs; 99.95% purity; diameter: 10-20 nm) with the powder of an approved plain bone cement brand (loading: 0.25, 0.50, and 1.00 wt/wt%)[61]. Against clinical isolates of MRSA, 1) live bacterial cells were reduced by up to approximately 55% on specimens of cement containing 1 wt/wt% Au NPs compared to specimens of the control cement (no loaded Au NPs); and 2) three-dimensional reconstruction of the biofilm showed a drop of biofilm thickness by approximately 74% when an ALAMBC was used[61].

A bioactive glass (SiO_2-Na_2O-CaO-P_2O_5-B_2O_3-Al_2O_3) was produced by melting the reactants in a. Pt crucible at 1450 °C for 1 h, then quenching the melt in water to obtain a frit that was milled and sieved to yield glass powder (SBA3 powder) (diameter < 20 mm)[62]. This powder was then subjected to an optimized ion-exchange process in a copper-containing aqueous solution, after which the Cu-doped powder was washed, filtered, and dried in air at 60 °C (Cu-SBA3 powder). An experimental AFAMBC was obtained by mechanically mixing 10 wt% of Cu-SBA3 powder with the powder of an approved plain cement brand, with three approved plain PMMA cement brands being used as controls[62]. Against *S. epidermidis* biofilm, a significant drop in bacteria viability was observed at each assayed time-point when an AFAMBC rather than a control cement was used (by a factor of between 2 and 4), indicating that the antibacterial potential of the AFAMBC is good[62]. The antibacterial action of the Cu-SBA3 cements was explained in terms of participation of reactive hydroxyl radicals that are generated in reactions that are harmful to cellular molecules, such as oxidation of proteins[77]. Notwithstanding these results, the resistance of some bacterial species, such as *E. coli*, against copper-containing biomaterials, was noted[62].

A bioactive glass (SiO_2-Na_2O-CaO-P_2O_5-B_2O_3-Al_2O_3) was produced by melting the reactants in a Pt crucible at 1450 °C, then the melt was quenched in water to obtain a frit that was milled and sieved to yield glass powder (SBA2 powder) (grain size < 20 mm or 20-45 mm)[63]. This powder was subjected to an optimized ion-exchange process in aqueous solution of $AgNO_3$, after which the silver-doped powder was dried in air and stored (Ag-SBA2 powder). An experimental AFAMBC was obtained by mechanically mixing 15 or 20 wt% of an Ag-SBA2 powder with the powder of an approved plain cement brand. Several combinations of process variables for producing the powder (drying temperature, storage mode, and mixing temperature) were used, resulting in 8 variants of powders. In an inhibition halo test in which a commercially-available *S. aureus* strain was used, the size of the halo zone when AFAMBC specimens were used was between approximately 2 and approximately 4 mm, indicating marked antibacterial activity of these cements[63].

An AFAMBC was prepared by incorporating sheets of CS and/or graphene oxide (GO) nanosheets, synthesized using the protocols given by Mangadlao *et al*[84], into the liquid of an experimental plain PMMA bone cement (CS- and GO-based cements)[64-66]. A plain cement served as the control cement. Against a commercially-available *S. aureus* strain, after 24 h incubation, the cements containing 0.2% GO (ABC-0.2GO cement), 0.3% GO (ABC-0.3GO cement), 0.5% GO (ABC-0.5GO cement), or 15% CS (ABC-15CS cement) showed significantly higher antimicrobial activity compared to that of the control cement [64,65]. Two mechanisms were postulated to explain the antimicrobial activity of the GO-based cement [64]. First, GO sheets directly contact the bacterial cell, thereby damaging them. Second, reactive oxygen species that are produced destroy the cell membrane subsequent to the GO sheets contacting the surface [64,65]. Synergistic antimicrobial activity was demonstrated in the cement that contained 0.5% GO and 15% CS (ABC-0.5GO-15CS cement)[64].

An experimental AFAMBC formulation (PMMA-NAC cement) was obtained by adding N-acetylcysteine powder (NAC) (an antibacterial agent) to PMMA bone cement in loadings ranging from 10 to 50% wt/vol[67]. At NAC loading ≥ 20% wt/vol, the antibacterial efficacy of the NAC-PMMA cement against planktonic forms of *S. aureus* and *E. coli* was significantly greater than that of the control cement (an approved plain cement brand). The same trend was seen against biofilm forms of the same bacterial strains.

Two variants of an experimental AFAMBC were prepared, the first one by mixing particles of a 5 wt/wt% of a bioglass (BGII-0.4; grain size: ≥ 40 mm), Ag NP powder (particle size: approximately 50 nm) (1.5 wt/wt%), and the powder of an approved plain cement brand (BC-BGII-0.4-AgNP cement)

[68]. BGII-0.4 was prepared using the Stober method modified by Zheng *et al*[85]. The composition of the other variant was the same that of the first one with the exception that a different bioglass was used (a sol-gel obtained SiO_2/CaO (70/30 mol%) bioglass; grain size: about 300 nm) (BG-MP)[68]). The antibacterial performance of each of the AFAMBC variants was determined in two tests using a hospital strain of *S. aureus*: inhibition of the growth of the strain after 4 h and effectiveness (methicillin resistance). In each of these tests, the BC-BGII-0.4-AgNP cement showed significant improvement compared to the control cement (an approved plain cement brand)[68].

In vitro cytotoxicity/cytocompatibility

On L929 mouse fibroblasts, the difference in release of lactate dehydrogenase (an indicator of cell integrity) when an experimental AFAMBC (NanoSilver-loaded cement) was used *vs* when an approved ALBC (control cement) was used, in a non-toxic cell culture medium, was not significant, a trend that was also observed both with protein content and number of vital cells, all of which showed that the lack of cytotoxicity of the AFAMBC[50]. Furthermore, on a human osteoblast cell line (hFOB), only a few dead osteoblasts were seen in live-dead staining in the NanoSilver bone cement specimens and osteoblasts that grew on these specimens were, in the main, vital and grew in a mesh-like manner, as just as in the cell culture medium, showing that the cement has high biocompatibility[50]. The results were explained in terms of Ag ions binding to cellular structures in the bacterial strain (especially, to their SH- groups), thereby interfering with the integrity, energy production, and conservation of the bacterial cell[50]. In contrast, bacterial resistance to the antibiotic in the control cement (gentamicin), being an aminoglycoside, can be acquired by single point mutations [50].

On mouse fibroblast cells (3T3), the difference in cytotoxicity between an experimental AFAMBC (15% CS-NPs or 15% QCS-NPs added to cement powder) and a negative control cement was not significant[51]. There was good adherence of cells (a commercially-available human osteosarcoma cell line; HOS TE85) on specimens of PMMA-15QAMA cement after 1 wk, indicating cytocompatibility of the cement[52].

On osteoblast cells (MC 3TC), the difference in cytotoxicity between the Ag nanoparticles-tiopronin cement and the control cement (an approved plain ALBC brand) was not significant, regardless of the nanoparticles loading of the cement[54].

On osteoblast cells (MC-3T3), the difference in cytotoxicity between an experimental AFAMBC (contained Ag NPs-TIO) and a counterpart control cement (same composition but no Ag NPs-TIO) was not significant regardless of the duration of exposure to the cells[56]. On osteoblast cells (MC-3T3), the difference in cytotoxicity between an experimental AFAMBC (contained the Ag NPs-OA) and the control cement (plain PMMA cement) was not significant, regardless of the nanoparticles loading of the cement[57]. On Jukrat cells (T-lymphocyte), an experimental AFAMBC (10TPGDA-G1 cement) was significantly less cytotoxic than a counterpart cement (same composition but no TPGDA)[59]. Using a continuous mouse fibroblast cell line (L-929; BS-CL-56), an experimental AFAMBC (Ag-SBA2 cement) was not cytotoxic and the difference in the viability of the cells on the cement and that of its plain counterpart cement was not significant[60].

On human osteoblast (HOb) cells, none of three experimental AFAMBCs (ABC-0.3GO, ABC-15CS, and ABC-0.3GO-15CS cements) showed cytotoxicity because the cellular viability in the presence of extracts taken between 1 d and 7 d increased with time and was > 90%[64]. When HOb was directly seeded on the surfaces of the specimens of each of the AFAMBCs, enhanced surface colonization and proliferation at the early stages (1 and 4 d) was obtained, compared to the case when specimens of plain ABC (control cement) were used[64]. The trends found in this work were also observed when the culture times were 14 d and 21 d[66]. In other words, in each of the AFAMBCs, GO and CS exerted desirable effects on cell adhesion, proliferation, and deposition[66]. These results are consistent with GO increasing the hydrophilicity of the cement surface, thereby allowing easy anchoring of hydroxyl groups to the surface of the cell[86] and the low toxicity of CS and its excellent ability to promote osteoblastic cell growth[87]. After cement immersion for 1 wk, PMMA-NAC cement with NAC loading about 30% wt/vol was significantly less toxic to human fibroblasts, human osteoblasts, and chondrocytes than was the case with control cement (an approved plain cement brand)[67].

The viability of periodontal ligament cells after 7 d of culture on BC-BGII-0.4-AgNP cement was significantly less than on control cement (an approved plain cement brand), with the same trend found for BC-BG-MP-AgNp cement[68]. In general, the results showed that the cytocompatibility of the BC-modified cement is a complex phenomenon, with relevant factors including, but not limited to, the amount of MMA released by a cement, bioactivity of the cement, and amount of BG[68].

Summary of antimicrobial activity and cytotoxicity/cytocompatibility results

The results of the studies summarized in the preceding two sub-sections provide ample evidence that, against micro-organisms that have been commonly found in PJI cases, an AFAMBC has excellent antimicrobial activity and is not cytotoxic and, by extension, has excellent biocompatibility and bioadherence. The first two mentioned characteristics translate to achievement of antimicrobial efficacy being achieved with a very small amount of an AFAMBC. The last-mentioned characteristics indicate that an AFAMBC limits the adherence of planktonic-forming bacteria on an implant surface, which is the first step in biofilm formation[82,83].

Other cement properties

The number of studies in which other cement properties were determined varied widely, from fewer than 5 (example properties: tensile modulus, tensile strength, fracture toughness, and radiopacity) to more than 20 (property: compressive strength) (Table 1). Among these results, there is clear evidence that for an AFAMBC, its maximum polymerization temperature is lower (which is desirable, because it lowers the potential for thermal necrosis of periprosthetic tissue), setting time is longer (which is not desirable, because it increases TJA surgery time), compressive strength and flexural modulus are each comparable (both of which indicate that the load-bearing ability of an implant anchored using either an ALBC or an AFAMBC would be comparable) and cell viability is higher (which is desirable because it indicates increased cell survival in the presence of an AFAMBC), relative to corresponding values for the control cement (which, in all but two studies, was a plain cement, that is one in which there was no antimicrobial additive). However, the trend in each of the other cement properties determined is unclear.

CRITICAL APPRAISAL OF THE LITERATURE

With reference to clinically-relevant properties other than those discussed in the previous Section, the literature has a few attractive features but many shortcomings.

Attractive features

First, the surfaces of specimens of formulated AFAMBCs have been extensively characterized, using an assortment of methods, such as scanning electron microscopy without and with energy dispersion spectroscopy[52,55,58-60,62-66], transmission electron microscopy[54], x-ray diffraction[55], Fourier transform infrared spectroscopy[58,59,64,65], x-ray photoelectron spectroscopy[58], atomic force microscopy[57,64], and Raman spectroscopy[64]. One noteworthy result from these characterization studies is that distribution of the GO in a GO-based AFAMBC, obtained using Raman mapping, showed that GO is well distributed within the cement matrix[64], which, it was suggested, will enhance mechanical properties of the AFAMBC[64].

Second, the literature contains a large assortment of *in vitro* properties of the formulated ALAMBCs, ranging from release of the antimicrobial agent and its activity against *S. aureus* to cytocompatibility against human osteoblast cell line and water uptake. In this regard, the studies by Prokopovich *et al*[57] and by Russo *et al*[61] merit special mention because their studies illuminate subtle differences in the mechanical behavior of AFABCs and their control cement counterparts. In the Prokopovich *et al*[57] study, near-surface values of elastic modulus were determined using a quasi-static nanoindentation technique (atomic force microscopy). One key finding was that for specimens conditioned in PBS, at 37 °C, for 4 wk before the test, the elastic moduli at the surface and the bulk of a specimen were about the same, regardless of whether the cement was an AFAMBC or its control cement counterpart (no antibacterial agent added). Russo *et al*[61] performed small punch tests on miniature disk-shaped cement specimens. The load-displacement curves obtained displayed an initial linear zone, followed by a decrease in slope, achievement of a peak load (P_{peak}), and, finally, a drop in load until fracture occurs. The results showed that P_{peak} for an AFAMBC with low loading (0.25% Au NPs) was significantly higher than that of the control cement but, with an AFAMBC that has a higher loading (0.5% and 1.0% Au NPs), P_{peak} was lower than that of the control cement. These results are consistent with the postulate that with high Au NP loading, either NP clusters form, which act as weak features, and/or a different ductility exists between the cement matrix and the Au NPs, which acts to weaken the cement by creating stress risers and discontinuities at the matrix-Au NPs interface[61].

Third, in a few studies, an additive used to formulate an AFAMBC bestowed an additional benefit of bioactivity to the cement. Lack of bioactivity (and, hence, poor osseointegration) is one of the shortcomings of ALBCs[20]. The aforementioned additives were the powder of a bioactive glass, chitosan, and graphene oxide nanosheets[55,60,62-66]. After 7-28 d of immersion of specimens of bioactive glass powder-loaded cement in simulated body fluid, at 37 °C, there was evidence of agglomerates on the specimen surface that were rich in calcium and phosphorus (hydroxyapaptite (HaP)) (Ca/P ratio = approximately 0.9 to approximately 4.0)[60,62,63]. Among other actions, Ca and P ions combine with local ions to form a HaP-like layer on the surface of components of a TJA, which enhances the ability of the surface to bond with both soft and hard tissues[88]. Furthermore, these agglomerates exhibited the globular morphology that was typical of HaP grown on the surfaces of biomaterial specimens[60,62,63].

Shortcomings

First, with only two exceptions[51,53], an ALBC was not used as the control cement in the studies. This means that comments cannot be made on the potential for AFAMBCs to replace ALBCs in clinical practice.

Table 1 Key trends[a] in a selection of properties of antibiotic-free antimicrobial poly (methyl methacrylate) bone cements

Property	Loaded additive[b] in AFAMBC formulation	Magnitude of trend[c]	Ref.
Tensile modulus	15%CS; 15% CS NP; 15% QCS NP; 10% QAMA; 5% TPGDA G1.0	↓; approximately; approximately; approximately; approximately	Shi *et al*[51]; Shi *et al*[51]; Shi *et al*[51]; Deb *et al*[52]; Abid *et al*[59]
Tensile strength	10% QAMA; 5% TPGDA G1.0	approximately; approximately	Deb *et al*[52]; Abid *et al*[59]
Compressive modulus	0.5% Ag NP; 5% TPGDA G1.0; 0.25% Au NP	↓; ↓; approximately	Slane *et al*[58]; Abid *et al*[59]; Russo *et al*[61]
Compressive strength	10% QAMA; 1% Ag-TIOP NP; 30% SBAG; 7% PP NP; 0.05% Ag-OA NP; 0.5% Ag NP; 5% TPGDA G1.0; 0.25% Au NP; 10% Cu-SBA3 NP; 0.3% GO; 15% CS; 0.3% GO-15% CS	approximately; approximately; approximately; approximately; approximately; ↓; approximately; approximately; approximately; approximately; ↓; ↓	Deb *et al*[52]; Prokopovich *et al*[54]; Miola *et al*[55]; Perni *et al*[56]; Prokopovich *et al*[57]; Slane *et al*[58]; Abid *et al*[59]; Russo *et al*[61]; Miola *et al*[62]; Zapata *et al*[64,66]; Zapata *et al*[64,66]; Zapata *et al*[64,66]
Flexural modulus	CS; CS NP; QCS NP; 0.5% Ag NP; 20% Ag-SBA2 NP; 10-50% NAC; 0.3% GO; 15% CS; 0.3% GO-15% CS	↓; approximately; approximately; approximately; approximately; ↓; approximately; ↓; ↓	Shi *et al*[51]; Shi *et al*[51]; Shi *et al*[51]; Slane *et al*[58]; Verne *et al*[63]; Sukhonthamarn *et al*[67]; Zapata *et al*[66]; Zapata *et al*[66]; Zapata *et al*[66]
Flexural strength	0.5% Ag NP; 20% Ag-SBA2 NP; 10-50% NAC; 0.3% GO; 15% CS; 0.3% GO-15% CS	approximately; ↓; ↓; approximately; ↓; approximately	Slane *et al*[58]; Verne *et al*[63]; Sukhonthamarn *et al*[67]; Zapata *et al*[66]; Zapata *et al*[66]; Zapata *et al*[66]
Fracture toughness	0.5% Ag NP	approximately	Slane *et al*[58]
Storage modulus and loss; modulus vs. time profile	7% PP NP	approximately	Perni *et al*[56]
Elastic modulus vs. depth	0.05% Ag-OA NP	approximately	Prokopovich *et al*[57]
Maximum polymerization	10% QAMA; 0.3% GO; 15% CS; 0.3% GO-15% CS; BC-BG-MP-Ag NP	↓; approximately; approximately; ↓; approximately	Deb *et al*[52]; Zapata *et al*[66]; Zapata *et al*[66]; Zapata *et al*[66]; Wekwejt *et al*[68]
Setting time	10% QAMA; 0.3% GO; 15% CS; 0.3% GO-15% CS; BC-BG-MP-Ag NP	↑; approximately; ↑; ↑; approximately	Deb *et al*[52]; Zapata *et al*[66]; Zapata *et al*[66]; Zapata *et al*[66]; Wekwejt *et al*[68]
Water contact angle	5% TPGDA G1.0; 10% TPDGA G1.0; 0.1% GO; 0.2% GO; 0.3% GO; 0.5% GO; BC-BGII-0.4-Ag NP; BC-BG-MP-Ag NP	↓; ↓; ↓; ↓; ↓; ↓; ↑; ↑	Abid *et al*[59]; Abid *et al*[59]; Zapata *et al*[65]; Zapata *et al*[65]; Zapata *et al*[65]; Zapata *et al*[65]; Wekwejt *et al*[68]; Wekwejt *et al*[68]
Radiopacity	10% QAMA; 20% Ag-SBA2 NP	approximately; ↑	Deb *et al*[52]; Verné *et al*[63]
Residual monomer content	15% CS; 0.3% GO-15% CS; 0.1% GO; 0.2% GO; 0.3% GO	↑; ↑; approximately; approximately; ↑; ↑	Zapata *et al*[64]; Zapata *et al*[64]; Zapata *et al*[65]; Zapata *et al*[65]; Zapata *et al*[65]; Zapata *et al*[65]
Uptake of PBS, at 37 °C, *vs* test time profile	0.05% Ag-OA NP; 15% CS; 0.3% GO-15% CS	approximately; ↑; ↑	Prokopovich *et al*[57]; Zapata *et al*[64]; Zapata *et al*[64]

[a]Trend is ratio of mean value of property of antibiotic-free antimicrobial poly (methyl methacrylate) bone cement (AFAMBC) to that of a plain counterpart control cement (no antimicrobial additive), except in the study by Shi *et al*[51], in which the counterpart control cement was an approved antibiotic-loaded bone cement.

[b]CS: chitosan.

[c]:↓: Ratio is much less than 1 (mean property value for AFAMBC significantly lower than that for control cement); Approximately: Ratio is about 1 (difference in mean property values not significant); ↑: Ratio is much greater than 1 (mean property value for AFAMBC significantly higher than that for control cement). CS NP: Chitosan nanoparticles; QCS NP: Quaternary ammonium chitosan derivative nanoparticles; QAMA: Quaternary amine dimethacrylate; TPGDA G1.0: Generation-1 tripropylene glycol diacrylate dendrimer; Ag NP: Silver nanoparticles; Au NP: Gold nanoparticles; Ag-TIOP NP: Silver nanoparticles capped with tiopronin; SBAG: Particles of Na_2O-CaO-P_2O_5-B2O_3-Al_2O_3-Ag_2O glass; PP NP: Propylparaben nanoparticles; Ag-OA NP: Silver nanoparticles capped with oleic acid; Cu-SBA3 NP: Powder of copper-doped bioactive glass (48% SiO_2-26% Na_2O-22% CaO-3% P_2O_5-0.43% B_2O_3 -0.57% Al2O3) nanoparticles; GO: Graphene oxide nanosheets; Ag-SBA2 NP: Powder of silver-doped bioactive glass (SiO_2-Na_2O-CaO-P_2O_5- B_2O_3-Al_2O_3) (< 20 mm) nanoparticles; NAC: N-acetylcysteine; BC-BG-MP-Ag NP: A composite cement comprising bone cement, a Bioglass (70 mol%SiO_2/30 mol%CaO), and silver nanoparticles; BC-BGII-Ag NP: A composite cement comprising a Bioglass and silver nanoparticles.

Second, in some studies, the plain cement that was used as the control contained a constituent that is not part of the composition of any approved plain cement brand (or, indeed, any approved ALBC brand); specifically, 2-(diethylamino) ethyl acrylate (DEAEA), and 2-(diethylamino) ethyl methacrylate (DEAEM) in the liquid[64-66].

Third, there was only one study in which, for the preparation of the cement dough, the powder (with or without antimicrobial additive(s)) and the liquid (with or without antimicrobial additive) were mixed under vacuum[50]. In all the other studies, the mixing method was either manual[51,52,54-56,59,64-66,68] or a mechanical mixer was used[62]; or, else, the mixing method used was not explicitly stated[57,60,

61,63,66]. It is well known that mixing method exerts a significant influence on the properties of curing and cured properties of PMMA bone cement[20].

Fourth, in the evaluation of the antimicrobial activity of the cements, a clinical/hospital strain of microorganisms that are commonly found in PJI cases (such as *S. aureus* and *S. epidermidis*) was used in only two studies[50,68]. More importantly, in very few studies was a biofilm utilized in the evaluation of antimicrobial activity of the cements[50,62]. This situation is unfortunate given universal acknowledgement that PJI is a form of biofilm-associated implant-related musculoskeletal infection[34,82,83,89-91]; specifically, there is a "race to the top" in which the released antibiotic is inefficacious if a biofilm forms on the surface of the implant before the released antimicrobial agent gets there[92-94].

Fifth, in only a few studies was a human cell line used in the evaluation of cytotoxicity of the cements [50,52,64-66,68]. To give studies clinical relevance, use of a human cell line is preferred to use of cell lines from animals, such as mouse fibroblast.

Sixth, determination of release of the antimicrobial agent from an AFAMBC was conducted in fewer than 30% of studies [54-57,60,62]. Comparing and contrasting the details of this profile to that from an ALBC counterpart[25] would have provided information that may be useful in the design of future AFAMBCs.

Seventh, *in vivo* evaluation of AFAMBCs have been performed in only two studies. In the first, the cements compared were an approved plain bone cement brand (PBC), two experimental cement formulations (an approved plain bone cement brand loaded with 0.6 or 1.0 wt/wt% Nanosilver) (EAGC)), and an approved ALBC brand (antibiotic: tobramycin) (TOBC)[53]. Into the medullary canal of the right femur of female New Zealand White rabbits was injected a cement dough after contamination with a commercially-available *S. aureus* strain[53]. After 14 d, 100% incidence of *S. aureus* was found in all the rabbits in which either PBC or EAGC used, whereas, when TOBC was used, the incidence was 17% (2 out of the 12 rabbits). These results suggest that EAGC may not be suitable for use in revision TJA, where bacteria are already in the periprosthetic tissues[53]. In the second study[66], a dough of the cement (plain, ABC-0.3GO, ABC-15CS, or ABC-0.3GO-15CS cements) was injected into 5 mm-diameter defect created in the parietal bone of Wistar rats (age and mean mass = 8 mo and 0.37 kg, respectively)[66]. After 3 mo of implantation, higher amounts of osseointegration and biocompatibility were obtained with each of the experimental AFAMBC formulations (ABC-0.3GO, ABC-15CS, and ABC-0.3GO-15CS) compared to the corresponding values when the plain bone cement brand was used[66].

Eighth, the quality of the statistical analysis of results presented in the reports was variable. In four reports, there was no mention that statistical analysis was performed[50,59,60,63] even though, in one of them, it was stated that there was "no significant difference in quantitative cytotoxicity testing between the NanoSilver bone cement and the non-toxic control group"[50]. In the vast majority of studies, a parametric test of comparison (Student *t*-test, or ANOVA) was used for intergroup comparisons[51,52,54-57,61,62,64-66]. In only two reports (those by Slane *et al*[58] and by Wekwejt *et al*[68]**)** was the correct methodology used; that is, test for normality and homogeneity of variance of the datasets was conducted before a parametric test of comparison was applied.

FUTURE PROSPECTS

The shortcomings of the literature, as expounded on in the immediately preceding Section, together with other considerations, lead to identification of potential areas for future research. Four are presented here.

First, detailed studies should be performed on the influence of an AFAMBC on the ability of bacteria to form biofilm on surfaces of alloys currently used to fabricate parts of TJA, such as the stem of a total hip arthroplasty (for example, Ti-6Al-4V and Co-Cr-Mo[95], and those proposed for such use (for example, Ti-34Nb-2Ta-0.5O[96], Ti-12Nb-12Zr-12Sn[97], Ti-13Nb-13Zr[98], 40Ti-60Ta composite[99], Ti-39Nb-6Zr-0.45Al[100], and cold groove-rolled Ti-35Nb-3.75Sn[101]). Specifically, these studies should focus on determining the effectiveness of an AFAMBC vis a vis biofilms; that is, the extent to which an AFAMBC: (1) Inhibits microbial adhesion to the surface and colonization; (2) Interferes with the signal molecules that modulate biofilm formation (and associated increased antibiotic tolerance) (for example, quorum sensing inhibitors and/or quorum quenching agents[102-105]; and (3) Disaggregates the biofilm matrix[89,90,92,93,104-110].

Second, studies should be conducted to determine cement properties that have been the subject of only a few studies, such as radiopacity, fracture toughness, and liquid contact angle (q), or have not been determined, examples being fatigue performance (fatigue life and/or fatigue strength), fatigue crack growth/propagation rate, and creep. With regard to q, it should be determined using a biosimulating solution, such as PBS or simulated body fluid, rather than water, as has been the case[59,68]. Fatigue performance should be determined following the method stipulated in the relevant bone cement testing standard (ASTM F2118 or ISO 16402[111,112]).

Third, there are number of novel antimicrobial materials that should be investigated for their suitability to be formulated into a suitable form to be used as additives for an AFAMBC. Examples of materials that could be added to the powder of a plain cement are a quorum-sensing inhibitor drug

[113], Ti-doped ZnO[114], nano-GO nanosheets[115], selenium nanoparticles[116], Ag-nanoparticle-reduced GO nanocomposite[117], chitosan hybrid nanoparticles[118], a Cu cluster molecule[119], powder prepared from extract from a Tunisian lichen[120], Yb-doped ZnO nanoparticles[121], and an analog of PKZ18 (PKZ18-22), a molecule that has been shown to block growth of antibiotic-resistant *S. aureus* in biofilm[122]. Examples of materials that could be added to the liquid of a plain cement are benzothiazole or one of its derivatives[123,124] and a natural antimicrobial agent (such as extract of *Salvadora persica*, *Olea europaea*, and *Ficus carcia* leaves[125] or biosynthesized ZnO nanoflowers[126]).

Fourth, in all studies, the control cement must be an ALBC, preferably an approved ALBC brand. This will ensure that the results of property determinations will be used as a basis for making a recommendation on the clinical use of an AFAMBC instead of an ALBC.

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REFERENCES

1 **Dale H**, Fenstad AM, Hallan G, Havelin LI, Furnes O, Overgaard S, Pedersen AB, Kärrholm J, Garellick G, Pulkkinen P, Eskelinen A, Mäkelä K, Engesæter LB. Increasing risk of prosthetic joint infection after total hip arthroplasty. *Acta Orthop* 2012; **83**: 449-458 [PMID: 23083433 DOI: 10.3109/17453674.2012.733918]
2 **Kurtz SM**, Lau EC, Son MS, Chang ET, Zimmerli W, Parvizi J. Are We Winning or Losing the Battle With Periprosthetic Joint Infection: Trends in Periprosthetic Joint Infection and Mortality Risk for the Medicare Population. *J Arthroplasty* 2018; **33**: 3238-3245 [PMID: 29914821 DOI: 10.1016/j.arth.2018.05.042]
3 **Kapadia BH**, McElroy MJ, Issa K, Johnson AJ, Bozic KJ, Mont MA. The economic impact of periprosthetic infections following total knee arthroplasty at a specialized tertiary-care center. *J Arthroplasty* 2014; **29**: 929-932 [PMID: 24140271 DOI: 10.1016/j.arth.2013.09.017]
4 **Kühn KD**. Management of periprosthetic joint infection: A global perspective on diagnosis, treatment options, prevention strategies and their economic impact. Springer, Berlin
5 **Jämsen E**, Nevalainen P, Eskelinen A, Huotari K, Kalliovalkama J, Moilanen T. Obesity, diabetes, and preoperative hyperglycemia as predictors of periprosthetic joint infection: a single-center analysis of 7181 primary hip and knee replacements for osteoarthritis. *J Bone Joint Surg Am* 2012; **94**: e101 [PMID: 22810408 DOI: 10.2106/JBJS.J.01935]
6 **Meehan JP**, Danielsen B, Kim SH, Jamali AA, White RH. Younger age is associated with a higher risk of early periprosthetic joint infection and aseptic mechanical failure after total knee arthroplasty. *J Bone Joint Surg Am* 2014; **96**: 529-535 [PMID: 24695918 DOI: 10.2106/JBJS.M.00545]
7 **Otto-Lambertz C**, Yagdiran A, Wallscheid F, Eysel P, Jung N. Periprosthetic Infection in Joint Replacement. *Dtsch Arztebl Int* 2017; **114**: 347-353 [PMID: 28610654 DOI: 10.3238/arztebl.2017.0347]
8 **Tubb CC**, Polkowksi GG, Krause B. Diagnosis and Prevention of Periprosthetic Joint Infections. *J Am Acad Orthop Surg* 2020; **28**: e340-e348 [PMID: 31972719 DOI: 10.5435/JAAOS-D-19-00405]
9 **Love C**, Marwin SE, Tomas MB, Krauss ES, Tronco GG, Bhargava KK, Nichols KJ, Palestro CJ. Diagnosing infection in the failed joint replacement: a comparison of coincidence detection 18F-FDG and 111In-labeled leukocyte/99mTc-sulfur colloid marrow imaging. *J Nucl Med* 2004; **45**: 1864-1871 [PMID: 15534056]

10 **McNally M**, Sousa R, Wouthuyzen-Bakker M, Chen AF, Soriano A, Vogely HC, Clauss M, Higuera CA, Trebše R. The EBJIS definition of periprosthetic joint infection. *Bone Joint J* 2021; **103-B**: 18-25 [PMID: 33380199 DOI: 10.1302/0301-620X.103B1.BJJ-2020-1381.R1]

11 **Lee YS**, Lee YK, Han SB, Nam CH, Parvizi J, Koo KH. Natural progress of D-dimer following total joint arthroplasty: a baseline for the diagnosis of the early postoperative infection. *J Orthop Surg Res* 2018; **13**: 36 [PMID: 29439725 DOI: 10.1186/s13018-018-0730-4]

12 **Tirumala V**, Klemt C, Xiong L, Chen W, van den Kieboom J, Kwon YM. Diagnostic Utility of Platelet Count/Lymphocyte Count Ratio and Platelet Count/Mean Platelet Volume Ratio in Periprosthetic Joint Infection Following Total Knee Arthroplasty. *J Arthroplasty* 2021; **36**: 291-297 [PMID: 32773272 DOI: 10.1016/j.arth.2020.07.038]

13 **Li R**, Li X, Ni M, Zheng QY, Zhang GQ, Chen JY. Anatomic Landmark-Guided Hip Aspiration in the Diagnosis of Periprosthetic Joint Infection. *Orthopedics* 2021; **44**: e85-e90 [PMID: 33089335 DOI: 10.3928/01477447-20201007-04]

14 **Vaz K**, Scarborough M, Bottomley N, Kendrick B, Taylor A, Price A, Alvand A, Jackson W. Debridement, antibiotics and implant retention (DAIR) for the management of knee prosthetic joint infection. *Knee* 2020; **27**: 2013-2015 [PMID: 32950374 DOI: 10.1016/j.knee.2020.08.011]

15 **Zhu MF**, Kim K, Cavadino A, Coleman B, Munro JT, Young SW. Success Rates of Debridement, Antibiotics, and Implant Retention in 230 Infected Total Knee Arthroplasties: Implications for Classification of Periprosthetic Joint Infection. *J Arthroplasty* 2021; **36**: 305-310.e1 [PMID: 32868114 DOI: 10.1016/j.arth.2020.07.081]

16 **Aggarwal VK**, Rasouli MR, Parvizi J. Periprosthetic joint infection: Current concept. *Indian J Orthop* 2013; **47**: 10-17 [PMID: 23531512]

17 **Osmon DR**, Berbari EF, Berendt AR, Lew D, Zimmerli W, Steckelberg JM, Rao N, Hanssen A, Wilson WR; Infectious Diseases Society of America. Executive summary: diagnosis and management of prosthetic joint infection: clinical practice guidelines by the Infectious Diseases Society of America. *Clin Infect Dis* 2013; **56**: 1-10 [PMID: 23230301 DOI: 10.1093/cid/cis966]

18 **Kunutsor SK**, Whitehouse MR, Blom AW, Board T, Kay P, Wroblewski BM, Zeller V, Chen SY, Hsieh PH, Masri BA, Herman A, Jenny JY, Schwarzkopf R, Whittaker JP, Burston B, Huang R, Restrepo C, Parvizi J, Rudelli S, Honda E, Uip DE, Bori G, Muñoz-Mahamud E, Darley E, Ribera A, Cañas E, Cabo J, Cordero-Ampuero J, Redó MLS, Strange S, Lenguerrand E, Gooberman-Hill R, Webb J, MacGowan A, Dieppe P, Wilson M, Beswick AD; Global Infection Orthopaedic Management Collaboration. One- and two-stage surgical revision of peri-prosthetic joint infection of the hip: a pooled individual participant data analysis of 44 cohort studies. *Eur J Epidemiol* 2018; **33**: 933-946 [PMID: 29623671 DOI: 10.1007/s10654-018-0377-9]

19 **Kildow BJ**, Della-Valle CJ, Springer BD. Single vs 2-Stage Revision for the Treatment of Periprosthetic Joint Infection. *J Arthroplasty* 2020; **35**: S24-S30 [PMID: 32046827 DOI: 10.1016/j.arth.2019.10.051]

20 **Lewis G**. Properties of antibiotic-loaded acrylic bone cements for use in cemented arthroplasties: a state-of-the-art review. *J Biomed Mater Res B Appl Biomater* 2009; **89**: 558-574 [PMID: 18823020 DOI: 10.1002/jbm.b.31220]

21 **Kühn KD**, Höntzsch D. Augmentation with PMMA cement. *Unfallchirurg* 2015; **118**: 737-748 [PMID: 26315391 DOI: 10.1007/s00113-015-0059-y]

22 **Villa JM**, Pannu TS, Theeb I, Buttaro MA, Oñativia JI, Carbo L, Rienzi DH, Fregeiro JI, Kornilov NN, Bozhkova SA, Sandiford NA, Piuzzi NS, Higuera CA, Kendoff DO. International Organism Profile of Periprosthetic Total Hip and Knee Infections. *J Arthroplasty* 2021; **36**: 274-278 [PMID: 32828620 DOI: 10.1016/j.arth.2020.07.020]

23 **Lewis G**, Brooks JL, Courtney HS, Li Y, Haggard WO. An Approach for determining antibiotic loading for a physician-directed antibiotic-loaded PMMA bone cement formulation. *Clin Orthop Relat Res* 2010; **468**: 2092-2100 [PMID: 20195806 DOI: 10.1007/s11999-010-1281-0]

24 **Lewis G**. Antibiotic release enhancement methods for antibiotic-loaded PMMA bone cement for periprosthetic joint infection prophylaxis in cemented total joint arthroplasties: current status and future prospects. *Journal of Materials Science Research and Reviews* 2020; **6**: 1-21

25 **Mensah LM**, Love BJ. A meta-analysis of bone cement mediated antibiotic release: Overkill, but a viable approach to eradicate osteomyelitis and other infections tied to open procedures. *Mater Sci Eng C Mater Biol Appl* 2021; **123**: 111999 [PMID: 33812619 DOI: 10.1016/j.msec.2021.111999]

26 **Cummins JS**, Tomek IM, Kantor SR, Furnes O, Engesaeter LB, Finlayson SR. Cost-effectiveness of antibiotic-impregnated bone cement used in primary total hip arthroplasty. *J Bone Joint Surg Am* 2009; **91**: 634-641 [PMID: 19255224 DOI: 10.2106/JBJS.G.01029]

27 **Qadir R**, Sidhu S, Ochsner JL, Meyer MS, Chimento GF. Risk stratified usage of antibiotic-loaded bone cement for primary total knee arthroplasty: short term infection outcomes with a standardized cement protocol. *J Arthroplasty* 2014; **29**: 1622-1624 [PMID: 24703363 DOI: 10.1016/j.arth.2014.02.032]

28 **Yi Z**, Bin S, Jing Y, Zongke Z, Pengde K, Fuxing P. No decreased infection rate when using antibiotic-impregnated cement in primary total joint arthroplasty. *Orthopedics* 2014; **37**: 839-845 [PMID: 25437076 DOI: 10.3928/01477447-20141124-07]

29 **Sanz-Ruiz P**, Matas-Diez JA, Sanchez-Somolinos M, Villanueva-Martinez M, Vaquero-Martín J. Is the Commercial Antibiotic-Loaded Bone Cement Useful in Prophylaxis and Cost Saving After Knee and Hip Joint Arthroplasty? *J Arthroplasty* 2017; **32**: 1095-1099 [PMID: 27919578 DOI: 10.1016/j.arth.2016.11.012]

30 **King JD**, Hamilton DH, Jacobs CA, Duncan ST. The Hidden Cost of Commercial Antibiotic-Loaded Bone Cement: A Systematic Review of Clinical Results and Cost Implications Following Total Knee Arthroplasty. *J Arthroplasty* 2018; **33**: 3789-3792 [PMID: 30217400 DOI: 10.1016/j.arth.2018.08.009]

31 **Bendich I**, Zhang N, Barry JJ, Ward DT, Whooley MA, Kuo AC. Antibiotic-Laden Bone Cement Use and Revision Risk After Primary Total Knee Arthroplasty in U.S. Veterans. *J Bone Joint Surg Am* 2020; **102**: 1939-1947 [PMID: 32890041 DOI: 10.2106/JBJS.20.00102]

32 **Namba RS**, Prentice HA, Paxton EW, Hinman AD, Kelly MP. Commercially Prepared Antibiotic-Loaded Bone Cement and Infection Risk Following Cemented Primary Total Knee Arthroplasty. *J Bone Joint Surg Am* 2020; **102**: 1930-1938

[PMID: 32826555 DOI: 10.2106/JBJS.19.01440]
33 **Pellegrini AV**, Suardi V. Antibiotics and cement: what I need to know? *Hip Int* 2020; **30**: 48-53 [PMID: 32290707 DOI: 10.1177/1120700020915463]
34 **Schwarz EM**, McLaren AC, Sculco TP, Brause B, Bostrom M, Kates SL, Parvizi J, Alt V, Arnold WV, Carli A, Chen AF, Choe H, Coraça-Huber DC, Cross M, Ghert M, Hickok N, Jennings JA, Joshi M, Metsemakers WJ, Ninomiya M, Nishitani K, Oh I, Padgett D, Ricciardi B, Saeed K, Sendi P, Springer B, Stoodley P, Wenke JC; Hospital for Special Surgery 2019 Biofilm Symposium Workgroup. Adjuvant antibiotic-loaded bone cement: Concerns with current use and research to make it work. *J Orthop Res* 2021; **39**: 227-239 [PMID: 31997412 DOI: 10.1002/jor.24616]
35 **Sebastian S**, Liu Y, Christensen R, Raina DB, Tägil M, Lidgren L. Antibiotic containing bone cement in prevention of hip and knee prosthetic joint infections: A systematic review and meta-analysis. *J Orthop Translat* 2020; **23**: 53-60 [PMID: 32489860 DOI: 10.1016/j.jot.2020.04.005]
36 **Farhan-Alanie MM**, Burnand HG, Whitehouse MR. The effect of antibiotic-loaded bone cement on risk of revision following hip and knee arthroplasty. *Bone Joint J* 2021; **103-B**: 7-15 [PMID: 33380204 DOI: 10.1302/0301-620X.103B1.BJJ-2020-0391.R1]
37 **Jiranek WA**, Hanssen AD, Greenwald AS. Antibiotic-loaded bone cement for infection prophylaxis in total joint replacement. *J Bone Joint Surg Am* 2006; **88**: 2487-2500 [PMID: 17079409 DOI: 10.2106/JBJS.E.01126]
38 **Wilairatana V**, Sinlapavilawan P, Honsawek S, Limpaphayom N. Alteration of inflammatory cytokine production in primary total knee arthroplasty using antibiotic-loaded bone cement. *J Orthop Traumatol* 2017; **18**: 51-57 [PMID: 27770338 DOI: 10.1007/s10195-016-0432-9]
39 **Hansen EN**, Adeli B, Kenyon R, Parvizi J. Routine use of antibiotic laden bone cement for primary total knee arthroplasty: impact on infecting microbial patterns and resistance profiles. *J Arthroplasty* 2014; **29**: 1123-1127 [PMID: 24418770 DOI: 10.1016/j.arth.2013.12.004]
40 **Sinclair KD**, Pham TX, Farnsworth RW, Williams DL, Loc-Carrillo C, Horne LA, Ingebretsen SH, Bloebaum RD. Development of a broad spectrum polymer-released antimicrobial coating for the prevention of resistant strain bacterial infections. *J Biomed Mater Res A* 2012; **100**: 2732-2738 [PMID: 22623404 DOI: 10.1002/jbm.a.34209]
41 **Jennings JA**, Carpenter DP, Troxel KS, Beenken KE, Smeltzer MS, Courtney HS, Haggard WO. Novel Antibiotic-loaded Point-of-care Implant Coating Inhibits Biofilm. *Clin Orthop Relat Res* 2015; **473**: 2270-2282 [PMID: 25604874 DOI: 10.1007/s11999-014-4130-8]
42 **Ozcelik B**, Ho KKK, Glattauer V, Willcox M, Kumar N, Thissen H. Poly(ethylene glycol)-Based Coatings Combining Low-Biofouling and Quorum-Sensing Inhibiting Properties to Reduce Bacterial Colonization. *ACS Biomater Sci Eng* 2017; **3**: 78-87 [PMID: 33429684 DOI: 10.1021/acsbiomaterials.6b00579]
43 **Tobin EJ**. Recent coating developments for combination devices in orthopedic and dental applications: A literature review. *Adv Drug Deliv Rev* 2017; **112**: 88-100 [PMID: 28159606 DOI: 10.1016/j.addr.2017.01.007]
44 **Han X**, Ji X, Zhao M, Li D. Mg/Ag ratios induced in vitro cell adhesion and preliminary antibacterial properties of TiN on medical Ti-6Al-4V alloy by Mg and Ag implantation. *Surf Coat Technol* 2020; **397**: 126020 [DOI: 10.1016/j.surfcoat.2020.126020]
45 **Kharat Z**, Sadri M, Kabiri M. Herbal extract loaded chitosan/PEO nanocomposites as antibacterial coatings of orthopaedic implants. *Fibers Polym* 2021; **22**: 989-999 [DOI: 10.1007/s12221-021-0490-3]
46 **Sivakumar B**, Vijaysegaran P, Chaudhuri A, Crawford S, Ottley M. Daptomycin resistance in prosthetic joint infections. *Orthopedics* 2012; **35**: e603-e606 [PMID: 22495870 DOI: 10.3928/01477447-20120327-42]
47 **Zborníková E**, Gallo J, Večeřová R, Bogdanová K, Kolář M, Vítovská D, Do Pham DD, Pačes O, Mojr V, Šanderová H, Ulrichová J, Galandáková A, Čadek D, Hrdlička Z, Krásný L, Rejman D. Evaluation of Second-Generation Lipophosphonoxins as Antimicrobial Additives in Bone Cement. *ACS Omega* 2020; **5**: 3165-3171 [PMID: 32118132 DOI: 10.1021/acsomega.9b03072]
48 **Suhardi VJ**, Bichara DA, Kwok S, Freiberg AA, Rubash H, Malchau H, Yun SH, Muratoglu OK, Oral E. A Fully Functional Drug-Eluting Joint Implant. *Nat Biomed Eng* 2017; **1** [PMID: 29354321 DOI: 10.1038/s41551-017-0080]
49 **Jenkins J**, Nobbs AH, Verkade P, Su B. Characterisation of bactericidal titanium surfaces using electron microscopy. *Microscopy Analysis* 2018; **32**: 15-19
50 **Alt V**, Bechert T, Steinrücke P, Wagener M, Seidel P, Dingeldein E, Domann E, Schnettler R. An in vitro assessment of the antibacterial properties and cytotoxicity of nanoparticulate silver bone cement. *Biomaterials* 2004; **25**: 4383-4391 [PMID: 15046929 DOI: 10.1016/j.biomaterials.2003.10.078]
51 **Shi Z**, Neoh KG, Kang ET, Wang W. Antibacterial and mechanical properties of bone cement impregnated with chitosan nanoparticles. *Biomaterials* 2006; **27**: 2440-2449 [PMID: 16338001 DOI: 10.1016/j.biomaterials.2005.11.036]
52 **Deb S**, Doiron R, Disilvio L, Punyani S, Singh H. PMMA bone cement containing a quaternary amine comonomer with potential antibacterial properties. *J Biomed Mater Res B Appl Biomater* 2008; **85**: 130-139 [PMID: 17806110 DOI: 10.1002/jbm.b.30925]
53 **Moojen DJF**, Vogely HC, Fleer A, Verbout AJ, Castelein RM, Dhert WJ. No efficacy of silver bone cement in the prevention of methicillin- sensitive Staphylococcal infections in a rabbit contaminated implant bed model. *J Orthop Res* 2009; **27**: 1002-1007 [PMID: 19165770 DOI: 10.1002/jor.20854]
54 **Prokopovich P**, Leech R, Carmalt CJ, Parkin IP, Perni S. A novel bone cement impregnated with silver-tiopronin nanoparticles: its antimicrobial, cytotoxic, and mechanical properties. *Int J Nanomedicine* 2013; **8**: 2227-2237 [PMID: 23818779 DOI: 10.2147/IJN.S42822]
55 **Miola M**, Bruno M, Maina G, Fucale G, Lucchetta G, Vernè E. Antibiotic-free composite bone cements with antibacterial and bioactive properties. A preliminary study. *Mater Sci Eng C Mater Biol Appl* 2014; **43**: 65-75 [PMID: 25175189 DOI: 10.1016/j.msec.2014.06.026]
56 **Perni S**, Thenault V, Abdo P, Margulis K, Magdassi S, Prokopovich P. Antimicrobial activity of bone cements embedded with organic nanoparticles. *Int J Nanomedicine* 2015; **10**: 6317-6329 [PMID: 26487803 DOI: 10.2147/IJN.S86440]
57 **Prokopovich P**, Köbrick M, Brousseau E, Perni S. Potent antimicrobial activity of bone cement encapsulating silver nanoparticles capped with oleic acid. *J Biomed Mater Res B Appl Biomater* 2015; **103**: 273-281 [PMID: 24819471 DOI:

10.1002/jbm.b.33196]
58 **Slane J**, Vivanco J, Rose W, Ploeg HL, Squire M. Mechanical, material, and antimicrobial properties of acrylic bone cement impregnated with silver nanoparticles. *Mater Sci Eng C Mater Biol Appl* 2015; **48**: 188-196 [PMID: 25579913 DOI: 10.1016/j.msec.2014.11.068]
59 **Abid CK**, Jain S, Jackeray R, Chattopadhyay S, Singh H. Formulation and characterization of antimicrobial quaternary ammonium dendrimer in poly(methyl methcarylate) bone cement. *J Biomed Mater Res B Appl Biomater* 2017; **105**: 521-530 [PMID: 26584408 DOI: 10.1002/jbm.b.33553]
60 **Miola M**, Fucale G, Maina G, Verné E. Composites bone cements with different viscosities loaded with a bioactive and antibacterial glass. *J Mater Sci* 2017; **52**: 5133-5146 [DOI: 10.1007/s10853-017-0750-1]
61 **Russo T**, Gloria A, De Santis R, D'Amora U, Balato G, Vollaro A, Oliviero O, Improta G, Triassi M, Ambrosio L. Preliminary focus on the mechanical and antibacterial activity of a PMMA-based bone cement loaded with gold nanoparticles. *Bioact Mater* 2017; **2**: 156-161 [PMID: 29744425 DOI: 10.1016/j.bioactmat.2017.05.002]
62 **Miola M**, Cochis A, Kumar A, Arciola CR, Rimondini L, Verné E. Copper-Doped Bioactive Glass as Filler for PMMA-Based Bone Cements: Morphological, Mechanical, Reactivity, and Preliminary Antibacterial Characterization. *Materials (Basel)* 2018; **11** [PMID: 29882763 DOI: 10.3390/ma11060961]
63 **Verné E**, Foroni F, Lucchetta G, Miola M. Antibacterial and bioactive composite bone cements. *Curr Mater Sci* 2020; **12**: 144-153 [DOI: 10.2174/1874464812666190819143740]
64 **Valencia Zapata ME**, Mina Hernandez JH, Grande Tovar CD, Valencia Llano CH, Diaz Escobar JA, Vázquez-Lasa B, San Román J, Rojo L. Novel Bioactive and Antibacterial Acrylic Bone Cement Nanocomposites Modified with Graphene Oxide and Chitosan. *Int J Mol Sci* 2019; **20** [PMID: 31208091 DOI: 10.3390/ijms20122938]
65 **Zapata MEV**, Ruiz Rojas LM, Mina Hernández JH, Delgado-Ospina J, Tovar CDG. Acrylic Bone Cements Modified with Graphene Oxide: Mechanical, Physical, and Antibacterial Properties. *Polymers (Basel)* 2020; **12** [PMID: 32784747 DOI: 10.3390/polym12081773]
66 **Zapata MEV**, Hernandez JHM, Grande Tovar CD, Llano CHV, Vázquez-Lasa B, San Román J, Rojo L. Osseointegration of antimicrobial acrylic bone cements modified with graphene oxide and chitosan. *Appl Sci* 2020; **10**: 6528 [DOI: 10.3390/app10186528]
67 **Sukhonthamarn K**, Cho J, Chisari E, Goswami K, Arnold WV, Parvizi J. N-acetylcysteine use as an adjuvant to bone cement to fight periprosthetic joint infections: A preliminary in vitro efficacy and biocompatibility study. *J Orthop Res* 2021; **39**: 356-364 [PMID: 33179364 DOI: 10.1002/jor.24910]
68 **Wekwejt M**, Chen S, Kaczmarek-Szczepańska B, Nadolska M, Łukowicz K, Pałubicka A, Michno A, Osyczka AM, Michálek M, Zieliński A. Nanosilver-loaded PMMA bone cement doped with different bioactive glasses - evaluation of cytocompatibility, antibacterial activity, and mechanical properties. *Biomater Sci* 2021; **9**: 3112-3126 [PMID: 33704333 DOI: 10.1039/d1bm00079a]
69 **Bistolfi A**, Ferracini R, Albanese C, Vernè E, Miola M. PMMA-Based Bone Cements and the Problem of Joint Arthroplasty Infections: Status and New Perspectives. *Materials (Basel)* 2019; **12** [PMID: 31810305 DOI: 10.3390/ma12234002]
70 **Tan HL**, Ao HY, Ma R, Lin WT, Tang TT. In vivo effect of quaternized chitosan-loaded polymethylmethacrylate bone cement on methicillin-resistant Staphylococcus epidermidis infection of the tibial metaphysis in a rabbit model. *Antimicrob Agents Chemother* 2014; **58**: 6016-6023 [PMID: 25070107 DOI: 10.1128/AAC.03489-14]
71 **Wang M**, Sa Y, Li P, Guo Y, Du Y, Deng H, Jiang T, Wang Y. A versatile and injectable poly(methyl methacrylate) cement functionalized with quaternized chitosan-glycerophosphate/nanosized hydroxyapatite hydrogels. *Mater Sci Eng C Mater Biol Appl* 2018; **90**: 264-272 [PMID: 29853090 DOI: 10.1016/j.msec.2018.04.075]
72 **Wekwejt M**, Michno A, Truchan K, Pałubicka A, Świeczko-Żurek B, Osyczka AM, Zieliński A. Antibacterial Activity and Cytocompatibility of Bone Cement Enriched with Antibiotic, Nanosilver, and Nanocopper for Bone Regeneration. *Nanomaterials (Basel)* 2019; **9** [PMID: 31382557 DOI: 10.3390/nano9081114]
73 **Lin X**, Ge J, Wei D, Liu C, Tan L, Yang H, Yang K, Zhou H, Li B, Luo ZP, Yang L. Surface degradation-enabled osseointegrative, angiogenic and antiinfective properties of magnesium-modified acrylic bone cement. *J Orthop Translat* 2019; **17**: 121-132 [PMID: 31194022 DOI: 10.1016/j.jot.2019.04.007]
74 **Sathya S**, Murthy PS, Devi VG, Das A, Anandkumar B, Sathyaseelan VS, Doble M, Venugopalan VP. Antibacterial and cytotoxic assessment of poly (methyl methacrylate) based hybrid nanocomposites. *Mater Sci Eng C Mater Biol Appl* 2019; **100**: 886-896 [PMID: 30948126 DOI: 10.1016/j.msec.2019.03.053]
75 **Huh MW**, Kang I-K, Lee DH, Kim WS, Lee SP, Min KE, Seo KH. Surface characterization and antibacterial activity of chitosan-grafted poly(ethylene terephthalate) prepared by plasma glow discharge. *J Appl Polym Sci* 2001; **81**: 2769-2778 [DOI: 10.1002/app.1723]
76 **Marambio-Jones C**, Hoek EMV. A review of the antibacterial effects of silver nanomaterials and potential implications for human health and the environment. *J Nanoparticle Res* 2010; **12**: 1531-1551 [DOI: 10.1007/s11051-010-9900-y]
77 **Sadoon AA**, Khadka P, Freeland J, Gundampati RK, Manso RH, Ruiz M, Krishnamurthi VR, Thallapuranam SK, Chen J, Wang Y. Silver Ions Caused Faster Diffusive Dynamics of Histone-Like Nucleoid-Structuring Proteins in Live Bacteria. *Appl Environ Microbiol* 2020; **86** [PMID: 31953329 DOI: 10.1128/AEM.02479-19]
78 **Pollini M**, Paladini F, Catalano M, Taurino A, Licciulli A, Maffezzoli A, Sannino A. Antibacterial coatings on haemodialysis catheters by photochemical deposition of silver nanoparticles. *J Mater Sci Mater Med* 2011; **22**: 2005-2012 [PMID: 21691829 DOI: 10.1007/s10856-011-4380-x]
79 **Yoshida Y**, Furuta S, Niki E. Effects of metal chelating agents on the oxidation of lipids induced by copper and iron. *Biochim Biophys Acta* 1993; **1210**: 81-88 [PMID: 8257723 DOI: 10.1016/0005-2760(93)90052-b]
80 **Allan I**, Newman H, Wilson M. Antibacterial activity of particulate bioglass against supra- and subgingival bacteria. *Biomaterials* 2001; **22**: 1683-1687 [PMID: 11374470 DOI: 10.1016/s0142-9612(00)00330-6]
81 **Hu S**, Chang J, Liu M, Ning C. Study on antibacterial effect of 45S5 Bioglass. *J Mater Sci Mater Med* 2009; **20**: 281-286 [PMID: 18763024 DOI: 10.1007/s10856-008-3564-5]

82 **Samal S**, Das PK. Microbial biofilms: pathogenicity and treatment strategies. *Pharmatutor* 2018; **6**: 16-22 [DOI: 10.29161/pt.v6.i1.2018.16]
83 **Markowska K**, Grudniak AM, Wolska KI. Silver nanoparticles as an alternative strategy against bacterial biofilms. *Acta Biochim Pol* 2013; **60**: 523-530 [PMID: 24432308 DOI: 10.18388/abp.2013_2016]
84 **Mangadlao JD**, De Leon AC, Felipe MJ, Cao P, Advincula PA, Advincula RC. Grafted carbazole-assisted electrodeposition of graphene oxide. *ACS Appl Mater Interfaces* 2015; **7**: 10266-10274 [PMID: 25928838 DOI: 10.1021/acsami.5b00857]
85 **Zheng K**, Taccardi N, Beltrán AM, Sui B, Zhou T, Reddy Marthala VR, Hartmann M, Boccaccini AR. Timing of calcium nitrate addition affects morphology, dispersity and composition of bioactive glass nanoparticles. *RSC Adv* 2016; **6**: 95101-95111 [DOI: 10.1039/c6ra05548f]
86 **Pahlevanzadeh F**, Bakhsheshi-Rad HR, Hamzah E. In-vitro biocompatibility, bioactivity, and mechanical strength of PMMA-PCL polymer containing fluorapatite and graphene oxide bone cements. *J Mech Behav Biomed Mater* 2018; **82**: 257-267 [PMID: 29627737 DOI: 10.1016/j.jmbbm.2018.03.016]
87 **Hamilton V**, Yuan Y, Rigney DA. Bone cell attachment and growth on well-characterized chitosan films. *Polym Int* 2007; **56**: 641-647 [DOI: 10.1002/pi.2181]
88 **Soares P**, Dias-Netipanyj MF, Elifio-Esposito S, Leszczak V, Popat K. Effects of calcium and phosphorus incorporation on the properties and bioactivity of TiO_2 nanotubes. *J Biomater Appl* 2018; **33**: 410-421 [PMID: 30223734 DOI: 10.1177/0885328218797549]
89 **Rowson C**, Townsend R. Biofilms: prevention and treatment. *Br J Hosp Med (Lond)* 2016; **77**: 699-703 [PMID: 27937018 DOI: 10.12968/hmed.2016.77.12.699]
90 **Arciola CR**, Campoccia D, Montanaro L. Implant infections: adhesion, biofilm formation and immune evasion. *Nat Rev Microbiol* 2018; **16**: 397-409 [PMID: 29720707 DOI: 10.1038/s41579-018-0019-y]
91 **Scheper H**, Wubbolts JM, Verhagen JAM, de Visser AW, van der Wal RJP, Visser LG, de Boer MGJ, Nibbering PH. SAAP-148 Eradicates MRSA Persisters Within Mature Biofilm Models Simulating Prosthetic Joint Infection. *Front Microbiol* 2021; **12**: 625952 [PMID: 33584628 DOI: 10.3389/fmicb.2021.625952]
92 **Römling U**, Balsalobre C. Biofilm infections, their resilience to therapy and innovative treatment strategies. *J Intern Med* 2012; **272**: 541-561 [PMID: 23025745 DOI: 10.1111/joim.12004]
93 **Subramani R**, Jayaprakashvel M. Bacterial quorum sensing: biofilm formation, survival behaviour and antibiotic resistance. In: Bramhachari P. Implication of quorum sensing and biofilm formation in medicine, agriculture and food industry. Springer Singapore, 21-37 [DOI: 10.1007/978-981-32-9409-7_3]
94 **Aguilera-Correa J-J**, Esteban J, Romero-Garcia D. Mechanics of biofilm formation in clinically used biomaterials, In: Mitra A. Microbial biofilms: current research and practical implications. Caister Academic Press, Norfolk, UK
95 **Ratner BD**, Hoffman AS, Schoen FJ, Lemons JE. Biomaterials science: an introduction to materials in medicine, 2nd edition. Elsevier Academic Press, San Diego, CA, USA
96 **Acharya S**, Panicker AG, Gopal V, Dabas SS, Manivasagam G, Suwas S, Chatterjee K. Surface mechanical attrition treatment of low modulus Ti-Nb-Ta-O alloy for orthopedic applications. *Mater Sci Eng C Mater Biol Appl* 2020; **110**: 110729 [PMID: 32204039 DOI: 10.1016/j.msec.2020.110729]
97 **Wu CT**, Chang HZ, Wu CY, Chen SW, Huang SY, Huang M, Pan YT, Bradbury P, Chou J, Yen HW. Machine learning recommends affordable new Ti alloy with bone-like modulus. *Mater Today* 2020; **34**: 41-50 [DOI: 10.1016/j.mattod.2019.08.008]
98 **Hoppe V**, Szymczyk-Ziółkowska P, Rusińska M, Dybała B, Poradowski D, Janeczek M. Assessment of Mechanical, Chemical, and Biological Properties of Ti-Nb-Zr Alloy for Medical Applications. *Materials (Basel)* 2020; **14** [PMID: 33396757 DOI: 10.3390/ma14010126]
99 **Huang Q**, Xu S, Ouyang Z, Yang Y, Liu Y. Multi-scale nacre-inspired lamella-structured Ti-Ta composites with high strength and low modulus for load-bearing orthopedic and dental applications. *Mater Sci Eng C Mater Biol Appl* 2021; **118**: 111458 [PMID: 33255043 DOI: 10.1016/j.msec.2020.111458]
100 **Hwang YJ**, Choi YS, Hwang YH, Cho HW, Lee DG. Biocompatibility and Biological Corrosion Resistance of Ti-39Nb-6Zr-0.45Al Implant Alloy. *J Funct Biomater* 2020; **12** [PMID: 33383616 DOI: 10.3390/jfb12010002]
101 **Hanada S**, Masahashi N, Semboshi S, Jung TK. Low Young's modulus of cold groove-rolled β Ti-Nb-Sn alloys for orthopedic applications. *Mater Sci Eng A* 2021; **802**: 140645 [DOI: 10.1016/j.msea.2020.140645]
102 **Raina S**, De Vizio D, Odell M, Clements M, Vanhulle S, Keshavarz T. Microbial quorum sensing: a tool or a target for antimicrobial therapy? *Biotechnol Appl Biochem* 2009; **54**: 65-84 [PMID: 19594442 DOI: 10.1042/BA20090072]
103 **Kalia VC**, Wood TK, Kumar P. Evolution of resistance to quorum-sensing inhibitors. *Microb Ecol* 2014; **68**: 13-23 [PMID: 24194099 DOI: 10.1007/s00248-013-]
104 **Gajdács M**, Spengler G. The Role of Drug Repurposing in the Development of Novel Antimicrobial Drugs: Non-Antibiotic Pharmacological Agents as Quorum Sensing-Inhibitors. *Antibiotics (Basel)* 2019; **8** [PMID: 31861228 DOI: 10.3390/antibiotics8040270]
105 **Singh BP**, Ghosh S, Chauhan A. Development, dynamics and control of antimicrobial-resistant bacterial biofilms: a review. *Environ Chem Lett* 2021; **19**: 1983-1993 [DOI: 10.1007/s10311-020-01169-5]
106 **Bordi C**, de Bentzmann S. Hacking into bacterial biofilms: a new therapeutic challenge. *Ann Intensive Care* 2011; **1**: 19 [PMID: 21906350 DOI: 10.1186/2110-5820-1-19]
107 **Rogers GB**, Carroll MP, Bruce KD. Enhancing the utility of existing antibiotics by targeting bacterial behaviour? *Br J Pharmacol* 2012; **165**: 845-857 [PMID: 21864314 DOI: 10.1111/j.1476-5381.2011.01643.x]
108 **Whiteley M**, Diggle SP, Greenberg EP. Progress in and promise of bacterial quorum sensing research. *Nature* 2017; **551**: 313-320 [PMID: 29144467 DOI: 10.1038/nature24624]
109 **Carradori S**, Di Giacomo N, Lobefalo M, Luisi G, Campestre C, Sisto F. Biofilm and Quorum Sensing inhibitors: the road so far. *Expert Opin Ther Pat* 2020; **30**: 917-930 [PMID: 32985271 DOI: 10.1080/13543776.2020.1830059]
110 **Haque M**, Islam S, Sheikh MA, Dhingra S, Uwambaye P, Labricciosa FM, Iskandar K, Charan J, Abukabda AB, Jahan D. Quorum sensing: a new prospect for the management of antimicrobial-resistant infectious diseases. *Expert Rev Anti Infect*

Ther 2021; **19**: 571-586 [PMID: 33131352 DOI: 10.1080/14787210.2021.1843427]

111 **ASTM**. F2118-14 (2020) Standard test method for constant amplitude of force controlled fatigue testing of acrylic bone cement materials. [cited 20 July 2021]. Available from: https://www.astm.org/Standards/F2118.htm

112 **ISO**. ISO 16402:2008 (2020) Implants for surgery-Acrylic resin cement-Flexural fatigue testing of acrylic resin cements used in orthopaedics. [cited 20 July 2021]. Available from: https://www.iso.org/standard/32212.html

113 **Bjarnsholt T**, Ciofu O, Molin S, Givskov M, Høiby N. Applying insights from biofilm biology to drug development - can a new approach be developed? *Nat Rev Drug Discov* 2013; **12**: 791-808 [PMID: 24080700 DOI: 10.1038/nrd4000]

114 **Sun T**, Hao H, Hao WT, Yi SM, Li XP, Li JR. Preparation and antibacterial properties of titanium-doped ZnO from different zinc salts. *Nanoscale Res Lett* 2014; **9**: 98 [PMID: 24572014 DOI: 10.1186/1556-276X-9-98]

115 **Lee JH**, Jo JK, Kim DA, Patel KD, Kim HW, Lee HH. Nano-graphene oxide incorporated into PMMA resin to prevent microbial adhesion. *Dent Mater* 2018; **34**: e63-e72 [PMID: 29402540 DOI: 10.1016/j.dental.2018.01.019]

116 **Karahaliloglu Z**, Kilicay E. In vitro evaluation of bone cements impregnated with selenium nanoparticles stabilized by phosphatidylcholine (PC) for application in bone. *J Biomater Appl* 2020; **35**: 385-404 [PMID: 32567484 DOI: 10.1177/0885328220933781]

117 **Wu J**, Zhu B, Zhao Y, Shi M, He X, Xu H, Zhou Q. One-step eco-friendly synthesis of Ag-reduced graphene oxide nanocomposites for antibiofilm application. *J Mater Eng Perform* 2020; **29**: 2551-2559 [DOI: 10.1007/s11665-020-04742-9]

118 **Bueloni B**, Sanna D, Garribba E, Castro GR, León IE, Islan GA. Design of nalidixic acidvanadium complex loaded into chitosan hybrid nanoparticles as smart strategy to inhibit bacterial growth and quorum sensing. *Int J Biol Macromol* 2020; **161**: 1568-1580 [PMID: 32777416 DOI: 10.1016/j.ijbiomac.2020.07.304]

119 **Zhang X**, Zhang Z, Shu Q. Copper clusters: an effective antibacterial for eradicating multidrug-resistant bacterial infection in vitro and in vivo. *Adv Funct Mater* 2021; **31**: 2008720 [DOI: 10.1002/adfm.202008720]

120 **Mendili M**, Essghaier B, Seaward MRD, Khadhri A. In vitro evaluation of lysozyme activity and antimicrobial effect of extracts from four Tunisian lichens: Diploschistes ocellatus, Flavoparmelia caperata, Squamarina cartilaginea and Xanthoria parietina. *Arch Microbiol* 2021; **203**: 1461-1469 [PMID: 33388791 DOI: 10.1007/s00203-020-02129-x]

121 **Navarro-López DE**, Garcia-Varela R, Ceballos-Sanchez O, Sanchez-Martinez A, Sanchez-Ante G, Corona-Romero K, Buentello-Montoya DA, Elías-Zuñiga A, López-Mena ER. Effective antimicrobial activity of ZnO and Yb-doped ZnO nanoparticles against Staphylococcus aureus and Escherichia coli. *Mater Sci Eng C Mater Biol Appl* 2021; **123**: 112004 [PMID: 33812624 DOI: 10.1016/j.msec.2021.112004]

122 **Seyler TM**, Moore C, Kim H, Ramachandran S, Agris PF. A New Promising Anti-Infective Agent Inhibits Biofilm Growth by Targeting Simultaneously a Conserved RNA Function That Controls Multiple Genes. *Antibiotics (Basel)* 2021; **10** [PMID: 33406640 DOI: 10.3390/antibiotics10010041]

123 **Keri RS**, Patil MR, Patil SA, Budagumpi S. A comprehensive review in current developments of benzothiazole-based molecules in medicinal chemistry. *Eur J Med Chem* 2015; **89**: 207-251 [PMID: 25462241 DOI: 10.1016/j.ejmech.2014.10.059]

124 **Morsy MA**, Ali EM, Kandeel M, Venugopala KN, Nair AB, Greish K, El-Daly M. Screening and Molecular Docking of Novel Benzothiazole Derivatives as Potential Antimicrobial Agents. *Antibiotics (Basel)* 2020; **9** [PMID: 32365587 DOI: 10.3390/antibiotics9050221]

125 **Singer L**, Bierbaum G, Kehl K, Bourauel C. Evaluation of the antimicrobial activity and compressive strength of a dental cement modified using plant extract mixture. *J Mater Sci Mater Med* 2020; **31**: 116 [PMID: 33247427 DOI: 10.1007/s10856-020-06455-w]

126 **Hasan M**, Altaf M, Zafar A, Hassan SG, Ali Z, Mustafa G, Munawar T, Saif MS, Tariq T, Iqbal F, Khan MW, Mahmood A, Mahmood N, Shu X. Bioinspired synthesis of zinc oxide nano-flowers: A surface enhanced antibacterial and harvesting efficiency. *Mater Sci Eng C Mater Biol Appl* 2021; **119**: 111280 [PMID: 33321572 DOI: 10.1016/j.msec.2020.111280]

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MINIREVIEWS

Lateral epicondylitis: New trends and challenges in treatment

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Abstract

Lateral epicondylitis (LE) is a chronic aseptic inflammatory condition caused by repetitive microtrauma and excessive overload of the extensor carpi radialis brevis muscle. This is the most common cause of musculoskeletal pain syndrome in the elbow, inducing significant pain and limitation of the function of the upper limb. It affects approximately 1-3% of the population and is frequently seen in racquet sports and sports associated with functional overload of the elbow, such as tennis, squash, gymnastics, acrobatics, fitness, and weight lifting. Typewriters, artists, musicians, electricians, mechanics, and other professions requiring frequent repetitive movements in the elbow and wrists are also affected. LE is a leading causation for absence from work and lower sport results in athletes. The treatment includes a variety of conservative measures, but if those fail, surgery is indicated. This review summarizes the knowledge about this disease, focusing on risk factors, expected course, prognosis, and conservative and surgical treatment approaches.

Key Words: Diagnosis; Lateral epicondylitis; Tennis elbow; Treatment; Review

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Core Tip: Lateral epicondylitis (LE) is the most common cause of musculoskeletal pain in the elbow. LE is a leading causation for absence from work and lower sport results in athletes and has a negative impact on the job and social life of patients. Despite extensive research in the last few decades and the plenty of different articles concerning the causes, pathogenesis, and treatment, LE remains a challenge. In this article, we summarize the knowledge about this condition, emphasizing the risk factors, the development of symptoms and the prognostic value of individual factors, and the treatment approaches.

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INTRODUCTION

Lateral epicondylitis (LE) is the most common cause of musculoskeletal pain in the elbow and is associated with significant pain and severe limitation of upper limb function. This condition is also known as periostitis, tendinitis of extensor carpi radialis brevis muscle (ECRB), epicondyloalgia, radial epicondyliti, *etc*., but is most commonly described in the literature as tennis elbow (TE) or LE[1]. LE could be caused by previous trauma but is mainly associated with overload activities that require repetitive prono-supination of the forearm and full extension of the elbow. Other risk factors include degenerative changes of the tendons and disruption of the local blood supply in the area. Usually, there is no pain at rest, but the so-called "extensor activity" provokes pain. Statistics show that LE mainly targets patients of “active” age and has a negative impact on their job and social life, thus indirectly affecting the economics of the country. Although it has been highly researched in the last few decades and there are many different articles concerning the causes, pathogenesis, and treatment, it still presents a challenge for specialists. The aim of this article is to briefly summarize the existing knowledge about this condition, emphasizing the risk factors, the development of symptoms and the prognostic value of individual factors, as well as different treatment approaches. In this manuscript, we will critically review the available literature, including recent publications, and outline some future prospects for the development of research on LE.

HISTORY OF LE

In 1873, Runge first described LE as a "writer's cramp." The term “tennis elbow” was introduced by Morris in 1882, but it was Momberg in 1910, who first described this condition in detail[2]. In his monograph on TE in 1936, James Cyriax concluded that the natural course of LE is between six months and two years[3]. This statement has been widely accepted by different authors over the years, but currently, it is considered that the symptoms of LE could persist for many years and relapses are very common[4].

In 1979, Nirschl *et al*[5] were the first to present surgical treatment of LE, with 97.7% good and excellent results, and in 85.2% of the cases, patients returned to active sports.

EPIDEMIOLOGY AND RISK FACTORS

LE is a relatively common pathology, affecting between 1%-3% of the population. Approximately 4-7/1000 of the patients visit their general practitioners due to symptoms of LE. It is estimated that approximately 40% of all people show some symptoms of LE throughout their life. An interesting fact is that Sanders *et al*[6], in their population study, observed a significant decrease in the annual incidence of LE in 2000 from 4.5/1000 to 2.4/1000 in 2012. According to them, the lower frequency could be due to either changes in the diagnostic approach or to a real decrease in the LE cases. LE usually affects men and women aged between 30-50, and there is no gender predominance[7]. An interesting fact is that more than 50% of nonprofessional tennis players suffer from this disease, but only 5% of professional tennis players complain of LE. Players in other sports, such as badminton and squash, can also be affected. In athletes, the symptoms are associated with poor backhand performance, low grip of the racket, too tight cord of the racket or in cases when players use wet and heavy balls[8]. LE most commonly affects the dominant hand, especially when performing daily repetitive motions. It is the reason for some of the longest absences from work. Up to 17% of factory workers, as well as meat processors who have repetitive and similar hand movements, suffer from LE. Typists, artists, musicians, electricians, mechanics, and others can also be affected. It is well known that workers involved with repetitive movements of the hands and wrists have an increased risk of LE[9,10], are more resistant to treatment and have a worse prognosis[11,12]. One of the reasons for persistent pain in LE is central sensitization, associated with reduced thresholds of nociception and increased time summation[13]. There is evidence that patients with LE exhibit widespread hyperalgesia, which results in a higher score on the pain scale and prolonged duration of the symptoms. Herquelot *et al*[10] studied the influence of physical and psychological factors on the occurrence of elbow and LE diseases among a group of 3710 workers in France. Elbow pain without LE was reported in 10.5% of the workers, and LE was diagnosed in 2.4% of the workers. Age, body mass index (> 25) and low social support (men only) were significant

risk factors. Heavy exercise combined with repetitive elbow flexion/extension for more than two hours a day and wrist flexion for more than two hours a day were the most significant risk factors for elbow pain and LE.

According to Sanders *et al*[6], the most common professional activities of patients with LE are office workers or secretaries and medical staff, mainly nurses.

In a recently published case–control study of the influence of various factors on the occurrence of LE, Park *et al*[14] found that female sex, dominant hand involvement, manual labor, and ipsilateral rotator cuff rupture were risk factors for LE. The results of the study show that excessive use of the limb is a stronger risk factor for LE than metabolic factors[14].

According to some reports, there could be a link between LE and the use of fluoroquinolones. Such a consequence has been reported in Achilles tendon degeneration[15].

Studies show that LE leads to absences from work for up to 219 working days of the year, with a cost of $8099 per patient. Data from the Workcover Queensland show that diseases affecting the upper limb (shoulder and elbow) accounted for 18% of all occupational diseases from 2009 to 2013, which is equal to the prevalence of diseases in the back[16].

SYMPTOMS, DIAGNOSIS AND EVOLUTION

Clinical examination usually presents with increased sensitivity and pain during palpation in the lateral epicondyle area, which is exacerbated by prono-supination of the forearm. The pathognomonic sign of LE is the test in which pain is provoked by the extension of the wrist against resistance, as well as the "chair back test".

Precise evaluation of the pain should be assessed at the beginning of the symptoms because there is evidence that patients with more severe pain syndrome in the first presence of the disease have a higher potential for persistence of the pain at the twelfth month[17]. The "Patient Rated Tennis Elbow Evaluation" is an LE-specific questionnaire that includes pain and impairment scales that are collected to give an overall score from 0 (no pain or injury) to 100 (strongest pain or injury)[18]. A minimum change of 11 points or 37% of the baseline assessment is considered clinically significant[19]. The most common functional limitation in LE is grip pain, which can be measured as painless grip strength and is a reliable and valid indicator that is more sensitive than measuring maximum grip strength[20]. It is measured with the patient lying, the elbow is in a slight extension and the forearm is in pronation, as the patient squeezes the dynamometer until the first appearance of pain. The final calculation consists of the average of three tests performed at one-minute intervals.

From the imaging tools, the X-ray could exclude other pathological conditions of the elbow, and in rare cases, small calcifications could be observed. Ultrasound can provide more accurate data by visualizing the initial location of the muscle and the possible thickening of the tissues around the tendon as a result of the inflammatory process[21]. The most accurate assessment can be made by magnetic resonance imaging (MRI). It shows thickening of the proximal muscle insertion with increased signal in T1 and T2 presented in 2/3 of patients. These characteristics may persist for a long time after the symptoms have resolved[22]. Ultrasound and MRI are highly sensitive but are nonspecific for proving LE. However, the absence of a pathological finding from these tests can certainly rule out LE. The presence of a large rupture (≥ 6 mm) in the tendon or lateral collateral ligament is a crucial part of the differential diagnosis, as it is associated with unsuccessful conservative treatment[23]. Infrared thermography in 94%-100% of patients with LE shows abnormally increased epicondylar activity around the lateral epicondyle. Isotope testing is also positive in 72% of the patients[24], although these two methods are practically not used routinely.

Electromyography and cervical and thoracic spine examinations could also be helpful in diagnosing the source of pain symptoms in the spine. Although the influence of cervical and thoracic spinal diseases on LE is not fully understood, some studies show that neck pain is more common in people with LE[25]. Moreover, patients with LE who also complain of shoulder or neck pain have a worse prognosis[18].

Current data show that the disease usually develops over the years, with common recurrences. This changes the initial assessment that LE is limited from six months to two years. Over 50% of patients report that elbow pain still persists after 12 mo[26,27]. Follow-up of participants in a clinical trial[4] of nonsurgical treatment of LE showed that 20% of patients (27/134) reported pain after three to five years (3.9 years on average), regardless of treatment regimens, and that those with an initial severe pain syndrome had a 5.5 times higher rate of pain symptoms due to LE. Therefore, LE is considered a nonself-limiting condition and is associated with continuous pain in a large number of patients. Sanders *et al*[6] indicated an 8.5% recurrence rate over two years, and it remained constant over time. The surgically treated cases within two years after diagnosis have increased three times for the period of the study/2001-2012/, from 1.1% for the period between 2000-2002 up to 3.2% after 2009. One of ten patients with persistent symptoms at the sixth month required surgical treatment.

CONSERVATIVE TREATMENT

Conservative treatment of LE includes nonsteroidal anti-inflammatory drugs (NSAIDs), analgesics, topical corticosteroid application, rest, cryotherapy, acupuncture, kinesitherapy, physical therapy including ultrasound, iontophoresis, deep transverse frictions, shock wave and lazer therapy, manual therapy, exercises strengthening the muscles, *etc.* Wearing an epicondylar bandage is also a part of conservative treatment[28].

Although there is still no generally approved algorithm for the treatment of LE, it is now accepted that the start of the treatment should be with oral NSAIDs[29]. In the short term, oral NSAIDs affect pain compared to placebo, but there are still no data for the 6- to 12-mo period. There are insufficient data on the efficacy of NSAIDs on pain compared with injectable corticosteroids, but as a global effect on symptoms, NSAIDs have shown lower efficacy. In terms of arm function improvement, NSAID administration did not show a significant improvement compared with placebo[30]. Topical NSAIDs improve pain symptoms, but arm function compared with placebo effects is uncertain[30]. Studies in the treatment of LE have shown a significant improvement in the symptoms of topical corticosteroid injection compared with placebo or NSAIDs. A positive effect is reported in both pain and arm function. There is no comparison of efficacy with different types of corticosteroids[30]. In addition to the corticosteroid, a local anesthetic injection was given. The results of the studies showed an overall improvement in pain symptoms and arm function in both groups, with no significant difference between the groups treated with corticosteroids or anesthetics[31]. Interestingly, there is evidence that corticosteroid injections have a higher recurrence rate after 6 wk in patients with LE than in the placebo group or untreated patients. Additionally, compared with combined physical therapy, corticosteroid injections appear to cause a higher recurrence rate after 6 wk[30].

OTHER CONSERVATIVE TREATMENT OPTIONS

In 2011, Creaney *et al*[32] published the results of a prospective randomized study using growth factors to improve the healing processes of musculoskeletal injuries in sports medicine. It is believed that injecting autologous blood stimulates an inflammatory response, which would prompt healing stimulation. However, the benefit of the method has not been found in long-term follow-up, and its use is recommended only in those cases where other treatment options have failed. Autologous platelet-rich plasma (PRP) is another option used to treat LE. PRP is made by using a sample from the patient's own blood. It is widely used in orthopedics and sports medicine as a method of recovery after various soft tissue injuries or after surgical interventions. PRP is a potential treatment option in patients with LE in cases of physiotherapy failure[33]. Mishra *et al*[34] reported the results after PRP in a prospective cohort study in 230 patients who did not respond to at least three months of conservative treatment for LE. At 24 wk, PRP injection resulted in a significant improvement in pain compared to the control group (71.5% *vs* 56.1%, $P = 0.019$), as well as a significantly lower percentage of patients reporting residual sensitivity in the elbow area (29.1% *vs* 54.0%, $P = 0.009$). A study by Shim *et al*[35] found no difference between PRP administration and own blood injection. However, the significant differences between the various PRP systems and the different techniques used in producing them complicate the comparison of the results of the various studies[33]. Leukocyte concentration affects the quality of PRP. New data suggest that leukocyte-rich PRP may provide pain relief and good outcomes for LE patients compared to alternative topical injections. Additionally, better results are seen with the use of leukocyte-rich PRP than with the use of leukocyte-poor PRP[35]. In a pilot study of 12 patients with refractory LE, Connell *et al*[36] showed that collagen-producing tenocyte-like cells derived from autologous skin fibroblasts that were injected with a PRP-rich matrix led to clinical and ultrasound improvement. In 2013, Wang *et al*[37] published the results of a study on the use of autologous tenocytes derived from patellar tendon cells and injected under ultrasound control for the treatment of severe refractory LE in 16 patients. These cells are preferred because of their potential for collagen synthesis and rapid proliferation.

Botulinum toxin A has also been proposed for the treatment of LE. In 1997, Morré *et al*[38] first described its use in LE. The authors suggest that botulinum toxin injections could aid in the treatment of LE by causing reversible paresis of the extensors, especially m. ECRB, thus preventing the development of microtraumas in its proximal insertion. Placzek *et al*[39] conducted a multicenter randomized controlled trial in which 130 patients were treated with botulinum toxin or placebo. Patients treated with botulinum showed significant improvements in pain measured by the analog scale at the 6th, 12th, and 18th weeks. However, the application could provoke weakness in the wrist extensors and reduced grip strength. Regardless of the results obtained from these studies, Hayton *et al*[40] failed to prove a significant difference between the Botox-treated group and the control group.

PHYSICAL THERAPY

Physiotherapy and kinesitherapy play a significant role in the treatment of TE. Their use could start in the acute phase or immediately after diagnosis to reduce pain and continue in the early and late postoperative period to restore range of motion, joint function, recovery of muscle strength and prevention of contractures. In the different stages, specific combinations of the above-described methods could be used by preparing individual rehabilitation programs.

Different combinations of exercises have also been used for the treatment. They are usually part of a complex treatment. Despite controversial results, there is evidence from several randomized controlled trials that exercise may be more effective in reducing pain and improving arm function than other procedures, such as ultrasound, placebo ultrasound and manual therapy, but there is no difference in muscle strength and function between various types of exercises[30,41,42]. Manual therapy for the elbow, wrist and cervicothoracic spine can reduce pain and increase the strength of the pain-free grip immediately after treatment. Unfortunately, meta-analysis is not possible due to heterogeneity between manual therapy techniques and follow-up time. There is insufficient evidence of the long-term clinical effects of manual therapy alone in LE[43-47].

The use of ortheses is another popular LE treatment option. The variety of different orthotic devices and the different follow-up methods for evaluating their effectiveness makes it difficult to analyze the published data. Overall, there is generally controversial evidence for the effectiveness of orthoses as an improved method for arm function and pain relief compared to placebo or in untreated patients. There is no evidence of the superiority of one type of orthosis over others[48-52].

Topical application of ice is a traditional method for pain management. However, evidence for its effectiveness in LE is limited. In a controlled clinical trial, Manias *et al*[53] failed to demonstrate the advantage of using ice in combination with exercise over using exercise alone.

Acupuncture is used in the treatment of many musculoskeletal disorders, and LE is no exception. After reviewing the literature on the subject, Trinh *et al*[54] concluded that acupuncture is effective in relieving complaints in the short term. Acupuncture is shown to be more effective in relieving pain and improving function than ultrasound, both at the end of the treatment and at the six-month follow-up [55].

The use of laser therapy in LE is effective in the short term compared to placebo, but in the long term, however, no advantages are found compared to other physical methods. Lasers with a wavelength other than 904 nm did not show better efficacy than placebo[56-58]. The analysis of data from clinical trials on the effect of ultrasound therapy and iontophoresis in LE shows that they do not have an advantage over the use of placebo[30]. The data for the application of shock-wave therapy are similar and are not more effective than placebo or other physical methods[59].

Recently, published data from a meta-analysis show that in the conservative treatment of LE, electrophysiotherapy and physiotherapy should be given priority over other interventions[60].

SURGICAL TREATMENT

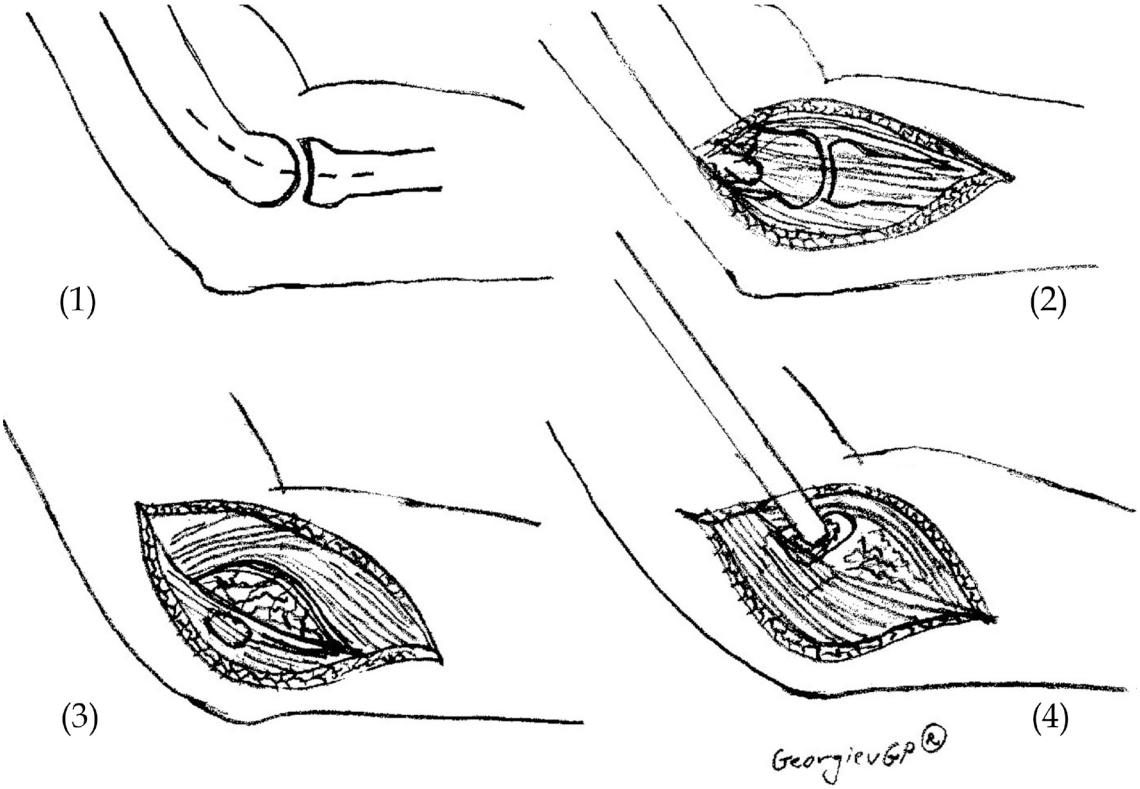
Usually, most patients respond to conservative treatment. Nonetheless, in some patients, the symptoms persist for a long time despite treatment. In such cases, a surgical approach is indicated. There are many surgical techniques (Figure 1 and 2), and most of them include debridement of the affected tendon of the m. ECRB and decortication of the lateral epicondyle. Surgery can be performed using open, percutaneous, or arthroscopic techniques.

Open surgery

In 1979, Nirshl *et al*[5] published an operative technique for the treatment of LE, which involved excision of all visibly damaged parts in the area of the insertion of the ECRB muscle. The authors reported an improvement in 97.7% of the patients after surgery. In 2008, Dunn *et al*[61] applied the Nirshl technique in 139 elbows and reported improvement in 97% of them. Numerous surgical techniques have been described in the literature: Excision of the painful area and ablation of the common extensor origin according to Garden; Hohmann surgery in which the initial attachment sites of the extensors are released from the lateral epicondyle; and Kaplan denervation of the humeroradial joint. The most popular technique is that of Boyd and McLeod, which eliminates all possible causes of the disease. It involves excision of the proximal part of the annular ligament, releasement of the insertion of the extensors, excision of the bursa in the area and excision of the synovium of the humeroradial joint. There is no evidence of an advantage of any of the open techniques for the treatment of LE over the others[30].

Percutaneous technique

In 1962, Loose performed a percutaneous technique for releasement of the proximal insertion of the ECRB with local anesthesia for the first time. Good results after percutaneous releasement have also been reported by different authors[62-65]. This procedure is effective in pain relief, uses a minimally



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Figure 1 Scheme presenting the open release of lateral epicondylitis. (1) Skin incision; (2) Extensor carpi radialis longus – extensor digitorum communis interface is identified; (3) Degenerated tissue at extensor carpi radialis brevis muscle is identified and incised; and (4) Osteotome decortication.

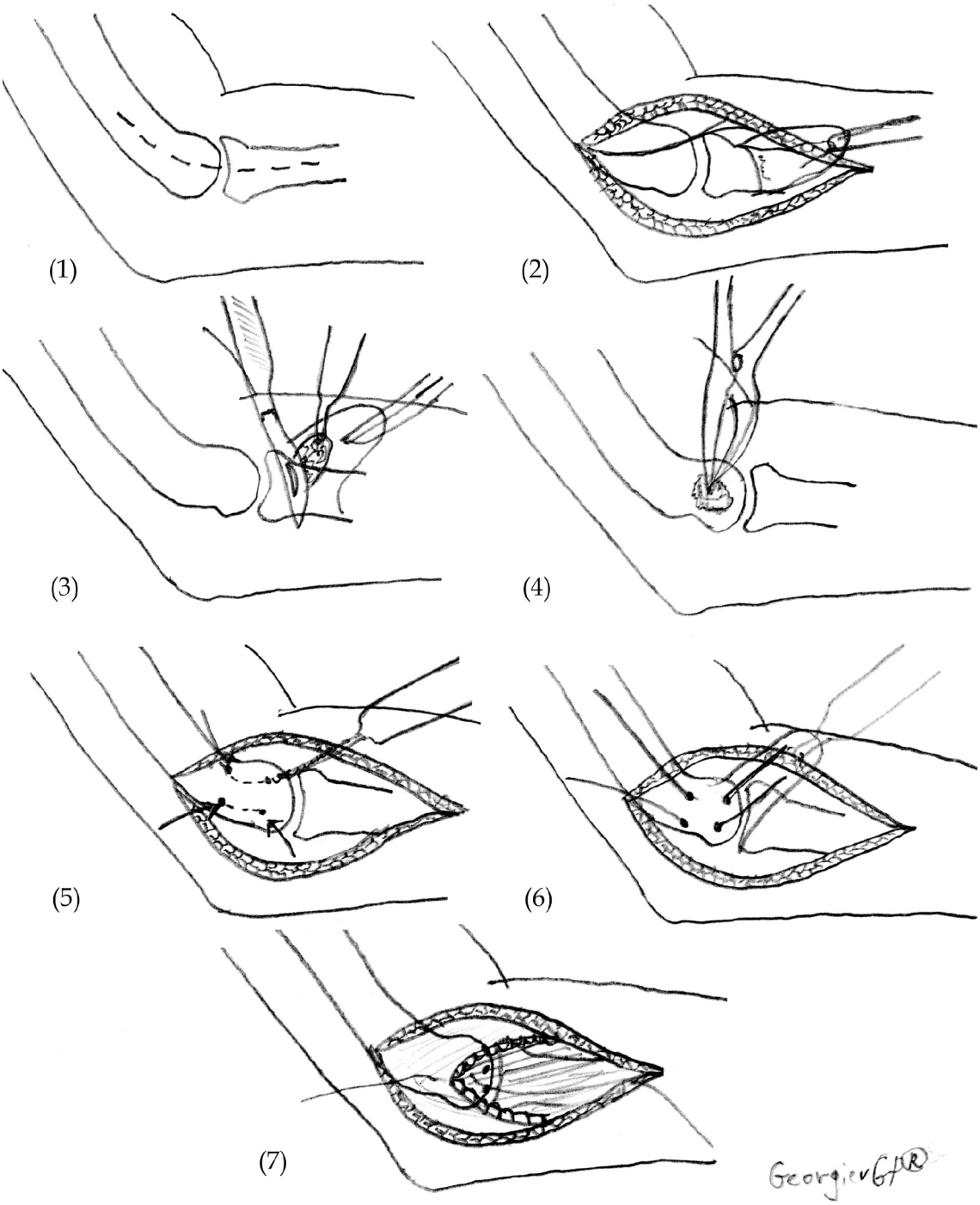
invasive approach and can be performed as a one-day surgery. However, the application of percutaneous operative techniques is still controversial. Recently, data on a new percutaneous technique called ultrasound guided percutaneous tenotomy (UGPT) have been published. It is safe and secure and leads to improvement of pain symptoms, hand function and ultrasound imaging at the one-year follow-up[66]. This new surgical technique is applied through an incision of five millimeters using ultrasound energy to remove damaged tissue and cause an inflammatory reaction that promotes the healing process in the tendon[67]. The technique requires the use of special equipment - the TX1 Tissue Removal System (Tenex Health, Lake Forest, CA). Seng *et al*[68] administered UGPT *via* the TX1 Tissue Removal System to a group of 20 patients with refractory LE, reporting improvement in arm function and pain relief after 3 years of follow-up. Boden *et al*[69] compared the results after treatment with PRP or UGPT in patients with medial or LE. No statistically significant difference was found between the two techniques. The authors conclude that both techniques are effective in the treatment of epicondylitis and lead to pain relief and improved arm function and quality of life.

Arthroscopic technique

Arthroscopic surgery is becoming increasingly popular in treating LE in the United States. This procedure involves arthroscopic release of the tendon of the ECRB. The potential benefit of arthroscopic surgery is a shorter recovery time and a better tolerance of the patient. The results of this technique have been reported mainly in a series of patients with positive results. Baker *et al*[70] were the first to apply arthroscopic operative techniques in LE treatment. In arthroscopic surgery, debridement of the pathological tissue is performed. The authors reported good results in 30 patients[71]. Jerosch *et al*[72] also reported good results from arthroscopic treatment in Germany. Currently, a prospective, single-center, double-blind, randomized, controlled study of the efficacy of arthroscopic release of ECRB in patients with LE is conducted[73]. The expected results will allow optimization of the therapeutic approach in patients with LE with a high degree of reliability.

LIMITATIONS AND FUTURE SCOPE

In this review, we used only English language sources from medical databases. It is worth mentioning here that some of the studies included in this literature review are gaining small sample sizes, which increases the likelihood of a type II error. There are significant methodological differences in the design



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Figure 2 Scheme presenting the technique for the surgical treatment of lateral epicondylitis. (1) Skin incision; (2) Reflection in the distal direction of the extensor mechanism; (3) Excision of pathologic tissue under the flap of the extensor mechanism; (4) Osteotome decortication; (5) Drilling of two V-shaped tunnels for reattachment of the extensors; (6) Reattachment of the extensor mechanism to the lateral epicondyle; and (7) Restoration of the extensor tendon mechanism.

of the studies between the different studies. In addition, we see a great variety in the methods used to evaluate the results, which means that meaningful data synthesis, which may counteract some of the limitations of individual studies, is difficult.

Although LE has been a known disease for centuries and numerous studies have been conducted on it, there is still a wide horizon for future research and supplementation of our knowledge regarding this disease. First, it is necessary to study in depth the importance of risk factors in light of developing strategies for primary prevention. Another promising area is the study and application of imaging methods using artificial intelligence, which are already entering medical practice[74-76]. Additionally, nonsurgical treatment using various cellular derivatives is a promising therapeutic method[77]. In the near future, we expect to improve the existing methods and introduce new minimally invasive methods of treatment. Researchers' efforts will also focus on establishing an effective therapeutic strategy for

patients with recurrent LE.

CONCLUSION

LE is a common musculoskeletal disorder caused by chronic repetitive overload of the proximal insertion of the extensor carpi radialis brevis muscle that results in local microinjuries, which heal partially and thus induce aseptic inflammation, swelling and pain. Without adequate treatment, this disease could become chronic and lead to significant limitations in daily activities and quality of life impairment. Knowing the nature of this disease is a prerequisite for the implementation of correct therapeutic strategies and therefore achieves a good therapeutic approach and positive results.

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REFERENCES

1 **Waseem M**, Nuhmani S, Ram CS, Sachin Y. Lateral epicondylitis: a review of the literature. *J Back Musculoskelet Rehabil* 2012; **25**: 131-142 [PMID: 22866337 DOI: 10.3233/bmr-2012-0328]
2 **Goldie I**. Epicondylitis lateralis humeri (epicondylalgia or tennis elbow). A pathogenetical study. *Acta Chir Scand Suppl* 1964; **57** SUPPL 339: 1+ [PMID: 14192714]
3 **Cyriax J**. The pathology and treatment of tennis elbow. *J Bone Joint Surg* 1936; **18**: 921-940
4 **Coombes BK**, Bisset L, Brooks P, Khan A, Vicenzino B. Effect of corticosteroid injection, physiotherapy, or both on clinical outcomes in patients with unilateral lateral epicondylalgia: a randomized controlled trial. *JAMA* 2013; **309**: 461-469 [PMID: 23385272 DOI: 10.1001/jama.2013.129]
5 **Nirschl RP**, Pettrone FA. Tennis elbow. The surgical treatment of lateral epicondylitis. *J Bone Joint Surg Am* 1979; **61**: 832-839 [PMID: 479229]
6 **Sanders TL Jr**, Maradit Kremers H, Bryan AJ, Ransom JE, Smith J, Morrey BF. The epidemiology and health care burden of tennis elbow: a population-based study. *Am J Sports Med* 2015; **43**: 1066-1071 [PMID: 25656546 DOI: 10.1177/0363546514568087]
7 **Chard MD**, Hazleman BL. Tennis elbow--a reappraisal. *Br J Rheumatol* 1989; **28**: 186-190 [PMID: 2659123 DOI: 10.1093/rheumatology/28.3.186]
8 **Ho C**. Extracorporeal shock wave treatment for chronic lateral epicondylitis (tennis elbow). *Issues Emerg Health Technol* 2007; 1-4 [PMID: 17302021]
9 **Bernard BP**. Musculoskeletal disorders and workplace fractures: a critical review of the epidemiological evidence for

work-related musculoskeletal disorders of the neck, upper extremity and low back. Washington: National Institute for Occupational Safety and Health, 1997
10 **Herquelot E**, Bodin J, Roquelaure Y, Ha C, Leclerc A, Goldberg M, Zins M, Descatha A. Work-related risk factors for lateral epicondylitis and other cause of elbow pain in the working population. *Am J Ind Med* 2013; **56**: 400-409 [PMID: 23152138 DOI: 10.1002/ajim.22140]
11 **Coonrad RW**, Hooper WR. Tennis elbow: its course, natural history, conservative and surgical management. *J Bone Joint Surg Am* 1973; **55**: 1177-1182 [PMID: 4758032]
12 **Haahr JP**, Andersen JH. Prognostic factors in lateral epicondylitis: a randomized trial with one-year follow-up in 266 new cases treated with minimal occupational intervention or the usual approach in general practice. *Rheumatology (Oxford)* 2003; **42**: 1216-1225 [PMID: 12810936 DOI: 10.1093/rheumatology/keg360]
13 **Jespersen A**, Amris K, Graven-Nielsen T, Arendt-Nielsen L, Bartels EM, Torp-Pedersen S, Bliddal H, Danneskiold-Samsoe B. Assessment of pressure-pain thresholds and central sensitization of pain in lateral epicondylalgia. *Pain Med* 2013; **14**: 297-304 [PMID: 23279601 DOI: 10.1111/pme.12021]
14 **Park HB**, Gwark JY, Im JH, Na JB. Factors Associated With Lateral Epicondylitis of the Elbow. *Orthop J Sports Med* 2021; **9**: 23259671211007734 [PMID: 34036114 DOI: 10.1177/23259671211007734]
15 **Le Huec JC**, Schaeverbeke T, Chauveaux D, Rivel J, Dehais J, Le Rebeller A. Epicondylitis after treatment with fluoroquinolone antibiotics. *J Bone Joint Surg Br* 1995; **77**: 293-295 [PMID: 7706350]
16 **Workcover Queensland**. Workcover Queensland annual report 2012-2013. Brisbane Qld, Australia, 2013
17 **Smidt N**, Lewis M, VAN DER Windt DA, Hay EM, Bouter LM, Croft P. Lateral epicondylitis in general practice: course and prognostic indicators of outcome. *J Rheumatol* 2006; **33**: 2053-2059 [PMID: 16881095]
18 **Rompe JD**, Overend TJ, MacDermid JC. Validation of the Patient-rated Tennis Elbow Evaluation Questionnaire. *J Hand Ther* 2007; **20**: 3-10; quiz 11 [PMID: 17254903 DOI: 10.1197/j.jht.2006.10.003]
19 **Poltawski L**, Watson T. Measuring clinically important change with the patient rated tennis elbow evaluation. *Hand Ther* 2011; **16**: 52-57 [DOI: 10.1258/ht.2011.011013]
20 **Stratford PW**, Levy DR. Assessing valid change over time in patients with lateral epicondylitis at the elbow. *Clin J Sports Med* 1994; **4**: 88-91 [DOI: 10.1097/00042752-199404000-00004]
21 **Heales LJ**, Broadhurst N, Mellor R, Hodges PW, Vicenzino B. Diagnostic ultrasound imaging for lateral epicondylalgia: a case-control study. *Med Sci Sports Exerc* 2014; **46**: 2070-2076 [PMID: 24848494 DOI: 10.1249/MSS.0000000000000345]
22 **Pasternack I**, Tuovinen EM, Lohman M, Vehmas T, Malmivaara A. MR findings in humeral epicondylitis. A systematic review. *Acta Radiol* 2001; **42**: 434-440 [PMID: 11552879]
23 **Clarke AW**, Ahmad M, Curtis M, Connell DA. Lateral elbow tendinopathy: correlation of ultrasound findings with pain and functional disability. *Am J Sports Med* 2010; **38**: 1209-1214 [PMID: 20335508 DOI: 10.1177/0363546509359066]
24 **Thomas D**, Siahamis G, Marion M, Boyle C. Computerised infrared thermography and isotopic bone scanning in tennis elbow. *Ann Rheum Dis* 1992; **51**: 103-107 [PMID: 1540012 DOI: 10.1136/ard.51.1.103]
25 **Berglund KM**, Persson BH, Denison E. Prevalence of pain and dysfunction in the cervical and thoracic spine in persons with and without lateral elbow pain. *Man Ther* 2008; **13**: 295-299 [PMID: 17942362 DOI: 10.1016/j.math.2007.01.015]
26 **Binder AI**, Hazleman BL. Lateral humeral epicondylitis--a study of natural history and the effect of conservative therapy. *Br J Rheumatol* 1983; **22**: 73-76 [PMID: 6850196 DOI: 10.1093/rheumatology/22.2.73]
27 **Bot SD**, van der Waal JM, Terwee CB, van der Windt DA, Bouter LM, Dekker J. Course and prognosis of elbow complaints: a cohort study in general practice. *Ann Rheum Dis* 2005; **64**: 1331-1336 [PMID: 15708885 DOI: 10.1136/ard.2004.030320]
28 **Schwarzman G**, Watson JN, Hutchinson MR. Lateral epicondylopathy (Aka. tennis elbow): a review of current concepts and treatment. *Ann Sports Med Res* 2017; **4**: 1117
29 **Pattanittum P**, Turner T, Green S, Buchbinder R. Non-steroidal anti-inflammatory drugs (NSAIDs) for treating lateral elbow pain in adults. *Cochrane Database Syst Rev* 2013; CD003686 [PMID: 23728646 DOI: 10.1002/14651858.CD003686.pub2]
30 **Bisset L**, Coombes B, Vicenzino B. Tennis elbow. *BMJ Clin Evid* 2011; **2011** [PMID: 21708051]
31 **Hsieh LF**, Kuo YC, Lee CC, Liu YF, Liu YC, Huang V. Comparison Between Corticosteroid and Lidocaine Injection in the Treatment of Tennis Elbow: A Randomized, Double-Blinded, Controlled Trial. *Am J Phys Med Rehabil* 2018; **97**: 83-89 [PMID: 28816704 DOI: 10.1097/PHM.0000000000000814]
32 **Creaney L**, Wallace A, Curtis M, Connell D. Growth factor-based therapies provide additional benefit beyond physical therapy in resistant elbow tendinopathy: a prospective, single-blind, randomised trial of autologous blood injections versus platelet-rich plasma injections. *Br J Sports Med* 2011; **45**: 966-971 [PMID: 21406450 DOI: 10.1136/bjsm.2010.082503]
33 **Le ADK**, Enweze L, DeBaun MR, Dragoo JL. Current Clinical Recommendations for Use of Platelet-Rich Plasma. *Curr Rev Musculoskelet Med* 2018; **11**: 624-634 [PMID: 30353479 DOI: 10.1007/s12178-018-9527-7]
34 **Mishra A**, Pavelko T. Treatment of chronic elbow tendinosis with buffered platelet-rich plasma. *Am J Sports Med* 2006; **34**: 1774-1778 [PMID: 16735582 DOI: 10.1177/0363546506288850]
35 **Shim JW**, Lee JS, Park YB, Cho HC, Jung HS. The effect of leucocyte concentration of platelet-rich plasma on outcomes in patients with lateral epicondylitis: a systematic review and meta-analysis. *J Shoulder Elbow Surg* 2022; **31**: 634-645 [PMID: 34861405 DOI: 10.1016/j.jse.2021.10.036]
36 **Connell D**, Datir A, Alyas F, Curtis M. Treatment of lateral epicondylitis using skin-derived tenocyte-like cells. *Br J Sports Med* 2009; **43**: 293-298 [PMID: 19224912 DOI: 10.1136/bjsm.2008.056457]
37 **Wang A**, Breidahl W, Mackie KE, Lin Z, Qin A, Chen J, Zheng MH. Autologous tenocyte injection for the treatment of severe, chronic resistant lateral epicondylitis: a pilot study. *Am J Sports Med* 2013; **41**: 2925-2932 [PMID: 24068695 DOI: 10.1177/0363546513504285]
38 **Morré HH**, Keizer SB, van Os JJ. Treatment of chronic tennis elbow with botulinum toxin. *Lancet* 1997; **349**: 1746 [PMID: 9193392 DOI: 10.1016/s0140-6736(05)62958-3]
39 **Placzek R**, Drescher W, Deuretzbacher G, Hempfing A, Meiss AL. Treatment of chronic radial epicondylitis with

botulinum toxin A. A double-blind, placebo-controlled, randomized multicenter study. *J Bone Joint Surg Am* 2007; **89**: 255-260 [PMID: 17272437 DOI: 10.2106/JBJS.F.00401]

40 **Hayton MJ**, Santini AJ, Hughes PJ, Frostick SP, Trail IA, Stanley JK. Botulinum toxin injection in the treatment of tennis elbow. A double-blind, randomized, controlled, pilot study. *J Bone Joint Surg Am* 2005; **87**: 503-507 [PMID: 15741614 DOI: 10.2106/JBJS.D.01896]

41 **Martinez-Silvestrini JA**, Newcomer KL, Gay RE, Schaefer MP, Kortebein P, Arendt KW. Chronic lateral epicondylitis: comparative effectiveness of a home exercise program including stretching alone versus stretching supplemented with eccentric or concentric strengthening. *J Hand Ther* 2005; **18**: 411-419, quiz 420 [PMID: 16271688 DOI: 10.1197/j.jht.2005.07.007]

42 **Yoon SY**, Kim YW, Shin IS, Kang S, Moon HI, Lee SC. The Beneficial Effects of Eccentric Exercise in the Management of Lateral Elbow Tendinopathy: A Systematic Review and Meta-Analysis. *J Clin Med* 2021; **10** [PMID: 34501416 DOI: 10.3390/jcm10173968]

43 **Nourbakhsh MR**, Fearon FJ. The effect of oscillating-energy manual therapy on lateral epicondylitis: a randomized, placebo-control, double-blinded study. *J Hand Ther* 2008; **21**: 4-13; quiz 14 [PMID: 18215746 DOI: 10.1197/j.jht.2007.09.005]

44 **Paungmali A**, O'Leary S, Souvlis T, Vicenzino B. Hypoalgesic and sympathoexcitatory effects of mobilization with movement for lateral epicondylalgia. *Phys Ther* 2003; **83**: 374-383 [PMID: 12665408]

45 **Vicenzino B**, Paungmali A, Buratowski S, Wright A. Specific manipulative therapy treatment for chronic lateral epicondylalgia produces uniquely characteristic hypoalgesia. *Man Ther* 2001; **6**: 205-212 [PMID: 11673930 DOI: 10.1054/math.2001.0411]

46 **Cleland JA**, Flynn TW, Palmer JA. Incorporation of manual therapy directed at the cervicothoracic spine in patients with lateral epicondylalgia: A pilot clinical trial. *J Man Manip Ther* 2005; **13**: 143-151 [DOI: 10.1179/106698105790824932]

47 **Fernández-Carnero J**, Fernández-de-las-Peñas C, Cleland JA. Immediate hypoalgesic and motor effects after a single cervical spine manipulation in subjects with lateral epicondylalgia. *J Manipulative Physiol Ther* 2008; **31**: 675-681 [PMID: 19028251 DOI: 10.1016/j.jmpt.2008.10.005]

48 **Faes M**, van den Akker B, de Lint JA, Kooloos JG, Hopman MT. Dynamic extensor brace for lateral epicondylitis. *Clin Orthop Relat Res* 2006; **442**: 149-157 [PMID: 16394754 DOI: 10.1097/01.blo.0000187057.35196.57]

49 **Kachanathu SJ**, Miglani S, Grover D, Zakaria AR. Forearm band vs elbow taping: as a management of lateral epicondylitis. *J Musculoskel Res* 2013; **16**: 1-9 [DOI: 10.1142/S0218957713500036]

50 **Bisset LM**, Collins NJ, Offord SS. Immediate effects of 2 types of braces on pain and grip strength in people with lateral epicondylalgia: a randomized controlled trial. *J Orthop Sports Phys Ther* 2014; **44**: 120-128 [PMID: 24405258 DOI: 10.2519/jospt.2014.4744]

51 **Van De Streek MD**, Van Der Schans CP, De Greef MH, Postema K. The effect of a forearm/hand splint compared with an elbow band as a treatment for lateral epicondylitis. *Prosthet Orthot Int* 2004; **28**: 183-189 [PMID: 15382812 DOI: 10.1080/03093640408726703]

52 **Forogh B**, Khalighi M, Javanshir MA, Ghoseiri K, Kamali M, Raissi G. The effects of a new designed forearm orthosis in treatment of lateral epicondylitis. *Disabil Rehabil Assist Technol* 2012; **7**: 336-339 [PMID: 22112040 DOI: 10.3109/17483107.2011.635330]

53 **Manias P**, Stasinopoulos D. A controlled clinical pilot trial to study the effectiveness of ice as a supplement to the exercise programme for the management of lateral elbow tendinopathy. *Br J Sports Med* 2006; **40**: 81-85 [PMID: 16371498 DOI: 10.1136/bjsm.2005.020909]

54 **Trinh KV**, Phillips SD, Ho E, Damsma K. Acupuncture for the alleviation of lateral epicondyle pain: a systematic review. *Rheumatology (Oxford)* 2004; **43**: 1085-1090 [PMID: 15213328 DOI: 10.1093/rheumatology/keh247]

55 **Davidson JH**, Vandervoort A, Lessard L, Miller L. The effect of acupuncture vs ultrasound on pain level, grip strength and disability in individuals with lateral epicondylitis: a pilot study. *Physiother Can* 2001; **53**: 195-202

56 **Bjordal JM**, Lopes-Martins RA, Joensen J, Couppe C, Ljunggren AE, Stergioulas A, Johnson MI. A systematic review with procedural assessments and meta-analysis of low level laser therapy in lateral elbow tendinopathy (tennis elbow). *BMC Musculoskelet Disord* 2008; **9**: 75 [PMID: 18510742 DOI: 10.1186/1471-2474-9-75]

57 **Roberts DB**, Kruse RJ, Stoll SF. The effectiveness of therapeutic class IV (10 W) laser treatment for epicondylitis. *Lasers Surg Med* 2013; **45**: 311-317 [PMID: 23733499 DOI: 10.1002/lsm.22140]

58 **Skorupska E**, Lisinski P, Samborski W. The effectiveness of the conservative vs myofascial pain physiotherapy in tennis elbow patients: double-blind randomized trial of 80 patients. *J Musculoskel Pain* 2012; **20**: 41-50 [DOI: 10.3109/10582452.2011.635846]

59 **Bisset L**, Paungmali A, Vicenzino B, Beller E. A systematic review and meta-analysis of clinical trials on physical interventions for lateral epicondylalgia. *Br J Sports Med* 2005; **39**: 411-22; discussion 411 [PMID: 15976161 DOI: 10.1136/bjsm.2004.016170]

60 **Kim YJ**, Wood SM, Yoon AP, Howard JC, Yang LY, Chung KC. Efficacy of Nonoperative Treatments for Lateral Epicondylitis: A Systematic Review and Meta-Analysis. *Plast Reconstr Surg* 2021; **147**: 112-125 [PMID: 33002980 DOI: 10.1097/PRS.0000000000007440]

61 **Dunn JH**, Kim JJ, Davis L, Nirschl RP. Ten- to 14-year follow-up of the Nirschl surgical technique for lateral epicondylitis. *Am J Sports Med* 2008; **36**: 261-266 [PMID: 18055917 DOI: 10.1177/0363546507308932]

62 **Nazar M**, Lipscombe S, Morapudi S, Tuvo G, Kebrle R, Marlow W, Waseem M. Percutaneous tennis elbow release under local anaesthesia. *Open Orthop J* 2012; **6**: 129-132 [PMID: 22509230 DOI: 10.2174/1874325001206010129]

63 **Grundberg AB**, Dobson JF. Percutaneous release of the common extensor origin for tennis elbow. *Clin Orthop Relat Res* 2000; 137-140 [PMID: 10906868 DOI: 10.1097/00003086-200007000-00019]

64 **Kaleli T**, Ozturk C, Temiz A, Tirelioglu O. Surgical treatment of tennis elbow: percutaneous release of the common extensor origin. *Acta Orthop Belg* 2004; **70**: 131-133 [PMID: 15165014]

65 **Cho BK**, Kim YM, Kim DS, Choi ES, Shon HC, Park KJ, Lee EM. Mini-open muscle resection procedure under local anesthesia for lateral and medial epicondylitis. *Clin Orthop Surg* 2009; **1**: 123-127 [PMID: 19885046 DOI:

10.4055/cios.2009.1.3.123]
66 **Barnes DE**, Beckley JM, Smith J. Percutaneous ultrasonic tenotomy for chronic elbow tendinosis: a prospective study. *J Shoulder Elbow Surg* 2015; **24**: 67-73 [PMID: 25306494 DOI: 10.1016/j.jse.2014.07.017]
67 **Jacobson JA**, Kim SM, Brigido MK. Ultrasound-Guided Percutaneous Tenotomy. *Semin Musculoskelet Radiol* 2016; **20**: 414-421 [PMID: 28002863 DOI: 10.1055/s-0036-1597545]
68 **Seng C**, Mohan PC, Koh SB, Howe TS, Lim YG, Lee BP, Morrey BF. Ultrasonic Percutaneous Tenotomy for Recalcitrant Lateral Elbow Tendinopathy: Sustainability and Sonographic Progression at 3 Years. *Am J Sports Med* 2016; **44**: 504-510 [PMID: 26602153 DOI: 10.1177/0363546515612758]
69 **Boden AL**, Scott MT, Dalwadi PP, Mautner K, Mason RA, Gottschalk MB. Platelet-rich plasma versus Tenex in the treatment of medial and lateral epicondylitis. *J Shoulder Elbow Surg* 2019; **28**: 112-119 [PMID: 30551782 DOI: 10.1016/j.jse.2018.08.032]
70 **Baker CL Jr**, Murphy KP, Gottlob CA, Curd DT. Arthroscopic classification and treatment of lateral epicondylitis: two-year clinical results. *J Shoulder Elbow Surg* 2000; **9**: 475-482 [PMID: 11155299 DOI: 10.1067/mse.2000.108533]
71 **Baker CL Jr**, Baker CL 3rd. Long-term follow-up of arthroscopic treatment of lateral epicondylitis. *Am J Sports Med* 2008; **36**: 254-260 [PMID: 18202296 DOI: 10.1177/0363546507311599]
72 **Jerosch J**, Schunck J. Arthroscopic treatment of lateral epicondylitis: indication, technique and early results. *Knee Surg Sports Traumatol Arthrosc* 2006; **14**: 379-382 [PMID: 16078089 DOI: 10.1007/s00167-005-0662-5]
73 **Matache BA**, Berdusco R, Momoli F, Lapner PL, Pollock JW. A randomized, double-blind sham-controlled trial on the efficacy of arthroscopic tennis elbow release for the management of chronic lateral epicondylitis. *BMC Musculoskelet Disord* 2016; **17**: 239 [PMID: 27245219 DOI: 10.1186/s12891-016-1093-9]
74 **Bharati S**, Podder P, Mondal MRH. Hybrid deep learning for detecting lung diseases from X-ray images. *Inform Med Unlocked* 2020; **20**: 100391 [PMID: 32835077 DOI: 10.1016/j.imu.2020.100391]
75 **Mondal MRH**, Bharati S, Podder P. CO-IRv2: Optimized InceptionResNetV2 for COVID-19 detection from chest CT images. *PLoS One* 2021; **16**: e0259179 [PMID: 34710175 DOI: 10.1371/journal.pone.0259179]
76 **Khamparia A**, Bharati S, Podder P, Gupta D, Khanna A, Phung TK, Thanh DNH. Diagnosis of breast cancer based on modern mammography using hybrid transfer learning. *Multidimens Syst Signal Process* 2021; **32**: 747-765 [PMID: 33456204 DOI: 10.1007/s11045-020-00756-7]
77 **Khoury M**, Tabben M, Rolón AU, Levi L, Chamari K, D'Hooghe P. Promising improvement of chronic lateral elbow tendinopathy by using adipose derived mesenchymal stromal cells: a pilot study. *J Exp Orthop* 2021; **8**: 6 [PMID: 33501619 DOI: 10.1186/s40634-020-00320-z]

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ORIGINAL ARTICLE

Retrospective Cohort Study

Is it necessary to fuse to the pelvis when correcting scoliosis in cerebral palsy?

Shane F Strom, Matthew C Hess, Achraf H Jardaly, Michael J Conklin, Shawn R Gilbert

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Abstract

BACKGROUND

Neuromuscular scoliosis is commonly associated with a large pelvic obliquity. Scoliosis in children with cerebral palsy is most commonly managed with posterior spinal instrumentation and fusion. While consensus is reached regarding the proximal starting point of fusion, controversy exists as to whether the distal level of spinal fusion should include the pelvis to correct the pelvic obliquity.

AIM

To assess the role of pelvic fusion in posterior spinal instrumentation and fusion, particularly it impact on pelvic obliquity correction, and to assess if the rate of complications differed as a function of pelvic fusion.

METHODS

This was a retrospective, cohort study in which we reviewed the medical records of children with cerebral palsy scoliosis treated with posterior instrumentation and fusion at a single institution. Minimum follow-up was six months. Patients were stratified into two groups: Those who were fused to the pelvis and those fused to L4/L5. The major outcomes were complications and radiographic parameters. The former were stratified into major and minor complications, and the latter consisted of preoperative and final Cobb angles, L5-S1 tilt and pelvic obliquity.

RESULTS

The study included 47 patients. The correction of the L5 tilt was 60% in patients fused to the pelvis and 67% in patients fused to L4/L5 (P = 0.22). The pelvic obliquity was corrected by 43% and 36% in each group, respectively (P = 0.12).

Regarding complications, patients fused to the pelvis had more total complications as compared to the other group (63.0% *vs* 30%, respectively, P = 0.025). After adjusting for differences in radiographic parameters (lumbar curve, L5 tilt, and pelvic obliquity), these patients had a 79% increased chance of developing complications (Relative risk = 1.79; 95%CI: 1.011-3.41).

CONCLUSION

Including the pelvis in the distal level of fusion for cerebral palsy scoliosis places patients at an increased risk of postoperative complications. The added value that pelvic fusion offers in terms of correcting pelvic obliquity is not clear, as these patients had similar percent correction of their pelvic obliquity and L5 tilt compared to children whose fusion was stopped at L4/L5. Therefore, in a select patient population, spinal fusion can be stopped at the distal lumbar levels without adversely affecting the surgical outcomes.

Key Words: Cerebral palsy; Scoliosis; Pelvic fusion; Pelvic obliquity; Spinal fusion; Distal lumbar level

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Core Tip: The value of including the pelvis in the distal level of fusion in children with cerebral palsy scoliosis is not clear with respect to correcting pelvic obliquity or L5 tilt. This does, however, increase the risk of complications. After careful patient selection, spinal fusion can be stopped at the distal lumbar levels without adversely affecting the surgical outcomes.

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INTRODUCTION

Patients with neuromuscular scoliosis may benefit from surgery with improved standing balance, sitting positioning, and overall better caregiver satisfaction[1]. However, these surgeries are challenging due to severe deformity and presence of comorbidities. Complications are high (20% to 40%) compared to adolescent idiopathic scoliosis (5% to 23%)[2-5]. Posterior spinal instrumentation and fusion is the most common procedure performed. Proximally, fusion is begun T1 or T2 to prevent the development of proximal junctional kyphosis (PJK) which can lead to pain and neurologic deficits[6,7]. The distal extent of the fusion, however, remains controversial. Neuromuscular scoliosis is commonly characterized by pelvic obliquity which affects sitting balance and the development of iliac ulcers[8]. There is debate as to whether pelvic fixation is necessary to correct pelvic obliquity with some authors advocating that those with pelvic obliquity less than 10°-15° do not require fixation to the pelvis[6-8]. The majority of authors, however, advocate for fusion to the pelvis to not only correct the pelvic obliquity but also decrease the risk of distal curve progression and revision surgery[9-11].

The studies that discuss pelvic fusion either focus on children with flaccid forms of paralysis or include a pooled patient cohort including both spastic and flaccid disorders[9-13]. Since these neuromuscular disorders have varying levels of pelvic obliquity and do not necessarily act the same way, we sought to analyze our patients with cerebral palsy (CP) with regards to radiographic outcomes and complications as a function of fusion to the pelvis compared with higher levels of fusion.

MATERIALS AND METHODS

Following institutional review board approval, we retrospectively reviewed our electronic medical records. Surgically treated CP scoliosis patients who had gross motor function classification system levels IV or V and were less than 21 years of age were included. Exclusion criteria were surgery for predominant kyphosis, follow-up less than six months, or incomplete charts. The analysis spanned records from 2007 to 2018 at a single institution. We excluded patients with other indications for surgery, patients with unavailable radiographs, and those with follow-up less than six months. Demographic information, operative details, and the development of complications were recorded. We stratified complications into major and minor as previously described.[14] Major complications were those that prolonged the duration of hospitalization or required additional surgical procedures. These

included severe pulmonary complications (pneumonia, respiratory failure), deep surgical site infections (SSI), hemodynamic instability, pseudarthrosis, and PJK. Minor complications were those that were asymptomatic, self-resolving, or effectively treated non-surgically. Examples include intraoperative durotomy, fever occurring more than 24 h after surgery, decubitus ulcers, superficial SSIs, and superficial wound dehiscence. Pre-operative and final follow up radiographs were measured and Cobb angles, L5-S1 tilt and pelvic obliquity using the Maloney method were recorded[14-17].

Statistical analysis was performed using the IBM SPSS Statistics for Windows, version 25 (IBM Corp., Armonk, NY, USA). *T*-tests and χ^2 tests were used when appropriate. The relative risk (RR) and 95%CI were calculated to assess whether the fusion level affected the risk of developing postoperative complications. *P* values ≤ 0.05 were considered statistically significant.

RESULTS

Over the study period, 65 children with CP had surgery for scoliosis at our hospital. We excluded 18 cases: 3 had predominant kyphosis rather than scoliosis, 8 had unavailable radiographs, and 7 were lost to follow-up. Our analysis therefore included 47 patients. These were 29 males and 18 females, with an average age of 13.9 years (range: 9.6–19.9 years). All procedures were posterior spinal fusion and instrumentation. The median number of fused vertebrae was 16 (range: 14-17), and 27 patients (57.4%) were fused to the pelvis. Median follow-up duration was 31 mo (range: 7–101 mo).

Patients fused to the pelvis and those fused to L4/L5 were similar with regards to their age, sex distribution, weight, follow-up, and comorbidities. The one exception was that fewer patients fused to the pelvis had seizures. Patient details are included in Table 1. The operative duration and blood loss were not different between both groups. Length of stay was also similar in both groups and was six days on average. With respect to pre-operative radiographic parameters, patients fused to the pelvis had a larger lumbar curve by 17˚ (P = 0.017), greater L5 tilt by 4˚ (P = 0.04), and greater pelvic obliquity by 10˚ (P = 0.0033). The thoracic curve magnitude was similar in both groups (P = 0.17). Table 2 includes the radiographic parameters immediately before surgery and at final follow-up. At the final follow-up, patients who were fused to the pelvis had their thoracic curve corrected by 53%, and their lumbar curve corrected by 38%. Corrections of their L5 tilt and pelvic obliquity were 60% and 43%, respectively. Patients who were fused to L4/L5 had 43% correction of their thoracic curve, 64% of their lumbar curve, 67% of their L5 tilt, and 36% of the pelvic obliquity. The degree of correction of the L5 tilt and pelvic obliquity was similar regardless of fusing to the pelvis (P = 0.22 and 0.12, respectively).

Pelvic obliquity of 10˚ is considered by some to be the threshold for pelvic fusion[6]. Twenty-one of 27 patients fused to the pelvis exceeded this threshold, with a mean of 25˚ (range: 11˚-59˚). This was corrected by 40% to 15˚ (range: 2˚-34˚). In the L4/L5 group, 10 of 20 also had a pelvic obliquity greater than 10˚, with an average of 18˚ (range: 11˚-30˚). Their pelvic obliquity was corrected by 44%, from a mean of 18˚ (range: 11˚–30˚) to 10˚ (range: 4˚-20˚). The magnitude of pelvic obliquity correction was clinically and statistically similar in both groups (P = 0.12). Table 3 stratifies patients according to their preoperative and final pelvic obliquity, and Figure 1 is sample cases of patients who were fused short of the pelvis or whose fusion included the pelvis, respectively.

The complications encountered are detailed in Table 4. The most frequent complications were pulmonary complications (14.9%), pressure ulcers (12.8%), and instrumentation (8.5%). No postoperative neurological deficits or deaths occurred. Two patients underwent reoperation for deep SSI and PJK. Both had been fused to the pelvis. Also two patients had hardware break and one had instrumentation prominence, but all were asymptomatic and were simply observed. Patients with fusion to the pelvis had more total complications (63.0% *vs* 30%, P = 0.025; RR = 2.099; 95%CI: 1.012–4.35, P = 0.046). Their RR for minor complications was 2.41 (95%CI: 0.92–6.29, P = 0.073) and for major complications was 1.48 (95%CI: 0.30–7.31, P = 0.63). Even after adjusting for the differences in radiographic parameters (lumbar curve, L5 tilt, and pelvic obliquity), the risk for complications remained increased (RR = 1.79; 95%CI: 1.011–3.41).

DISCUSSION

Children with CP scoliosis frequently have pelvic obliquity that affects their sitting balance and interferes with transfers. To correct pelvic obliquity and reduce risk of distal adding on, fusion to the pelvis is often recommended[1,10]. Pelvic fusion, however, can lead to surgical morbidity and complications[11,18]. In this study, we compare outcomes in children with CP scoliosis with regards to the distal extent of spine fusion. Pelvic fusion did not increase the operative time or blood loss compared to higher levels of fusion. Published studies have differed, with some demonstrating longer surgeries and more blood loss with pelvic fixation, while other studies did not find a difference[13,19-21]. The long duration of surgery and magnitude of blood loss along with case to case variation may make it difficult to detect differences with statistical significance.

Table 1 Characteristics of patients with cerebral palsy scoliosis

Characteristics	Fusion to pelvis (*n* = 27)	Fusion to L4/L5 (*n* = 20)	*P* value
Demographics			
Average age (yr)	14.2	13.4	0.303
Sex, number of males	19	13	0.52
Average weight (kg)	34.2	35.6	0.66
Average follow-up (mo)	41.7	31.0	0.11
Gastrostomy (*n*)	15	6	0.061
VP shunt (*n*)	4	3	0.95
Seizures (*n*)	10[a]	14[a]	0.050
Operative details			
Average operative duration (min)	341	334	0.72
Average blood loss (mL)	989	1049	0.74

[a]$P \leq 0.05$, between the groups.
VP shunt: Ventriculoperitoneal shunt.

Table 2 Radiographic parameters

	Pre-operative values, mean (Range)	Final values, mean (Range)
Fusion to pelvis		
Thoracic curve (degrees)	30 (0–64)	14 (0-38)
Lumbar curve (degrees)	56 (4–106)	32 (0-68)
L5 tilt (degrees)	10 (0-41)	4 (0-16)
Pelvic obliquity (degrees)	21 (1-59)	12 (0-34)
Fusion to L4/L5		
Thoracic curve (degrees)	42 (2-109)	24 (1-88)
Lumbar curve (degrees)	39 (5-75)	14 (1-47)
L5 tilt (degrees)	6 (0-13)	2 (0-8)
Pelvic obliquity (degrees)	11 (1-30)	7 (2-20)

Table 3 Preoperative and final pelvic obliquity of patients

	Pelvic obliquity		
	< 10°	10°-15°	> 15°
Fusion to pelvis			
Preoperative	6	6	15
Final	12	6	9
Fusion to L4/L5			
Preoperative	10	5	5
Final	15	1	4

We did find differences in complication rates. In our cohort, children fused to the pelvis had an increased risk to develop post-operative complications, with a RR of 2.099, mainly attributable to higher occurrences of minor complications, most notably pressure ulcers and hardware complications. Pelvic fusion leads to a more rigid seating position[1]. In patients with limited mobility, this could increase

Table 4 Complications encountered in both groups, *n* (%)

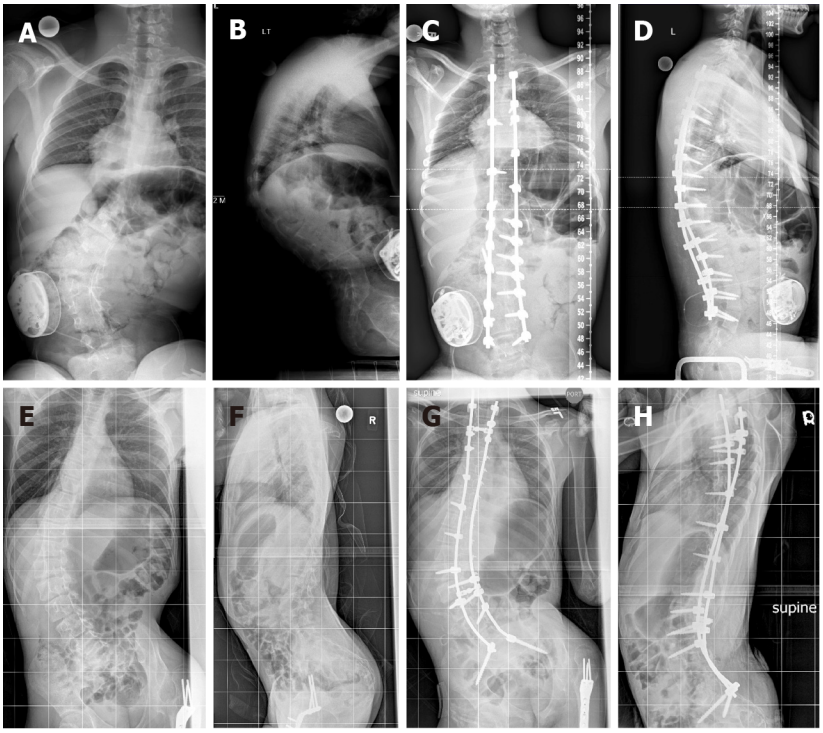
Complications	Fusion to pelvis (*n* = 27)	Fusion to L4/L5 (*n* = 20)	Total (*n* = 47)
Pulmonary complications			
Respiratory failure[1]	1 (3.7)	1 (5)	2 (4.2)
Atelectasis	3 (11.1)	1 (5)	4 (8.5)
Pneumonia[1]	0	1(5)	1 (2.1)
Pressure ulcer	5 (18.5)	1 (5)	6 (12.8)
Instrumentation			
Hardware break or prominence	3 (11.1)	0	3 (6.4)
PJK[1]	1 (3.7)	0	1 (2.1)
Superficial SSI	0	2 (10)	2 (4.2)
Deep SSI[1]	1 (3.7)	0	1 (2.1)
Wound dehiscence	1 (3.7)	0	1 (2.1)
SIRS[1]	1 (3.7)	0	1 (2.1)
Durotomy	1 (3.7)	0	1 (2.1)
Total	17 (63)	6 (30)	23 (49.9)

[1]Major complications.
SIRS: Systemic inflammatory response syndrome; SSI: Surgical site infection; PJK: Proximal junctional kyphosis.

their risk for decubitus ulcers. We only had few occurrences of SSIs and wound complications, but they are also an important consideration. Deep SSIs are a common cause for reoperation which puts patients at repeated risks of anesthetic complications, bleeding, and injury due to reinstrumentation. This is particularly important in patients with GMFCS levels IV and V, who have significant co-morbidities, are frequently malnourished, and are at increased risk for abnormal wound healing and infections. Again, published reports have conflicting results. Toll *et al*[14] in their evaluation of risk factors following scoliosis surgery in neuromuscular patients did not find that fusion to the pelvis was a risk factor for complications. On the other hand, other studies found an increased risk[22,23]. One possible explanation of this discrepancy is the heterogeneity of the reports which include different neuromuscular conditions in the same analysis.

The two most commonly used determinants for including the pelvis in the fusion are L5 stability and pelvic obliquity. The L5-sacrum articulation is considered stable when the L5 tilt is less than 15°, and it is considered unstable when it is greater than 15°. Fusion to the pelvis is also recommended for pelvic obliquity greater than 10°. In our cohort, even though decision making was not standardized, all patients with a large L5 tilt were fused to the pelvis. However, not all patients with pelvic tilt were fused to the pelvis. The pelvic fusion did have greater L5 tilt and pelvic obliquity than patients fused to L4/L5. Interestingly, the degree of correction of both parameters was similar in both groups. The L5 tilt was corrected by 60% with pelvic fusion and by 67% with fusion to L4/L5 (P = 0.22). Similarly, the pelvic obliquity was corrected by 43% and 36% in each group, respectively (P = 0.12), so fusing to the pelvis did not offer a significantly greater correction of pelvic obliquity. This was also true for the subset of patients with a pelvic obliquity greater than 10°. In this population, correction of pelvic obliquity was 40% for patients fused to the pelvis and 44% for those fused to L4/L5, indicating that even with patients who have a large pelvic tilt, fusion to the pelvis does not necessarily achieve better pelvic obliquity correction. Therefore, a large pelvic obliquity by itself might not be an indication to include the pelvis in the distal extent of the spinal fusion, particularly since these patients experience more complications. Furthermore, fusion to the pelvis may not be necessary in all children with CP scoliosis. This could still lead to satisfactory surgical outcomes including pelvic tilt while decreasing the risk of postoperative complications. Future studies can better delineate selection criteria regarding whether to fuse to the pelvis or not in these children.

Our study has several limitations. As a retrospective study, information was gathered from the medical records, which might lead to some inaccuracies. We aimed to have a homogenous cohort, so we only included children with CP, making our sample size moderate. This made the study underpowered to detect differences at the level of individual complications, but did allow identification of higher total complication rate. Sagittal plane deformities were not assessed. There were no predetermined selection criteria for choosing distal fusion level to the pelvis. Although traditional criteria for fusion to the pelvis were not strictly followed, patients who were fused to the pelvis had more pelvic and L5 tilt, indicating



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Figure 1 Sample cases of patients who were fused short of the pelvis or whose fusion included the pelvis. A, B: Preoperative anteroposterior (A) and lateral (B) radiographs demonstrating scoliosis with a lumbar curve Cobb angle of 58° and pelvic obliquity of 12°; C, D: Fusion was stopped at L5, and postoperative anteroposterior (C) and lateral (D) radiographs show the lumbar curve Cobb angle at 8° and pelvic obliquity at 3°; E, F: Preoperative anteroposterior (E) and lateral (F) radiographs demonstrating scoliosis with a lumbar curve Cobb angle of 52° and pelvic obliquity of 19°; G, H: Fusion was carried out to the pelvis, and postoperative anteroposterior (G) and lateral (H) radiographs show a lumbar curve Cobb angle of 48° and pelvic obliquity of 12°.

selection bias. This might limit the generalizability of the present study, but the conclusion that in a select patient population, posterior fusion does not necessarily have to include the pelvis remains valid. In addition, our outcomes focused on complications. Other factors that can affect surgical planning, like patient and caregiver satisfaction, were not assessed. Additional studies that focus on patient reported outcomes in this patient population will provide valuable insights.

CONCLUSION

In conclusion, this study demonstrated that in children with CP scoliosis, fusion short of the pelvis can lead to acceptable final pelvic tilt in some cases and may decrease the risk of developing post-operative complications.

ARTICLE HIGHLIGHTS

Research background

The distal extent of the fusion in children with cerebral palsy scoliosis is a controversial topic. There is not enough evidence on whether it is necessary to include the pelvis in the distal fusion to correct for pelvic obliquity in these patients.

Research motivation

This study was carried out to fill the gap in the literature on whether it is necessary to fuse to the pelvis when correcting cerebral palsy scoliosis. The need for a homogeneous cohort (*i.e.* children with cerebral palsy and not other forms of neuromuscular scoliosis) was an additional reason for carrying out the study.

Research objectives

The primary objective was to compare the radiographic outcome (Cobb angles and pelvic obliquity) of cerebral palsy scoliosis treatment in children who were fused to the pelvis *vs* those who were fused to

L4/L5. The secondary objective was to determine the complications associated with each of the two procedures.

Research methods

The study was a retrospective, cohort study that utilized chart and radiographic review to determine the outcomes and complications associated with cerebral palsy scoliosis correction in children who were fused to L4/L5 as compared to those fused to the pelvis.

Research results

In the analysis of 47 patients, the L5 tilt was corrected by 60% in patients fused to the pelvis, comparable to the 67% achieved in patients fused to L4/L5 (P = 0.22). The pelvic obliquity was also corrected by a similar degree; 43% in patients fused to the pelvis and 36% in patients fused to L4/L5 (P = 0.12). As for complications, patients fused to the pelvis had a higher number of total complications (63.0% *vs* 30%, respectively, P = 0.025).

Research conclusions

Fusing to the pelvis in cerebral palsy scoliosis did not achieve better correction of patients' pelvic obliquity and L5 tilt. However, it did increase the risk of postoperative complications. Therefore, spinal fusion can be stopped at the distal lumbar levels in a select patient population, without necessarily compromising the surgical outcomes.

Research perspectives

Future studies can investigate delineating specifically which patients might benefit from including the pelvis in their distal fusion. This might aid the surgeons in their preoperative planning and in guiding their choice of surgical technique.

FOOTNOTES

Author contributions: Jardaly AH, Conklin MJ, and Gilbert SR designed the research study; Strom SF, Hess MC, Jardaly AH, Conklin MJ, and Gilbert SR performed the data collection; Jardaly AH analyzed the data; Strom SS, Hess MC, and Jardaly AH wrote the manuscript; all authors thoroughly edited the manuscript; all authors have read and approve the final manuscript.

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REFERENCES

1 **Halawi MJ**, Lark RK, Fitch RD. Neuromuscular Scoliosis: Current Concepts. *Orthopedics* 2015; **38**: e452-e456 [PMID: 26091215 DOI: 10.3928/01477447-20150603-50]

2 **Hasler CC**. Operative treatment for spinal deformities in cerebral palsy. *J Child Orthop* 2013; **7**: 419-423 [PMID: 24432105 DOI: 10.1007/s11832-013-0517-4]

3 **Reames DL**, Smith JS, Fu KM, Polly DW Jr, Ames CP, Berven SH, Perra JH, Glassman SD, McCarthy RE, Knapp RD Jr, Heary R, Shaffrey CI; Scoliosis Research Society Morbidity and Mortality Committee. Complications in the surgical treatment of 19,360 cases of pediatric scoliosis: a review of the Scoliosis Research Society Morbidity and Mortality database. *Spine (Phila Pa 1976)* 2011; **36**: 1484-1491 [PMID: 21037528 DOI: 10.1097/BRS.0b013e3181f3a326]

4 **Murphy RF**, Mooney JF 3rd. Current concepts in neuromuscular scoliosis. *Curr Rev Musculoskelet Med* 2019; **12**: 220-227 [PMID: 30941730 DOI: 10.1007/s12178-019-09552-8]

5 **Sink EL**, Newton PO, Mubarak SJ, Wenger DR. Maintenance of sagittal plane alignment after surgical correction of spinal deformity in patients with cerebral palsy. *Spine (Phila Pa 1976)* 2003; **28**: 1396-1403 [PMID: 12838097 DOI: 10.1097/01.BRS.0000067088.99346.73]

6 **Hasler C**, Brunner R, Grundshtein A, Ovadia D. Spine deformities in patients with cerebral palsy; the role of the pelvis. *J Child Orthop* 2020; **14**: 9-16 [PMID: 32165976 DOI: 10.1302/1863-2548.14.190141]

7 **Takaso M**, Nakazawa T, Imura T, Fukuda M, Takahashi K, Ohtori S. Segmental Pedicle Screw Instrumentation and Fusion Only to L5 in the Surgical Treatment of Flaccid Neuromuscular Scoliosis. *Spine (Phila Pa 1976)* 2018; **43**: 331-338 [PMID: 29095413 DOI: 10.1097/BRS.0000000000000996]

8 **Modi HN**, Suh SW, Song HR, Yang JH, Jajodia N. Evaluation of pelvic fixation in neuromuscular scoliosis: a retrospective study in 55 patients. *Int Orthop* 2010; **34**: 89-96 [PMID: 19052744 DOI: 10.1007/s00264-008-0703-z]

9 **Howard J**, Sees J, Shrader W. Management of Spine Deformity in Cerebral Palsy. *JPOSNA* 2019; **1**: 1

10 **Peelle MW**, Lenke LG, Bridwell KH, Sides B. Comparison of pelvic fixation techniques in neuromuscular spinal deformity correction: Galveston rod versus iliac and lumbosacral screws. *Spine (Phila Pa 1976)* 2006; **31**: 2392-8; discussion 2399 [PMID: 16985470 DOI: 10.1097/01.brs.0000238973.13294.16]

11 **Janjua MB**, Toll B, Ghandi S, Sebert ME, Swift DM, Pahys JM, Samdani AF, Hwang SW. Risk Factors for Wound Infections after Deformity Correction Surgery in Neuromuscular Scoliosis. *Pediatr Neurosurg* 2019; **54**: 108-115 [PMID: 30783030 DOI: 10.1159/000496693]

12 **Nielsen E**, Andras LM, Bellaire LL, Fletcher ND, Minkara A, Vitale MG, Troy M, Glotzbecker M, Skaggs DL. Don't You Wish You Had Fused to the Pelvis the First Time: A Comparison of Reoperation Rate and Correction of Pelvic Obliquity. *Spine (Phila Pa 1976)* 2019; **44**: E465-E469 [PMID: 30299416 DOI: 10.1097/BRS.0000000000002888]

13 **Tøndevold N**, Lastikka M, Andersen T, Gehrchen M, Helenius I. Should instrumented spinal fusion in nonambulatory children with neuromuscular scoliosis be extended to L5 or the pelvis? *Bone Joint J* 2020; **102-B**: 261-267 [PMID: 32009441 DOI: 10.1302/0301-620X.102B2.BJJ-2019-0772.R2]

14 **Toll BJ**, Samdani AF, Janjua MB, Gandhi S, Pahys JM, Hwang SW. Perioperative complications and risk factors in neuromuscular scoliosis surgery. *J Neurosurg Pediatr* 2018; **22**: 207-213 [PMID: 29749884 DOI: 10.3171/2018.2.PEDS17724]

15 **McCall RE**, Hayes B. Long-term outcome in neuromuscular scoliosis fused only to lumbar 5. *Spine (Phila Pa 1976)* 2005; **30**: 2056-2060 [PMID: 16166895 DOI: 10.1097/01.brs.0000178817.34368.16]

16 **Maloney WJ**, Rinsky LA, Gamble JG. Simultaneous correction of pelvic obliquity, frontal plane, and sagittal plane deformities in neuromuscular scoliosis using a unit rod with segmental sublaminar wires: a preliminary report. *J Pediatr Orthop* 1990; **10**: 742-749 [PMID: 2250058 DOI: 10.1097/01241398-199011000-00007]

17 **Brooks JT**, Sponseller PD. What's New in the Management of Neuromuscular Scoliosis. *J Pediatr Orthop* 2016; **36**: 627-633 [PMID: 25887834 DOI: 10.1097/BPO.0000000000000497]

18 **Subramanyam R**, Schaffzin J, Cudilo EM, Rao MB, Varughese AM. Systematic review of risk factors for surgical site infection in pediatric scoliosis surgery. *Spine J* 2015; **15**: 1422-1431 [PMID: 25796355 DOI: 10.1016/j.spinee.2015.03.005]

19 **Sharma S**, Wu C, Andersen T, Wang Y, Hansen ES, Bünger CE. Prevalence of complications in neuromuscular scoliosis surgery: a literature meta-analysis from the past 15 years. *Eur Spine J* 2013; **22**: 1230-1249 [PMID: 23085815 DOI: 10.1007/s00586-012-2542-2]

20 **Kothari P**, Somani S, Lee NJ, Guzman JZ, Leven DM, Skovrlj B, Steinberger J, Kim J, Cho SK. Thirty-Day Morbidity Associated with Pelvic Fixation in Adult Patients Undergoing Fusion for Spinal Deformity: A Propensity-Matched Analysis. *Global Spine J* 2017; **7**: 39-46 [PMID: 28451508 DOI: 10.1055/s-0036-1583946]

21 **Ramo BA**, Roberts DW, Tuason D, McClung A, Paraison LE, Moore HG 4th, Sucato DJ. Surgical site infections after posterior spinal fusion for neuromuscular scoliosis: a thirty-year experience at a single institution. *J Bone Joint Surg Am* 2014; **96**: 2038-2048 [PMID: 25520337 DOI: 10.2106/JBJS.N.00277]

22 **Labbé AC**, Demers AM, Rodrigues R, Arlet V, Tanguay K, Moore DL. Surgical-site infection following spinal fusion: a case-control study in a children's hospital. *Infect Control Hosp Epidemiol* 2003; **24**: 591-595 [PMID: 12940580 DOI: 10.1086/502259]

23 **Perry JW**, Montgomerie JZ, Swank S, Gilmore DS, Maeder K. Wound infections following spinal fusion with posterior segmental spinal instrumentation. *Clin Infect Dis* 1997; **24**: 558-561 [PMID: 9145726 DOI: 10.1093/clind/24.4.558]

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Comparing complications of outpatient management of slipped capital femoral epiphysis and Blount's disease: A database study

Achraf Jardaly, Timothy W Torrez, Gerald McGwin, Shawn R Gilbert

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Abstract

BACKGROUND

Currents trends in pediatric orthopaedics has seen an increase in surgeries being successfully completed in an outpatient setting. Two recent examples include slipped capital femoral epiphysis (SCFE) and Blount's disease. Surgical indications are well-studied for each pathology, but to our knowledge, there is an absence in literature analyzing safety and efficacy of inpatient *vs* outpatient management of either condition. We believed there would be no increase in adverse outcomes associated with outpatient treatment of either conditions.

AIM

To investigate whether outpatient surgery for SCFE and Blount's disease is associated with increased risk of adverse outcomes.

METHODS

The 2015-2017 American College of Surgeons National Surgical Quality Improvement Program Pediatric Registries were used to compare patient characteristics, rates of complications, and readmissions between outpatient and inpatient surgery for SCFE and Blount's disease.

RESULTS

Total 1788 SCFE database entries were included, 30% were performed in an

outpatient setting. *In situ* pinning was used in 98.5% of outpatient surgeries and 87.8% of inpatient surgeries ($P < 0.0001$). Inpatients had a greater percent of total complications than outpatients 2.57% and 1.65% respectively. Regarding Blount's disease, outpatient surgeries constituted 41.2% of the 189 procedures included in our study. The majority of inpatients were treated with a tibial osteotomy, while the majority of outpatients had a physeal arrest ($P < 0.0001$). Complications were encountered in 7.4% of patients, with superficial surgical site infections and wound dehiscence being the most common. 1.6% of patients had a readmission. No differences in complication and readmission risks were found between inpatients and outpatients.

CONCLUSION

The current trend is shifting towards earlier discharges and performing procedures in an outpatient setting. This can be safely performed for a large portion of children with SCFE and Blount's disease without increasing the risk of complications or readmissions. Osteotomies are more commonly performed in an inpatient setting where monitoring is available.

Key Words: Outpatient surgery; Early discharge; Slipped capital femoral epiphysis; Blount's disease

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Core Tip: In our retrospective analysis of common complications of both slipped capital femoral epiphysis and Blount's disease using National Surgical Quality Improvement Program database. We showed equivocally that treating both these conditions as an outpatient was safe and effective.

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INTRODUCTION

In recent years, an increasing number of orthopaedic surgeries have been performed in an outpatient setting[1]. A study examining pediatric fracture trends demonstrated a threefold increase in the use of outpatient services for the surgical fixation of fractures from 1996 to 2006[2]. Though outpatient surgery provides a lower initial cost, several factors like patient safety, complications, and readmissions need to be considered[3].

Obesity in children has reached epidemic proportions. According to the Centers of Disease Control and Prevention, 1 out of 5 individuals less than 19 years of age are obese[4]. As such, it is anticipated that adverse health outcomes related to obesity will increase. From an orthopaedic perspective, childhood obesity is considered to be a significant risk factor for both slipped capital femoral epiphysis (SCFE) and Blount's disease[5,6]. A better understanding of both diseases and their respective treatment options would benefit children and their families.

Despite the surgical options for SCFE and Blount's disease being well-studied, to our knowledge, there is no literature comparing inpatient *vs* outpatient management of either condition[6,7]. Therefore, we sought to use a large pediatric database to compare the complication and readmission rates between treatment in the inpatient and outpatient setting. Our hypothesis was that there would be no increased risk of adverse outcomes associated with the outpatient treatment of both conditions.

MATERIALS AND METHODS

The American College of Surgeons National Surgical Quality Improvement Program (NSQIP) Pediatric Registry was queried for the years 2015, 2016, and 2017[8]. As information in this database is de-identified and HIPAA compliant, institutional review board approval is not required.

NSQIP prospectively collects data on patient demographics, risk factors, and operative details. The database follows patients for 30 d after surgeries to document discharge status, complications, readmission, and reoperation. The 2017 NSQIP Pediatric database includes 113922 cases from 109 hospitals. Cases with codes corresponding for the International Classification of Diseases, ninth and tenth revisions (ICD-9 and ICD-10) primary diagnosis of SCFE or Blount's disease were selected. Procedures were defined as outpatient if patients were discharged on the day of the surgery.

For SCFE, patients from 9 to 16 years were included. Treatment options were divided into *in situ* pinning and open treatment. Open treatment includes osteotomy, open reduction, and internal fixation. For pediatric Blount's disease, patients older than 10 years were excluded. Treatment was categorized as external fixation, osteotomy, or physeal arrest. Osteotomy includes proximal tibial osteotomy with or without fibular osteotomy or excision. Physeal arrest includes epiphysiodesis and hemiepiphysiodesis with any method (*e.g.* guided growth). Patients were excluded if their primary surgery was not congruent with their primary diagnosis (*e.g.* distal femur lengthening for SCFE, or tumor/cyst excision for Blount's disease).

In addition to the common complications documented in the database, we considered a discharge to an acute care setting or facility which was not home as a complication. If a case had multiple related complications, then it was recorded as one complication. For example, a patient with both superficial wound dehiscence and superficial surgical site infection (SSI) was counted as one complication under superficial SSI. No patient had multiple unrelated complications. We included both reoperations and readmissions not requiring an operation in "readmissions.".

Statistical analysis was carried out using IBM SPSS Statistics for Windows, version 25 (IBM Corp., Armonk, N.Y., USA). ANOVA, Wilcoxon signed rank-test, Fisher's exact tests, and χ^2 tests were used to compare variables between the outpatient and the inpatient settings. Odds ratios (OR) with 95%CI were calculated when differences in adverse outcomes were exhibited between the inpatient and outpatient settings. P values < 0.05 were considered to be statistically significant.

RESULTS

SCFE

Out of 1797 procedures for SCFE, 46% were performed as an outpatient. 93.6% of children admitted postoperatively were discharged within 3 days, with 47.7% being discharged on postop day (POD) 1 and 39.4% on POD 2. Patients in both settings were similar with respect to age. Small differences existed regarding the weight, sex, and race of patients. There were more males and white patients receiving outpatient surgeries in comparison to the inpatient setting noting more female and black patients. Outpatients had a higher percentage of American Society of Anesthesiologists Classification (ASA) classes 1 and 2 and a lower percentage of ASA class 3 compared to inpatients. Patient details can be found in Table 1. *In situ* pinning was the most common procedure, constituting 98.5% of outpatient surgeries and 87.8% of inpatient surgeries (P < 0.0001).

Total 1.6% of outpatients and 1.2% of inpatients had complications (P = 0.50), and the readmissions rates were 1.1% and 1.44%, respectively (P = 0.89). The nature of complications and causes of readmission are found in Table 2. There was no statistically significant difference in individual adverse outcomes except for bleeding. Bleeding was the most common complication among inpatients and did not occur in outpatients. None of these patients had a preoperative bleeding disorder. 12 of the 15 cases of bleeding requiring transfusion occurred with open procedures (Osteotomy and internal fixation) while 3 occurred during in situ pinning (P < 0.0083). The overall risks of SCFE recurrence and femoral neck fractures for outpatient and inpatient was 0.55% and 0.64% respectively. Three inpatients initially discharged on POD 1 required readmission for postop pain management.

There were 3.5x the total number of complications in the inpatient SCFE group but the mean number of complications between the two groups was not significant (P = 0.292). There were 3.3x the number patients that developed complications but OR was not statistically significant (OR = 0.66, 95%CI: 0.31-1.41). Similarly, no difference was found regarding odds of readmission (OR = 1.12, 95%CI: 0.20–6.16).

Blount's disease

Total 189 procedures for Blount's disease were included. 41.2% were performed in an outpatient setting. 54.1% of admitted patients were discharged on POD 1, and 30.6% were discharged on POD 2. Patients in both settings had similar sex, race, BMI, and ASA distributions, but statistically significant differences were found in their age. Outpatients were younger by (0.7 year) (Table 1). There were also differences in the procedures used in both settings (P < 0.0001). Osteotomy was the most common procedure among inpatients (64%), whereas it was not performed in an outpatient setting. 98.7% of outpatients were treated with physeal arrest, as compared to 34.2% of inpatients.1.3% of inpatients and 1.8% of outpatients were treated with external fixation.

7.4% of patients experienced complications (Table 3). Superficial SSI and wound dehiscence were the most frequent complications. Individual and total risk of complications and readmissions were not different between both settings (P > 0.05) so no ORs were calculated.

DISCUSSION

There is a shifting trend towards performing procedures in an outpatient setting[9]. In the current study

Table 1 Patient demographics, *n* (%)

	SCFE		Blount's disease	
	Outpatient (*n* = 553)	Inpatient (*n* = 1244)	Outpatient (*n* = 78)	Inpatient (*n* = 111)
Age (yr), mean ± SD	12.6 ± 1.4	12.5 ± 1.6	6.0 ± 2.8[a]	6.7 ± 2.0[a]
Sex				
Female	181 (32.73)[a]	490 (39.39)[a]	52 (66.7)	70 (63.1)
Male	372 (67.27)[a]	754 (60.61)[a]	26 (33.3)	41 (36.9)
Weight (kg), mean ± SD	71.5 ± 18.2	73.3 ± 20.3	38.6 ± 23.5[a]	48.6 ± 27.1[a]
Missing	2	3	0	0
Race				
White	248 (44.85)[a]	429 (34.49)[a]	17 (21.8)	20 (18.0)
Black	153 (27.67)[a]	441 (35.45)[a]	46 (60.2)	63 (56.8)
Hispanic	74 (13.38)[a]	158 (12.7)[a]	6 (7.7)	13 (11.7)
Other minorities	33 (5.6)[a]	41 (3.29)[a]	3 (3.8)	5 (4.5)
Unknown/Not reported	47(8.5)[a]	175 (14.07)[a]	6 (7.7)	10 (9.0)
ASA				
1	182 (32.91)	399 (32.07)	24 (30.8)	21 (18.9)
2	340 (61.48)	725 (58.28)	42 (53.8)	61 (55.0)
3	29 (5.24)	116 (9.32)	12 (15.4)	27 (24.3)
4	1 (0.18)	1 (0.08)	0	2 (1.8)
None assigned	1 (0.18)	3 (0.24)	0	0

[a]$P < 0.05$ between groups.

ASA: American Society of Anesthesiologists Classification; SCFE: Slipped capital femoral epiphysis.

based on results from the NSQIP Pediatric database, 46% of SCFE procedures and 41% of Blount's procedures were performed as outpatients.

Several studies report a decline in the incidence of SCFE[10-12]. As obesity rates have been increasing, it is unusual for fewer children to suffer from SCFE. One thing to consider is the methodology of the studies, which rely on databases. Most large registries report inpatient admissions. Same-day surgeries and procedures performed in ambulatory surgery centers are more difficult to capture, but the shift towards outpatient surgery could contribute to the apparent decrease in the incidence of SCFE. In 2000, outpatient SCFE procedures represented 23% of operatively treated SCFEs[13]. This percentage more than doubled according to our results. In addition, NSQIP does not include data from ambulatory centers, so outpatient procedures might constitute more than half of all SCFE surgical correction. Future studies investigating the true incidence of SCFE with outpatient adjustment would provide valuable information.

Performing procedures in an outpatient setting has several advantages. One significant benefit is the lower patient and hospital cost associated with early patient discharge[14]. In addition, several studies showed that patient satisfaction is inversely correlated with the length of hospital stay[15]. A study comparing inpatients and outpatients satisfaction following hip and knee arthroplasty demonstrated that satisfaction was high in both groups, but in areas of differences, outpatients had higher scores[16]. For children, this effect might be more pronounced, and performing outpatient surgeries can benefit their psychological well-being[17]. However, outpatient surgeries can have higher rates of adverse outcomes in some contexts, particularly with SSI[18]. Arshi *et al*[19] found that outpatient total knee arthroplasties had a higher chance of revision compared with inpatient care. Therefore, comparative studies for specific conditions are needed in this area.

Though an outpatient setting is an attractive option for patients and physicians, postoperative pain needs be considered[17]. Previous studies showed that children discharged home at the day of surgery had higher pain score than inpatients[20]. Even in admitted patients, Mather and Mackie reported that 17% of children had severe pain on POD 1[21]. In the present analysis, only 3 SCFE patients (0.24%) required readmission for pain. These patients were initially discharged on POD 1. None of the SCFE outpatients or any patients treated for Blount's disease had pain requiring readmission. Therefore, it is possible for the vast majority of surgical patients to benefit from early discharge without the need for

Table 2 Adverse outcomes in slipped capital femoral epiphysis patients, *n* (%)

	Outpatient (*n* = 544)	Inpatient (*n* = 1244)
Complication		
Non-routine discharge	6 (1.1)	5 (0.40)
Superficial SSI	1 (0.18)	5 (0.40)
Superficial wound dehiscence	1 (0.18)	6 (0.48)
Postop *C. diff* infection	1 (0.18)	0
Bleeding requiring transfusion	0[a]	15 (1.21)[a]
Venous thrombosis	0	1 (0.08)
Total number of patients with complications	9 (1.65)	30 (2.41)
Total number of complications	9 (1.65)	32 (2.57)
Reoperation		
SCFE	0	7 (0.56)
Hip infection	0	1 (0.08)
Femoral neck fracture	3 (0.55)	1 (0.08)
Closed reduction of hip dislocation	1 (0.18)	0
Fracture of hip/pelvis	0	1 (0.08)
Not documented	0	2 (0.20)
Total complication	4 (0.73)	12 (0.96)
Readmission without operation		
Superficial SSI	0	1 (0.08)
Pain	0	3 (0.24)
Not documented	2 (0.24)	4 (0.32)
Total readmission	6	18

[a]$P < 0.05$ between groups.
SCFE: Slipped capital femoral epiphysis; SSI: Surgical site infection.

inpatient management of pain. Techniques for anesthesia have improved significantly, and adequate postoperative analgesia can be achieved by giving caregivers ample pediatric-specific instructions and using multimodal medications[20].

Disease-specific and surgery-specific considerations also need to be investigated. One such consideration is the early return to weight-bearing which could increase the risk of femoral neck fractures in patients with SCFE[22]. Femur fractures in our SCFE population were rare and did not differ significantly based on the treatment setting. Nonetheless, for unstable slips where physician judgment deems strict non-weight-bearing to be necessary, patients might benefit from hospital admission (with inpatient physical therapy) to help enforce weight-bearing restrictions when compliance is an issue. The most common complications of SCFE include osteonecrosis, chondrolysis, fixation failure, and slip progression[23]. Osteonecrosis and chondrolysis are largely related to the nature of the slips rather than the surgical approach[23]. 0.56% of patients required a reoperation for SCFE, indicating fixation failure and/or slip progression. This rate was not different based on the setting of the surgery. Other common complications like SSI and wound dehiscence were also similar between the groups. The only individual complication that was different between both groups was bleeding requiring a transfusion. However, this was confounded with open procedures. Open procedures are more invasive, and bleeding is a well-known complication[7]. Such procedures are reserved for severe slips requiring more complex procedures, and it is recommended that they be admitted for inpatient monitoring. After adjusting the analysis for the type of surgery, the inpatient and outpatient settings did not have different odds ratio of complications or readmissions.

Surgery for Blount's disease, though technically difficult, is not commonly associated with major complications other than recurrence[24]. Infections, nerve injuries, and compartment syndromes can still occur[25]. 7.4% of Blount's patients had a complication in this study, most commonly superficial SSI and wound dehiscence. Patients selected to be treated in an outpatient setting can benefit from

Table 3 Adverse outcomes in Blount's patients, *n* (%)

Adverse outcome	Outpatient (*n* = 78)	Inpatient (*n* = 111)
Complication		
Non-routine discharge	1 (1.3)	0
Superficial SSI	1 (1.3)	5 (4.5)
Superficial wound dehiscence	4 (5.1)	2 (1.8)
Sepsis	1 (1.3)	0
Total complications	7 (9.0)	7 (6.3)
Readmission without operation		
Not documented	0	1 (0.9)
Reoperation		
Incision and drainage	1 (1.3)	0
Neuroplasty (common peroneal nerve)	0	1 (0.9)
Total readmissions	1 (1.3)	2 (1.8)

No *P* values < 0.05. SSI: Surgical site infection.

education about meticulous wound care and early signs of infection, and our results showed that rates of infections and overall complications were not different between both settings. This confirms our hypothesis that outpatient procedures are not associated with increased morbidity.

Careful patient selection is still needed to limit complications and readmissions. Patients with ASA 1 or 2 are considered suitable for outpatient surgery[17]. 90.3% of all the patients included in this study meet this requirement. Those with ASA 3 can still receive outpatient surgery, but they might have an increased risk of admission[17]. In addition, attention should be given to comorbidities and prior surgical or anesthetic complications. Nonetheless, a large portion of children with SCFE and Blount's disease can benefit from outpatient surgery.

To capture a large number of procedures, we used the NSQIP Pediatric Database. This is not without limitations. Data collected was from numerous hospitals, so there could be differences in the surgical techniques, indications for surgery, and selection criteria for inpatient *vs* outpatient procedures. Also, all cases included are surgeries performed in a hospital setting. Cases from ambulatory surgery centers are not part of the database. This means that even more procedures are performed in the outpatient setting. However, numerous studies have shown that ambulatory centers have similar outcomes to hospital outpatients, so the conclusion that outpatient surgery does not increase the risk of complications is not undermined[25,26]. In addition, patients were followed for 30 d. Long term complications like growth arrest and femoroacetabular impingement for SCFE and recurrence of Blount's disease may differ. Symptoms before and after surgery are not available. Despite these limitations, this study provides a representative sample of surgically managed cases of SCFE and Blount's disease and is the first to investigate short-term readmission and complication rates between of these outpatient procedures. Additionally, the prospective data collection and a priori definitions of complications improve the quality of data regarding complications compared to retrospective data collection or databases utilizing only coded complications.

CONCLUSION

In conclusion, our results indicate that performing outpatient surgeries for SCFE and Blount's disease is a viable option. Careful selection criteria need to be applied, but a large number of children can be surgically-treated as outpatients which does not affect the odds for early postoperative complications or readmissions.

ARTICLE HIGHLIGHTS

Research background

Currents trends in pediatric orthopaedics has seen an increase in surgeries being successfully completed

in an outpatient setting.

Research motivation
Limited data is available on safety and efficacy of managing slipped capital femoral epipphysis and Blount's disease in the outpatient setting.

Research objectives
Is outpatient management safe and effective for slipped capital femoral epipphysis and Blount's disease in the outpatient setting.

Research methods
Retrospective analysis of a large multi-institutional database.

Research results
In summary complications were minimal in outpatient surgical management for slipped capital femoral epiphysis and Blount's disease in the outpatient setting.

Research conclusions
Surgeons should consider outpatient management for both slipped capital femoral epiphysis and Blount's disease.

Research perspectives
This study should prompt future research in outcomes of outpatient management of other previous inpatient pediatric orthopaedic procedures.

FOOTNOTES

Author contributions: Jardaly A contributed to the manuscript preparation, data collection, revisions; Torrez TW contributed to the manuscript preparation, data collection, revisions; McGwin G contributed to the data analysis and statistics; Gilbert SR contributed to the manuscript preparation and was the principal investigator.

Institutional review board statement: This study was institutional review board exempt.

Informed consent statement: Informed consent was waived as per the University of Alabama at Birmingham's IRB guidelines.

Conflict-of-interest statement: The authors do not endorse any conflict of interests.

Data sharing statement: Technical appendix, statistical code, and dataset available from the corresponding author at achraf.jardaly@lau.edu.

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REFERENCES

1 **Webster P**. An outpatient "evolution" in orthopedic surgery. *CMAJ* 2017; **189**: E1568 [PMID: 29255105 DOI: 10.1503/cmaj.109-5534]
2 **Bernstein DT**, Chen C, Zhang W, McKay SD. National Trends in Operative Treatment of Pediatric Fractures in the Ambulatory Setting. *Orthopedics* 2015; **38**: e869-e873 [PMID: 26488780 DOI: 10.3928/01477447-20151002-52]
3 **Makarewich CA**, Stotts AK, Yoo M, Nelson RE, Rothberg DL. Inpatient Versus Outpatient Treatment of Gartland Type II

Supracondylar Humerus Fractures: A Cost and Safety Comparison. *J Pediatr Orthop* 2020; **40**: 211-217 [PMID: 31415017 DOI: 10.1097/BPO.0000000000001442]

4 **ACDC**. Childhood Obesity Facts, 2019. [accessed 2020 Feb 24]. Available from: https://www.cdc.gov/obesity/data/childhood.html

5 **Perry DC**, Metcalfe D, Costa ML, Van Staa T. A nationwide cohort study of slipped capital femoral epiphysis. *Arch Dis Child* 2017; **102**: 1132-1136 [PMID: 28663349 DOI: 10.1136/archdischild-2016-312328]

6 **Sabharwal S**. Blount disease. *J Bone Joint Surg Am* 2009; **91**: 1758-1776 [PMID: 19571101 DOI: 10.2106/JBJS.H.01348]

7 **Loder RT**, Dietz FR. What is the best evidence for the treatment of slipped capital femoral epiphysis? *J Pediatr Orthop* 2012; **32** Suppl 2: S158-S165 [PMID: 22890456 DOI: 10.1097/BPO.0b013e318259f2d1]

8 **American College of Surgeons**. About ACS NSQIP pediatric. [accessed 2020 Mar 3]. Available from: https://www.facs.org/quality-programs/acs-nsqip/about

9 **Goldfarb CA**, Bansal A, Brophy RH. Ambulatory Surgical Centers: A Review of Complications and Adverse Events. *J Am Acad Orthop Surg* 2017; **25**: 12-22 [PMID: 28002212 DOI: 10.5435/JAAOS-D-15-00632]

10 **Tucker A**, Ballard J, Cosgrove A. Temporal changes in slipped upper femoral epiphysis at a regional level: a declining incidence and literature review. *J Child Orthop* 2019; **13**: 445-456 [PMID: 31695811 DOI: 10.1302/1863-2548.13.190037]

11 **Ravinsky R**, Rofaiel J, Escott BG, Lim Z, Ravi B, Howard A. Epidemiology of Slipped Capital Femoral Epiphysis in Ontario, Canada. *J Pediatr Orthop* 2019; **39**: e165-e167 [PMID: 30199462 DOI: 10.1097/BPO.0000000000001254]

12 **Gutman IM**, Gilbert SR. Trends in slipped capital femoral epiphysis: is the rate declining? *J Child Orthop* 2018; **12**: 428-433 [PMID: 30294366 DOI: 10.1302/1863-2548.12.180081]

13 **Lehmann CL**, Arons RR, Loder RT, Vitale MG. The epidemiology of slipped capital femoral epiphysis: an update. *J Pediatr Orthop* 2006; **26**: 286-290 [PMID: 16670536 DOI: 10.1097/01.bpo.0000217718.10728.70]

14 **Crawford DC**, Li CS, Sprague S, Bhandari M. Clinical and Cost Implications of Inpatient Versus Outpatient Orthopedic Surgeries: A Systematic Review of the Published Literature. *Orthop Rev (Pavia)* 2015; **7**: 6177 [PMID: 26793295 DOI: 10.4081/or.2015.6177]

15 **Peres-da-Silva A**, Kleeman LT, Wellman SS, Green CL, Attarian DE, Bolognesi MP, Seyler TM. What Factors Drive Inpatient Satisfaction After Knee Arthroplasty? *J Arthroplasty* 2017; **32**: 1769-1772 [PMID: 28274618 DOI: 10.1016/j.arth.2017.01.036]

16 **Kelly MP**, Calkins TE, Culvern C, Kogan M, Della Valle CJ. Inpatient Versus Outpatient Hip and Knee Arthroplasty: Which Has Higher Patient Satisfaction? *J Arthroplasty* 2018; **33**: 3402-3406 [PMID: 30143333 DOI: 10.1016/j.arth.2018.07.025]

17 **Miller DJ**, Nelson SE, Shah AS, Ganley TJ, Flynn JJM. Outpatient Pediatric Orthopedic Surgery. *Orthop Clin North Am* 2018; **49**: 55-62 [PMID: 29145984 DOI: 10.1016/j.ocl.2017.08.007]

18 **Arshi A**, Leong NL, Wang C, Buser Z, Wang JC, Vezeridis PS, McAllister DR, Petrigliano FA. Relative Complications and Trends of Outpatient Total Shoulder Arthroplasty. *Orthopedics* 2018; **41**: e400-e409 [PMID: 29658980 DOI: 10.3928/01477447-20180409-01]

19 **Arshi A**, Leong NL, D'Oro A, Wang C, Buser Z, Wang JC, Jones KJ, Petrigliano FA, SooHoo NF. Outpatient Total Knee Arthroplasty Is Associated with Higher Risk of Perioperative Complications. *J Bone Joint Surg Am* 2017; **99**: 1978-1986 [PMID: 29206787 DOI: 10.2106/JBJS.16.01332]

20 **Shum S**, Lim J, Page T, Lamb E, Gow J, Ansermino JM, Lauder G. An audit of pain management following pediatric day surgery at British Columbia Children's Hospital. *Pain Res Manag* 2012; **17**: 328-334 [PMID: 23061083 DOI: 10.1155/2012/541751]

21 **Mather L**, Mackie J. The incidence of postoperative pain in children. *Pain* 1983; **15**: 271-282 [PMID: 6134266 DOI: 10.1016/0304-3959(83)90062-3]

22 **Johari AN**, Pandey RA. Controversies in management of slipped capital femoral epiphysis. *World J Orthop* 2016; **7**: 78-81 [PMID: 26925378 DOI: 10.5312/wjo.v7.i2.78]

23 **Roaten J**, Spence DD. Complications Related to the Treatment of Slipped Capital Femoral Epiphysis. *Orthop Clin North Am* 2016; **47**: 405-413 [PMID: 26772949 DOI: 10.1016/j.ocl.2015.09.013]

24 **Edwards TA**, Hughes R, Monsell F. The challenges of a comprehensive surgical approach to Blount's disease. *J Child Orthop* 2017; **11**: 479-487 [PMID: 29263762 DOI: 10.1302/1863-2548.11.170082]

25 **Cody JP**, Pfefferle KJ, Ammeen DJ, Fricka KB. Is Outpatient Unicompartmental Knee Arthroplasty Safe to Perform at an Ambulatory Surgery Center? *J Arthroplasty* 2018; **33**: 673-676 [PMID: 29103779 DOI: 10.1016/j.arth.2017.10.007]

26 **Sershon RA**, McDonald JF 3rd, Ho H, Goyal N, Hamilton WG. Outpatient Total Hip Arthroplasty Performed at an Ambulatory Surgery Center *vs* Hospital Outpatient Setting: Complications, Revisions, and Readmissions. *J Arthroplasty* 2019; **34**: 2861-2865 [PMID: 31445867 DOI: 10.1016/j.arth.2019.07.032]

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ORIGINAL ARTICLE

Retrospective Study

Minimally invasive outpatient management of iliopsoas muscle abscess in complicated spondylodiscitis

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Abstract

BACKGROUND

Iliopsoas muscle abscess (IPA) and spondylodiscitis are two clinical conditions often related to atypical presentation and challenging management. They are both frequently related to underlying conditions, such as immunosuppression, and in many cases they are combined. IPA can be primary due to the hematogenous spread of a microorganism to the muscle or secondary from a direct expansion of an inflammatory process, including spondylodiscitis. Computed tomography-guided percutaneous drainage has been established in the current management of this condition.

AIM

To present a retrospective analysis of a series of 8 immunocompromised patients suffering from spondylodiscitis complicated with IPA and treated with percutaneous computed tomography-guided drainage and drain insertion in an outpatient setting.

METHODS

Patient demographics, clinical presentation, underlying conditions, isolated microorganisms, antibiotic regimes used, abscess size, days until the withdrawal of the catheter, and final treatment outcomes were recorded and analyzed.

RESULTS

All patients presented with night back pain and local stiffness with no fever. The laboratory tests revealed elevated inflammatory markers. Radiological findings of

spondylodiscitis with unilateral or bilateral IPA were present in all cases. *Staphylococcus aureus* was isolated in 3 patients and *Mycobacterium tuberculosis* in 2 patients. Negative cultures were found in the remaining 3 patients. The treatment protocol included percutaneous computed tomography-guided abscess drainage and drain insertion along with a course of targeted or empiric antibiotic therapy. All procedures were done in an outpatient setting with no need for patient hospitalization.

CONCLUSION
The minimally invasive outpatient management of IPA is a safe and effective approach with a high success rate and low morbidity.

Key Words: Iliopsoas abscess; Spondylodiscitis; Percutaneous drainage; Minimally invasive; Outpatient; Immunocompromised

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Core Tip: Eight patients diagnosed with spondylodiscitis complicated with iliopsoas muscle abscess were managed with minimally invasive percutaneous computed tomography-guided drainage, placement of a drain, and proper antibiotic treatment in an outpatient setting. Complete recession of the symptoms with no recurrence after 6 mo was observed. The minimally invasive outpatient management of iliopsoas muscle abscess is a safe and effective approach with a high success rate and low morbidity.

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INTRODUCTION

Iliopsoas muscle abscess (IPA) is a rare infective clinical condition often related to nonspecific symptoms and a variety of etiologies[1]. It was first described by Mynter in 1881 and was characterized as "acute psoitis"[2]. Two proposed mechanisms lead to IPA. Primary IPAs are caused by a hematogenous spread of an infective microorganism that leads to IPA formation due to the muscle's rich vascularity, especially in immunocompromised patients. Secondary IPAs are developed by a contiguous spread of an intra-abdominal inflammatory process or by musculoskeletal conditions such as spondylodiscitis, sacroiliitis, or tuberculosis of the spine[1,3,4].

Spondylodiscitis is the most common form of spinal infection, affecting the intervertebral disc and the adjacent vertebral bodies and can present isolated or combined with other underlying conditions such as infections, malignancy, and immunosuppression[5]. Pyogenic spondylodiscitis can result in IPA due to direct expansion into the iliopsoas.

Symptoms of IPA may be insidious and nonspecific due to the location of the iliopsoas muscle, but the classical clinical presentation described in the literature includes the triad of fever, back pain, and limp[6,7]. Due to the atypical clinical features, diagnosis is oftentimes delayed leading to increased morbidity and mortality. Once an IPA is suspected, computed tomography (CT) scan is recommended, with a high sensitivity rate approaching 100%, whereas magnetic resonance imaging (MRI) of the spine is the most indicative imaging for spondylodiscitis[4,8]. There is no uniform treatment strategy for IPA. Traditionally, surgical drainage of the abscess along with a broad-spectrum antibiotic treatment was the preferred treatment[1,9,10]. However, more recent literature reports that the percutaneous CT-guided abscess drainage is a safe and equally effective alternative[1,8,11]. The purpose of the current study was to present and evaluate a case series of 8 patients diagnosed with spondylodiscitis complicated with IPA. The patients were managed with antimicrobial therapy, minimally invasive percutaneous CT-guided drainage, and the addition of a short-term drain insertion in an outpatient setting.

MATERIALS AND METHODS

A retrospective collection and analysis of all radiologically diagnosed cases of IPA that were treated with CT-guided percutaneous drainage from 2016 to 2020 in the department of Interventional Radiology of a tertiary University hospital was performed. All cases initially presented to the spinal outpatient

clinic complaining of back pain and were diagnosed with spondylodiscitis and IPA formation after an MRI and a CT scan. Records were extracted from the Interventional Radiology department's database. Data were reviewed for patient demographics, underlying conditions, isolated microorganisms, antibiotic regimes used, abscess size, days until the withdrawal of the catheter, and final outcome.

All abscesses were defined as secondary IPAs due to the concurrent presence of spondylodiscitis. Two patients were diagnosed specifically with tuberculosis of the spine. There was no neurological compromise, spinal instability, or bone deformity present due to spondylodiscitis.

Treatment success was marked by clinical and laboratory improvement along with radiological confirmation of recession of the abscess and eventually catheter removal. All patients were clinically evaluated 6 mo after the end of their treatment.

CT-guided percutaneous drainage

All draining procedures were performed by direct insertion of a 12 Fr pigtail catheter into the abscess cavity. Before the procedure, a CT and MRI scan were performed. Values of international normalized ratio less than 1.5 and platelet count greater than 50000/μL were required to proceed with the drainage, and antiplatelet or anticoagulation medication had to be discontinued accordingly. Patients were placed in the prone position in most cases (7 out of 8 patients). The placement decision was made depending on the best approach to the abscess cavity. All procedures were performed under local anesthesia and aseptic conditions. After an initial CT scan for approach planning, the trocar pigtail catheter was advanced into the abscess cavity under CT guidance. When the trocar reached the middle of the fluid collection it was withdrawn while the catheter was advanced and secured in position (Figure 1). Manual aspiration of the fluid was then performed, and the catheter was connected to a drainage bag. The inserted drain was removed if there was no drainage for 48 h.

RESULTS

A total of 8 patients that underwent CT-guided percutaneous IPA drainage were included in the study (Table 1). Their mean age was 52.6 ± 20.8-years-old, and there were six unilateral and two bilateral cases, a total of 10 abscesses. All cases were secondary; six were in immunocompromised patients [renal failure, HIV, intravenous (IV) drugs] with spondylodiscitis and two were in patients diagnosed with tuberculosis of the spine.

All patients presented at the spine outpatient clinic complaining of back pain for at least 3 mo with worsening at night, and 1 patient also mentioned weight loss. At clinical examination, there was local sensitivity and palpable muscle spasm found in all patients with no neurological compromise. All patients remained afebrile. From the laboratory investigation, there was an increase in inflammatory markers (C-reactive protein and erythrocyte sedimentation rate).

The diagnosis was confirmed by MRI followed by CT. According to imaging calculations, the mean abscess size was 6.3 ± 2.1 cm. There was no bone deformity or spinal degeneration observed. The drainage procedure was arranged immediately and performed in the next 1-3 d from the initial diagnosis. A 12 Fr pigtail drain was inserted in all cases, as previously described. The average time until the withdrawal of the catheter was 10 ± 2 d.

Microbiology samples from the abscess fluid were sent in all cases. *Staphylococcus aureus* was isolated in 3 cases, *Mycobacterium tuberculosis* was isolated in 2 patients, and there was no specific microorganism isolated in 2 renal impairment/dialysis patients and 1 IV drug user. All patients initially received empiric antibiotic therapy with ciprofloxacin and clindamycin orally. After the culture results, patients with *Staphylococcus aureus* culture isolation received a targeted 2-wk course of intravenous vancomycin and oral rifampicin with daily outpatient visits, followed by oral linezolid and rifampicin for another 6 wk. The tuberculosis patients underwent a 9-mo antimicrobial treatment with oral isoniazid, ethambutol, and rifampicin, whereas the patients with no specific microorganism isolated received an 8-wk empiric antibiotic treatment as presented in Table 2. All abscesses were successfully drained on the first attempt, and all patients had a complete resolution of symptoms. There were no recurrences at the 6-mo follow-up.

DISCUSSION

We present a case series of 8 patients suffering from spondylodiscitis complicated with IPA, successfully treated with a minimally invasive approach of combined percutaneous abscess drainage with drain insertion and antibiotic therapy. Immunosuppression is the predominant underlying condition in IPA and may be responsible for the insidious presenting signs and symptoms[9]. In the current series, there was a higher prevalence of IPA in patients that were on renal dialysis, immunocompromised by HIV, or IV drug users. Moreover, tuberculosis is linked to secondary IPA due to vertebral involvement[11-13]. Although tuberculosis is rare, there were 2 cases of secondary IPA in patients with tuberculosis of the

Table 1 Patient's demographics

Patient	Sex	Age in yr	Underlying condition	Site	Position	Size in cm	Procedure time in min	Presenting complaint	Catheter withdrawal in d	Microbiologic cultures
1	Male	76	Renal failure-dialysis	Unilateral	Prone	4.5	15	Back pain	8	Negative
2	Female	69	Renal failure-dialysis	Unilateral	Prone	6.4	15	Back pain, weight loss	10	Negative
3	Male	74	Renal failure-dialysis	Bilateral	Prone	7.5/4.5	25	Back pain	8	*Staphylococcus aureus*
4	Female	68	Renal failure-dialysis	Unilateral	Prone	4.4	10	Back pain	9	*Staphylococcus aureus*
5	Female	34	HIV	Bilateral	Prone	5.5/4.3	25	Back pain	8	*Staphylococcus aureus*
6	Male	35	IV drug user	Unilateral	Supine	8.3	10	Back pain	13	Negative
7	Male	38	Tuberculosis	Unilateral	Prone	7.5	15	Back pain	11	*Mycobacterium tuberculosis*
8	Female	27	Tuberculosis	Unilateral	Prone	10.4	15	Back pain	14	*Mycobacterium tuberculosis*

IV: Intravenous.

Table 2 Culture results and antibiotic treatment

Microorganism	*n*	Antibiotic treatment	Duration
Staphylococcus aureus	3	Rifampicin PO - Vancomycin IV	2 wk
		Rifampicin PO - Linezolid PO	6 wk
Mycobacterium tuberculosis	2	Rifampicin PO - Isoniazid PO - Ethambutol PO	9 mo
Negative cultures, renal impairment patients	2	Vancomycin IV - Ciprofloxacin PO	8 wk
Negative cultures, IV drug user	1	Ciprofloxacin PO - Clindamycin PO	4 wk
		Ciprofloxacin PO - Rifampicin PO	3 wk

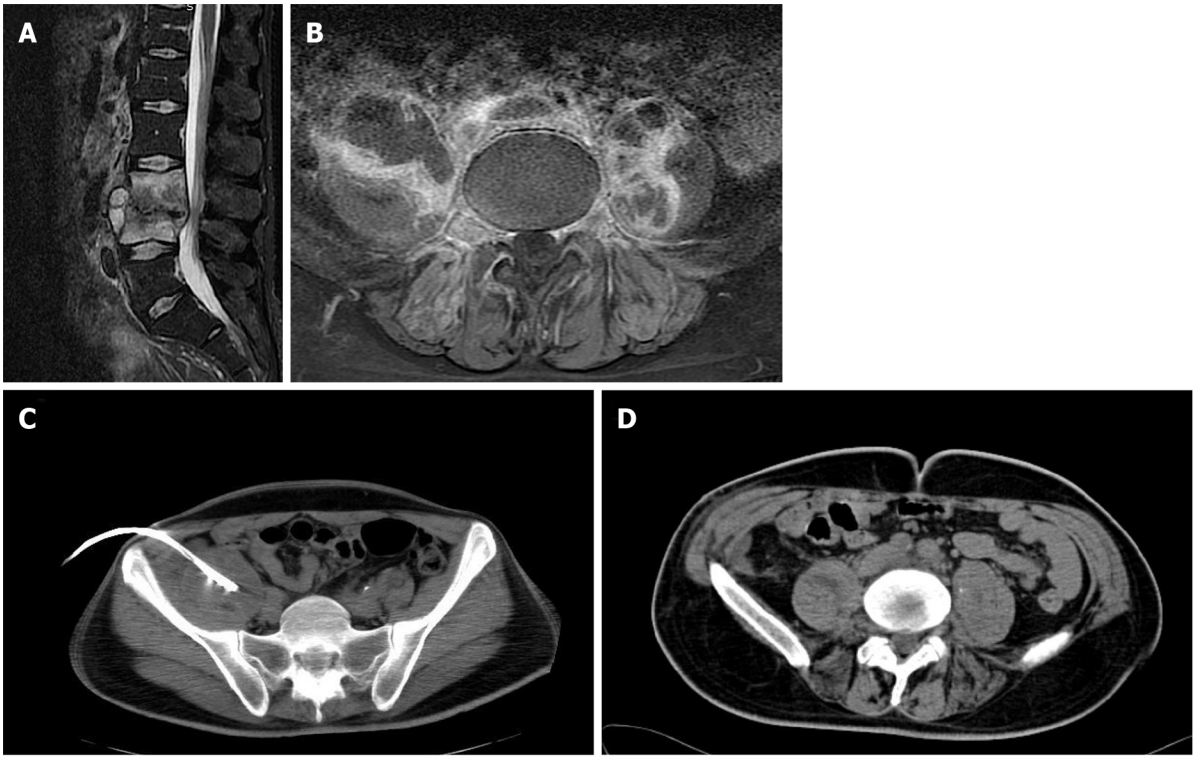
IV: Intravenous; PO: By mouth (*per* os).

spine.

The clinical triad of IPA symptoms as described by Mynter[2] in 1881 includes back pain, limping, and fever. Subsequent studies have identified more nonspecific symptoms such as weight loss, lower extremity pain, lower extremity edema, gastrointestinal symptoms, and a palpable mass[8]. The laboratory findings include elevated white blood cell count, C-reactive protein, and erythrocyte sedimentation rate as well as anemia[3,4]. In the present case series, none of the patients presented with the typical IPA symptomatology. The patients' underlying conditions along with the raised inflammatory markers guided the physicians to suspect an inflammatory condition of the spine.

The final diagnosis of IPA is confirmed by the imaging findings. Several studies recommend ultrasound as the initial radiological investigation. However, it is an operator-dependent procedure with a low diagnostic rate[1,9,14]. CT scan is considered to be the "gold standard" for a definitive diagnosis of IPA, and MRI adds more detailed imaging of the abscess wall, the soft tissues, and the surrounding structures without the need for IV contrast infusion[3,15-17]. Both MRI and CT scans were performed in the current study and revealed signs of spondylodiscitis with unilateral or bilateral IPA formation in all patients. Although IPA is mainly described as an outcome of spondylodiscitis[7], literature also describes spondylodiscitis as a complication of an established IPA[18]. Therefore, it could not be clearly stated which condition was presented first. Spondylodiscitis, however, did not require invasive treatment in contrast to the IPA formation.

The literature traditionally suggests early surgical management of the IPA, which suggests a long in-hospital stay. The surgical procedure of choice, according to Ricci *et al*[9] in 1986, was abscess drainage through a lower abdominal muscle-splitting, extraperitoneal incision. In more recent years, with the evolution of interventional radiology, minimally invasive percutaneous drainage of retroperitoneal abscesses, including IPA, is the treatment method of choice[11]. This approach is preferred especially for



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Figure 1 A 35-year-old patient with a history of intravenous drug use presenting with severe low back pain. A: T2 weighted image sagittal image reveals a high-intensity signal of the L3-L4 vertebrae, disk involvement, and paravertebral fluid collections; B: T1 weighted image axial image with contrast enhancement reveals bilateral iliopsoas abscesses; C: The corresponding computed tomography image with the pigtail catheter inserted in the right iliopsoas abscess; D: The computed tomography image after the catheter removal revealed complete resolution of the abscess.

immunocompromised patients, as it eliminates the need for general anesthesia and is also associated with a shorter hospital stay, minimizing morbidity and mortality. There is currently no literature describing the management of such patients with a drain insertion in an outpatient setting. In the current series, all patients were managed as outpatients. All patients underwent CT-guided drainage and drain insertion without delay from the time of diagnosis. The drain insertion increased the success rate of the drainage, and no repeat procedures were necessary.

Empiric antibiotic therapy should cover against *Staphylococcus aureus* and gram-negative and gram-positive microorganisms, including bowel flora and common urinary tract infection bacteria, and targeted therapy should be commenced immediately after the culture results[14]. For mycobacterial infections, a 9-mo conventional antituberculosis therapy was applied. For non-mycobacterial infections, as all cases presented with vertebral involvement, the minimum duration of the antibiotic treatment was 8 wk, including at least 2 wk of IV vancomycin, and prolonged according to laboratory and radiological findings. Those receiving IV vancomycin visited the outpatient clinic daily for the first 2 wk for the infusions.

The drain catheter remained in place until no drainage was observed for 2 consecutive days. A follow-up CT scan was performed between days 7 and 14 to confirm abscess recession.

The current study has several limitations. First, it is a single-center study of a small pilot patient group, which reflects the rarity of the condition. Second, no control group was recruited. Moreover, the retrospective study design might introduce recall or patient selection bias.

CONCLUSION

The minimally invasive outpatient management of IPA is a safe and effective approach with a high success rate and low morbidity.

ARTICLE HIGHLIGHTS

Research background

There has been an evolution in the management of complicated spondylodiscitis with iliopsoas muscle abscess (IPA) formation through the years and computed tomography (CT)-guided drain insertion with antibiotic therapy being the current practice.

Research motivation

Complicated spondylodiscitis with IPA formation in immunocompromised patients could be managed in an outpatient setting.

Research objectives

The purpose of the current study was to describe the care management of complicated spondylodiscitis.

Research methods

A 4-year retrospective collection and analysis of all radiologically diagnosed cases of IPA that were treated with CT-guided percutaneous drainage. Data included patient demographics, underlying conditions, isolated microorganisms, antibiotic regimes used, abscess size, days until the withdrawal of the catheter, and final outcome. All draining procedures were performed by direct insertion of a 12 Fr pigtail catheter into the abscess cavity.

Research results

All 8 patients were diagnosed with IPA formation secondary to complicated spondylodiscitis, and two of them were diagnosed with spinal tuberculosis. All 8 patients showed complete recession of the symptoms and radiological findings after the CT-guided abscess drainage and the long-term antibiotic therapy. The microbiology cultures identified *Staphylococcus aureus* in 3 cases and *Mycobacterium tuberculosis* in 2 cases and were negative in the remaining 3 cases. There was no need for patient hospitalization.

Research conclusions

The minimally invasive outpatient management of IPA, which combines CT-guided percutaneous drainage and placement of a drain with proper antibiotic treatment, proved to be a safe and effective approach with a high success rate and low morbidity.

Research perspectives

More studies should be performed in order to prove the cost effectiveness and the decreased morbidity of the minimally invasive outpatient management of these patients.

FOOTNOTES

Author contributions: Fesatidou V wrote the manuscript; Kitridis D reviewed the manuscript, performed a critical revision, and submitted the manuscript; Petsatodis E acquired and analyzed the data; Samoladas E and Givissis P supervised the study and contributed to patient care.

Institutional review board statement: The study was approved by the Institutional Review Board.

Informed consent statement: All study participants, or their legal guardian, provided informed written consent prior to study enrollment.

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Data sharing statement: No additional data are available.

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REFERENCES

1 **Shields D**, Robinson P, Crowley TP. Iliopsoas abscess--a review and update on the literature. *Int J Surg* 2012; **10**: 466-469 [PMID: 22960467 DOI: 10.1016/j.ijsu.2012.08.016]
2 **Mynter H**. Acute psoitis. *Buffalo Med Surg J* 1881; **21**: 202-210
3 **Mallick IH**, Thoufeeq MH, Rajendran TP. Iliopsoas abscesses. *Postgrad Med J* 2004; **80**: 459-462 [PMID: 15299155 DOI: 10.1136/pgmj.2003.017665]
4 **Taiwo B**. Psoas abscess: a primer for the internist. *South Med J* 2001; **94**: 2-5 [PMID: 11213936]
5 **Tsantes AG**, Papadopoulos DV, Vrioni G, Sioutis S, Sapkas G, Benzakour A, Benzakour T, Angelini A, Ruggieri P, Mavrogenis AF; World Association Against Infection In Orthopedics And Trauma W A I O T Study Group On Bone And Joint Infection Definitions. Spinal Infections: An Update. *Microorganisms* 2020; **8** [PMID: 32230730 DOI: 10.3390/microorganisms8040476]
6 **Hsieh MS**, Huang SC, Loh el-W, Tsai CA, Hung YY, Tsan YT, Huang JA, Wang LM, Hu SY. Features and treatment modality of iliopsoas abscess and its outcome: a 6-year hospital-based study. *BMC Infect Dis* 2013; **13**: 578 [PMID: 24321123 DOI: 10.1186/1471-2334-13-578]
7 **Ouellette L**, Hamati M, Flannigan M, Singh M, Bush C, Jones J. Epidemiology of and risk factors for iliopsoas abscess in a large community-based study. *Am J Emerg Med* 2019; **37**: 158-159 [PMID: 29784279 DOI: 10.1016/j.ajem.2018.05.021]
8 **Tabrizian P**, Nguyen SQ, Greenstein A, Rajhbeharrysingh U, Divino CM. Management and treatment of iliopsoas abscess. *Arch Surg* 2009; **144**: 946-949 [PMID: 19841363 DOI: 10.1001/archsurg.2009.144]
9 **Ricci MA**, Rose FB, Meyer KK. Pyogenic psoas abscess: worldwide variations in etiology. *World J Surg* 1986; **10**: 834-843 [PMID: 3776220 DOI: 10.1007/BF01655254]
10 **Yacoub WN**, Sohn HJ, Chan S, Petrosyan M, Vermaire HM, Kelso RL, Towfigh S, Mason RJ. Psoas abscess rarely requires surgical intervention. *Am J Surg* 2008; **196**: 223-227 [PMID: 18466865 DOI: 10.1016/j.amjsurg.2007.07.032]
11 **Akhan O**, Durmaz H, Balcı S, Birgi E, Çiftçi T, Akıncı D. Percutaneous drainage of retroperitoneal abscesses: variables for success, failure, and recurrence. *Diagn Interv Radiol* 2020; **26**: 124-130 [PMID: 32116220 DOI: 10.5152/dir.2019.19199]
12 **Procaccino JA**, Lavery IC, Fazio VW, Oakley JR. Psoas abscess: difficulties encountered. *Dis Colon Rectum* 1991; **34**: 784-789 [PMID: 1914744 DOI: 10.1007/BF02051071]
13 **López VN**, Ramos JM, Meseguer V, Pérez Arellano JL, Serrano R, Ordóñez MAG, Peralta G, Boix V, Pardo J, Conde A, Salgado F, Gutiérrez F; GTI-SEMI Group. Microbiology and outcome of iliopsoas abscess in 124 patients. *Medicine (Baltimore)* 2009; **88**: 120-130 [PMID: 19282703 DOI: 10.1097/MD.0b013e31819d2748]
14 **Huang JJ**, Ruaan MK, Lan RR, Wang MC. Acute pyogenic iliopsoas abscess in Taiwan: clinical features, diagnosis, treatments and outcome. *J Infect* 2000; **40**: 248-255 [PMID: 10908019 DOI: 10.1053/jinf.2000.0643]
15 **Wu TL**, Huang CH, Hwang DY, Lai JH, Su RY. Primary pyogenic abscess of the psoas muscle. *Int Orthop* 1998; **22**: 41-43 [PMID: 9549580 DOI: 10.1007/s002640050205]
16 **Qureshi NH**, O'Brien DP, Allcutt DA. Psoas abscess secondary to discitis: a case report of conservative management. *J Spinal Disord* 2000; **13**: 73-76 [PMID: 10710154 DOI: 10.1097/00002517-200002000-00014]
17 **Zissin R**, Gayer G, Kots E, Werner M, Shapiro-Feinberg M, Hertz M. Iliopsoas abscess: a report of 24 patients diagnosed by CT. *Abdom Imaging* 2001; **26**: 533-539 [PMID: 11503095 DOI: 10.1007/s002610000201]
18 **Yemisci OU**, Cosar SN, Oztop P, Karatas M. Spondylodiscitis associated with multiple level involvement and negative microbiological tests: an unusual case. *Spine (Phila Pa 1976)* 2010; **35**: E1006-E1009 [PMID: 20395882 DOI: 10.1097/BRS.0b013e3181c52d56]

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ORIGINAL ARTICLE

Retrospective Study

Direct anterior approach hip arthroplasty: How to reduce complications - A 10-years single center experience and literature review

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Abstract

BACKGROUND

The direct anterior approach for total hip arthroplasty (DAA-THA) is increasing in popularity due to some advantages such as less surgical trauma, minimal dissection of soft tissues, shorter rehabilitation times, faster return to daily activities, lower incidence of dislocation. On the other hand, the literature reports a high rate of intraoperative complications, with many different rates and complication types in the published papers.

AIM

To analyze our complications comparing results with the literature; to report measures that we have taken to reduce complications rate.

METHODS

All DAA-THA patients with one year minimum follow up who were operated at a single high-volume centre, between January 2010 and December 2019 were included in this retrospective study. All surgeries were performed using cementless short anatomical or straight stems and press fit cups. Patients' follow-up was performed, at 6 wk, 3 mo, then annually post-surgery with clinical and radiological evaluation. Primary outcomes were stem revision for aseptic loosening and all-cause stem revision. Second outcome was intra-operative and post-operative complications identification.

RESULTS

A total of 394 patients underwent DDA-THA from January 2010 and December 2019, for a total of 412 hips; twelve patients lost to follow-up and one patient who died from causes not related to surgery were excluded from the study. The

average age at the time of surgery was 61 years (range from 28 to 78 years). Mean follow-up time was 64.8 mo (range 12-120 mo). Seven stems were revised. One cortical perforation, one trochanteric and lateral cortical wall intraoperative fracture, one diaphyseal fracture, three clinically symptomatic early subsidence and one late aseptic loosening. We also observed 3 periprosthetic fractures B1 according to the Vancouver Classification. Other minor complications not requiring stem revision were 5 un-displaced fractures of the calcar region treated with preventive cerclage, one early infection, one case of late posterior dislocation, 18 case of asymptomatic stem subsidence, 6 cases of lateral cutaneous femoral nerve dysesthesia.

CONCLUSION
DAA is associated to good outcomes and lower incidence of dislocation. Complication rate can be reduced by mindful patient selection, thorough preoperative planning, sufficient learning curve and use of intraoperative imaging.

Key Words: Hip arthroplasty; Direct anterior approach; Short hip stem; Minimally invasive surgery; Complications

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Core Tip: Direct anterior approach for total hip arthroplasty is increasing in popularity due to some advantages such as less surgical trauma, shorter rehabilitation times, faster return to daily activities, lower incidence of dislocation. Moreover, the literature reports a high rate of intraoperative complications, with many different rates and complication types in the published papers. The aim of this paper is to analyze our complications comparing the results obtained in a total of 412 hips at a mean follow-up of 64.8 mo with those reported in the literature and to describe measures that we have taken to reduce complications rate.

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INTRODUCTION

The direct anterior approach (DAA) was first described by Heuter in 1881 but popularized by Judet starting in 1947[1]. However, it has only recently become popular. In particular, this happened in 2005 following publications by Matta *et al*[2,3]. The increase in popularity of DDA is due to the advantages such as less surgical trauma, minimal dissection of soft tissues, shorter rehabilitation times, faster return to daily activities, lower incidence of dislocation. However, the literature reports a higher rate of perioperative DAA complications than other approaches[4-8] like periprosthetic fracture, prosthesis loosening and nerve injury, but the reported complication rates vary widely in the published literature both in the incidence rate and in the type of complication[9-13]. There is not yet consensus concerning the best approach for total hip arthroplasty (THA) and debates are ongoing[14]. The interest on DAA complications is growing in the recent literature, also compared with those of other hip approaches[15-17]. The aim of our study is to analyze the complication incidence rate in a study group with a maximum follow up of 10 years and compare the results with the literature. Furthermore, from the analysis of our learning curve, we can derive the technical and organizational measures that we have taken to reduce the incidence of complications with the use of DAA for THA.

MATERIALS AND METHODS

All DAA-THA patients with one year minimum follow up who were operated at a single high-volume centre (> 450 arthroplasties/year), between January 2010 and December 2019 were included in this study. The exclusion criteria for the use of DAA in our practice were: age more than 80 years, arthroplasties in hip fractures or in osteolytic lesions, patients with body mass index > 35. Clinical data (gender, age, weight and height) and comorbidities (cardiovascular, respiratory, gastrointestinal, nutritional, endocrine, genitourinary) were collected retrospectively from medical records and outpatient control cards. Radiographic data was taken from the hospital database (Picture archiving and

communication system).

All surgeries were performed using cementless short stems and press fit cup by three surgeons experienced in DAA. Two cementless design of the stem were used. Minimax stem and Versafit press-fit cup (Medacta International, Castel San Pietro, Switzerland) and Fitmore stem and Continuum press-fit cup (Zimmer Biomet, Warsaw, IN, USA). Minimax is anatomically designed, collarless, and made of titanium-niobium alloy (Ti-6Al-7Nb) stem. The neck has a 127 degrees neck-shaft angle with an anteversion of 9 degrees. Minimax stem can be classified as type 6 according to Khanuja *et al*[18] because it is curved, anatomic stems that match the proximal femoral endosteal geometry. Fitmore is a straight designed, tapered, collarless and made of titanium stem which is coated proximally with Ti-VPS (Titanium Vacuum Plasma Spray) and rough-blasted distally. The neck has a neck-shaft angle of 127°, 129°, 137° or 140° without anteversion. Fitmore stem can be classified as type 2 according to Khanuja *et al*[18] because it is a tapered, wedged and proximal porous coated stem that achieves fixation proximally. According to short stem classification[19], Fitmore stem can be classified as type 4, shortened conventional wedged design.

Final decision whether to use DAA was made by the orthopaedic surgeon, in compliance with the exclusion criteria, operating based on age, fragility, bone morphology, and level of activity of the patient. In a same way, decision whether implant straight or anatomical stem was made by orthopaedic surgeon in compliance with proximal femoral anatomy after pre-operative planning[20,21]. Ceramic on ceramic coupling was chosen and 32 mm or 36 mm head diameter were used in all cases.

All surgeries were done in all patients with the support of the standard operating room table or the Amis Mobile Leg positioner (Medacta International, Castel San Pietro, Switzerland).

Primary outcomes were stem revision for aseptic loosening and all-cause stem revision. Second outcome was intra-operative and post-operative complications identification. Patient follow-up was performed at 6 wk, 3 mo and then annually post-surgery.

During preoperative and postoperative radiographic controls, anteroposterior and axial hip radiographs were taken with the foot in a neutral rotational position. Femoral geometries were categorized according to the Door classification system[22] using preoperative anteroposterior radiographs of the hip. The calcar-to-canal ratio was calculated by dividing the canal width, measured at 10 cm below the lesser trochanter, by the calcar width, measured at the middle level of the lesser trochanter. Femurs with a ratio of 0-0.5 were considered type A, 0.5-0.75 as type B, and 0.75-1 as type C [23,24].

Alignment of the stem was considered neutral when the vertical axis of the stem was between 0 and 2° with respect to the femoral shaft axis. A varus-valgus alignment was classified as mild in case of misalignment between 2° and 5° and severe when the misalignment of the stem was greater than 5°. The most recent radiographs were compared to the first postoperative clinic radiographs to evaluate bony remodeling and changes in implant positioning. Stem subsidence was diagnosed in the presence of a stem sinking greater than 3 mm, measured on a perpendicular line drawn from the greater trochanter to the lateral edge of the implant. Implant loosening was diagnosed in the presence of subsidence and/or axial deviation in varus/valgus. We judged early subsidence or axis deviation within 6 mo of surgery, late when observed after 6 mo post-operative.

RESULTS

We retrospectively reviewed a group of 394 consecutive patients who underwent DDA-THA from January 2010 to December 2019 of whom 18 were operated bilaterally in a single procedure, for a total of 412 hips; twelve patients lost to three-month follow-up and one patient who died from causes not related to surgery were excluded from the study. The remaining 381 patients (399 hips) were 263 (65.9%) female and 136 (34.1%) male. The average age at the time of surgery was 61 years (range from 28 to 78 years). The preoperative diagnosis was primary osteoarthritis in 328 cases (14 bilateral), avascular necrosis of the femoral head in 38 cases (3 bilateral), rheumatoid arthritis in 11 cases (1 bilateral), traumatic osteoarthritis in 18 cases, and other causes in 4 cases. Demographic data of patients are sumarized in Table 1. Mean follow-up time was 64.8 mo (range 12-120 mo). In 238 cases an anatomical stem was used, in 161 cases a straight stem was used. Three hundred forty-four surgeries were performed *via* the DAA using a standard operating room table (86.2%) and 44 (13.8%) surgeries were performed using the AMIS mobile leg.

Seven stems were revised. One cortical perforation was observed on postoperative radiographic control and then revised. One trochanteric and lateral cortical wall fracture was intraoperative observed and fixed with cerclage and stem revision. One diaphyseal fracture was treated by plate fixation. Three clinically symptomatic early subsidence revised respectively 5, 6 and 7 mo after surgery. One aseptic loosening 4 years after surgery (Figure 1). We also observed 3 periprosthetic fractures B1 according to the Vancouver Classification. The intra operative complications observed, in addition to the cortical perforation, the diaphyseal fracture and the trochanteric fracture, were 5 un-displaced fractures of the calcar region treated with preventive cerclage (Figure 2). One early infection was treated with surgical washing and head and liner revision followed by antibiotic therapy. One posterior dislocation was

Table 1 Demographic data of patients

Parameters	Values
No. of patients	381
No. of hips	399
Gender (male/female), *n* (%)	136 (34.1)/263 (65.9)
mean age (yr)	61 (28-78)
mean follow-up (mo)	64,8 (12 –120)
Diagnosis (No. hips)	
Osteoarthritis	328 (14 bilateral)
Avascular necrosis	38 (3 bilateral)
Rheumatoid arthritis	11 (1 bilateral)
Traumatic osteoarthritis	18
Other causes	4
Surgical technique, *n* (%)	
Standard operating room table	445 (86.4)
AMIS mobile leg positioner	54 (19.4)

observed one year after surgery (Figure 3). Patient referred dislocation during a squat on the ground with the loss of balance. Dislocation was reduced without anesthesia, no further dislocations were observed one year after reduction. Six patients referred numbness or paresthesias within the cutaneous distribution of the anterolateral thigh at follow-up.

According to Dorr classification[17], 168 hips (42%) were graded as Dorr A, 192 hips (48%) as Door B and 39 hips (10%) as Dorr C. In our experience pre-operative planning showed more suitable Fitmore stem for a femoral geometry type A (84/168), according to the Door classification system. This is due to the tapering of the tip adaptable to a narrow femoral canal. Minimax stem is instead more suitable for a femoral geometry type C due to more filling metaphyseal portion (37/39). For this reason, the two groups of patients treated with Fitmore stem and Minimax stem appear not homogeneous and their incidence of complications is not comparable.

In 307 (77%) cases the alignment of the stem was considered neutral, in 76 (19%) cases it was considered mild varus-valgus and in 15 (4%) cases severe varus-valgus. Trabeculae hypertrophy was observed in 84 cases (21%) at zone 3, in 45 cases (11%) at zone 5 and 5 cases (2%) at zone 4. There was grade 1 stress shielding (calcar round-off) in 5 cases (2%). No hypertrophy at zones 8-14 (lateral view) were observed. Stem subsidence > 3 mm, in addition to the one symptomatic case revised, was observed 4 more times (4 mm, 7mm, 6 mm and 10 mm respectively). In all these 4 cases, the absence of pain and the tolerated leg length discrepancy did not compromise the good final functional result.

Finally, 445 (86.4%) surgeries (11 bilateral) were performed *via* the DAA using a standard operating room table and 54 (19.4%) surgeries (7 bilateral) were performed using the Amis Mobile Leg. Comparison between demographic characteristics and the incidence of complications in the two patient groups (anatomical and straight stem) did not reveal significant differences (Table 2).

DISCUSSION

This study was undertaken to evaluate DAA-THA complication rates. For this reason, we retrospectively evaluated clinical and radiographic complications at a mean follow-up of 64.8 mo (range 12-120 mo) in 381 patients (399 hips). All patients received a cementless anatomical short stem or a tapered wedged short stem according to inclusion criteria.

Incidence of dislocation is certainly the most relevant result of our study. Commonly considered to be lower than that of others approaches, the small dislocation rate of the DAA is one of the reasons for the great popularity of this approach, although a widely accepted consensus has not been reached yet and some authors report higher complication rates[25].

We found one case of hip dislocation on 399 hips (0.2%) (Figure 3), which represents the one of the lower dislocation incidences reported in literature in case of large study group[26], with the latest works reporting dislocation rate from 0.23% to 2.5%[27,28].

Table 2 Major and minor complications

Complications	Anatomical stem (*n* = 238)	Straight stem (*n* = 161)
Major complication (with stem revision)	6	4
Acute mobilization	1	1
Trochanter fracture	-	2
Diaphyseal fracture	1	-
Aseptic loosening	1	-
Subidence	1	-
Periprosthetic fractures	2	1
Minor complication	18	9
Calcar fractures (Intraoperative cerclage)	5	1
Ossification	-	1
Subsidence		
Conservative treatment ≤ 3 mm	9	5
Conservative treatment > 3 mm	3	1
Dislocation	-	1
Early infection	1	-
LCFN dysesthesia	4	2

LCFN: Lateral cutaneous femoral nerve.

Unexpectedly, the case of hip dislocation found in our study was a posterior dislocation occurred after hip hyper-flexion and adduction, factually suggesting an inadequate cup anteversion, since the dislocation after THA performed with the DAA is usually anterior also due to the preservation of the musculo-tendinous attachments of the short external rotators which are important for hip stabilization after arthroplasty. Nevertheless, also Barnett *et al*[27] reported a prevalence of posterior dislocation.

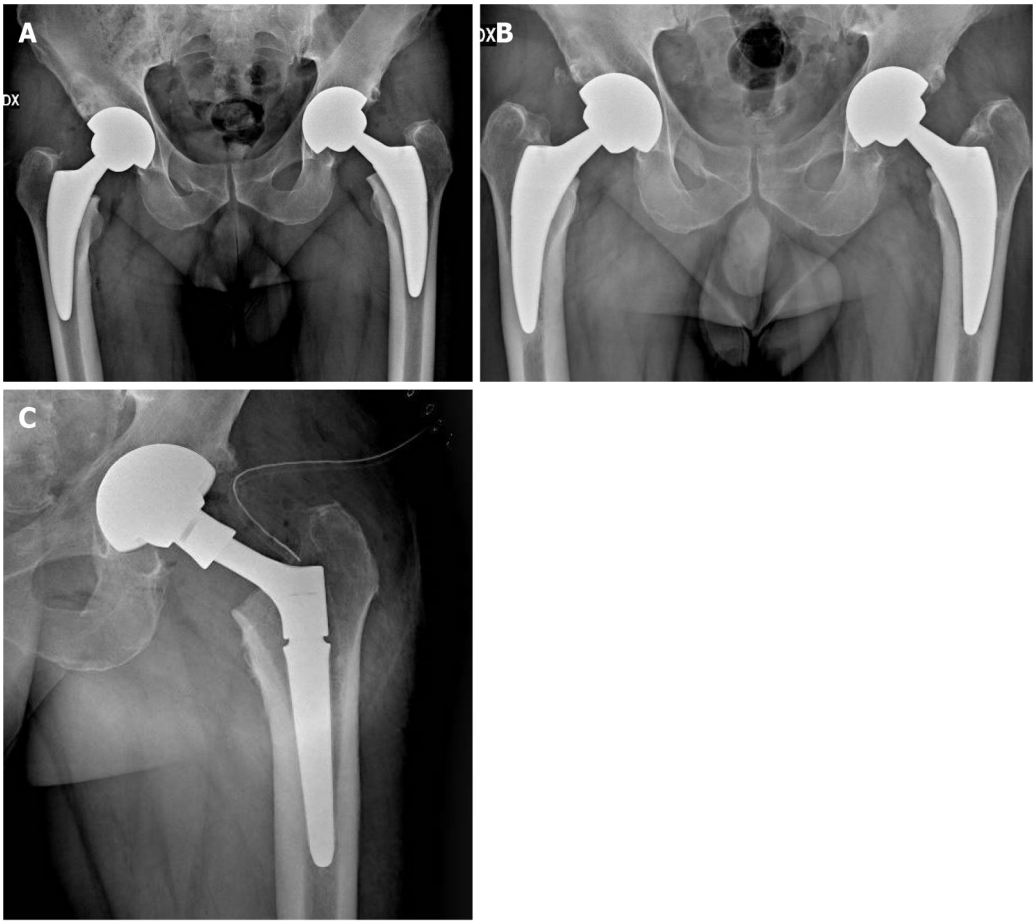
Acetabular cup anteversion and inclination are a key point for the long-term success of THA and seen as a challenge in DAA-THA. There are some studies suggesting alternative solutions on this issue; Hu *et al*[29] described satisfactory clinical and radiographic outcomes achieved by DAA-THA performed in the lateral position. Fluoroscopic guidance is reported to be used to improve component positioning during anterior approach THA, but with still debated results; for example, Rathod *et al*[30] depicted a reduction of variability of acetabular cup anteversion using fluoroscopy with the patient in the supine position during direct anterior THA, while Kobayashi *et al*[31] revealed potential excessive cup anteversion and flexion implantation of the stem obtained from fluoroscopic assistance by surgeons in their early experience with DAA. In our practice, we do use intraoperative imaging, but especially to check stem size and alignment in order to mitigate the tendency to undersize the femoral implant associated to DAA-THA, as described in our previous work[32].

Although the use of different femoral heads size has been described in many studies[33,34], it's known that the use of larger femoral heads increases the head-neck ratio and consequently increases the range of movement before reaching the point of primary impingement thus reducing dislocation rates, as reported in the published literature[35-37]. Also aware of this, in our series we used only 32 mm or 36 mm diameter heads.

An analysis of the Norwegian Arthroplasty Register found overall similar revision rates between hip approaches, but the posterior approach was associated with more than twice the risk of revision due to dislocation when compared with alternate approaches[38].

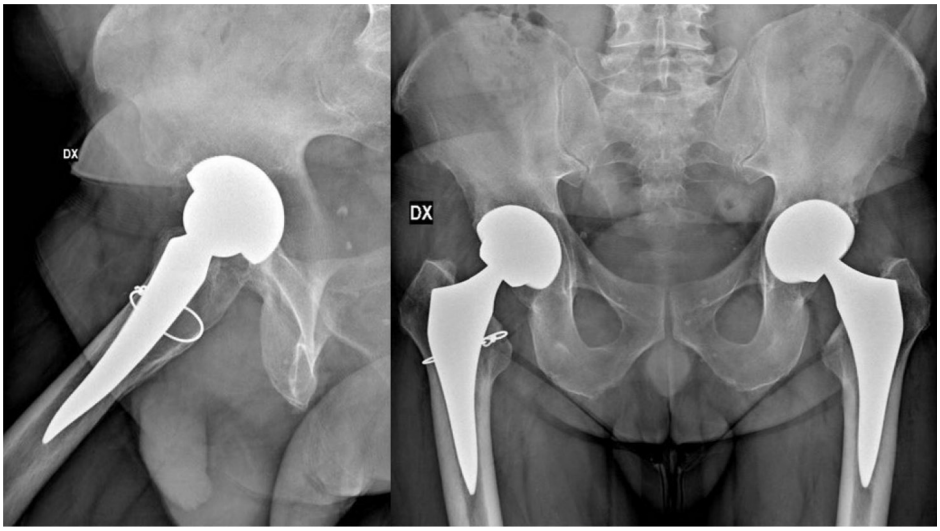
In the literature are reported various revision rates, rising from 0%[39] to 3.3%[28] with different follow up time. In our series, the global revision rate was 1.8% and revision rate for aseptic loosening was 1% at a mean follow up of 65 mo, with particular attention to three clinically symptomatic early subsidence revised respectively 5, 6 and 7 mo after surgery; especially in these cases it is critical, in our opinion, the intraoperative imaging to mitigate the tendency to undersize the femoral implant associated to DAA-THA[32].

The risk of intraoperative fractures is due to the difficult exposure of the femur. Early studies reported a high complication rate with the use of a fracture table[40]. Most of these were avulsions of the greater trochanter. The evolution of specialized traction tables for DAA, promoting greater patient hip positioning than patient hip traction, has reduced the incidence of complications. Although the



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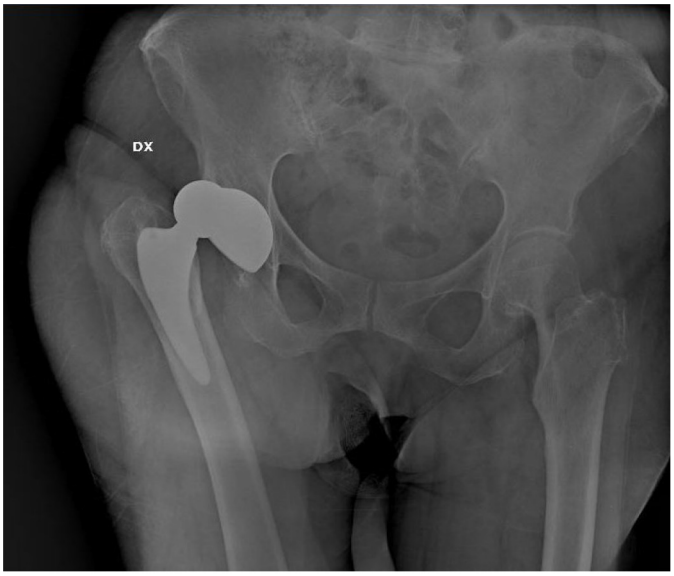
Figure 1 A 55 years old man undergone bilateral one-stage direct anterior approach for total hip arthroplasty. A: Postperative X-ray control; B: Radiological evidence of left femoral stem loosening after 4 years from the surgery; C: Revision of the loosed femoral stem.



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Figure 2 A 48 years old man undergone bilateral one-stage direct anterior approach for total hip arthroplasty; intraoperative right femur cerclage due to calcar incomplete fracture.

differences between complications during the traction table or the standard table are still debated in the current literature, the incidence of intraoperative fracture in DAA is reported between 1.3% and 2.4% [41-43]. The use of short femoral stems is described as a reduction in the risk of intraoperative fractures [44-46]. Dietrich *et al*[44] reported a significantly reduced fracture rate of 1.6% *vs* 6.8% in 457 DAA with



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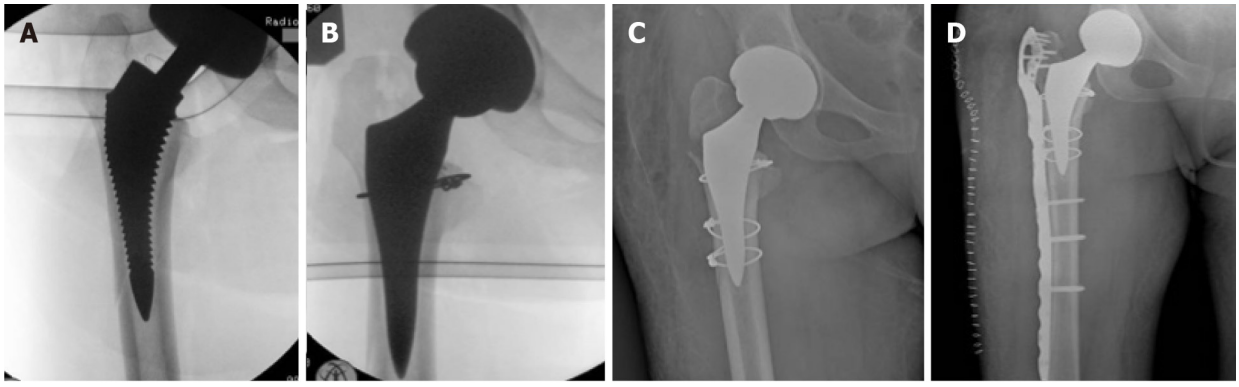
Figure 3 Posterior hip dislocation in 80 years old woman one year after direct anterior approach for total hip arthroplasty.

conventional straight stems. Luger *et al*[45] reported 0.9% of intraoperative fractures after 1052 DAA-THA with the same straight stem used in our study. In our opinion, the use of short stems with specific instruments for DAA favors the introduction into the femoral canal, decreases the points of conflict with cortices during introduction and decreases the incidence of complications. We observed 3 major complications (0.7%) related to intraoperative fractures (Figure 4). Our rate of intraoperative fracture increases to 2% including minor complications (intraoperative cerclages due to calcar incomplete fractures). Our results encourage us to continue our experience with short stems, both with the use of the standard table and the traction table[8]. Surprisingly, however, Greco *et al*[42] report an opposite experience. They observed higher femoral complications (1.27%) with short stem standard profile as compared to full length standard profile (0.77%). The Authors concluded that short stem may impart greater stress concentration in the proximal femur during broaching and stem insertion which could increase the risk of fracture. On the contrary, a longer stem aids with the direction of broaching and may prevent inappropriate contact against the femoral cortices. One of the Authors has decided to avoid use of the short stem option in elderly female patients given the compounded risk of femoral complication.

Despite DAA utilizes an internervous plane between Tensor fasciae lata and Gluteus medius muscles (Superior gluteal nerve) and Sartorius and Rectus femoris muscles (Femoral nerve), nerve complications are however possible.

Injury to lateral cutaneous femoral nerve (LCFN) is a not rare minor complication. LCFN is a pure sensory nerve is a sensory nerve that forms from the roots of L2 and L3; travels along the posterolateral aspect of the psoas e iliac muscles through the anterosuperior iliac spine, ending superficially at the sartorius muscle. Then LCFN pierces the fascia lata beneath the inguinal ligament and runs laterally and distally within the subcutaneous tissue of the anterolateral region of the thigh. Some authors describe a division of the LFCN into an anterior (femoral) and posterior (gluteal) branch after passing behind or through the inguinal ligament. Rudin *et al*[47] classified the branching pattern of the LFCN in three as Sartorius-type (dominant anterior branch on the lateral border of the Sartorius muscle and further branches in the anterior aspect of the thigh), posterior-type [strong posterior branch equal in thickness to, or thicker than, the anterior branch. It runs laterally and crosses the medial border of the tensor fascia lata (TFL) muscle distal to the anterior superior iliac spine (ASIS)] or fan-type (multiple nerve branches of equal thickness on the anterolateral region of the proximal aspect of the thigh, crossing over the TFL and the lateral border of the Sartorius). They reported 36% of sartorius-type, 32% of posterior-type and 32 of fan-type after dissection of twenty-eight cadaveric hemipelves from 18 donors. In contrast to this data, Thaler *et al*[48], after a study on 44 Limbs and hemipelves from 22 formalin-preserved cadavers, showed a Sartorius-type branch pattern (70.5%) of the LFCN in the majority of cases, while a posterior-type and a fan-type were detected in 13.6% and 15.9% of cases, respectively. If these data were confirmed, injury to branches of the LFCN should be avoided in most cases by a skin incision 2 cm lateral to the ASIS end its distal extension as lateral as possible.

The true incidence of this complication remains unclear. The reported incidence in literature ranges from 0.1% to 81%. This is due to both the diagnostic difficulty and the degree of accuracy of the clinical examination at follow up. In fact, symptoms ranging from hypoesthesia to painful paresthesias and there is no validated diagnostic tool for LFCN neuropraxia. Patients with LFCN injury often report numbness, paresthesias, or even dysesthesias analogous to meralgia paresthetica within the cutaneous



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Figure 4 A 61 years old woman undergone direct anterior approach for total hip arthroplasty. A, B: Lateral femoral wall fracture showed at intraoperative control and then fixed with cerclage; C: Evidence of undiagnosed trochanteric fracture at postoperative control; D: X-rays control after periprosthetic plate and screws.

distribution of the anterolateral thigh. In our experience, patients often do not report dysesthesia during postoperative follow-up. The disorder is in fact reported only if the patient is directly questioned about the problem of skin sensitivity. Only in 6 cases patients did report dysesthesia or numbness as a symptom that occasionally caused discomfort. We did not include direct skin sensitivity assessment forms in our follow-up, this is a possible reason of our low incidence (1.5%) of LCFN injury. Homma *et al*[49] investigating skin sensitivity problems using a dedicated questionnaire, showed 31.9% of LFCN injury. In the same way Patton *et al*[50] reported numbness in 37% of patients with decreasing of incidence to 11% of patients from 6-8 years post op. The fact that symptoms related to LCFN lesion are often reported only after a specific question further suggests that it is a minor complication. Furthermore, in most cases, the presence of LCFN lesions appears to be independent of hip function scores and does not affect final result.

The superior gluteal nerve is a motor nerve, which is formed from the roots of L4 and L5 and the first sacral spinal nerves that supply the gluteus medius, gluteus minimus, and TFL muscles. It runs sideways between the gluteus medius and minimus and then divides into upper and lower branches. Both the upper and lower branches innervate the gluteus medius and minimal muscles. Furthermore, the terminal branches of the inferior branch run anteriorly and supply the tensor of the fascia lata. Precisely these terminal branches represent the anatomical structure at risk. Overstretching the TFL muscle using retractors during surgery or coagulation of the near ascending branch of the lateral circumflex femoral artery can be causes of Injury. There is little information in the literature regarding injury to the TFL with respect to the DAA[51]. The consequences of atrophy of the tensor fasciae are cosmetic, but potential functional deficit is unknow.

Even if in our study we did not consider blood loss, it is reported that DAA THA is related to lower intraoperative blood loss and smaller changes in pre- and postoperative hemoglobin values, less blood drained, and lower volumes of blood transfusions required[52]. Moreover, Zhao *et al*[53] described no statistically significant differences in the rate of blood transfusion, hematoma, or re-bleeding between patients undergone ligation of the branches of the lateral circumflex femoral artery pedicle *vs* those treated with electrocautery.

There are some uncommon complications that are still to be taken into account; Hogerzeil *et al*[6] reported the case of a 69-year-old male patient who developed acute compartment syndrome of the thigh after elective DAA THA while using therapeutic low molecular weight heparin as bridging for regular oral anticoagulation. Also the risk of excessive radiation exposure to both the patients and the surgeons has to be considered; Jinnai *et al*[54] compared the intraoperative fluoroscopy time of DAA-THA with that of osteosynthesis for proximal femoral fracture to determine if the level of radiation exposure exceeded safety limits and concluding that the intraoperative exposure level was significantly lower and the fluoroscopy time was significantly shorter in DAA-THA than in osteosynthesis.

There are some limitations in this paper. First, the main weakness of our work is the retrospective design of the study. Second, we did not include direct skin sensitivity assessment forms in our follow-up controls and this could be a possible reason of our low incidence of LCFN injury. Third, the exclusion of ages of more than 80 could be considered a selection bias, improving clinical outcome and reducing the revision rate. Fourth, we did not use radiostereometric analysis to evaluate for stem subsidence, but only manual techniques of measurement.

CONCLUSION

DAA is associated to less surgical trauma, minimal dissection of soft tissues, lower blood loss, shorter rehabilitation times and lower incidence of dislocation. Complication rate can be reduced by mindful patient selection, preoperative planning with proper implant choice, sufficient learning curve, use of intraoperative imaging to check cup and stem orientation and to mitigate the tendency to undersize the femoral implant.

ARTICLE HIGHLIGHTS

Research background

The direct anterior approach for total hip arthroplasty (DAA-THA) is increasing in popularity due to some advantages such as less surgical trauma, minimal dissection of soft tissues, shorter rehabilitation times, faster return to daily activities, lower incidence of dislocation with different reports in the published papers.

Research motivation

Some literature reports a high rate of perioperative complications, with many different rates and complication types among the published papers without reaching a clear consensus.

Research objectives

Objectives of our study are to analyze our complications and comparing results with the literature reports and to report measures that we have taken to reduce complications rate.

Research methods

We retrospectively collected data of all DAA-THA patients with one year minimum follow up who were operated at a single high-volume centre, between January 2010 and December 2019. All surgeries were performed using cementless short anatomical or straight stems and press fit cups. Patients' follow-up was performed with clinical and radiological evaluation. Primary outcomes were stem revision for aseptic loosening and all-cause stem revision. Second outcome was intra-operative and post-operative complications identification.

Research results

The authors collected 394 patients underwent DDA-THA from January 2010 and December 2019, for a total of 412 hips; twelve patients lost to follow-up and one patient who died from causes not related to surgery were excluded from the study. Mean follow-up time was 64.8 mo (range 12–120 mo). Seven stems were revised. One cortical perforation, one trochanteric and lateral cortical wall intraoperative fracture, one diaphyseal fracture, three clinically symptomatic early subsidence and one late aseptic loosening. We also observed 3 periprosthetic fractures B1 according to the Vancouver Classification. Other minor complications not requiring stem revision were 5 undisplaced fractures of the calcar region treated with preventive cerclage, one early infection, one case of late posterior dislocation, 18 case of asymptomatic stem subsidence, 6 cases of lateral cutaneous femoral nerve dysesthesia.

Research conclusions

In our experience DAA is associated to good outcomes and lower incidence of dislocation. According to our results complication rate can be reduced by mindful patient selection, thorough preoperative planning, sufficient learning curve and use of intraoperative imaging.

Research perspectives

Despite these good results, the choice of the ideal surgical approach of THA is still controversial and studies on larger samples are needed.

FOOTNOTES

Author contributions: All authors gave substantial contributions to conception and design of the study, acquisition of data, or analysis and interpretation of data, drafting the article and making critical revisions related to important intellectual content of the manuscript and final approval of the version of the article to be published.

Institutional review board statement: The study and follow-up, respecting the criteria of the Declaration of Helsinki, were approved by the ASN/Sav Institutional Review Board.

Informed consent statement: In this retrospective analysis we used anonymous clinical data that were obtained after each patient agreed to treatment by written consent form; all patients accepted the proposed treatment and follow-up after adequate information and gave written consent. For full disclosure, paper copy is available at SS Annunziata Hospital, Savigliano, Italy.

Conflict-of-interest statement: The authors declare that they have no conflict of interest to this study.

Data sharing statement: Technical appendix, statistical code, and dataset available from the corresponding author at rivgio@libero.it. The presented data are anonymized and risk of identification is very low.

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REFERENCES

1 **Judet J**, Judet H. [Anterior approach in total hip arthroplasty]. *Presse Med* 1985; **14**: 1031-1033 [PMID: 3158949]
2 **Matta JM**, Shahrdar C, Ferguson T. Single-incision anterior approach for total hip arthroplasty on an orthopaedic table. *Clin Orthop Relat Res* 2005; **441**: 115-124 [PMID: 16330993 DOI: 10.1097/01.blo.0000194309.70518.cb]
3 **Connolly KP**, Kamath AF. Direct anterior total hip arthroplasty: Literature review of variations in surgical technique. *World J Orthop* 2016; **7**: 38-43 [PMID: 26807354 DOI: 10.5312/wjo.v7.i1.38]
4 **Aggarwal VK**, Weintraub S, Klock J, Stachel A, Phillips M, Schwarzkopf R, Iorio R, Bosco J, Zuckerman JD, Vigdorchik JM, Long WJ. 2019 Frank Stinchfield Award: A comparison of prosthetic joint infection rates between direct anterior and non-anterior approach total hip arthroplasty. *Bone Joint J* 2019; **101-B**: 2-8 [PMID: 31146560 DOI: 10.1302/0301-620X.101B6.BJJ-2018-0786.R1]
5 **Post ZD**, Orozco F, Diaz-Ledezma C, Hozack WJ, Ong A. Direct anterior approach for total hip arthroplasty: indications, technique, and results. *J Am Acad Orthop Surg* 2014; **22**: 595-603 [PMID: 25157041]
6 **Hogerzeil DP**, Muradin I, Zwitser EW, Jansen JA. Acute compartment syndrome of the thigh following hip replacement by anterior approach in a patient using oral anticoagulants. *World J Orthop* 2017; **8**: 964-967 [PMID: 29312856 DOI: 10.5312/wjo.v8.i12.964]
7 **Alvarez-Pinzon AM**, Mutnal A, Suarez JC, Jack M, Friedman D, Barsoum WK, Patel PD. Evaluation of wound healing after direct anterior total hip arthroplasty with use of a novel retraction device. *Am J Orthop (Belle Mead NJ)* 2015; **44**: E17-E24 [PMID: 25566560]
8 **Rivera F**, Bardelli A, Giolitti A. Promising medium-term results of anterior approach with an anatomical short stem in primary hip arthroplasty. *J Orthop Traumatol* 2021; **22**: 8 [PMID: 33675436 DOI: 10.1186/s10195-021-00567-x]
9 **Goulding K**, Beaulé PE, Kim PR, Fazekas A. Incidence of lateral femoral cutaneous nerve neuropraxia after anterior approach hip arthroplasty. *Clin Orthop Relat Res* 2010; **468**: 2397-2404 [PMID: 20532717 DOI: 10.1007/s11999-010-1406-5]
10 **Woolson ST**, Pouliot MA, Huddleston JI. Primary total hip arthroplasty using an anterior approach and a fracture table: short-term results from a community hospital. *J Arthroplasty* 2009; **24**: 999-1005 [PMID: 19493651 DOI: 10.1016/j.arth.2009.04.001]
11 **De Geest T**, Vansintjan P, De Loore G. Direct anterior total hip arthroplasty: complications and early outcome in a series of 300 cases. *Acta Orthop Belg* 2013; **79**: 166-173 [PMID: 23821968]
12 **Ukai T**, Ebihara G, Watanabe M. Comparison of short-term outcomes of anterolateral supine approach and posterolateral approach for primary total hip arthroplasty: a retrospective study. *J Orthop Traumatol* 2021; **22**: 6 [PMID: 33638733 DOI: 10.1186/s10195-021-00570-2]
13 **Dall'Oca C**, Ceccato A, Cresceri M, Scaglia M, Guglielmini M, Pelizzari G, Valentini R, Magnan B. Facing complications of direct anterior approach in total hip arthroplasty during the learning curve. *Acta Biomed* 2020; **91**: 103-109 [PMID: 32555084 DOI: 10.23750/abm.v91i4-S.9728]
14 **Migliorini F**, Trivellas A, Eschweiler J, El Mansy Y, Mazzanti MC, Tingart M, Aretini P. Hospitalization length, surgical duration, and blood lost among the approaches for total hip arthroplasty: a Bayesian network meta-analysis. *Musculoskelet Surg* 2020; **104**: 257-266 [PMID: 32248344 DOI: 10.1007/s12306-020-00657-9]
15 **Huang XT**, Liu DG, Jia B, Xu YX. Comparisons between Direct Anterior Approach and Lateral Approach for Primary Total Hip Arthroplasty in Postoperative Orthopaedic Complications: A Systematic Review and Meta-Analysis. *Orthop Surg*

2021; **13**: 1707-1720 [PMID: 34351056 DOI: 10.1111/os.13101]

16 **Vles GF**, Corten K, Driesen R, van Elst C, Ghijselings SG. Hidden blood loss in direct anterior total hip arthroplasty: a prospective, double blind, randomized controlled trial on topical versus intravenous tranexamic acid. *Musculoskelet Surg* 2021; **105**: 267-273 [PMID: 32152813 DOI: 10.1007/s12306-020-00652-0]

17 **Bendich I**, Landy DC, Do H, Krell E, Diane A, Boettner F, Rodriguez J, Alexiades M, Gonzalez Della Valle A. Intraoperative Complications and Early Return to the Operating Room in Total Hip Arthroplasty Performed Through the Direct Anterior and Posterior Approaches. An Institutional Experience of Surgeons After Their Learning Curve. *J Arthroplasty* 2021; **36**: 2829-2835 [PMID: 33865647 DOI: 10.1016/j.arth.2021.03.046]

18 **Khanuja HS**, Vakil JJ, Goddard MS, Mont MA. Cementless femoral fixation in total hip arthroplasty. *J Bone Joint Surg Am* 2011; **93**: 500-509 [PMID: 21368083 DOI: 10.2106/JBJS.J.00774]

19 **Khanuja HS**, Banerjee S, Jain D, Pivec R, Mont MA. Short bone-conserving stems in cementless hip arthroplasty. *J Bone Joint Surg Am* 2014; **96**: 1742-1752 [PMID: 25320202 DOI: 10.2106/JBJS.M.00780]

20 **von Engelhardt LV**, Breil-Wirth A, Kothny C, Seeger JB, Grasselli C, Jerosch J. Long-term results of an anatomically implanted hip arthroplasty with a short stem prosthesis (MiniHip™). *World J Orthop* 2018; **9**: 210-219 [PMID: 30364820 DOI: 10.5312/wjo.v9.i10.210]

21 **Tootsi K**, Lees L, Geiko B, Märtson A. Intraoperative complications in total hip arthroplasty using a new cementless femoral implant (SP-CL®). *J Orthop Traumatol* 2020; **21**: 8 [PMID: 32451636 DOI: 10.1186/s10195-020-00548-6]

22 **Dorr LD**, Faugere MC, Mackel AM, Gruen TA, Bognar B, Malluche HH. Structural and cellular assessment of bone quality of proximal femur. *Bone* 1993; **14**: 231-242 [PMID: 8363862 DOI: 10.1016/8756-3282(93)90146-2]

23 **Summers S**, Nigh E, Sabeh K, Robinson R. Clinical and radiographic outcomes of total hip replacement with a 3-part metaphyseal osseointegrated titanium alloy stem enhanced with low plasticity burnishing: a mean 5-year follow-up study. *Arthroplast Today* 2019; **5**: 352-357 [PMID: 31516981 DOI: 10.1016/j.artd.2019.07.004]

24 **Solarino G**, Vicenti G, Piazzolla A, Maruccia F, Notarnicola A, Moretti B. Total hip arthroplasty for dysplastic coxarthrosis using a cementless Wagner Cone stem. *J Orthop Traumatol* 2021; **22**: 16 [PMID: 33864539 DOI: 10.1186/s10195-021-00578-8]

25 **Pincus D**, Jenkinson R, Paterson M, Leroux T, Ravi B. Association Between Surgical Approach and Major Surgical Complications in Patients Undergoing Total Hip Arthroplasty. *JAMA* 2020; **323**: 1070-1076 [PMID: 32181847 DOI: 10.1001/jama.2020.0785]

26 **Chen W**, Sun JN, Zhang Y, Chen XY, Feng S. Direct anterior versus posterolateral approaches for clinical outcomes after total hip arthroplasty: a systematic review and meta-analysis. *J Orthop Surg Res* 2020; **15**: 231 [PMID: 32576223 DOI: 10.1186/s13018-020-01747-x]

27 **Barnett SL**, Peters DJ, Hamilton WG, Ziran NM, Gorab RS, Matta JM. Is the Anterior Approach Safe? *J Arthroplasty* 2016; **31**: 2291-2294 [PMID: 26897487 DOI: 10.1016/j.arth.2015.07.008]

28 **Rahm S**, Tondelli T, Steinmetz S, Schenk P, Dora C, Zingg PO. Uncemented Total Hip Arthroplasty Through the Direct Anterior Approach: Analysis of a Consecutive Series of 275 Hips With a Minimum Follow-Up of 10 Years. *J Arthroplasty* 2019; **34**: 1132-1138 [PMID: 30795936 DOI: 10.1016/j.arth.2019.01.062]

29 **Hu F**, Shang X, Zhang X, Chen M. Direct anterior approach in lateral position achieves superior cup orientation in total hip arthroplasty: a radiological comparative study of two consecutive series. *Int Orthop* 2020; **44**: 453-459 [PMID: 31900573 DOI: 10.1007/s00264-019-04461-4]

30 **Rathod PA**, Bhalla S, Deshmukh AJ, Rodriguez JA. Does fluoroscopy with anterior hip arthroplasty decrease acetabular cup variability compared with a nonguided posterior approach? *Clin Orthop Relat Res* 2014; **472**: 1877-1885 [PMID: 24549773 DOI: 10.1007/s11999-014-3512-2]

31 **Kobayashi H**, Homma Y, Baba T, Ochi H, Matsumoto M, Yuasa T, Kaneko K. Surgeons changing the approach for total hip arthroplasty from posterior to direct anterior with fluoroscopy should consider potential excessive cup anteversion and flexion implantation of the stem in their early experience. *Int Orthop* 2016; **40**: 1813-1819 [PMID: 26634579 DOI: 10.1007/s00264-015-3059-1]

32 **Rivera F**, Leonardi F, Evangelista A, Pierannunzii L. Risk of stem undersizing with direct anterior approach for total hip arthroplasty. *Hip Int* 2016; **26**: 249-253 [PMID: 27013489 DOI: 10.5301/hipint.5000337]

33 **Barrett WP**, Turner SE, Murphy JA, Flener JL, Alton TB. Prospective, Randomized Study of Direct Anterior Approach vs Posterolateral Approach Total Hip Arthroplasty: A Concise 5-Year Follow-Up Evaluation. *J Arthroplasty* 2019; **34**: 1139-1142 [PMID: 30885407 DOI: 10.1016/j.arth.2019.01.060]

34 **Klasan A**, Neri T, Oberkircher L, Malcherczyk D, Heyse TJ, Bliemel C. Complications after direct anterior versus Watson-Jones approach in total hip arthroplasty: results from a matched pair analysis on 1408 patients. *BMC Musculoskelet Disord* 2019; **20**: 77 [PMID: 30764879 DOI: 10.1186/s12891-019-2463-x]

35 **Ho KW**, Whitwell GS, Young SK. Reducing the rate of early primary hip dislocation by combining a change in surgical technique and an increase in femoral head diameter to 36 mm. *Arch Orthop Trauma Surg* 2012; **132**: 1031-1036 [PMID: 22460352 DOI: 10.1007/s00402-012-1508-5]

36 **Berry DJ**, von Knoch M, Schleck CD, Harmsen WS. Effect of femoral head diameter and operative approach on risk of dislocation after primary total hip arthroplasty. *J Bone Joint Surg Am* 2005; **87**: 2456-2463 [PMID: 16264121 DOI: 10.2106/JBJS.D.02860]

37 **van Loon J**, Hoornenborg D, van der Vis HM, Sierevelt IN, Opdam KT, Kerkhoffs GM, Haverkamp D. Ceramic-on-ceramic *vs* ceramic-on-polyethylene, a comparative study with 10-year follow-up. *World J Orthop* 2021; **12**: 14-23 [PMID: 33520678 DOI: 10.5312/wjo.v12.i1.14]

38 **Mjaaland KE**, Svenningsen S, Fenstad AM, Havelin LI, Furnes O, Nordsletten L. Implant Survival After Minimally Invasive Anterior or Anterolateral Vs. Conventional Posterior or Direct Lateral Approach: An Analysis of 21,860 Total Hip Arthroplasties from the Norwegian Arthroplasty Register (2008 to 2013). *J Bone Joint Surg Am* 2017; **99**: 840-847 [PMID: 28509824 DOI: 10.2106/JBJS.16.00494]

39 **Henri Bauwens P**, Fary C, Servien E, Lustig S, Batailler C. Early low complication rate of ceramic-on-ceramic total hip arthroplasty by direct anterior approach. *SICOT J* 2020; **6**: 30 [PMID: 32749213 DOI: 10.1051/sicotj/2020027]

40 **Jewett BA**, Collis DK. High complication rate with anterior total hip arthroplasties on a fracture table. *Clin Orthop Relat Res* 2011; **469**: 503-507 [PMID: 20886324 DOI: 10.1007/s11999-010-1568-1]

41 **Sarraj M**, Chen A, Ekhtiari S, Rubinger L. Traction table versus standard table total hip arthroplasty through the direct anterior approach: a systematic review. *Hip Int* 2020; **30**: 662-672 [PMID: 31994425 DOI: 10.1177/1120700019900987]

42 **Greco NJ**, Lombardi AV Jr, Morris MJ, Hobbs GR, Berend KR. Direct Anterior Approach and Perioperative Fracture With a Single-Taper Wedge Femoral Component. *J Arthroplasty* 2019; **34**: 145-150 [PMID: 30301574 DOI: 10.1016/j.arth.2018.09.003]

43 **Cohen EM**, Vaughn JJ, Ritterman SA, Eisenson DL, Rubin LE. Intraoperative Femur Fracture Risk During Primary Direct Anterior Approach Cementless Total Hip Arthroplasty With and Without a Fracture Table. *J Arthroplasty* 2017; **32**: 2847-2851 [PMID: 28511947 DOI: 10.1016/j.arth.2017.04.020]

44 **Dietrich M**, Kabelitz M, Dora C, Zingg PO. Perioperative Fractures in Cementless Total Hip Arthroplasty Using the Direct Anterior Minimally Invasive Approach: Reduced Risk With Short Stems. *J Arthroplasty* 2018; **33**: 548-554 [PMID: 28993084 DOI: 10.1016/j.arth.2017.09.015]

45 **Luger M**, Hipmair G, Schopper C, Schauer B, Hochgatterer R, Allerstorfer J, Gotterbarm T, Klasan A. Low rate of early periprosthetic fractures in cementless short-stem total hip arthroplasty using a minimally invasive anterolateral approach. *J Orthop Traumatol* 2021; **22**: 19 [PMID: 34019194 DOI: 10.1186/s10195-021-00583-x]

46 **Drosos GI**, Tottas S, Kougioumtzis I, Tilkeridis K, Chatzipapas C, Ververidis A. Total hip replacement using MINIMA® short stem: A short-term follow-up study. *World J Orthop* 2020; **11**: 232-242 [PMID: 32405472 DOI: 10.5312/wjo.v11.i4.232]

47 **Rudin D**, Manestar M, Ullrich O, Erhardt J, Grob K. The Anatomical Course of the Lateral Femoral Cutaneous Nerve with Special Attention to the Anterior Approach to the Hip Joint. *J Bone Joint Surg Am* 2016; **98**: 561-567 [PMID: 27053584 DOI: 10.2106/JBJS.15.01022]

48 **Thaler M**, Dammerer D, Hechenberger F, Hörmann R, Van Beeck A, Stofferin H. The Anatomical Course of the Lateral Femoral Cutaneous Nerve in Relation to Various Skin Incisions Used for Primary and Revision Total Hip Arthroplasty With the Direct Anterior Approach. *J Arthroplasty* 2021; **36**: 368-373 [PMID: 32826147 DOI: 10.1016/j.arth.2020.07.052]

49 **Homma Y**, Baba T, Sano K, Ochi H, Matsumoto M, Kobayashi H, Yuasa T, Maruyama Y, Kaneko K. Lateral femoral cutaneous nerve injury with the direct anterior approach for total hip arthroplasty. *Int Orthop* 2016; **40**: 1587-1593 [PMID: 26224618 DOI: 10.1007/s00264-015-2942-0]

50 **Patton RS**, Runner RP, Lyons RJ, Bradbury TL. Clinical Outcomes of Patients With Lateral Femoral Cutaneous Nerve Injury After Direct Anterior Total Hip Arthroplasty. *J Arthroplasty* 2018; **33**: 2919-2926.e1 [PMID: 29807793 DOI: 10.1016/j.arth.2018.04.032]

51 **Zhao G**, Zhu R, Jiang S, Xu N, Bao H, Wang Y. Using the anterior capsule of the hip joint to protect the tensor fascia lata muscle during direct anterior total hip arthroplasty: a randomized prospective trial. *BMC Musculoskelet Disord* 2020; **21**: 21 [PMID: 31926554 DOI: 10.1186/s12891-019-3035-9]

52 **Alecci V**, Valente M, Crucil M, Minerva M, Pellegrino CM, Sabbadini DD. Comparison of primary total hip replacements performed with a direct anterior approach versus the standard lateral approach: perioperative findings. *J Orthop Traumatol* 2011; **12**: 123-129 [PMID: 21748384 DOI: 10.1007/s10195-011-0144-0]

53 **Zhao GY**, Wang YJ, Xu NW, Liu F. Dissection and ligation of the lateral circumflex femoral artery is not necessary when using the direct anterior approach for total hip arthroplasty. *World J Clin Cases* 2019; **7**: 4226-4233 [PMID: 31911903 DOI: 10.12998/wjcc.v7.i24.4226]

54 **Jinnai Y**, Baba T, Zhuang X, Tanabe H, Banno S, Watari T, Homma Y, Kaneko K. Does a fluoro-assisted direct anterior approach for total hip arthroplasty pose an excessive risk of radiation exposure to the surgeon? *SICOT J* 2020; **6**: 6 [PMID: 32068533 DOI: 10.1051/sicotj/2020004]

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ORIGINAL ARTICLE

Retrospective Study

Integrity of the hip capsule measured with magnetic resonance imaging after capsular repair or unrepaired capsulotomy in hip arthroscopy

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Abstract

BACKGROUND

Current literature shows no clear answer on the question how to manage the capsule after hip arthroscopy. Regarding patient reported outcome measures there seems to be no difference between capsular repair or unrepaired capsulotomy.

AIM

To evaluate and compare the integrity of the hip capsule measured on a magnetic resonance imaging (MRI) scan after capsular repair or unrepaired capsulotomy.

METHODS

A case series study was performed; a random sample of patients included in a trial comparing capsular repair *vs* unrepaired capsulotomy had a postoperative MRI scan. The presence of a capsular defect and gap size were independently evaluated on MRI.

RESULTS

A total of 28 patients (29 hips) were included. Patient demographics were comparable between treatment groups. There were 2 capsular defects in the capsular repair group and 7 capsular defects in the unrepaired capsulotomy group (P = 0.13). In the group of patients with a defect, median gap sizes at the acetabular side were 5.9 mm (range: 2.7-9.0) in the repaired and 8.0 mm (range: 4.5-18.0) in the unrepaired group (P = 0.462). At the muscular side gap sizes were 6.6 mm (range: 4.1-9.0) in the repaired group and 11.5 mm (range: 3.0-18.0) in the unrepaired group (P = 0.857). The calculated Odds ratio (OR) for having a capsular defect with an increasing lateral center-edge (CE) angle was 1.12 (P = 0.06). The OR for having a capsular defect is lower in the group of patients that underwent a labral repair with an OR of 0.1 (P = 0.05).

CONCLUSION

There is no significant difference in capsular defects between capsular repair or unrepaired capsulotomy. Regarding clinical characteristics our case series shows that a larger CE angle increases the likelihood of a capsular defect and the presence of a labral repair decreases the likelihood of a capsular defect.

Key Words: Hip; Arthroscopy; Magnetic resonance imaging; Capsule; Thickness

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Core Tip: In this case series we evaluated the integrity of the hip capsule after hip arthroscopy with a magnetic resonance imaging scan and compared between patients in a capsular repair group and unrepaired capsulotomy group. The magnetic resonance imaging scan of 29 hips was observed to determine whether there was a capsular defect or not. After 12 mo follow-up no difference was found between groups regarding the presence of a capsular defect or not.

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INTRODUCTION

Hip arthroscopy is a more and more popular technique to address intra-articular pathology of the hip[1,2]. Entrance to the hip is made by several portals and usually an interportal or T-shaped capsulotomy is performed to improve workspace in the joint[3]. In the early days of hip arthroscopy these capsulotomies were usually left unrepaired[4]. In recent years there has been debate on what to do with the capsulotomy at the end of the procedure. Some papers suggest that routine capsular closure might result in improved outcomes after surgery where other papers report conflicting evidence and show no superiority of routine capsular repair[5-10]. However, there are cadaveric studies that show the biomechanical importance of complete capsular repair[11,12]. Restoration of the hip joint capsule results in hip joint kinematics to near normal levels after interportal or T-shaped capsulotomy[12]. The unrepaired hip capsulotomy might be a reason for developing postoperative iatrogenic hip instability[13,14]. As the (un)repaired capsulotomy might be a contributor to postoperative complaints of patients with iatrogenic hip instability, this may be quantified by assessment of the quality and morphologic appearance of the hip capsule with magnetic resonance imaging (MRI)[15].

The purpose of this study is to evaluate the integrity of the hip capsule after capsular repair or unrepaired capsulotomy measured with MRI. Our secondary aim is to evaluate the association between pre- and perioperative details and the quality and integrity of the capsule.

MATERIALS AND METHODS

Study design and participants

For the current study a random sample of 28 patients (29 hips) with residual hip complaints after surgery or complaints of the contralateral hip had an MRI scan postoperatively and were enrolled in the current study. All patients were part of a trial that was designed and approved after local medical ethical committee approval (NL55669.048.15). Inclusion criteria for the trial were age between 18-65 years, a body mass index (BMI) lower than 35 and good understanding of Dutch/English language and with intra-articular hip pathology who opt for hip arthroscopy. Exclusion criteria were revision hip arthroscopy, extra-articular hip pathology, a documented systemic connective tissue disease or hypermobility, a center-edge (CE) angle of less than 25 degrees, prior hip surgery or a hip fracture in the past. After randomization patients were either allocated to repaired capsulotomy or the unrepaired capsulotomy group. All patients were operated by the senior author. Functional outcome was measured at baseline and after 12 mo follow-up with the Copenhagen Hip and Groin Outcome Score (HAGOS) [16].

The postoperative MRI scans were independently evaluated for capsular integrity by Bech NH and Haverkamp D to assess inter observer reliability. Both authors were blinded to clinical and detailed operative information to prevent bias.

Final cohort consisted of 29 hips (28 patients) of which 16 were in the unrepaired group and 13 in the capsular repair (repair) group that had received a postoperative MRI scan.

Surgical technique

Patients were operated *via* standard technique and 2 or 3 portals were made. An interportal capsulotomy was done in all patients. No T-shaped capsulotomies were done. Repair of the capsule took approximately 15 min of operating time. The capsular repair was done with 2 or 3 sutures by arthroscopic technique (Capsular Close Scorpion, Arthrex). Standard sutures were used (Fibrewire, Arthrex).

Postoperative protocol

In both groups the rehabilitation protocol was similar. The first 4 wk no weight bearing was allowed. After that, patients started weight bearing with crutches. From week 5 till week 12 patients started with passive and active exercises and were guided by a physiotherapy. After week 12 there were no more restrictions. All patients received standard 4 wk of non-steroid anti-inflammatory drugs (diclofenac) to inhibit heterotopic ossification.

Capsular quality assessment on MRI

The used technique for measuring capsular defects has been previously described in the paper of Strickland *et al*[17]. Capsular integrity was measured on a proton weighted density sequence or the T2 weighted fat-saturated sequence in the coronal plane. First step was to determine if there was a capsular defect (Figure 1). The definition of a capsular defect was described by Weber *et al*[18]; being any visual disruption of the iliofemoral ligament or any appearance of communication between the joint and the iliofemoral bursa seen with contrast (Figure 1A and B)[18]. Furthermore, we measured 2 parameters: Gap length on the acetabular side and the gap length on the muscular side of the defect (Figure 1A and B)

Statistical analysis

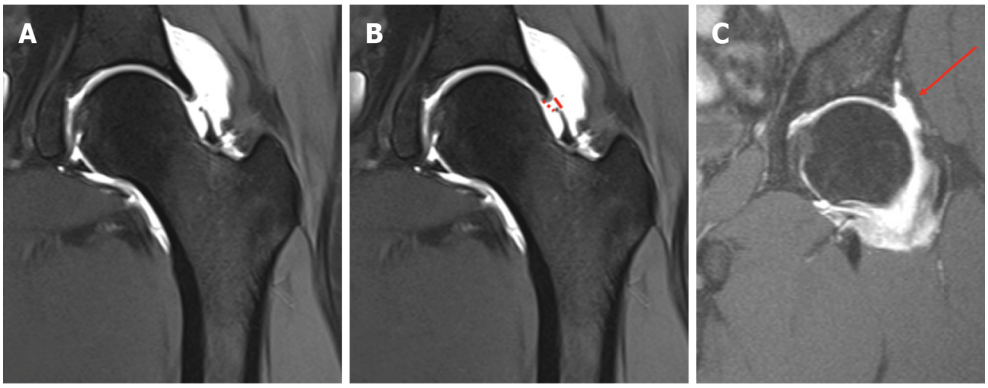
Patient and clinical characteristics are described as means ± SD in case of normally distributed continuous variables. Otherwise, medians with ranges are presented. Comparisons between repair groups were performed by use of *t*-tests or non-parametric Mann Whitney *U*-tests where appropriate. Categorical variables are presented as numbers with accompanying proportions and analyzed by use of χ^2 tests or Fischer Exact-tests (in case of expected numbers < 5). For the presence of a capsular gap, absolute agreement was calculated to present inter observer reliability. The association between pre- and perioperative details and the presence of a defect was analyzed by use of a univariate logistic regression analysis and Odds ratios (OR) with 95%CI were calculated. Intra class correlation coefficients ($ICC_{agreement}$, 2-way random effect model) were calculated for both acetabular and muscular gap length. A P value < 0.05 was considered statistically significant.

Analysis was performed by use of SPSS statistical software (IBM Corp. IBM SPSS Statistics for Macintosh Version 26.0. Armonk, NY: IBM Corp).

RESULTS

Patient demographics

The mean age in the unrepaired group was 33.3 ± 6.1 and in the repair group 31.4 ± 9.1. Average follow-



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Figure 1 Example of capsular defect and intact capsule on magnetic resonance imaging-arthrography. A: example of a capsular defect on magnetic resonance imaging (MRI)-arthrography with extracapsular contrast leakage to the adjacent soft-tissue; B: Gap length measurement; solid line: gap length muscular side. Dotted line: Gap length acetabular side; C: Example of an intact capsule on MRI-arthrography (Arrow). There is no contrast leakage to the adjacent soft-tissue.

up in the repair group was 15.8 ± 6.5 mo and in the unrepaired group 12.6 ± 6.7 mo. Regarding baseline characteristics there were no significant differences between both groups (Table 1).

Regarding the HAGOS functional outcome score both baseline and 12 mo follow-up values are given in Table 2. In the capsule defect group, 7 patients reached the 12 mo follow-up, in the capsule intact group, 16 patients reached the 12 mo follow-up. Between the capsule intact and the capsular defect group, there were no differences on all 5 domains of the HAGOS outcome score (Table 2).

Capsular defects

In total there were 9 capsular defects measured on MRI, 20 hips did not have a capsular defect. For the assessment of the presence of capsular defect there was 100% agreement between observers. In the repair group, there were 2 patients (15.4%) with a measurable capsular defect on MRI, and in the unrepaired group 7 patients (43.8%) (P = 0.13).

In the capsular repair group, there were 2 failures. The first was a 23-year-old woman with a large CE angle (44 degrees) and a BMI of 24,6. The second patient was a 45-year-old woman with a hip that had already some signs of osteoarthritis, a CE angle of 36.9 degrees and a BMI of 33.3.

Gap size

Inter observer reliability of gap size measurements was good to excellent with ICC values of 0.83 and 0.94 of the gap measurements at the acetabular and muscular side.

Among patients with a capsular defect, median gap sizes at the acetabular side were 5.9 mm (range: 2.7-9.0) and 8.0 mm (range: 4.5-18.0) in the repaired and unrepaired group, respectively (P = 0.462). At the muscular side, gap sizes were 6.6 mm (range: 4.1-9.0) and 11.5 mm (range: 3.0-18.0), respectively (P = 0.857).

Clinical characteristics and capsular defect

Although not significant patients with a larger CE angle were more likely to have a capsular defect on MRI with an OR of 1.12 (P = 0.06).

In the group of patients with a capsular defect, there were 2 with a CAM-type deformity and 5 with a pincer-type deformity. In the capsule intact group, there were 6 patients with a CAM-type deformity and 9 patients with a pincer-type deformity. There was no significant association between the presence of a CAM or pincer deformity and a capsular defect (Table 3).

In the capsular defect group, there was 1 patient that underwent a labral repair; in the capsule intact group, 11 patients underwent a labral repair. Patients with a labral repair were less likely to have a capsular defect on MRI with an OR of 0.1 compared to patients without labral repair (P = 0.05) (Table 3).

DISCUSSION

In this case series we found that the incidence of a capsular defect, although not significant, was higher in the unrepaired capsulotomy group than in the repaired group. Our results are comparable to available current literature. In the randomized controlled trial of Strickland *et al*[17] they investigated 30 hips and compared capsular closure *vs* unrepaired interportal capsulotomy during simultaneous bilateral arthroscopy. They measured the capsular defect and the quality of the capsule postoperatively

Table 1 Patient demographics

	Repaired (*n* = 13)	Unrepaired (*n* = 16)	*P* value
Sex			0.36
Male	4 (30.8)	2 (12.5)	
Female	9 (69.2)	14 (87.5)	
BMI	23.8 ± 3.9	23.1 ± 2.3	0.67
Age (yr)	31.4 ± 9.1	33.3 ± 6.1	0.49
Follow-up (mo)	15.8 ± 6.5	12.6 ± 6.7	0.72
Impingement type			
CAM	5 (38.5)	3 (18.8)	0.62
Pincer	5 (38.5)	9 (56.3)	0.34
Labral repair	5 (38.5)	7 (43.8)	0.22
CE angle at time of MRI (degrees)	38.2 ± 7.7	34.0 ± 9.8	0.48

Data are presented as *n* (%) or mean ± SD. BMI: Body mass index; CE: Center-edge; MRI: magnetic resonance imaging.

Table 2 Hip and Groin Outcome Score functional outcome score at baseline and after 12 mo follow-up

	Capsular intact (*n* = 20)	Capsular defect (*n* = 9)	*P* value
Baseline			
HAGOS, median (IQR)			
Symptoms	44.6 (35.7-58.9)	35.7 (28.6-37.5)	0.08
Pain	43.8 (32.5-54.4)	35.0 (31.3-48.8)	0.39
ADL	47.5 (26.3-65.0)	40.0 (40.0-67.5)	0.84
Sport	32.8 (19.5-43.0)	25.0 (19.5-37.5)	0.71
QoL	25.0 (15.0-35.0)	25.0 (21.3-38.8)	0.64
12 mo FU			
HAGOS, median (IQR)			
Symptoms	51.8 (32.1-74.1)	39.3 (35.7-64.3)	0.82
Pain	70.0 (48.8-86.3)	60.0 (40.0-92.5)	0.87
ADL	67.5 (40.0-90.0)	60.0 (50.0-95.0)	0.62
Sport	53.6 (25.8-80.5)	53.1 (35.7-81.3)	0.87
QoL	40.0 (26.3-53.8)	60.0 (40.0-60.0)	0.28

HAGOS: Hip and Groin Outcome Score; IQR: Interquartile Range; FU: Follow-up; ADL: Activity of daily living; QoL: Quality of life.

and report no significant differences between treatment groups at final endpoint at 24 wk after surgery. Kraeutler *et al*[19] performed a multicenter randomized trial between capsular repair and unrepaired capsulotomy. They also report no differences between both treatment groups regarding healing of the capsule measured on MRI[19].

In the paper of Weber *et al*[18] symptomatic patients were evaluated with MRI after capsular repair. They reported that 1 year after surgery 92.5% of the repaired capsules remained closed and that the capsule was thickened at the site of the repaired capsulotomy compared to the unaffected contralateral hip capsule[18].

To our best knowledge there is no literature that investigated the association between the size of the CE-angle and the presence of a capsular defect. In our series the likelihood of a capsular defect was larger with an increasing CE angle. An explanation for this finding could be that in this group the incidence of pincer impingement was higher. As part of the procedure of pincer impingement the surgeon must resect a part of the acetabulum and detach a part of the iliofemoral ligament. Extended

Table 3 Association between clinical characteristics and presence of a capsular defect

	OR (95%CI)	*P* value
CE angle at time of MRI	1.12 (1.00-1.26)	0.06
CAM	0.67 (0.11-4.20)	0.67
Pincer	1.53 (0.31-7.44)	0.60
Labral repair	0.10 (0.01-0.98)	0.05

CE: Center-edge; MRI: magnetic resonance imaging.

resection and concomitant ligament damage could lead to possible higher incidence of capsular defects after surgery. In our series there were only 2 failures in the capsular repair group that showed a capsular defect on MRI. Possibly the rather large CE angle in both patients was of influence and led to subsequent failure of capsular healing.

Regarding labral repair there was a significant larger portion of patients with an intact capsule in the labral repair group. It is unsure where the difference in capsular defects between labral repair and no repair originates from. A possibility is that more stability from a repaired labrum influences the capsular healing. Cadaveric studies show that an intact labrum absorbs a lot of strain during motion of the hip [20]. Without the intact labrum the hip capsule might have to compensate for these forces resulting in possibly a higher incidence of capsular defects.

Strengths

A strength of this study is that the capsular defect was measured by two authors separately and that an intra classifier coefficient was calculated to verify the accuracy of the measured defects.

Limitations

The first limitation of this study is that small number of patients were included. We expect that although there was a clinically relevant difference in measurable defect between the groups, this difference was not statistically different because of the small sample size. Secondly, only symptomatic patients or patients with complaints of the contralateral hip had an MRI scan and this could have introduced a bias in our results.

CONCLUSION

Our current study shows that there is no significant difference in capsular healing on MRI between capsular repair or unrepaired capsulotomy. Furthermore, a higher CE angle increases the likelihood of having a capsular defect and the presence of a labral repair decreases the likelihood of a capsular defect. Although there seems to be no reason for routinely capsular closure after hip arthroscopy, knowing these patient specific factors might help the orthopedic surgeon to decide to perform a capsular repair in specific cases.

ARTICLE HIGHLIGHTS

Research background

Capsular management after hip arthroscopy remains topic of debate after an interportal capsulotomy

Research motivation

More studies are needed to determine what the effect is of capsular repair on capsular healing after hip arthroscopy.

Research objectives

To determine whether capsular repair or not may result in a capsular defect measured on an MRI scan. Secondary objective is to determine of the presence of a capsular defect might influence the clinical outcome after hip arthroscopy.

Research methods

A random sample of patients were enrolled in this case series. All were operated and had a magnetic

resonance imaging (MRI) scan in the postoperative phase. Patients were part of an earlier performed randomized trial and were randomized into a capsular repair or unrepaired capsulotomy group. Outcome was the presence of a capsular defect on MRI and the Copenhagen Hip and Groin Outcome Score (HAGOS).

Research results

A total of 29 hips were included. There was no significant different number of capsular defects between the capsular repair or unrepaired capsulotomy groups. There was also no difference in outcome measured with HAGOS outcome score between the capsular defect or capsule intact group.

Research conclusions

There was no difference in the number of capsular defects between the capsular repair or unrepaired capsulotomy group.

Research perspectives

Future larger studies are needed to confirm that capsular repair or unrepaired capsulotomy has no influence on the presence of a capsular defect or not. In addition; long term analysis needs to be done to determine whether the presence of a capsular defect might result in long term complications or influence outcome.

FOOTNOTES

Author contributions: Bech NH drafted the manuscript, was involved with data collection, and assisted with data analysis; van Dijk LA drafted the manuscript and participated in design of the study; de Waard S was involved with data collection, and assisted with data analysis; Vuurberg G drafted the manuscript, and assisted with data analysis; Sierevelt IN participated in study design and performed statistical analysis; Kerkhoffs GM participated in study design; Haverkamp D participated in design of the study drafted the manuscript and was involved with data collection; and all authors read and approved the final manuscript.

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REFERENCES

1 **Truntzer JN**, Shapiro LM, Hoppe DJ, Abrams GD, Safran MR. Hip arthroscopy in the United States: an update following coding changes in 2011. *J Hip Preserv Surg* 2017; **4**: 250-257 [PMID: 28948037 DOI: 10.1093/jhps/hnx004]
2 **Griffin DR**, Dickenson EJ, Wall PDH, Achana F, Donovan JL, Griffin J, Hobson R, Hutchinson CE, Jepson M, Parsons NR, Petrou S, Realpe A, Smith J, Foster NE; FASHIoN Study Group. Hip arthroscopy versus best conservative care for the treatment of femoroacetabular impingement syndrome (UK FASHIoN): a multicentre randomised controlled trial. *Lancet* 2018; **391**: 2225-2235 [PMID: 29893223 DOI: 10.1016/S0140-6736(18)31202-9]

3 **Larson CM**, Guanche CA, Kelly BT, Clohisy JC, Ranawat AS. Advanced techniques in hip arthroscopy. *Instr Course Lect* 2009; **58**: 423-436 [PMID: 19385552]

4 **Byrd JW**, Jones KS. Hip arthroscopy for labral pathology: prospective analysis with 10-year follow-up. *Arthroscopy* 2009; **25**: 365-368 [PMID: 19341922 DOI: 10.1016/j.arthro.2009.02.001]

5 **Domb BG**, Stake CE, Finley ZJ, Chen T, Giordano BD. Influence of capsular repair versus unrepaired capsulotomy on 2-year clinical outcomes after arthroscopic hip preservation surgery. *Arthroscopy* 2015; **31**: 643-650 [PMID: 25530511 DOI: 10.1016/j.arthro.2014.10.014]

6 **Economopoulos KJ**, Chhabra A, Kweon C. Prospective Randomized Comparison of Capsular Management Techniques During Hip Arthroscopy. *Am J Sports Med* 2020; **48**: 395-402 [PMID: 31891553 DOI: 10.1177/0363546519894301]

7 **Acuña AJ**, Samuel LT, Roth A, Emara AK, Kamath AF. How capsular management strategies impact outcomes: A systematic review and meta-analysis of comparative studies. *J Orthop* 2020; **19**: 237-243 [PMID: 32071521 DOI: 10.1016/j.jor.2020.02.002]

8 **Lund B**, Mygind-Klavsen B, Grønbech Nielsen T, Maagaard N, Kraemer O, Hölmich P, Winge S, Lind M. Danish Hip Arthroscopy Registry (DHAR): the outcome of patients with femoroacetabular impingement (FAI). *J Hip Preserv Surg* 2017; **4**: 170-177 [PMID: 28630739 DOI: 10.1093/jhps/hnx009]

9 **Atzmon R**, Sharfman ZT, Haviv B, Frankl M, Rotem G, Amar E, Drexler M, Rath E. Does capsular closure influence patient-reported outcomes in hip arthroscopy for femoroacetabular impingement and labral tear? *J Hip Preserv Surg* 2019; **6**: 199-206 [PMID: 31798927 DOI: 10.1093/jhps/hnz025]

10 **Bech NH**, Sierevelt IN, de Waard S, Joling BSH, Kerkhoffs GMMJ, Haverkamp D. Capsular closure versus unrepaired interportal capsulotomy after hip arthroscopy in patients with femoroacetabular impingement, results of a patient-blinded randomised controlled trial. *Hip Int* 2021; 11207000211005762 [PMID: 33845615 DOI: 10.1177/11207000211005762]

11 **Khair MM**, Grzybowski JS, Kuhns BD, Wuerz TH, Shewman E, Nho SJ. The Effect of Capsulotomy and Capsular Repair on Hip Distraction: A Cadaveric Investigation. *Arthroscopy* 2017; **33**: 559-565 [PMID: 28012635 DOI: 10.1016/j.arthro.2016.09.019]

12 **Baha P**, Burkhart TA, Getgood A, Degen RM. Complete Capsular Repair Restores Native Kinematics After Interportal and T-Capsulotomy. *Am J Sports Med* 2019; **47**: 1451-1458 [PMID: 30946598 DOI: 10.1177/0363546519832868]

13 **Abrams GD**, Hart MA, Takami K, Bayne CO, Kelly BT, Espinoza Orías AA, Nho SJ. Biomechanical Evaluation of Capsulotomy, Capsulectomy, and Capsular Repair on Hip Rotation. *Arthroscopy* 2015; **31**: 1511-1517 [PMID: 25882176 DOI: 10.1016/j.arthro.2015.02.031]

14 **Bayne CO**, Stanley R, Simon P, Espinoza-Orias A, Salata MJ, Bush-Joseph CA, Inoue N, Nho SJ. Effect of capsulotomy on hip stability-a consideration during hip arthroscopy. *Am J Orthop (Belle Mead NJ)* 2014; **43**: 160-165 [PMID: 24730000]

15 **Wagner FV**, Negrão JR, Campos J, Ward SR, Haghighi P, Trudell DJ, Resnick D. Capsular ligaments of the hip: anatomic, histologic, and positional study in cadaveric specimens with MR arthrography. *Radiology* 2012; **263**: 189-198 [PMID: 22371607 DOI: 10.1148/radiol.12111320]

16 **Thorborg K**, Hölmich P, Christensen R, Petersen J, Roos EM. The Copenhagen Hip and Groin Outcome Score (HAGOS): development and validation according to the COSMIN checklist. *Br J Sports Med* 2011; **45**: 478-491 [PMID: 21478502 DOI: 10.1136/bjsm.2010.080937]

17 **Strickland CD**, Kraeutler MJ, Brick MJ, Garabekyan T, Woon JTK, Chadayammuri V, Mei-Dan O. MRI Evaluation of Repaired Versus Unrepaired Interportal Capsulotomy in Simultaneous Bilateral Hip Arthroscopy: A Double-Blind, Randomized Controlled Trial. *J Bone Joint Surg Am* 2018; **100**: 91-98 [PMID: 29342058 DOI: 10.2106/JBJS.17.00365]

18 **Weber AE**, Kuhns BD, Cvetanovich GL, Lewis PB, Mather RC, Salata MJ, Nho SJ. Does the Hip Capsule Remain Closed After Hip Arthroscopy With Routine Capsular Closure for Femoroacetabular Impingement? *Arthroscopy* 2017; **33**: 108-115 [PMID: 27720303 DOI: 10.1016/j.arthro.2016.07.022]

19 **Kraeutler MJ**, Strickland CD, Brick MJ, Garabekyan T, Woon JTK, Chadayammuri V, Mei-Dan O. A multicenter, double-blind, randomized controlled trial comparing magnetic resonance imaging evaluation of repaired versus unrepaired interportal capsulotomy in patients undergoing hip arthroscopy for femoroacetabular impingement. *J Hip Preserv Surg* 2018; **5**: 349-356 [PMID: 30647924 DOI: 10.1093/jhps/hny045]

20 **Safran MR**, Giordano G, Lindsey DP, Gold GE, Rosenberg J, Zaffagnini S, Giori NJ. Strains across the acetabular labrum during hip motion: a cadaveric model. *Am J Sports Med* 2011; **39** Suppl: 92S-102S [PMID: 21709038 DOI: 10.1177/0363546511414017]

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LETTER TO THE EDITOR

Existing fixation modalities for Jones type fifth metatarsal fracture fixation pose high rates of complications and nonunion

Albert Thomas Anastasio, Selene G Parekh

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Abstract

Jones type fifth metatarsal fractures pose a challenge to the foot and ankle surgeon, given documented high nonunion rates as well as high complication rates including hardware prominence, nerve injury, and screw breakage for existing treatment modalities including screw and plantar plate fixation. We call for the design of innovative Jones-fracture specific implants which contour to the natural curve of the fifth metatarsal. Future research should aim to expand upon existing literature for Jones fracture fixation and evaluate efficacy of novel implants which are designed to address unacceptably high complication rates for existing treatment modalities.

Key Words: Jones; Metatarsal base; Fifth metatarsal; Athlete; Nonunion; Malunion

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Core Tip: Jones type fifth metatarsal fractures have high rates of complications and fixation failure. While intramedullary screw fixation is the current accepted treatment modality, we call for innovation in the treatment options for Jones fracture fixation to more appropriately address the challenges seen with this fracture pattern in the high level athlete.

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TO THE EDITOR

We read with interest a review article from Albloushi *et al*[1], who present an excellent overview of pathoanatomy, classification, and current concepts of fixation modalities for Jones type fifth metatarsal fracture. We thank the authors for this valuable contribution, and we agree with their conclusion that there remains a lack of consensus on the effective management of Jones fractures, especially in the high-level athlete group. In part, we believe this lack of consensus may be due to unacceptably high complication rates of existing surgical treatments.

Both delayed union and nonunion remain a challenging problem after Jones fracture fixation. The authors note that delayed union in zone 2 and 3 fractures are often the result of choosing screws that are smaller than 4.5 mm in diameter. They recommend utilization of larger screw diameters, especially in the athlete population. While we agree that smaller diameter screws often contribute to nonunion after Jones fixation, we also draw attention to the risk of cortical perforation and subsequent impingement related symptoms, and even potential nerve injury with use of the larger diameter screws[2]. The authors also mention the challenge in adequately appreciating the natural curvature of the fifth metatarsal during fracture fixation. The authors note that failure to maintain the screw within the cortical bone of the 5th metatarsal remains a major cause of nerve injury[3], and recommend meticulous choice of proper entry point of the guidewire and screw with the correct trajectory within the medullary canal. Still, achieving proper positioning of a straight screw within a bone with natural curvature is difficult, and the challenge is expounded when attempting to utilize a larger diameter screw in the case of the elite athlete. Moreover, cannulated screws have been shown to lack proper strength to withstand the significant and repetitive forces the fifth metatarsal must sustain and have been shown to be associated with screw breakage[4].

Despite the difficulties encountered with screw fixation of Jones fracture, plate fixation is also associated with substantial complication risk[5]. Nonunion rates have been unacceptably high in some series[6], and calcaneus autograft has become commonplace for the procedure, denoting an additional area of potential patient morbidity[7]. Hardware prominence also presents a unique challenge in the plating of the Jones fracture. Furthermore, soft tissue injury with the dissection required for proper plate placement flush against the cortical bone can be associated with nerve injury and periosteal stripping with destruction of native bone biology potentially impeding bony union.

With the high complication rates associated with the existing fixation modalities (intramedullary screw fixation and plantar plate fixation), there remains area for innovation with regards to treatment modalities for Jones fracture. Our institution has begun use of an intramedullary implant created specifically for Jones fracture fixation which we hope will be effective in reducing some of the listed complications. This implant has an inherent curve which is fabricated to closely aligned to the natural curvature of the fifth metatarsal. Furthermore, the implant has an end cap which serves to both compress across the fracture site and to reduce hardware prominence at the insertion site. To further enhance fixation at the distal end of the metatarsal, the implant has a talon based mechanism which once activated, provides further implant purchase distally to prevent screw pullout. A study at our institution is currently underway to evaluate whether or not these features lead to decreased complication rates and increased return to play and decreased time to bony union after Jones fracture fixation.

In summary, Jones fracture fixation remains a challenging problem for the foot and ankle surgeon. Existing treatment modalities are associated with high complication rates. Future research should aim to improve upon design elements of existing implants in an effort to effectively manage patients with this condition.

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REFERENCES

1 **Albloushi M**, Alshanqiti A, Qasem M, Abitbol A, Gregory T. Jones type fifth metatarsal fracture fixation in athletes: A review and current concept. *World J Orthop* 2021; **12**: 640-650 [PMID: 34631448 DOI: 10.5312/wjo.v12.i9.640]
2 **Watson GI**, Karnovsky SC, Konin G, Drakos MC. Optimal Starting Point for Fifth Metatarsal Zone II Fractures: A Cadaveric Study. *Foot Ankle Int* 2017; **38**: 802-807 [PMID: 28482680 DOI: 10.1177/1071100717702688]
3 **Aynardi MWK**, Wisbeck JM. Intramedullary Screw Fixation of Jones Fracture: The Crucial Starting Point and Minimizing Complications. *Orthop J Harvard Med Sch* 2019; **20**: 42-45 [DOI: 10.1016/j.fuspru.2011.10.005]
4 **Granata JD**, Berlet GC, Philbin TM, Jones G, Kaeding CC, Peterson KS. Failed Surgical Management of Acute Proximal Fifth Metatarsal (Jones) Fractures: A Retrospective Case Series and Literature Review. *Foot Ankle Spec* 2015; **8**: 454-459 [PMID: 26130624 DOI: 10.1177/1938640015592836]
5 **Haslan H**, Zar CT, Yahaya MY. Decision making in management of proximal fifth metatarsal fracture: a short review. *Med Health* 2016; **11**: 131-138 [DOI: 10.17576/MH.2016.1102.03]
6 **Bernstein DT**, Mitchell RJ, McCulloch PC, Harris JD, Varner KE. Treatment of Proximal Fifth Metatarsal Fractures and Refractures With Plantar Plating in Elite Athletes. *Foot Ankle Int* 2018; **39**: 1410-1415 [PMID: 30079768 DOI: 10.1177/1071100718791835]
7 **O'Malley MJ**, Sayres SC, Saleem O, Levine D, Roberts M, Deland JT, Ellis S. Morbidity and complications following percutaneous calcaneal autograft bone harvest. *Foot Ankle Int* 2014; **35**: 30-37 [PMID: 24318626 DOI: 10.1177/1071100713511806]



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The primary aim of *World Journal of Orthopedics* (*WJO*, *World J Orthop*) is to provide scholars and readers from various fields of orthopedics with a platform to publish high-quality basic and clinical research articles and communicate their research findings online.

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REVIEW

Update in combined musculoskeletal and vascular injuries of the extremities

Nikolaos Stefanou, Christina Arnaoutoglou, Fotios Papageorgiou, Miltiadis Matsagkas, Sokratis E Varitimidis, Zoe H Dailiana

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Abstract

Combined musculoskeletal and vascular injuries of the extremities are conditions in which a multidisciplinary approach is a *sine qua non* to ensure life initially and limb viability secondarily. Vascular injuries as part of musculoskeletal trauma are usually the result of the release of a high energy load in the wound site so that the prognosis is determined by the degree of soft-tissue damage, duration of limb ischemia, patient's medical status and presence of associated injuries. The management of these injuries is challenging and requires a specific algorithm of action, because they are usually characterized by increased morbidity, amputation rate, infection, neurological and functional deficits, and they could be life threatening. Although vascular injuries are rare and occur either isolated or in the context of major combined musculoskeletal trauma, the high index of suspicion, imaging control, and timely referral of the patient to organized trauma centers ensure the best functional outcome of the extremity in such challenging cases. Even after a successful initial treatment of a combined trauma pattern, long-term follow-up is crucial to prevent and detect early possible complications. The purpose of this manuscript is to provide an update on diagnosis and treatment of combined musculoskeletal and vascular injuries of the extremities, from an orthopedic point of view.

Key Words: Vascular injury; Musculoskeletal trauma; Combined injury; Arterial injury; Mangled extremity; Limb salvage

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Core Tip: A complex extremity injury that, in addition to a fracture, dislocation or even crush, involves a vascular injury represents a rare trauma pattern. Historically, control of hemorrhage following trauma has been of interest as far as vascular injury is a leading cause of death and disability. We here discuss the epidemiology, diagnosis and team management of combined musculoskeletal and vascular injuries of the extremities.

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INTRODUCTION

A complex extremity injury that, in addition to a fracture, dislocation or even crush, involves a vascular injury represents a rare trauma pattern. It is a part of combined extremity injury or mangled extremity, and an emergency condition in which multidisciplinary approach is a *sine qua non* to ensure life initially and limb viability secondarily[1]. Historically, control of hemorrhage following trauma has been of interest as vascular injury is a leading cause of death and disability. Moreover, limb salvage in patients with combined musculoskeletal and vascular injuries is distinctly dependent on the severity of soft-tissue injury, duration of limb ischemia and early, accurate diagnosis and treatment of vascular damage [2]. The management of these injuries is challenging and requires a specific algorithm of action, because they are usually characterized by increased morbidity, amputation rate, infection, neurological and functional deficits, and they could be life threatening.

The purpose of this review is to provide an update on diagnosis and treatment of combined musculoskeletal and vascular extremity injuries, from an orthopedic point of view. Combined injuries of the hand, despite possible vascular implication, are not included to this update, due to unique characteristics requiring special treatment and reconstructive pathway.

HISTORY

For many centuries, the manipulation of any hemorrhagic scenario, especially on the battlefield, was controlled by compressive dressings, styptics, hot iron, raw ligature of vessels and improvised tourniquets[3]. The first arterial repair was performed by Dr. Hallowell in 1759 at Newcastle upon Tyne in England and the case was reported by Dr. Richard Lambert in 1761[4]. At the end of the 19th century, in 1896, John B. Murphy carried out an end-to-end anastomosis at Mercy Hospital in Chicago, followed in only one decade by Alexis Carrel and Charles C. Guthrie who established other vascular operative techniques, thus providing a more refined approach in the management of vascular trauma[5-7]. Since a dry and distinct surgical field is necessary for the management of a vascular injury, the gradual widespread use of the tourniquet has greatly helped in the development of surgical techniques. Johannes Friedrich August von Esmarch who was one of the Bernhard von Langenbeck's assistants, developed in 1873 the famous apparatus widely known as the Esmarch bandage[8,9]. Ligations and amputations have been common practice during the Balkan Wars (1911–1913), the First World War (1914–1918) and until the end of World War II (1939–1945), when the use of effective antibiotics and the presence of blood banking improved significantly vascular injury treatment options[10-12].

The time for the predominance of vascular repair over amputation was initially the Korean War (1950–1953), in which amputation rate was about 13% compared to approximately 49% that followed arterial ligation in World War II, and then the Vietnam War (1955–1975)[8,13-15]. Over the years and reaching the Iraq war, the early amputation rate was about 5%-10%[16,17]. All the techniques of vascular rehabilitation and the management algorithms of multiple-trauma patients have been further improved until early 21st century (expanded Advanced Trauma Life Support protocol, utilization of tourniquet, temporary intraluminal shunts, medical air evacuation, high quality intensive care units, sophisticated pharmaceutical agents) and extended recording, statistical analysis, long-term follow-up and publishing of data in recent decades both from the battlefields (Iraq and Afghanistan) and the major urban centers provided significant help in that direction[18-22].

EPIDEMIOLOGY

Trauma patterns and the incidence of vascular complications differ greatly between urban centers and war zones, while the existing geographical distribution reflects the impact of high velocity weapons, motor vehicle accidents, industrialization, socioeconomic status and increasing criminality[22-24]. Vascular injuries of the upper and lower extremities following trauma are relatively uncommon and represent almost 2%-3% of all civilian trauma including blunt, penetrating and gunshot injuries[24]. According to Barmparas *et al*[25] vascular trauma occurs in only 0.6% of all pediatric trauma patients and in 1.6% of adults, predominantly young men (Figure 1).

In general, the amount of energy transferred on tissues during an injury increases proportionally the possibility of vascular insult[26]. In patients with severe crush injuries associated with extensive bone (segmental shaft fracture, floating joint) and soft-tissue damage, the index of suspicion for associated arterial injury must be high. Closed diaphyseal long bone fractures carry a reported risk of vascular injury of 0.1% but open fractures have a 3.6-fold increase in the chance of vascular injury[27]. Five percent of open fractures present with a vascular injury requiring repair (type IIIc), with an amputation rate of about 16%[28]. Severe open tibial fractures are associated with a 9% incidence of vascular injury, whereas knee dislocations, especially posterior, have been associated with vascular injury in up to 16% (KD-IV > KD-V > KD-III according to Schenck classification). Femoral and popliteal artery injuries are associated with a fracture in the adjacent bone structures in a percentage of about 2% and injury of the brachial artery can occur in 8%-12% of children suffering from a supracondylar humeral fracture, usually a Gartland III fracture[21,24,26,29].

DIAGNOSIS

Clinical presentation

Clinical diagnosis of combined vascular injuries in musculoskeletal trauma patients represents the first challenging step in an overall demanding treatment pathway. Physical examination is not always able to detect a limb-threatening injury in the absence of obvious signs of vascular impairment[26].

Given the fact that these injuries are in the context of major trauma, in polytrauma patients, the initial approach is performed *via* the well-established Advanced Trauma Life Support (ATLS) protocols[30]. In case of major bleeding, direct pressure, potential tourniquet application and resuscitation are the initial actions according to ATLS principles. After initial resuscitation and primary evaluation, a detailed clinical examination with neurological and vascular status documentation, is performed during the patient's secondary evaluation. In this step, palpation of distal pulses, extremity color and temperature, time required for skin capillary refill in the distal digits, and sensory and motor deficits are assessed, compared with the contralateral limb, and recorded. Reassessment is required after any intervention, manipulation, or reduction maneuver to exclude secondary provoked vascular injury[31]. However, high index of suspicion and low threshold for vascular imaging is required because vascular injury might be present in the first place, with normal pulse palpation in a rate of 5%-15%[32].

To establish an objective approach and clinical criteria for further treatment, findings of the physical examination are classified into hard and soft signs of extremity for vascular injury (Table 1). Hard signs include massive bleeding, presence of rapidly expanding hematoma, detection of one classic sign of arterial occlusion (6Ps: Pulselessness, pallor, paresthesia, pain, paralysis and poikilothermia), palpable thrill or audible bruit[33]. The presence of hard signs has 92%-95% sensitivity for incidence of vascular injuries requiring surgical intervention with a positive predictive value of 95%[34,35]. In these cases, immediate operative intervention – injury site exploration in the presence of any hard sign – is strongly suggested by the literature without further delay for additional advanced vascular imaging [computed tomography (CT) or conventional angiography] (Figure 2)[36,37]. Soft signs for vascular injury include history of arterial bleeding at the accident scene or during transit to the hospital, proximity of penetrating or blunt injury to an artery of the limb, small, no pulsatile hematoma over a named artery, and presence of neurological deficit affecting nerves with proximity to a named artery. In these cases, incidence of vascular injuries ranges from 3% to 25%, depending on which one or which soft sign combination exists (Figure 2)[38,39].

Besides physical examination, an arterial pressure index (API) or injured extremity index (IEI) (analogous to the ankle–brachial index – ABI) should be performed. The API/IEI is the ratio of the highest systolic occlusion pressure in the injured extremity at the level of the dorsalis pedis, posterior tibial or radial/ulnar arteries divided by the systolic pressure in a proximal vessel in an uninjured extremity (most often the brachial artery)[40,41]. Normal API values (> 0.9) are highly specific for exclusion of vascular injury in cases of blunt and penetrating injuries, making further vascular imaging unnecessary[42,43]. In cases with diminished peripheral pulses or API < 0.9 an imaging study, typically arteriography, should be performed.

Special consideration is required in cases of older diabetic patients with pre-existing peripheral vascular compromise, due to possible Monckeberg's medial calcific sclerosis with clinically false normal API index of ≥ 1[44]. Recent literature, however, demonstrates high accuracy and good agreement of

Table 1 Hard and soft signs in combined musculoskeletal and vascular injuries of the extremities

Hard signs	Soft signs (or subtle signs)
Active pulsatile or massive bleeding	History of arterial bleeding at the trauma scene
Rapidly expanding or pulsatile hematoma	Proximity-related injury
Bruit/thrill	Neurologic findings from nerve adjacent to a named artery
Evidence of arterial insufficiency and ischemia (6P: Pallor; pain; paresthesia; paralysis; pulseless; poikilothermia)	Hematoma over a named artery
	Diminished unilateral distal pulse

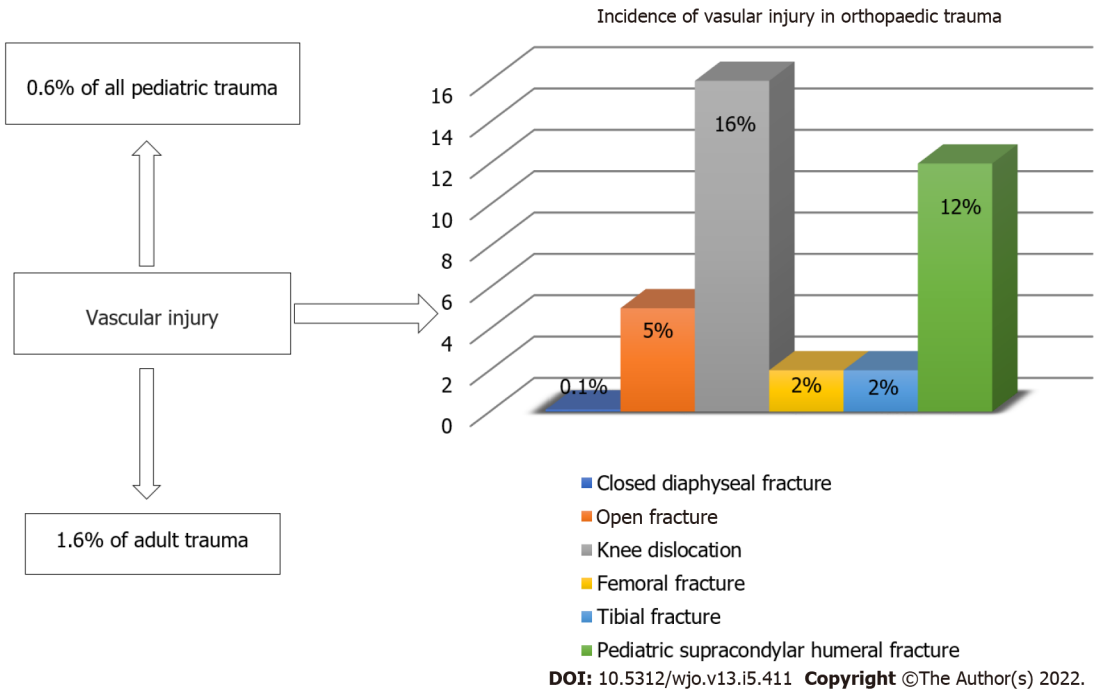


Figure 1 Epidemiology of vascular injuries in musculoskeletal trauma.

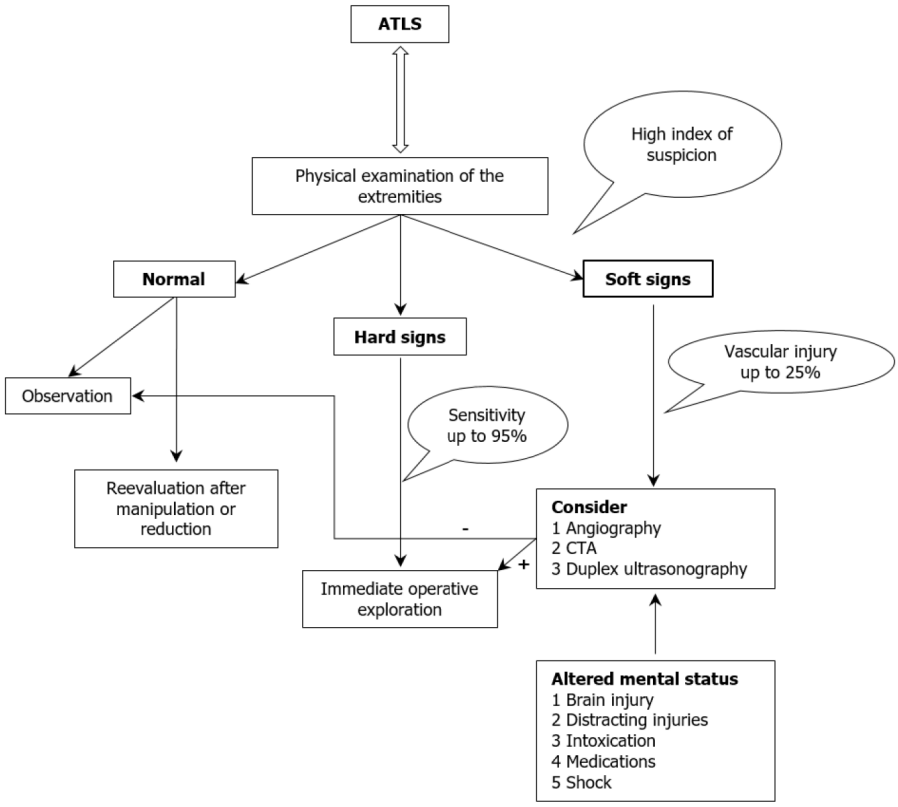
ankle–brachial index duplex ultrasonography in patients with type 2 diabetes and peripheral artery disease[45].

A specific, well known, clinical scenario is the knee dislocation and its association with popliteal artery injury. In these cases, clinical examination should include assessment of the stability of the knee joint, as laxity may suggest presence of a knee dislocation with spontaneous reduction. For further advanced imaging, current literature data are conflicting, with many authors advocating low threshold for vascular imaging in such an injury pattern and others being against routine imaging after spontaneous or performed reduction of a knee dislocation if normal pulses are present[38,46].

Supracondylar fractures represent another well-known clinical scenario. These fractures are of the most common traumatic fractures seen in children aged 5-7 years, with the urgency depending on whether the hand remains perfused or not, as rich collateral circulation may be sufficient despite vascular injury. In the case of absent distal pulses in supracondylar fractures of the humerus in children, the decision to explore is based on quality of extremity perfusion rather than absence of pulse. Generally, a well-perfused extremity is warm and pink in contrast to a poorly perfused extremity that is cold and pale with an arterial capillary refill > 2 s. Some studies recommend early aggressive surgical intervention for both patterns of vascular compromise in order to prevent limb loss and serious long-term complications such as Volkmann's ischemic contracture[21,24,25,29].

Imaging

Imaging modalities used in the diagnosis of vascular injuries in musculoskeletal trauma include conventional angiography, computed tomography angiography (CTA) and duplex ultrasound. Conventional catheter-based angiography provides accurate diagnosis of arterial injuries, even in minor injuries such as intimal tears, after intra-arterial or intravenous contrast agent injection[47,48]. As conventional angiography has several disadvantages such as cost, delay, need of specialized team, and possible renal



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Figure 2 Diagnostic algorithm for the management of vascular injuries in musculoskeletal trauma.

toxicity, it is currently preserved for intraoperative use and not for routine imaging at an Emergency Department basis[49].

Duplex ultrasound scanning (DUS) represents a combination of B-mode real-time ultrasound and pulsed Doppler flow. DUS is accurate in assessing vascular injury with reported sensitivity from 50% to 100% and specificity exceeding 95%[50,51]. It is also noninvasive and cost-effective but can be time-consuming and significantly operator-dependent. Therefore, many surgeons consider it unreliable for the detection of vascular injuries in extremity trauma. In contrast, it may have a role in the surveillance of known vascular injuries in which nonoperative treatment has been selected[52].

CTA is established as the gold standard imaging method when dealing with vascular injuries in the extremity trauma[53-55]. CTA provides a rapid confirmation of the presence and location of vascular injury with simultaneous detection of bone and soft-tissue injuries/defects, without being an interventional examination and with high cost-effectiveness index[56]. It can highlight radiological findings like hematoma, active bleeding (contrast medium extravasation), arterial dissection, transection or occlusion, pseudoaneurysm, arteriovenous fistulas, focal narrowing or spasm, as well as anatomical variants of vascular origin like bifurcation with an hypoplastic posterior tibial artery or popliteal artery trifurcation in the popliteal fossa[53]. The study has limitations in cases with CT artifacts in the presence of foreign body such as metallic fragments at the study field, suboptimal accuracy in poor timing of intravenous contrast agent administration and the potential risk for renal damage from contrast medium[57]. As mentioned above, presence of obvious hard signs dictates operative treatment on an emergency basis without further imaging. However, trauma teams can consider the execution of CTA in the case of hemodynamically stable patients despite hard signs for vascular injury, for preoperative planning so as to avoid extended exploration intraoperatively and to decrease surgical time[58].

Magnetic resonance angiography seems to have limited role in the detection of vascular compromise in trauma emergencies. CTA provides better spatial resolution and faster isotropic image acquisition, is more readily available and avoids potential hazards of prolonged imaging[59].

TREATMENT

Initial management

As mentioned above, patients with combined musculoskeletal and vascular injuries are approached in the first place according to ATLS principles, having in mind the "life over limb" quote. Current

universal guidelines for severely multiple injured patients agree on the early administration of tranexamic acid followed by Massive Transfusion Protocol with packed red blood cells, fresh frozen plasma and platelets, as well as an antifibrinolytic agent, to treat/prevent massive hemorrhage and trauma-induced coagulopathy[60-62]. Bleeding can be controlled by direct digital or dressing compression and proximal tourniquet application, for a limited time, which is preserved for special circumstances in hospital environment, where local hemorrhage cessation cannot be achieved with other manipulations[63]. Patients with diminished peripheral pulses and associated obvious gross limb deformity, such as displaced long bone fracture or joint dislocation, should undergo immediate manipulation to restore limb axis realignment and joint reduction respectively. The neurovascular status is consequently reassessed[64]. Reassessment is also required in cases of initial shock or hypothermia, after patient's resuscitation and rewarming, because vascular status under these circumstances can be misleading[65].

Limb salvage versus amputation

A crucial question to be answered early after patient presentation and initial resuscitation, is the one of limb salvage *versus* primary amputation, and in case of amputation, the timing and level of amputation. This decision is usually hard for patients, families and trauma surgeons. Patients in most cases are young and active with long remaining working lifespan, not willing to integrate a major, permanent physical modification. Surgical teams, however, usually experience amputation as a therapeutic failure and sometimes multiple, complex salvage procedures are guided, with uncertain outcome but with preservation of the patient's body image, at least initially. Progress and ongoing experience in microsurgical and reconstructive techniques provides wide range of surgical options, but limb salvage choice with extended indications, has often remarkable functional and emotional cost for the patients [66].

The Lower Extremity Assessment Project, a prospective multicenter study of patients with severe lower extremity injuries, stated that these limb-threatening injuries are likely associated with poor functional outcomes regardless of the choice between limb salvage and amputation[67]. Analogous results were presented by MacKenzie *et al*[68], in a series of 397 patients with severe lower limb trauma. The functional results were equally poor after amputation and limb reconstruction, and the outcome scores indicated substantial disability in 50% of patients.

Predictive factors for complications and poor outcomes in patients with combined musculoskeletal and vascular injuries are evaluated by variable injury scoring systems (MESS, NISSSA, LSI, PSI and HFS) including extensive soft-tissue injury, presence of open fracture, ischemic period exceeding 6 h, neurological deficit and other associated major injuries[69,70]. MESS (Mangled Extremity Severity Score) is predictive of amputation but its clinical validity is still in debate. MESS has been devised as a treatment decision aid; a score of ≥ 7 points usually indicates the need for primary amputation[71]. In 1994, Shanmuganathan[72] proposed the NISSSA score (Nerve Injury, Ischemia, Soft tissue injury, Skeletal injury, Shock and Age of the patient), which had the additional component of nerve injury – especially the loss of plantar sensation – apart of the bone and soft tissue injury components. Both scores were highly predictive of amputation, but the NISSSA had better sensitivity (81.8% *vs* 63.6%) and specificity (92.3% *vs* 69.2%) compared to MESS[72]. The Predictive Salvage Index (PSI) was proposed by Bosse *et al*[67] in 1987, with a reported sensitivity and specificity of 78% and 100%, respectively. The limb salvage index (LSI) was proposed by Russell in 1991 and although not utilized widely, the score was found more predictable than the MESS, PSI, NISSSA, and HFS-97 when assessing type III tibial fractures. Primary amputation is recommended after significant distal trauma, extensive crush, severe nerve dysfunction, an ischemic limb with duration exceeding 4 h of warm ischemia, segmental bone loss over one third of the length of the tibia, muscle loss in more than two compartments, and severe open foot injuries[73]. Besides injury characteristics, factors like non-Caucasian race, older age, female sex, lower educational level, lower economic status, smoking, and poor reported pre-injury general health condition, seem to play an important role in patients with less-than-optimal results[68].

Amputation

Limb amputation is a realistic solution in an emergency and could be life-saving in the setting of sepsis or ongoing bleeding in a hemodynamically unstable trauma patient, with the advantages of shorter hospitalization, fewer secondary procedures, and faster rehabilitation period. A published case series of nonsalvageable limb injuries reported that a delay of up to 5 d can be tolerated without negative impact on stump infection risk, giving the time for patient preparation and procedure planning on a semi-elective basis[74]. It must be underlined that long-term costs of prosthetics could likely make amputation an ultimately more expensive procedure[75].

Amputation level, determined by the nature of injury, is another crucial point of interest related with long-term functional outcome. It is well recognized that preservation of the knee joint provides a significant functional advantage. With a stump of sufficient length, the prosthesis has better support and less energy for movement is demanded[76]. Transtibial amputees perform better than transfemoral or through-knee ones, with decreased rehabilitation time[77,78]. However, the tissue condition after traumatic injuries requiring below-knee amputation is not always adequate to provide a lengthy and durable stump able to support a prosthesis, given the fact that at least 10 cm from medial tibial plateau

is recommended[76,79]. In such cases, composite flaps harvested from the amputated limb and spare-part surgery concept may provide stump lengthening, thus avoiding a more proximal amputation or the use of flap[80,81].

Limb salvage

Preoperative planning: Patient's clinical situation, other major trauma (trunk, visceral or craniocerebral) than extremity injury requiring surgical treatment or nonoperative surveillance and determination of the type of vascular injury, are factors considered when proceeding to the operating theater. A necessary condition for fast and safe surgical management includes grouping of injured tissues, planning of the procedure and defining the appropriate equipment for successful cooperation between different specialties. Furthermore, possible required equipment and devises should be confirmed, including magnifying loupes and vascular surgery – microsurgical instrumentation, external and internal fixation systems, and shunts.

In the presence of acute life-threatening injuries, like intracranial hematoma, thoracic, abdominal or pelvic bleeding, team management with two operating teams should be considered to manage the life-threatening injury, and control bleeding and re-establish perfusion at the injured extremity. In such cases, temporary measures, such as external fixation systems and intraluminal shunts, are the chosen treatment options following the Damage Control Surgery principles[82-84].

Types of vascular injury: Vascular injuries include a variety of lesions from arterial spasm to complete transection. Pre- or intraoperative accurate diagnosis of injury type is crucial as it guides the treatment modality. Overall, vascular injuries include complete wall defects with hemorrhage or pseudoaneurysm, intimal tears like disruption, flap or subintimal hematomas, complete transections with hemorrhage/ occlusion, arteriovenous fistulas and vascular spasm[21,64].

Regarding the injury mechanism, penetrating trauma is most associated with complete transections, wall defects or secondary development of arteriovenous fistulas. Blunt trauma, however, is usually associated with intimal defects or subintimal hematomas. Arterial spasm can be a result of either blunt or penetrating injury, more commonly in young patients[65].

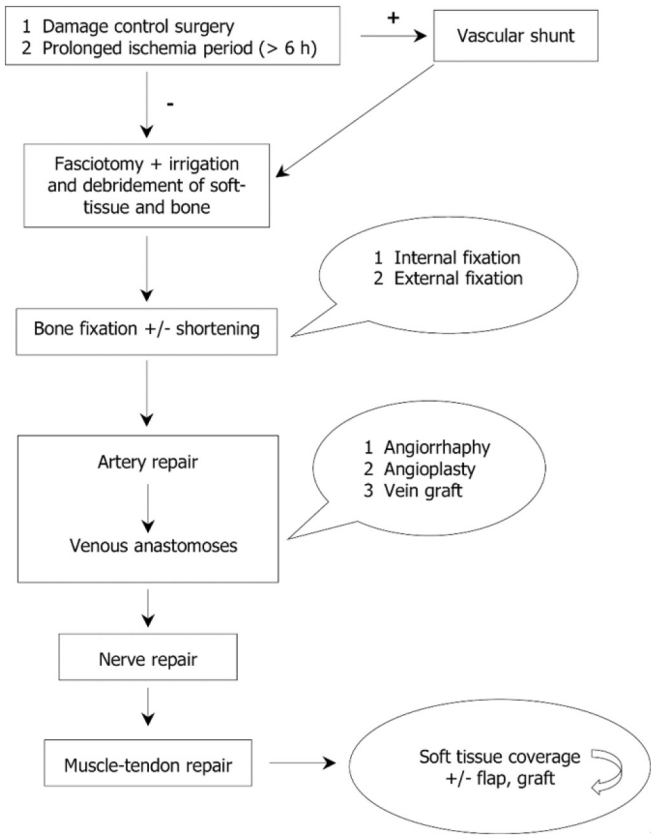
Vascular injuries that are nonocclusive, like arterial spasm, intramural hematomas, or intimal flaps have a satisfactory healing potential with nonoperative treatment, with reported rates of 87%-95%[85,86]. Single vessel occlusion located peripherally – distal to knee/elbow – does not constitute risk for the viability of the limb. In these cases, in the absence of mangled extremity or severe soft tissue damage, observation with close clinical and imaging surveillance is a viable option. Other treatment options, besides open vascular repair, have a role in selected, isolated traumatic aneurysms where embolization can be performed[64]. Moreover, small pseudoaneurysms and intimal flaps or tears can be amenable to endovascular treatments, placing endovascular stents or stent grafts[87,88].

Operative treatment: Care should be taken from the operative team to establish the best conditions required for major surgical intervention. An operative tourniquet can replace the bleeding-control apparatus used at the emergency department. Skin aseptic preparation and draping should encompass potential areas of distal and proximal vascular control, fasciotomy sites and ipsilateral limb from groin to toenails for possible greater or lesser saphenous vein retrieval[52,64]. Adequate surgical approach is essential, with proximal and distal extension of the injury zone, to control hemorrhage and determine type and extend of arterial injury.

Sequence of intervention when orthopedic and vascular surgeons are implicated, remains an area of relative debate, despite being reported that this surgical sequence probably does not affect lower limb amputations rates[89]. Fracture reduction and fixation offers a stable skeletal "scaffold" for subsequent vascular repair (Figure 3). Vascular repair decreases warm ischemia time of the affected extremity[26,90]. Ischemia is crucial and determines the sequence of surgical intervention, with 6 h generally being the cutoff time interval for higher limb salvage rates[89,91]. It must be underlined that ischemia time is never accurate and in most cases is underestimated by patient, relatives, ambulance crew or other healthcare professional. As a general rule, in cases with cold ischemia (pulseless limb with no capillary refill) and in patients with prolonged period of warm ischemia (present capillary refill), vascular intervention should be performed first so as to restore perfusion as soon as possible *via* temporary intraluminal vascular shunt insertion[64,92,93]. Fracture fixation can be performed first when there is no evidence of cold or prolonged warm ischemia, especially in concomitant presence of unstable, comminuted fracture pattern.

Concerning operative treatment of coexisting fracture, the dilemma between temporary *versus* definitive fracture fixation turns towards temporary external fixation by most authors, in order to offer prospective for bone defect management and avoid infection, "second hit" phenomenon related to coagulopathy, systematic inflammatory immune system response and fat/pulmonary embolism[94-96]. Bone transport as well as induced membrane or Masquelet technique are options for large, segmental bone defects[97-99].

Regarding operative options for vascular injury manipulation, they include direct repair – anastomosis, vein patch angioplasty, bypass anastomosis with interposition graft placement, endovascular stents, and temporary intraluminal vascular shunts.



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Figure 3 A proposed algorithm for the sequential anatomical restoration of injured structures in combined musculoskeletal and vascular trauma of the extremities.

In cases of small lacerations, lateral angiorrhaphy with or without vein patch angioplasty is adequate as repair option. Injuries involving complete artery transection are addressed with central and peripheral debridement till healthy intima followed by end-to-end anastomosis[100,101]. If the anastomosis is not free of tension, a substitute conduit must be interposed. Conduit of choice for the most cases of peripheral vascular injuries is the autogenous reversed saphenous vein graft from the contralateral, uninjured lower limb with the alternatives of cephalic or basilic upper limb veins and synthetic grafts[100,102].

A keynote step in the operative treatment pathway of vascular injuries is the early recognition of patients indicated for temporary intraluminal shunt insertion, rather than definitive vascular repair and prior to bone stabilization. These indications include critically injured patients as part of damage control surgery, Gustilo IIIC open fractures, prolonged ischemia period, need for distal perfusion while another complex revascularization procedure like extra-anatomical bypass is performed and prior to replantation perfusion of an amputated upper extremity part[103,104].

Vein injuries and possible repair are usually addressed with less caution, in the presence of arterial injuries that are limb threatening. Peripheral vein ligation rarely consists a threat for limb salvage, but increases postoperative swelling and venous soft-tissue hemorrhage, having transient adverse effects on arterial inflow and leading to increased morbidity and infection risk. Operative options for peripheral venous repair include venous patch angioplasty, thoracostomy tubes as intraluminal venous shunts, or interposition graft placement from contralateral greater saphenous vein, common femoral vein, or axillary vein[105].

Injured structures are identified from superficial to deep layer, based on the knowledge of the cross-sectional anatomy, and reconstruction starts from the deeper layer. Nerves are repaired after bone and vascular structures followed by muscle and tendons, which are the last to be reapproximated. Careful documentation by photos and/or video is mandatory, not only to accurately define the postoperative rehabilitation protocol, but for medicolegal purposes too. Tension-free nerve restoration is advocated, as neuroma formation is a common complication when nerve repair is performed incorrectly or under tension. Soft tissue coverage is the last stage that will ensure the rapid healing of the tissues. Decision for coverage should be taken in conjunction with reconstruction surgeon, including muscle flap transportation or extra-anatomical bypass graft fashioning[101,105,106].

The use of negative pressure wound therapy as an alternative treatment of soft tissue defects, seems to improve angiogenesis, regulate perfusion, and promote local microvascular maturation. However, its

use is limited and its efficacy and superiority over conventional dressing is questionable according to current multicenter randomized control trials and to Wound management of open lower limb fractures (WOLLF) study[107-109].

Secondary procedures: Cases with combined musculoskeletal and vascular injuries almost never have a unique surgical intervention. Second look for surgical site infection, soft-tissue viability and confirmation of vascular perfusion is routinely performed 24-48 h after initial surgery. The fasciotomy incision closure is performed after 7-10 d in case of optimal postoperative findings. At the same time, definite skeletal stabilization should be performed (external to internal fixation modification or unilateral external fixation system conversion to circular frame/hybrid fixation system) to minimize the risk of surgical site infection after the definite treatment, in case of preceding pin track infection.

COMPLICATIONS

Compartment syndrome – fasciotomies

Compartment syndrome is defined as the increased pressure within a closed fascial space, leading to reduction of capillary perfusion to less than required level for tissue viability, well recognized as cause for poor limb functional outcome[110,111]. It is the result of external compression or fascia closure and after increased compartment pressure in cases of ischemia–reperfusion, fractures, soft-tissue contusion, and venous outflow obstruction. In this concept, situations like crush injury, significant limb swelling, combined arterial and venous injuries requiring simultaneous clamping, need for arterial/venous ligation, early thrombosis of vascular repair, ongoing hypotension/continuing resuscitation and delayed treatment with no arterial perfusion for 4-6 h, determine high-risk patients for compartment syndrome development after combined trauma. Early clinical findings related to compartment syndrome are pain on passive movement of the involved compartments' muscles and patients' pain considered out of proportion to the injury, while classical 6 Ps (pulselessness, pallor, paresthesia, pain, paralysis, poikilothermia) are frequently not present in trauma patients with possible altered mental status and associated injuries and represent late signs of established compartment syndrome on the injured extremity[110].

Fasciotomies performed concomitantly with limb revascularization are associated with a four-times decrease in eventual amputation. There are also trauma surgeons who routinely perform prophylactic fasciotomies in the presence of high-risk scenarios[112]. This established intraoperative choice is possibly the reason for the low incidence of compartment syndrome after peripheral vascular injury [111]. Moreover, this approach may lead to possible conversion of a closed to open fracture, wound management related complications, altered sensation and chronic limb pain[113]. Still, these potential risks are easily overcome when there is a high chance of developing compartment syndrome and early fasciotomies should be considered in cases of revascularization following vascular trauma, multiple fractures or dislocation and /or multiple arterial injuries[21,112].

Infection

In addition to the basic complication of the already-mentioned compartment syndrome, bone and soft-tissue infection following combined musculoskeletal and vascular injuries, represents the major cause for late extremity amputation[114-117]. Gustilo *et al*[118], classifying open fractures reported an infection rate as high as 42% associated with vascular damage requiring repair (Gustilo IIIC fractures). Moreover, infection seems also being related with vascular thrombosis[119].

Nonunion

Vascular compromise, which often indicates the release of high energy in the fracture area, is a well-established predictive indicator for a nonunion in Gustilo–Anderson grade IIIC injuries[120]. Moreover, the coexistence of even a subclinical compartment syndrome appears to delay or prevent the process of long bones union[121].

Secondary amputation

Secondary amputations can be expected in 5.5%-28% of Gustilo type IIIC open tibial fractures[122,123]. The main reasons for secondary amputation include delayed revascularization, lack of adequate collateral blood flow, extensive soft tissue necrosis, infection, distal thrombosis, or postoperative arterial disruption[124].

Venous insufficiency

There is increasing evidence that primary or secondary venous insufficiency, particularly in the setting of combined peripheral arterial and venous injuries, may impair the chance of limb salvage. A proposed benefit to venous patency is that maintaining adequate venous drainage of an injured extremity can minimize extremity swelling, hemorrhage, and compartment syndrome. Feliciano argued that these acute benefits are an indication for immediate venous reconstruction, even if the fate of the repair will

likely be to thrombose later[102]. Other local vascular complications such as arterial disruption, pseudoaneurysm and emboli may result in a vicious circle of both regional and systemic adverse effects, like myocardial infarction, respiratory distress due to pulmonary embolism, acute renal failure, *etc*[125].

LONG TERM FOLLOW-UP

Even after a successful initial, multidisciplinary-guided treatment of a combined musculoskeletal and vascular injury, long term follow-up is crucial to prevent and detect early possible complications. This follow-up evaluation is performed by both orthopedic and vascular surgeons, with additional consultation from reconstructive surgeons, if necessary[126]. Alternatively, orthopedic surgeons with microsurgical background and competence can follow these patients, as they can solely perform all-around surgery for these combined injuries. Postoperative evaluations can be delayed in cases of segmental fractures, associated bone loss, or infection. In case of team management, the vascular surgeon will evaluate the arterial perfusion and venous flow and determine the shift from prophylactic thromboprophylaxis to antiplatelet agents 3-6 mo postoperatively. The vascular repair should be followed with ABI testing as well as graft duplex scan.

In addition, the continuous cooperation with the radiologists, physiatrists and physiotherapists at the follow-up period ensures rapid recovery without serious complications, or their detection and management in a timely manner. Finally, due to the functional impairment frequently left after these complex injuries, long-term psychological support is often necessary.

DISCUSSION

Limb salvage in patients with combined musculoskeletal and vascular injuries is distinctly dependent on the severity of soft-tissue injury, the duration of limb ischemia and the early, accurate diagnosis and treatment of vascular damage. In general, the amount of energy transferred on tissues during an injury increases proportionally the possibility of vascular insult[26]. In patients with severe crush injuries associated with extensive bone (segmental shaft fracture or floating joint) and soft-tissue damage, the index of suspicion for associated arterial injury must be high. Closed diaphyseal long bone fractures carry a reported risk of vascular injury of 0.1% but open fractures have a 3.6-fold increase in the chance of vascular injury[27]. It is therefore clear that the basic principle of early detection of a potentially catastrophic vascular lesion in orthopedic trauma must be secured in advance with the high degree of suspicion on the part of the surgeon.

The level of alertness is always determined by (1) The pattern of the injury (open or closed, fracture or dislocation, single or multiple injury, calibration of injury scores); (2) The anatomical area of the injury (open tibial fractures, knee dislocations and supracondylar elbow fractures in children of type III due to Gartland classification have rates of concomitant vascular injuries > 10%)[21,24,26,28,29]; and (3) The type of arterial lesion that the literature correlates with specific trauma patterns. Vascular injuries that are nonocclusive, like arterial spasm, intramural hematomas, or intimal flaps have a satisfactory healing potential with nonoperative treatment, with reported rates of 87%-95%. Therapeutic choices usually consist in monitoring the patient during follow-up, by means of physical examination and ultrasound scan. Single vessel occlusion located peripherally – distal to knee/elbow – does not constitute a risk to the viability of the limb. In these cases, in the absence of mangled extremity or severe soft tissue damage, observation with close clinical and imaging surveillance is a viable option[85,86].

A fundamental dimension of the successful outcome of combined orthopedic and vascular injuries is the speed and accuracy of patient management. Most of the time lost in the treatment approach of the injured patient, after the arrival to the trauma center, concerns the definite diagnosis of the vascular injury and the decision-making procedure. Orthopedic pathology is defined in the majority of cases with a simple X-ray (usually already done in primary or secondary survey). The presence of hard signs has 92%-95% sensitivity for incidence of vascular injuries requiring surgical intervention with a positive predictive value of 95%[33-35]. In these cases, immediate operative intervention – injury site exploration in the presence of any hard sign – is strongly suggested by the literature without further delay for additional advanced vascular imaging (CT or conventional angiography)[36,37]. Rapid decisions are ensured by the use of trauma classifications which assist the surgeons' judgment in adjunct to clinical evaluation and facilitate in-depth guidance of patients and their families prior to definitive surgical treatment. Predictive factors for complications and poor outcomes in patients with combined musculoskeletal and vascular injuries are evaluated by variable injury scoring systems (MESS, NISSSA, LSI, PSI and HFS)[69,70].

It is also necessary in the future to establish common action protocols between orthopedic, vascular and general surgeons, and for each tertiary trauma center to have a clearly defined action protocol that will be applied in the same way each time and will be included in the training program of young doctors.

As a general rule, in cases with cold ischemia (pulseless limb with no capillary refill) and in patients with prolonged period of warm ischemia (present capillary refill), vascular intervention should be performed first so as to restore perfusion as soon as possible *via* temporary intraluminal vascular shunt insertion. Fracture fixation can be performed first when there is no evidence of cold or prolonged warm ischemia, especially in concomitant presence of unstable, comminuted fracture pattern. Failure to perform fasciotomies after revascu larization of an acutely ischemic limb is the most common cause of preventable limb loss. Finally, a bed in the intensive care unit ideally should be reserved for early postoperative monitoring. Although open surgical repair has always been the gold standard for treating vascular trauma, the application of endovascular techniques should be a more beneficial future perspective according to specific indications.

CONCLUSION

Although vascular injuries are rare, they may occur in the context of major combined musculoskeletal trauma. The high index of suspicion, the imaging evaluation, and the timely referral of these patients to organized trauma centers ensure firstly the survival of the patient and the extremity and secondarily the best functional outcome in such challenging cases. Vascular injuries as part of musculoskeletal trauma are usually the result of the release of a high-energy load at the wound site so that the prognosis is strongly determined by the degree of soft-tissue damage, the duration of limb ischemia, the patients' general medical status and the presence of associated injuries. We therefore consider that distinct guidelines and multidisciplinary team management are *sine qua non* preconditions in dealing with combined musculoskeletal and vascular injuries of the extremities.

FOOTNOTES

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REFERENCES

1 **Mullis B**, Fajardo A, Smith T, Laughlin M. Team Approach: Combined Orthopaedic and Vascular Injury. *JBJS Rev* 2017; **5**: e2 [PMID: 28763353 DOI: 10.2106/JBJS.RVW.16.00027]
2 **Rasmussen TE**, Woodson J, Rich NM, Mattox KL. Vascular trauma at a crossroads. *J Trauma* 2011; **70**: 1291-1293 [PMID: 21610443 DOI: 10.1097/TA.0b013e3182178994]
3 **Rich NM**, Mattox KL, Hirshberg A. Vascular Trauma. 2nd ed. Philadelphia, PA: Elsevier Saunders; 2004
4 **Lambert R**. surgeon at Newcastle upon Tyne, to Dr. Hunter; giving an account of a new method of treating an aneurysm. *Med Observ Inq London* 1762; **2**: 360
5 **Murphy JB**. Resection of arteries and veins injured in continuity-end-to-end of suture-experimental clinical research. *Med Rec* 1897; **51**: 73
6 **Carrel A**. The surgery of blood vessels. *Bull Johns Hopkins Hosp* 1907; **18**: 18-28
7 **Guthrie C**. Blood Vessel Surgery and Its Applications. London, United Kingdom: Edward Arnold; 1912

8 **Rich NM**, Rhee P. An historical tour of vascular injury management: from its inception to the new millennium. *Surg Clin North Am* 2001; **81**: 1199-1215 [PMID: 11766173 DOI: 10.1016/s0039-6109(01)80005-0]
9 **Esmarch F**. The Surgeons Handbook of the Treatment of the Wounded in War. New York, NY: LW Schmidt; 1878
10 **Rich NM**. Vascular trauma historical notes. *Perspect Vasc Surg Endovasc Ther* 2011; **23**: 7-12 [PMID: 21502112 DOI: 10.1177/1531003511403496]
11 Soubbotitch V. Military experiences of traumatic aneurysms. *Lancet* 1913; **182**: 720- 721
12 **Debakey ME**, Simeone FA. Battle Injuries of the Arteries in World War II : An Analysis of 2,471 Cases. *Ann Surg* 1946; **123**: 534-579 [PMID: 17858758]
13 **Hughes CW**. The primary repair of wounds of major arteries; an analysis of experience in Korea in 1953. *Ann Surg* 1955; **141**: 297-303 [PMID: 14350568 DOI: 10.1097/00000658-195503000-00002]
14 **McNamara JH**, Brief DK, Beasley W, Wright JK. Vascular injury in Vietnam combat casualties: results of treatment at the 24th Evacuation Hospital 1 July 1967 to 12 August 1969. *Ann Surg* 1973; **178**: 143-147 [PMID: 4723422 DOI: 10.1097/00000658-197308000-00006]
15 **Rich NM**, Hughes CW. Vietnam vascular registry: a preliminary report. *Surgery* 1969; **65**: 218-226 [PMID: 5762414]
16 **Chambers LW**, Rhee P, Baker BC, Perciballi J, Cubano M, Compeggie M, Nace M, Bohman HR. Initial experience of US Marine Corps forward resuscitative surgical system during Operation Iraqi Freedom. *Arch Surg* 2005; **140**: 26-32 [PMID: 15655202 DOI: 10.1001/archsurg.140.1.26]
17 **Rotondo MF**, Zonies DH. The damage control sequence and underlying logic. *Surg Clin North Am* 1997; **77**: 761-777 [PMID: 9291979 DOI: 10.1016/s0039-6109(05)70582-x]
18 **Kragh JF Jr**, Walters TJ, Baer DG, Fox CJ, Wade CE, Salinas J, Holcomb JB. Survival with emergency tourniquet use to stop bleeding in major limb trauma. *Ann Surg* 2009; **249**: 1-7 [PMID: 19106667 DOI: 10.1097/SLA.0b013e31818842ba]
19 **Martin MJ**, Long WB. Vascular trauma: epidemiology and natural history. In: Cronenwett JL, Johnston KW, eds. Rutherford's Vascular Surgery. Vol 2. 8th ed. Philadelphia, PA: Saunders; 2014: 2422-2437
20 **Feliciano DV**. For the patient-Evolution in the management of vascular trauma. *J Trauma Acute Care Surg* 2017; **83**: 1205-1212 [PMID: 28863083 DOI: 10.1097/TA.0000000000001689]
21 **Mavrogenis AF**, Panagopoulos GN, Kokkalis ZT, Koulouvaris P, Megaloikonomos PD, Igoumenou V, Mantas G, Moulakakis KG, Sfyroeras GS, Lazaris A, Soucacos PN. Vascular Injury in Orthopedic Trauma. *Orthopedics* 2016; **39**: 249-259 [PMID: 27322172 DOI: 10.3928/01477447-20160610-06]
22 **Xu Y**, Xu W, Wang A, Meng H, Wang Y, Liu S, Li R, Lu S, Peng J. Diagnosis and treatment of traumatic vascular injury of limbs in military and emergency medicine: A systematic review. *Medicine (Baltimore)* 2019; **98**: e15406 [PMID: 31045795 DOI: 10.1097/MD.0000000000015406]
23 **Beranger F**, Lesquen H, Aoun O, Roqueplo C, Meyrat L, Natale C, Avaro JP. Management of war-related vascular wounds in French role 3 hospital during the Afghan campaign. *Injury* 2017; **48**: 1906-1910 [PMID: 28622832 DOI: 10.1016/j.injury.2017.06.004]
24 **Feliciano DV**, Rasmussen TE. Evaluation and treatment of vascular injuries. In: Browner BD, Jupiter JB, Kretteck C, eds. Skeletal Trauma. Basic Science, Management and Reconstruction. Philadelphia: Elsevier Saunders; 2015: 423e435
25 **Barmparas G**, Inaba K, Talving P, David JS, Lam L, Plurad D, Green D, Demetriades D. Pediatric vs adult vascular trauma: a National Trauma Databank review. *J Pediatr Surg* 2010; **45**: 1404-1412 [PMID: 20638516 DOI: 10.1016/j.jpedsurg.2009.09.017]
26 **Halvorson JJ**, Anz A, Langfitt M, Deonanan JK, Scott A, Teasdall RD, Carroll EA. Vascular injury associated with extremity trauma: initial diagnosis and management. *J Am Acad Orthop Surg* 2011; **19**: 495-504 [PMID: 21807917 DOI: 10.5435/00124635-201108000-00005]
27 **Monazzam S**, Goodell PB, Salcedo ES, Nelson SH, Wolinsky PR. When are CT angiograms indicated for patients with lower extremity fractures? *J Trauma Acute Care Surg* 2017; **82**: 133-137 [PMID: 27602910 DOI: 10.1097/TA.0000000000001258]
28 **Soni A**, Tzafetta K, Knight S, Giannoudis PV. Gustilo IIIC fractures in the lower limb: our 15-year experience. *J Bone Joint Surg Br* 2012; **94**: 698-703 [PMID: 22529094 DOI: 10.1302/0301-620X.94B5.27948]
29 **Brahmamdam P**, Plummer M, Modrall JG, Megison SM, Clagett GP, Valentine RJ. Hand ischemia associated with elbow trauma in children. *J Vasc Surg* 2011; **54**: 773-778 [PMID: 21571488 DOI: 10.1016/j.jvs.2011.03.004]
30 **American College of Surgeons**. ATLS: Advanced Trauma Life Support for Doctors.8th ed. Chicago, IL: American College of Surgeons, 2008
31 **Rozycki GS**, Tremblay LN, Feliciano DV, McClelland WB. Blunt vascular trauma in the extremity: diagnosis, management, and outcome. *J Trauma* 2003; **55**: 814-824 [PMID: 14608150 DOI: 10.1097/01.TA.0000087807.44105.AE]
32 **Barnes CJ**, Pietrobon R, Higgins LD. Does the pulse examination in patients with traumatic knee dislocation predict a surgical arterial injury? *J Trauma* 2002; **53**: 1109-1114 [PMID: 12478036 DOI: 10.1097/00005373-200212000-00013]
33 **Manthey DE**, Nicks BA. Penetrating trauma to the extremity. *J Emerg Med* 2008; **34**: 187-193 [PMID: 17976791 DOI: 10.1016/j.jemermed.2007.03.038]
34 **Gonzalez RP**, Falimirski ME. The utility of physical examination in proximity penetrating extremity trauma. *Am Surg* 1999; **65**: 784-789 [PMID: 10432092]
35 **Inaba K**, Branco BC, Reddy S, Park JJ, Green D, Plurad D, Talving P, Lam L, Demetriades D. Prospective evaluation of multidetector computed tomography for extremity vascular trauma. *J Trauma* 2011; **70**: 808-815 [PMID: 21610388 DOI: 10.1097/TA.0b013e3182118384]
36 **US**. Army Institute of Surgical Research. Joint Trauma System clinical practice guidelines. Accessed May 11, 2015. Available from: http://www.usaisr.amedd.army.mil/cpgs.html
37 **Fox CJ**, Starnes BW. Vascular surgery on the modern battlefield. *Surg Clin North Am* 2007; **87**: 1193-1211, xi [PMID: 17936482 DOI: 10.1016/j.suc.2007.07.015]
38 **Miranda FE**, Dennis JW, Veldenz HC, Dovgan PS, Frykberg ER. Confirmation of the safety and accuracy of physical examination in the evaluation of knee dislocation for injury of the popliteal artery: a prospective study. *J Trauma* 2002; **52**: 247-51; discussion 251 [PMID: 11834983 DOI: 10.1097/00005373-200202000-00008]

39 **Johansen K**, Lynch K, Paun M, Copass M. Non-invasive vascular tests reliably exclude occult arterial trauma in injured extremities. *J Trauma* 1991; **31**: 515-9; discussion 519 [PMID: 2020038]

40 **Modrall JG**, Weaver FA, Yellin AE. Vascular considerations in extremity trauma. *Orthop Clin North Am* 1993; **24**: 557-563 [PMID: 8341528]

41 **Lynch K**, Johansen K. Can Doppler pressure measurement replace "exclusion" arteriography in the diagnosis of occult extremity arterial trauma? *Ann Surg* 1991; **214**: 737-741 [PMID: 1741655 DOI: 10.1097/00000658-199112000-00016]

42 **Mills WJ**, Barei DP, McNair P. The value of the ankle-brachial index for diagnosing arterial injury after knee dislocation: a prospective study. *J Trauma* 2004; **56**: 1261-1265 [PMID: 15211135 DOI: 10.1097/01.ta.0000068995.63201.0b]

43 **Hemingway J**, Adjei E, Desikan S, Gross J, Tran N, Singh N, Starnes B, Quiroga E. Lowering the Ankle-Brachial Index Threshold in Blunt Lower Extremity Trauma May Prevent Unnecessary Imaging. *Ann Vasc Surg* 2020; **62**: 106-113 [PMID: 31394233 DOI: 10.1016/j.avsg.2019.05.052]

44 **Gherman D**, Dumitrescu CI, Ciocan A, Melincovici CS. Histopathological changes in major amputations due to diabetic foot - a review. *Rom J Morphol Embryol* 2018; **59**: 699-702 [PMID: 30534807]

45 **Ugwu E**, Anyanwu A, Olamoyegun M. Ankle brachial index as a surrogate to vascular imaging in evaluation of peripheral artery disease in patients with type 2 diabetes. *BMC Cardiovasc Disord* 2021; **21**: 10 [PMID: 33407158 DOI: 10.1186/s12872-020-01821-6]

46 **Gable DR**, Allen JW, Richardson JD. Blunt popliteal artery injury: is physical examination alone enough for evaluation? *J Trauma* 1997; **43**: 541-544 [PMID: 9314325 DOI: 10.1097/00005373-199709000-00029]

47 **Miller-Thomas MM**, West OC, Cohen AM. Diagnosing traumatic arterial injury in the extremities with CT angiography: pearls and pitfalls. *Radiographics* 2005; **25** Suppl 1: S133-S142 [PMID: 16227487 DOI: 10.1148/rg.25si055511]

48 **Itani KM**, Burch JM, Spjut-Patrinely V, Richardson R, Martin RR, Mattox KL. Emergency center arteriography. *J Trauma* 1992; **32**: 302-6; discussion 306 [PMID: 1548718 DOI: 10.1097/00005373-199203000-00007]

49 **Kauvar DS**, Kraiss LW. Vascular trauma: extremity. In: Cronenwett JL, Johnston KW, eds. Rutherford's Vascular Surgery. Vol 2. 8th ed. Philadelphia, PA: Saunders; 2014: 2485-2500

50 **Gagne PJ**, Cone JB, McFarland D, Troillett R, Bitzer LG, Vitti MJ, Eidt JF. Proximity penetrating extremity trauma: the role of duplex ultrasound in the detection of occult venous injuries. *J Trauma* 1995; **39**: 1157-1163 [PMID: 7500412 DOI: 10.1097/00005373-199512000-00026]

51 **Knudson MM**, Lewis FR, Atkinson K, Neuhaus A. The role of duplex ultrasound arterial imaging in patients with penetrating extremity trauma. *Arch Surg* 1993; **128**: 1033-7; discussion 1037 [PMID: 8368921 DOI: 10.1001/archsurg.1993.01420210097013]

52 **Schwartz M**, Weaver F, Yellin A, Ralls P. The utility of color flow Doppler examination in penetrating extremity arterial trauma. *Am Surg* 1993; **59**: 375-378 [PMID: 8507063]

53 **Cellina M**, Gibelli D, Martinenghi C, Oliva G, Floridi C. CT angiography of lower extremities from anatomy to traumatic and nontraumatic lesions: a pictorial review. *Emerg Radiol* 2020; **27**: 441-450 [PMID: 32221718 DOI: 10.1007/s10140-020-01770-9]

54 **Fleiter TR**, Mervis S. The role of 3D-CTA in the assessment of peripheral vascular lesions in trauma patients. *Eur J Radiol* 2007; **64**: 92-102 [PMID: 17869471 DOI: 10.1016/j.ejrad.2007.07.018]

55 **Seamon MJ**, Smoger D, Torres DM, Pathak AS, Gaughan JP, Santora TA, Cohen G, Goldberg AJ. A prospective validation of a current practice: the detection of extremity vascular injury with CT angiography. *J Trauma* 2009; **67**: 238-43; discussion 243 [PMID: 19667874 DOI: 10.1097/TA.0b013e3181a51bf9]

56 **Rieger M**, Mallouhi A, Tauscher T, Lutz M, Jaschke WR. Traumatic arterial injuries of the extremities: initial evaluation with MDCT angiography. *AJR Am J Roentgenol* 2006; **186**: 656-664 [PMID: 16498092 DOI: 10.2214/AJR.04.0756]

57 **White PW**, Gillespie DL, Feurstein I, Aidinian G, Phinney S, Cox MW, Adams E, Fox CJ. Sixty-four slice multidetector computed tomographic angiography in the evaluation of vascular trauma. *J Trauma* 2010; **68**: 96-102 [PMID: 19779310 DOI: 10.1097/TA.0b013e318190c4ca]

58 **Compton C**, Rhee R. Peripheral vascular trauma. *Perspect Vasc Surg Endovasc Ther* 2005; **17**: 297-307 [PMID: 16389424 DOI: 10.1177/153100350501700404]

59 **Patterson BO**, Holt PJ, Cleanthis M, Tai N, Carrell T, Loosemore TM; London Vascular Injuries Working Group. Imaging vascular trauma. *Br J Surg* 2012; **99**: 494-505 [PMID: 22190106 DOI: 10.1002/bjs.7763]

60 **Polytrauma Guideline Update Group**. Level 3 guideline on the treatment of patients with severe/multiple injuries: AWMF Register-Nr. 012/019. *Eur J Trauma Emerg Surg* 2018; **44**: 3-271 [PMID: 29654333 DOI: 10.1007/s00068-018-0922-y]

61 **Llau JV**, Acosta FJ, Escolar G, Fernández-Mondéjar E, Guasch E, Marco P, Paniagua P, Páramo JA, Quintana M, Torrabadella P. Multidisciplinary consensus document on the management of massive haemorrhage (HEMOMAS document). *Med Intensiva* 2015; **39**: 483-504 [PMID: 26233588 DOI: 10.1016/j.medin.2015.05.002]

62 **Cornero SG**, Maegele M, Lefering R, Abbati C, Gupta S, Sammartano F, Cimbanassi S, Chiara O. Predictive Factors for Massive Transfusion in Trauma: A Novel Clinical Score from an Italian Trauma Center and German Trauma Registry. *J Clin Med* 2020; **9** [PMID: 33050378 DOI: 10.3390/jcm9103235]

63 **Welling DR**, Burris DG, Hutton JE, Minken SL, Rich NM. A balanced approach to tourniquet use: lessons learned and relearned. *J Am Coll Surg* 2006; **203**: 106-115 [PMID: 16798493 DOI: 10.1016/j.jamcollsurg.2006.02.034]

64 **Feliciano DV**. Evaluation and treatment of vascular injuries. In: Browner BD, Jupiter JB, Levine AM, Trafton PG, Krettek C, eds. Skeletal Trauma. Basic Science, Management, and Reconstruction. 4th ed. Philadelphia, PA: Elsevier Saunders; 2009: 323-340

65 **Feliciano DV**, Moore FA, Moore EE, West MA, Davis JW, Cocanour CS, Kozar RA, McIntyre RC Jr. Evaluation and management of peripheral vascular injury. Part 1. Western Trauma Association/critical decisions in trauma. *J Trauma* 2011; **70**: 1551-1556 [PMID: 21817992 DOI: 10.1097/TA.0b013e31821b5bdd]

66 **Korompilias AV**, Beris AE, Lykissas MG, Vekris MD, Kontogeorgakos VA, Soucacos PN. The mangled extremity and attempt for limb salvage. *J Orthop Surg Res* 2009; **4**: 4 [PMID: 19216787 DOI: 10.1186/1749-799X-4-4]

67 **Bosse MJ**, McCarthy ML, Jones AL, Webb LX, Sims SH, Sanders RW, MacKenzie EJ; Lower Extremity Assessment

Project (Leap) Study Group. The insensate foot following severe lower extremity trauma: an indication for amputation? *J Bone Joint Surg Am* 2005; **87**: 2601-2608 [PMID: 16322607 DOI: 10.2106/JBJS.C.00671]

68 **MacKenzie EJ**, Bosse MJ, Pollak AN, Webb LX, Swiontkowski MF, Kellam JF, Smith DG, Sanders RW, Jones AL, Starr AJ, McAndrew MP, Patterson BM, Burgess AR, Castillo RC. Long-term persistence of disability following severe lower-limb trauma. Results of a seven-year follow-up. *J Bone Joint Surg Am* 2005; **87**: 1801-1809 [PMID: 16085622 DOI: 10.2106/JBJS.E.00032]

69 **Schlickewei W**, Kuner EH, Mullaji AB, Götze B. Upper and lower limb fractures with concomitant arterial injury. *J Bone Joint Surg Br* 1992; **74**: 181-188 [PMID: 1544948 DOI: 10.1302/0301-620X.74B2.1544948]

70 **Mullenix PS**, Steele SR, Andersen CA, Starnes BW, Salim A, Martin MJ. Limb salvage and outcomes among patients with traumatic popliteal vascular injury: an analysis of the National Trauma Data Bank. *J Vasc Surg* 2006; **44**: 94-100 [PMID: 16828431 DOI: 10.1016/j.jvs.2006.02.052]

71 **Johansen K**, Daines M, Howey T, Helfet D, Hansen ST Jr. Objective criteria accurately predict amputation following lower extremity trauma. *J Trauma* 1990; **30**: 568-72; discussion 572 [PMID: 2342140 DOI: 10.1097/00005373-199005000-00007]

72 **Shanmuganathan R**. The utility of scores in the decision to salvage or amputation in severely injured limbs. *Indian J Orthop* 2008; **42**: 368-376 [PMID: 19753223 DOI: 10.4103/0019-5413.43371]

73 **Trickett RW**, Rahman S, Page P, Pallister I. From guidelines to standards of care for open tibial fractures. *Ann R Coll Surg Engl* 2015; **97**: 469-475 [PMID: 26274742 DOI: 10.1308/rcsann.2015.0020]

74 **Jain A**, Glass GE, Ahmadi H, Mackey S, Simmons J, Hettiaratchy S, Pearse M, Nanchahal J. Delayed amputation following trauma increases residual lower limb infection. *J Plast Reconstr Aesthet Surg* 2013; **66**: 531-537 [PMID: 23245916 DOI: 10.1016/j.bjps.2012.11.026]

75 **MacKenzie EJ**, Jones AS, Bosse MJ, Castillo RC, Pollak AN, Webb LX, Swiontkowski MF, Kellam JF, Smith DG, Sanders RW, Jones AL, Starr AJ, McAndrew MP, Patterson BM, Burgess AR. Health-care costs associated with amputation or reconstruction of a limb-threatening injury. *J Bone Joint Surg Am* 2007; **89**: 1685-1692 [PMID: 17671005 DOI: 10.2106/JBJS.F.01350]

76 **Januszkiewicz JS**, Mehrotra ON, Brown GE. Calcaneal fillet flap: a new osteocutaneous free tissue transfer for emergency salvage of traumatic below-knee amputation stumps. *Plast Reconstr Surg* 1996; **98**: 538-541 [PMID: 8700996 DOI: 10.1097/00006534-199609000-00030]

77 **MacKenzie EJ**, Bosse MJ, Castillo RC, Smith DG, Webb LX, Kellam JF, Burgess AR, Swiontkowski MF, Sanders RW, Jones AL, McAndrew MP, Patterson BM, Travison TG, McCarthy ML. Functional outcomes following trauma-related lower-extremity amputation. *J Bone Joint Surg Am* 2004; **86**: 1636-1645 [PMID: 15292410 DOI: 10.2106/00004623-200408000-00006]

78 **Gonzalez EG**, Corcoran PJ, Reyes RL. Energy expenditure in below-knee amputees: correlation with stump length. *Arch Phys Med Rehabil* 1974; **55**: 111-119 [PMID: 4817680]

79 **Khan MA**, Javed AA, Rao DJ, Corner JA, Rosenfield P. Pediatric Traumatic Limb Amputation: The Principles of Management and Optimal Residual Limb Lengths. *World J Plast Surg* 2016; **5**: 7-14 [PMID: 27308235]

80 **Peng YP**, Lahiri A. Spare-part surgery. *Semin Plast Surg* 2013; **27**: 190-197 [PMID: 24872768 DOI: 10.1055/s-0033-1360586]

81 **Garcia-Vilariño E**, Perez-Garcia A, Salmeron-Gonzalez E, Sanchez-Garcia A, Bas JL, Simon-Sanz E. Avoiding Above-the-Knee Amputation with a Free Tibiofibular-Talocalcaneal Fillet Flap and Free Latissimus Dorsi Flap. *Indian J Plast Surg* 2020; **53**: 135-139 [PMID: 32367929 DOI: 10.1055/s-0040-1708226]

82 **Benz D**, Balogh ZJ. Damage control surgery: current state and future directions. *Curr Opin Crit Care* 2017; **23**: 491-497 [PMID: 29035926 DOI: 10.1097/MCC.0000000000000465]

83 **Feliciano DV**. Pitfalls in the management of peripheral vascular injuries. *Trauma Surg Acute Care Open* 2017; **2**: e000110 [PMID: 29766105 DOI: 10.1136/tsaco-2017-000110]

84 **Feliciano DV**, Subramanian A. Temporary vascular shunts. *Eur J Trauma Emerg Surg* 2013; **39**: 553-560 [PMID: 26815539 DOI: 10.1007/s00068-011-0171-9]

85 **Frykberg ER**, Dennis JW, Bishop K, Laneve L, Alexander RH. The reliability of physical examination in the evaluation of penetrating extremity trauma for vascular injury: results at one year. *J Trauma* 1991; **31**: 502-511 [PMID: 2020036 DOI: 10.1097/00005373-199104000-00009]

86 **Frykberg ER**, Vines FS, Alexander RH. The natural history of clinically occult arterial injuries: a prospective evaluation. *J Trauma* 1989; **29**: 577-583 [PMID: 2657082 DOI: 10.1097/00005373-198905000-00006]

87 **Simmons JD**, Walker WB, Gunter Iii JW, Ahmed N. Role of endovascular grafts in combined vascular and skeletal injuries of the lower extremity: a preliminary report. *Arch Trauma Res* 2013; **2**: 40-45 [PMID: 24396789 DOI: 10.5812/atr.10862]

88 **Reuben BC**, Whitten MG, Sarfati M, Kraiss LW. Increasing use of endovascular therapy in acute arterial injuries: analysis of the National Trauma Data Bank. *J Vasc Surg* 2007; **46**: 1222-1226 [PMID: 18154998 DOI: 10.1016/j.jvs.2007.08.023]

89 **Fowler J**, Macintyre N, Rehman S, Gaughan JP, Leslie S. The importance of surgical sequence in the treatment of lower extremity injuries with concomitant vascular injury: A meta-analysis. *Injury* 2009; **40**: 72-76 [PMID: 19070837 DOI: 10.1016/j.injury.2008.08.043]

90 **Huynh TT**, Pham M, Griffin LW, Villa MA, Przybyla JA, Torres RH, Keyhani K, Safi HJ, Moore FA. Management of distal femoral and popliteal arterial injuries: an update. *Am J Surg* 2006; **192**: 773-778 [PMID: 17161092 DOI: 10.1016/j.amjsurg.2006.08.043]

91 **Tunali O**, Saglam Y, Balci HI, Kochai A, Sahbaz NA, Sayin OA, Yazicioglu O. Gustilo type IIIC open tibia fractures with vascular repair: minimum 2-year follow-up. *Eur J Trauma Emerg Surg* 2017; **43**: 505-512 [PMID: 27273011 DOI: 10.1007/s00068-016-0689-y]

92 **Wyrzykowski AD**, Feliciano DV. Trauma damage control. In: Feliciano DV, Mattox KL, Moore EE, eds. Trauma. 6th ed. New York, NY: McGraw-Hill; 2008: 851-870

93 **Glass GE**, Pearse MF, Nanchahal J. Improving lower limb salvage following fractures with vascular injury: a systematic review and new management algorithm. *J Plast Reconstr Aesthet Surg* 2009; **62**: 571-579 [PMID: 19201270 DOI: 10.1016/j.bjps.2008.11.117]

94 **Allen MJ**, Nash JR, Ioannidies TT, Bell PR. Major vascular injuries associated with orthopaedic injuries to the lower limb. *Ann R Coll Surg Engl* 1984; **66**: 101-104 [PMID: 6703619]

95 **Howard PW**, Makin GS. Lower limb fractures with associated vascular injury. *J Bone Joint Surg Br* 1990; **72**: 116-120 [PMID: 2298768 DOI: 10.1302/0301-620X.72B1.2298768]

96 **Lasanianos NG**, Kanakaris NK, Dimitriou R, Pape HC, Giannoudis PV. Second hit phenomenon: existing evidence of clinical implications. *Injury* 2011; **42**: 617-629 [PMID: 21459378 DOI: 10.1016/j.injury.2011.02.011]

97 **Grubor P**, Milicevic S, Grubor M, Meccariello L. Treatment of Bone Defects in War Wounds: Retrospective Study. *Med Arch* 2015; **69**: 260-264 [PMID: 26543315 DOI: 10.5455/medarh.2015.69.260-264]

98 **Masquelet AC**, Begue T. The concept of induced membrane for reconstruction of long bone defects. *Orthop Clin North Am* 2010; **41**: 27-37; table of contents [PMID: 19931050 DOI: 10.1016/j.ocl.2009.07.011]

99 **Olesen UK**, Eckardt H, Bosemark P, Paulsen AW, Dahl B, Hede A. The Masquelet technique of induced membrane for healing of bone defects. A review of 8 cases. *Injury* 2015; **46** Suppl 8: S44-S47 [PMID: 26747918 DOI: 10.1016/S0020-1383(15)30054-1]

100 **Feliciano DV**, Moore EE, West MA, Moore FA, Davis JW, Cocanour CS, Scalea TM, McIntyre RC Jr. Western Trauma Association critical decisions in trauma: evaluation and management of peripheral vascular injury, part II. *J Trauma Acute Care Surg* 2013; **75**: 391-397 [PMID: 23928739 DOI: 10.1097/TA.0b013e3182994b4]

101 **Feliciano DV**. Heroic procedures in vascular injury management: the role of extra-anatomic bypasses. *Surg Clin North Am* 2002; **82**: 115-124 [PMID: 11905941 DOI: 10.1016/S0039-6109(03)00144-0]

102 **Feliciano DV**, Mattox KL, Graham JM, Bitondo CG. Five-year experience with PTFE grafts in vascular wounds. *J Trauma* 1985; **25**: 71-82 [PMID: 3965739 DOI: 10.1097/00005373-198501000-00012]

103 **Subramanian A**, Vercruysse G, Dente C, Wyrzykowski A, King E, Feliciano DV. A decade's experience with temporary intravascular shunts at a civilian level I trauma center. *J Trauma* 2008; **65**: 316-24; discussion 324 [PMID: 18695465 DOI: 10.1097/TA.0b013e31817e5132]

104 **Inaba K**, Aksoy H, Seamon MJ, Marks JA, Duchesne J, Schroll R, Fox CJ, Pieracci FM, Moore EE, Joseph B, Haider AA, Harvin JA, Lawless RA, Cannon J, Holland SR, Demetriades D; Multicenter Shunt Study Group. Multicenter evaluation of temporary intravascular shunt use in vascular trauma. *J Trauma Acute Care Surg* 2016; **80**: 359-64; discussion 364 [PMID: 26713968 DOI: 10.1097/TA.0000000000000949]

105 **Parry NG**, Feliciano DV, Burke RM, Cava RA, Nicholas JM, Dente CJ, Rozycki GS. Management and short-term patency of lower extremity venous injuries with various repairs. *Am J Surg* 2003; **186**: 631-635 [PMID: 14672770 DOI: 10.1016/j.amjsurg.2003.08.006]

106 **Strinden WD**, Dibbell DG Sr, Turnipseed WD, Acher CW, Rao VK, Mixter RC. Coverage of acute vascular injuries of the axilla and groin with transposition muscle flaps: case reports. *J Trauma* 1989; **29**: 512-516 [PMID: 2709462 DOI: 10.1097/00005373-198904000-00018]

107 **Borgquist O**, Ingemansson R, Malmsjö M. Wound edge microvascular blood flow during negative-pressure wound therapy: examining the effects of pressures from -10 to -175 mmHg. *Plast Reconstr Surg* 2010; **125**: 502-509 [PMID: 20124835 DOI: 10.1097/PRS.0b013e3181c82e1f]

108 **Tahir M**, Chaudhry EA, Zimri FK, Ahmed N, Shaikh SA, Khan S, Choudry UK, Aziz A, Jamali AR. [RETRACTED] Negative pressure wound therapy versus conventional dressing for open fractures in lower extremity trauma. *Bone Joint J* 2020; **102-B**: 912-917 [PMID: 32600140 DOI: 10.1302/0301-620X.102B7.BJJ-2019-1462.R1]

109 **Costa ML**, Achten J, Bruce J, Tutton E, Petrou S, Lamb SE, Parsons NR; UK WOLLF Collaboration. Effect of Negative Pressure Wound Therapy vs Standard Wound Management on 12-Month Disability Among Adults With Severe Open Fracture of the Lower Limb: The WOLLF Randomized Clinical Trial. *JAMA* 2018; **319**: 2280-2288 [PMID: 29896626 DOI: 10.1001/jama.2018.6452]

110 **British Orthopaedic Association**. BOAST 10: diagnosis and management of compartment syndrome of the limbs. Accessed May 20, 2015. Available from: http://www.boa.ac.uk/wp-content/uploads/2015/01/BOAST-10.pdf

111 **Branco BC**, Inaba K, Barmparas G, Schnüriger B, Lustenberger T, Talving P, Lam L, Demetriades D. Incidence and predictors for the need for fasciotomy after extremity trauma: a 10-year review in a mature level I trauma centre. *Injury* 2011; **42**: 1157-1163 [PMID: 20678764 DOI: 10.1016/j.injury.2010.07.243]

112 **Farber A**, Tan TW, Hamburg NM, Kalish JA, Joglar F, Onigman T, Rybin D, Doros G, Eberhardt RT. Early fasciotomy in patients with extremity vascular injury is associated with decreased risk of adverse limb outcomes: a review of the National Trauma Data Bank. *Injury* 2012; **43**: 1486-1491 [PMID: 21719009 DOI: 10.1016/j.injury.2011.06.006]

113 **Fitzgerald AM**, Gaston P, Wilson Y, Quaba A, McQueen MM. Long-term sequelae of fasciotomy wounds. *Br J Plast Surg* 2000; **53**: 690-693 [PMID: 11090326 DOI: 10.1054/bjps.2000.3444]

114 **Thakore RV**, Francois EL, Nwosu SK, Attum B, Whiting PS, Siuta MA, Benvenuti MA, Smith AK, Shen MS, Mousavi I, Obremskey WT, Sethi MK. The Gustilo-Anderson classification system as predictor of nonunion and infection in open tibia fractures. *Eur J Trauma Emerg Surg* 2017; **43**: 651-656 [PMID: 27658943 DOI: 10.1007/s00068-016-0725-y]

115 **Arnež ZM**, Papa G, Ramella V, Novati FC, Ahcan U, Stocco C. Limb and Flap Salvage in Gustilo IIIC Injuries Treated by Vascular Repair and Emergency Free Flap Transfer. *J Reconstr Microsurg* 2017; **33**: S03-S07 [PMID: 28985632 DOI: 10.1055/s-0037-1603737]

116 **Warkentien TE**, Lewandowski LR, Potter BK, Petfield JL, Stinner DJ, Krauss M, Murray CK, Tribble DR; Trauma Infectious Disease Outcomes Study Group. Osteomyelitis Risk Factors Related to Combat Trauma Open Upper Extremity Fractures: A Case-Control Analysis. *J Orthop Trauma* 2019; **33**: e475-e483 [PMID: 31356447 DOI: 10.1097/BOT.0000000000001593]

117 **Wang G**, Tang Y, Wu X, Yang H. Masquelet technique combined with microsurgical technique for treatment of Gustilo IIIC open distal tibial fractures: a retrospective single-center cohort study. *J Int Med Res* 2020; **48**: 300060520910024 [PMID: 32237939 DOI: 10.1177/0300060520910024]

118 **Gustilo RB**, Mendoza RM, Williams DN. Problems in the management of type III (severe) open fractures: a new classification of type III open fractures. *J Trauma* 1984; **24**: 742-746 [PMID: 6471139 DOI: 10.1097/00005373-198408000-00009]

119 **Brown KV**, Ramasamy A, Tai N, MacLeod J, Midwinter M, Clasper JC. Complications of extremity vascular injuries in conflict. *J Trauma* 2009; **66**: S145-S149 [PMID: 19359958 DOI: 10.1097/TA.0b013e31819cdd82]

120 **Tian R**, Zheng F, Zhao W, Zhang Y, Yuan J, Zhang B, Li L. Prevalence and influencing factors of nonunion in patients with tibial fracture: systematic review and meta-analysis. *J Orthop Surg Res* 2020; **15**: 377 [PMID: 32883313 DOI: 10.1186/s13018-020-01904-2]

121 **Reverte MM**, Dimitriou R, Kanakaris NK, Giannoudis PV. What is the effect of compartment syndrome and fasciotomies on fracture healing in tibial fractures? *Injury* 2011; **42**: 1402-1407 [PMID: 21993369 DOI: 10.1016/j.injury.2011.09.007]

122 **Seligson D**, Ostermann PA, Henry SL, Wolley T. The management of open fractures associated with arterial injury requiring vascular repair. *J Trauma* 1994; **37**: 938-940 [PMID: 7996607 DOI: 10.1097/00005373-199412000-00011]

123 **Alexander JJ**, Piotrowski JJ, Graham D, Franceschi D, King T. Outcome of complex vascular and orthopedic injuries of the lower extremity. *Am J Surg* 1991; **162**: 111-116 [PMID: 1862831 DOI: 10.1016/0002-9610(91)90170-i]

124 **McNutt R**, Seabrook GR, Schmitt DD, Aprahamian C, Bandyk DF, Towne JB. Blunt tibial artery trauma: predicting the irretrievable extremity. *J Trauma* 1989; **29**: 1624-1627 [PMID: 2593189]

125 **Martin MJ**, Perez-Alonso AJ, Asensio JA. Vascular complications and special problems in vascular trauma. *Eur J Trauma Emerg Surg* 2013; **39**: 569-589 [PMID: 26815541 DOI: 10.1007/s00068-013-0336-9]

126 **Boriani F**, Ul Haq A, Baldini T, Urso R, Granchi D, Baldini N, Tigani D, Tarar M, Khan U. Orthoplastic surgical collaboration is required to optimise the treatment of severe limb injuries: A multi-centre, prospective cohort study. *J Plast Reconstr Aesthet Surg* 2017; **70**: 715-722 [PMID: 28351609 DOI: 10.1016/j.bjps.2017.02.017]

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REVIEW

Coronal plane deformity around the knee in the skeletally immature population: A review of principles of evaluation and treatment

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Abstract

Coronal plane deformity around the knee, also known as genu varum or genu valgum, is a common finding in clinical practice for pediatricians and orthopedists. These deformities can be physiological or pathological. If untreated, pathological deformities can lead to abnormal joint loading and a consequent risk of premature osteoarthritis. The aim of this review is to provide a framework for the diagnosis and management of genu varum and genu valgum in skeletally immature patients.

Key Words: Genu varum; Genu valgum; Pediatric deformity; Knee deformity; Guided growth; Osteotomy; Lower limb deformity

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Core Tip: Physiological angulation requires no treatment other than clinical observation. If the clinical picture is doubtful, a long-standing X-ray of the lower limb is required for clarification. Once a pathological alignment is determined by X-ray, a differential diagnosis is needed to establish whether the deformity is idiopathic or a secondary condition. Furthermore, any associated deformities in other planes (*e.g.*, rotation or length difference) should be evaluated. Pathological alignment should be treated for at least two reasons: To interrupt the vicious circle described by the Hueter-Volkmann law and to prevent premature degeneration of the joint. Both of these conditions stem from abnormal load distribution. Guided growth should be considered every time a coronal deformity of the knee is foreseen in a skeletally immature patient. Although comparative studies are lacking in the literature, this technique has a high success rate with few complications and a low impact on the patient and the family.

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INTRODUCTION

Coronal angular deformities around the knee in children are a common finding in pediatric orthopedic surgery. However, a majority of these deformities, such as genu varum and genu valgum, are physiological and correspond to the normal changes in mechanical axis (MA) alignment that take place from birth to adolescence.

The purpose of this paper is to provide a review of the recent literature concerning: (1) The definition of normal (physiological) alignment and pathological genu valgum and genu varum; (2) The practical clinical approach for patients with a coronal angular deformity around the knee; and (3) A brief description of specific pathologies.

The Medline, Embase, Web of Science, and Cochrane Systematic Review databases were searched for studies published in English up to 31 August 2020. The primary search terms were "knee" AND "valgum"; "knee" AND "varum"; "normal" AND "lower" AND "limb" AND "alignment". Papers were screened by title and abstract to identify relevant articles. Their reference lists were checked manually for additional articles. Studies involving skeletally mature patients were excluded (these studies were only included in the analysis of the lower limb alignment range).

Definition of normal alignment and the natural history of coronal angular deformity of the knee in the skeletally immature

To understand deformities of the lower extremity, it is first important to understand and establish the parameters and thresholds of normal alignment. Every long bone, such as the femur and the tibia, has a mechanical and an anatomical axis (AA) (Figure 1). The MA of the lower limb is the line connecting the center of the femoral head and the midpoint of the tibiotalar joint. The femorotibial mechanical angle (FTMA) is the angle formed by the intersection of the mechanical axes of the femur (MAF) and the tibia (MAT). The AA of the lower limb is the AA of the femur and the tibia, which forms the femorotibial anatomical angle (FTAA). The MA deviation (MAD) is defined as the distance between the center of the knee and the MA[1].

Salenius and Vankka[2] reported that the femorotibial angle (FTA) develops physiologically from a varus alignment in the newborn (with an angulation of 10 to 15 degrees) to a neutral alignment at 18-20 mo and a valgus alignment at 3 years. Indeed, the mature FTAA is reached at approximately 8 years and is approximately 6 degrees of valgus (8 degrees in females and 7 degrees in males)[2-4]. Therefore, the persistence of genu varum beyond 2 years may be considered abnormal[5], whereas a valgus deformity greater than 15 degrees that persists after 8-10 years rarely corrects itself with growth[6].

A wide range of values for normal lower limb alignment has been reported in the literature[2,7]. However, it has been established that the FTMA tends to be neutral or slightly varus (1.3 ± 2 degrees) with the MA passing through or immediately medial to the center of the knee[1,8,9]. Indeed, the normal MAD is reported to be 8 ± 7 mm medial to the center of the knee joint line[1]. The knee joint line is reported to be approximately 3 degrees off the perpendicular line, as a consequence of a 3-degree valgus inclination of the distal femur and a 3-degree varus inclination of the proximal tibia[4]. The MAD falls away from the center of the knee in coronal angular deformities of the knee. Genu varum is defined as an increased FTA with the MA passing through the medial portion of the knee joint. Genu valgum is defined as a reduced FTA with the MA passing through the lateral portion of the knee joint[1].

ASSESSMENT

History

A careful medical history can help to differentiate between physiological and pathological coronal angular deformity (Table 1). A family history of short stature, varus or valgus alignment, and metabolic or genetic diseases should be ascertained. Personal history taking should also consider the child's stage of development and rule out any traumatic or pathological conditions (*e.g.*, infectious or rheumatic diseases)[5,6].

Physical examination

The clinical evaluation should include the patient's general appearance, stature, and height percentile.

Table 1 Principal causes of pathological genu varum and genu valgum

Genu varum	Genu valgum
Idiopathic	
Tibia vara (blount disease)	
Infantile form	
Adolescent form	
Post-traumatic	
Physeal bar	
Malunion	
	Cozen's phenomenon
Metabolic	
Rickets	
Renal disease	
Local disorders	
Infectious	
Tumor or tumor-like lesion	
Generalized disorders	
Metabolic (*e.g.*, rickets, renal osteodystrophy)	
Constitutional disease of bone (*i.e.*, bone dysplasia)	
Juvenile arthritis	
Neuromuscular	

Femoral anteversion, tibial torsion, and the foot's appearance should be assessed. The evaluation of the lower limb should look for any coronal plane, sagittal plane, or translational deformities. This paper will only discuss coronal plane deformities.

The intermalleolar (IM) and intercondylar (IC) distances are used to assess coronal plane deformity, although some researchers dispute the clinical utility of this, on account of poor reproducibility[5,6,10,11]. Staheli[7] states that knee angle variations measured using FTA, IM, or IC and falling within the range of two standard deviations above or below the mean are physiological conditions. Thus, pathological genu varum and genu valgum are true frontal plane deformities that are outside the normal range of two standard deviations above or below the mean[6,12,13].

Specifically, persistent varus deformity with an IC distance greater than 5 cm in patients older than 3 years, and valgus deformity (IM distance greater than 7 cm) in patients older than 7 years should be considered abnormal[10,12,14,15]. Obesity, femoral anteversion, external rotation of the tibia, and flat foot with out-toed stance can exaggerate the IM distance and the appearance of genu valgum, whereas internal tibial torsion can give an overestimated IC distance and the appearance of genu varum[10].

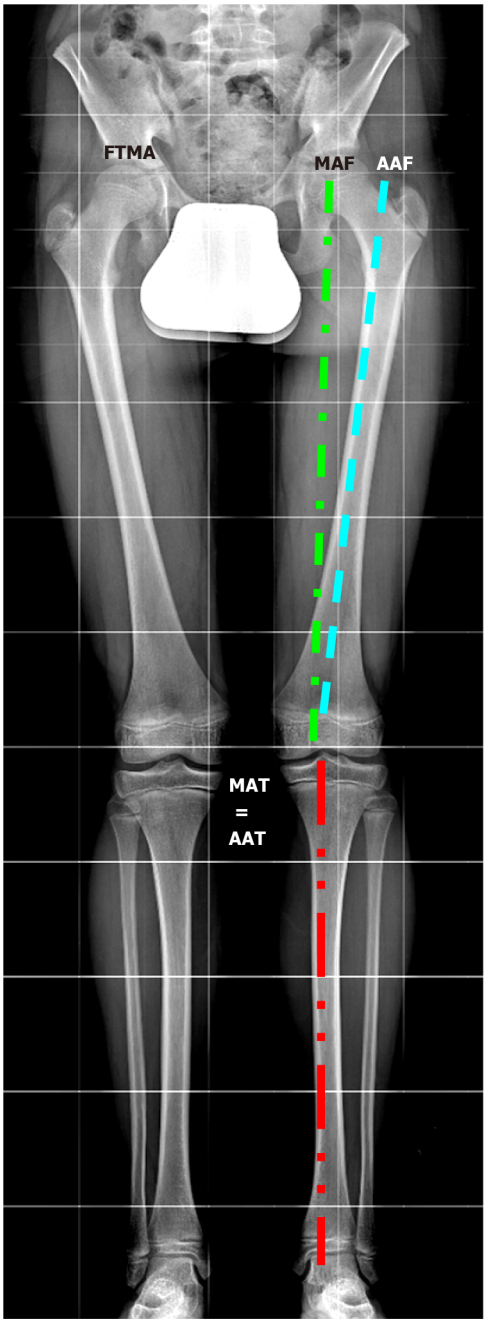
Radiographs

A long-standing, weight-bearing radiograph (including the pelvis, the hips, the knees, and the ankle) should be obtained every time pathological genu valgum or genu varum is suspected. In particular, a varus deformity should be evaluated by radiograph if[16]: (1) It persists or progresses beyond 18-24 mo of age or does not resolve; and (2) There is asymmetric deformity.

Radiographs should be obtained for genu valgum if[6]: (1) The patient is older than 7 years with a tibiofemoral angle greater than 15 degrees and/or an IM distance of more than 7 cm; (2) The genu valgum is associated with short stature (below the 25th percentile) or if there are other musculoskeletal abnormalities; and (3) There is asymmetric involvement.

Radiograph parameters

Paley and Tetsworth[17], Paley *et al*[18] standardized the approach to the radiographic evaluation of lower limb deformities and summarized and published it as a step-by-step method called "the malalignment test", which determines the source(s) of the malalignment (Figure 2). Long-standing films (anteroposterior and lateral) should be obtained including the hips, knees, and ankles. Proper positioning is important: The knees should be straight and the patella facing forward.



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Figure 1 Lower limb axes evaluated in long standing X-ray. FTMA: Femorotibial mechanical axis; MAF: Mechanical axis of the femur; AAF: Anatomical axis of the femur; MAT: Mechanical axis of the tibia; AAT: Anatomical axis of the tibia.

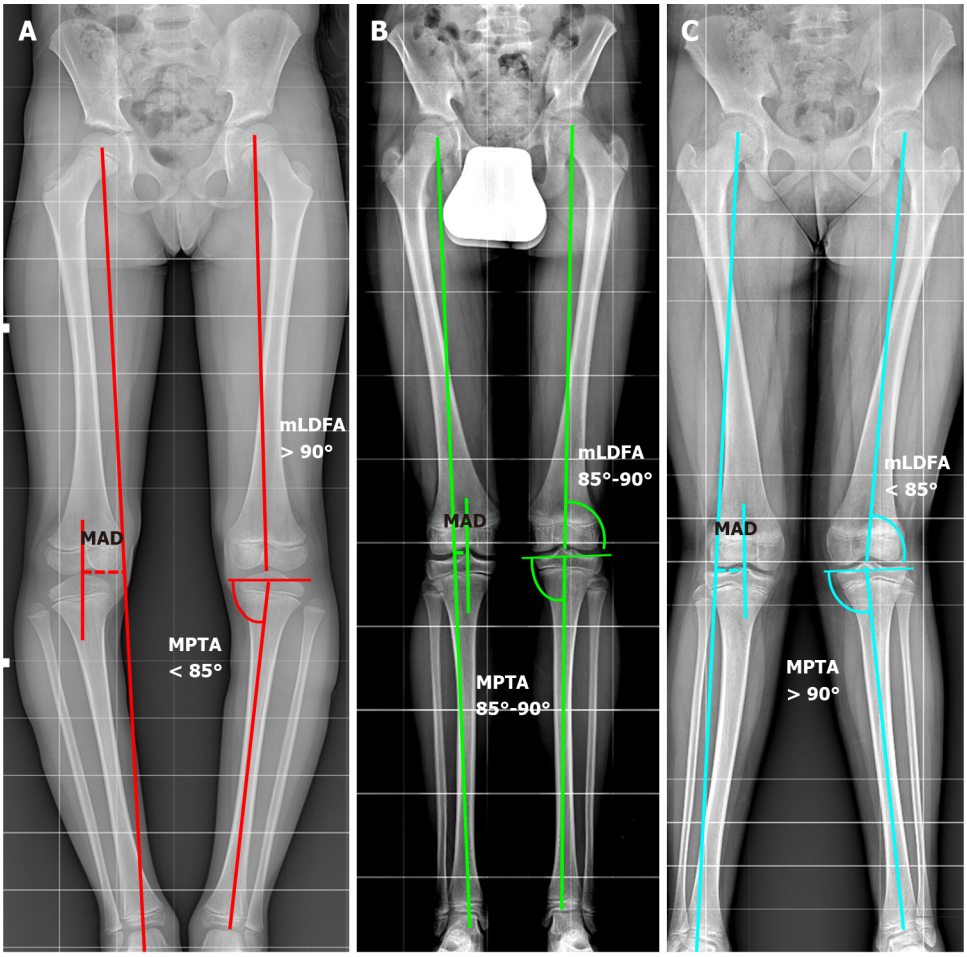
TREATMENT

Observation

Patients with physiological varus or valgus knee (that is, who fall within the two standard deviations from the normal value for their age or within the second zone on the X-ray) require no treatment other than observation. Parents should be reassured that it is not a true deformity or disease, but a variant of normal lower limb alignment, which usually corrects spontaneously. These patients should be clinically evaluated every 3-6 mo to monitor the deformity. Radiographic assessment should be repeated if there is suspicion of clinical worsening[6]. Conservative treatment (*e.g.*, shoe wedges or bracing) is not effective, is poorly tolerated, and is unnecessary in cases of physiological deviation[5-7,10].

Surgical treatment

It is generally accepted that a significant deformity that persists into preadolescence will not correct spontaneously. Physiological alignment of the lower limb is crucial for the symmetrical distribution of weight over the surfaces of the joints, especially the knee. Indeed, severe coronal malalignment has been



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Figure 2 The malalignment test. The mechanical axis (MA) is traced from the center of the femoral head to the center of the ankle. The metaphyseal-diaphyseal angle (MAD) is calculated in millimeters (dotted lines in the image traced from center of knee and MA). If the MAD exceeds the threshold of normality, it is necessary to find the source of the deformity. The mechanical lateral distal femur angle. Medial proximal tibial angle are evaluated. A: Varus; B: Normal; C: Valgus. MAD: Metaphyseal-diaphyseal angle; MPTA: Medial proximal tibial angle; mLDFA: Mechanical lateral distal femur angle.

linked to knee pain, altered gait, and occasionally patellofemoral problems[19]. Moreover, it can contribute to the development of osteoarthritis of the knee[11,20-22]. Additionally, MA deviation in the lateral or medial compartment can lead to compression in the lateral or medial physis, thereby further delaying growth as a result of the Hueter-Volkmann effect[23].

Preoperative planning

Preoperative planning could involve the malalignment test on a long-standing X-ray, as described by Paley and Tetsworth[17] (Figure 2): (1) Evaluation of MA and MAD. The first step is tracing the MA of the lower limb (*e.g.*, from the center of the femoral head to the center of the ankle). The MA should pass through the center of the knee joint. If the MA axis does not go through the center of the knee joint, there is a MAD. Furthermore, the MA deviation can be classified into three zones as defined by Müller and Müller-Färber[24]. When the MAD exceeds the normal range (*e.g.*, > 8 ± 7 mm medial to the center of the knee joint line[1]) or the MA passes to the first zone[23,24] a pathological malalignment is present and the following steps will determine the origin of the deformity; (2) Measurement of the mechanical lateral distal femur angle (n.v. = 87.5 ± 2.5): The lateral angle between the MAF and the line through the femoral condyles; (3) Measurement of the medial proximal tibial angle (n.v. = 87.5 ± 2.5): The medial angle between the MAT and the line through the tibial plateaus; (4) Measurement of the joint line convergence angle (n.v. = 0-2 degrees medial convergence): The angle between the femoral condyle and the tibial plateau joint line. This helps to evaluate any source from the ligament or capsular laxity or joint cartilage loss; (5) Ruling out a medial or lateral subluxation: The midpoints of the femur and the tibia should be aligned; and (6) Ruling out an intraarticular origin of the malalignment: The femoral condyles and the tibial plateaus should be aligned with respect to each other. A depressed or elevated femoral condyle or tibial plateau may indicate an intraarticular source of malorientation.

The method described evaluates deformities near the knee. Deformities away from the knee should be investigated using the center of rotation of angulation (CORA) method and other angles such as the



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Figure 3 Staple hemiepiphysiodesis.

lateral proximal femur angle and the lateral distal tibial angle[25] whose description is beyond the scope of this article.

The authors stress that these measurements are only reliable if the X-ray projection is anteroposterior with the knee in the frontal plane, which is defined as the position where the patella is centered in the femoral condyles[18,26]. This means that care must be taken to place the patient in the patella forward position, rather than in the feet forward position, as the latter is affected by tibial torsion and leads to incorrect measurement[18].

General indications

Surgical correction of coronal angular knee deformities is indicated if: (1) The MA falls within zone 2 and the patient is symptomatic; and (2) The MA is beyond zone 2[23,24]. If the deformity only involves the distal femur or the proximal tibia, the correction should only take place within the affected bone. If the deformity originates from both the femur and the tibia and is symmetrical, both bones should be treated. If, on the other hand, the deformity is asymmetrical, only the bone whose angle (LTFA and MTFA) deviates more than 5 degrees from the reference values should be treated[7,27].

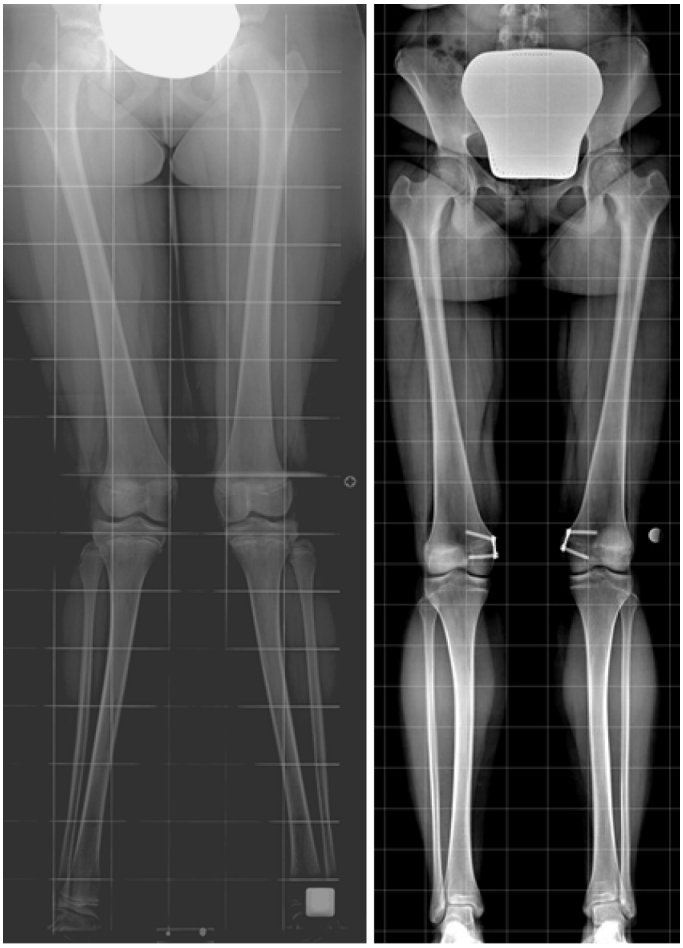
How to treat pathological genu varum and genu valgum

In growing children, the treatment strategies for coronal angular deformities around the knee are: (1) Hemiepiphysiodesis; and (2) Osteotomy.

Hemiepiphysiodesis: It is well known that the physis is the area where bones grow. Epiphysiodesis is a surgical procedure that consists of the iatrogenic arrest of the growth plate to control the growth of immature bone. Epiphysiodesis can be partial (hemiepiphysiodesis) or complete and its duration can be permanent or (potentially) reversible[28].

Hemiepiphysiodesis on the convex side of the deformity should be preferred to osteotomy in skeletally immature patients with coronal angular deformity around the knee and who have reasonably sufficient growth remaining for them to reach the expected correction[28]. The prerequisites for coronal angular deformity correction include a minimum of 2 years of growth remaining and a deformity originating from or in the immediate vicinity of the growth plate[10].

Permanent hemiepiphysiodesis: Phemister[29] described an open procedure for surgical closure of the growth plate. In 1993 Terry Canale[30] reported a percutaneous epiphysiodesis technique involving mechanical disruption of the growth plate induced by a combination of drills, burrs, and/or curettes.



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Figure 4 Tension band plate hemiepiphysiodesis for correcting genu valgum deformity.

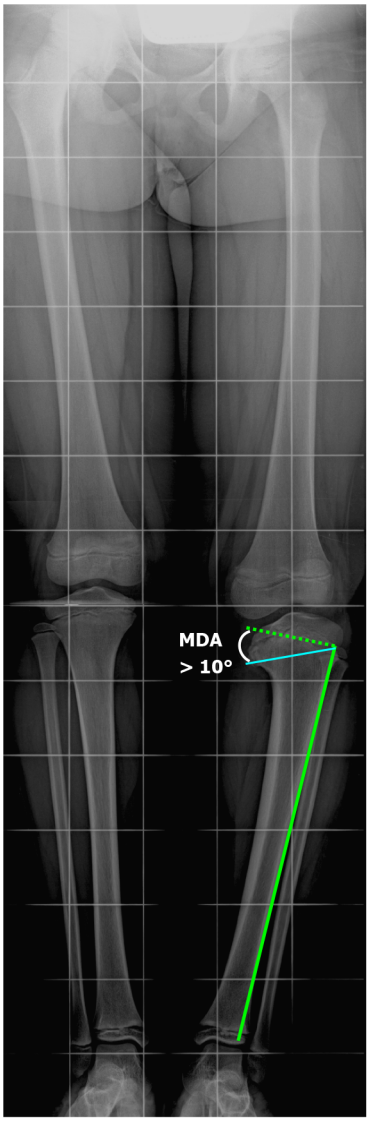
In 1998 Métaizeau *et al*[31] described percutaneous epiphysiodesis using transphyseal screws (PETS), which uses the compressive force of fully threaded cannulated screws to inhibit the growth of the physis. The screw is inserted into the metaphysis, crosswise through the growth plate and into the epiphysis on the opposite side, or in a straight direction into the epiphysis on the same side. It is reported that at least four screw threads should be engaged within the epiphysis to achieve sufficient compression[32]. PETS is sometimes referred to as reversible epiphysiodesis with screw removal. However, some authors report that the physis fuses quite quickly after screw placement and that the technique is not reliably reversible[33].

Permanent epiphysiodesis for coronal deformity is associated with low cost, minimally invasive procedures, and low cosmetic impact. It is an attractive option for patients who are near skeletal maturity because it eliminates implant-related complications and the unpredictability of the rebound effect. However, this technique requires accurate preoperative planning in order to time the procedure precisely, which is essential for achieving the exact estimated correction[11]. Inappropriate timing of surgery could lead to under- or overcorrection of the deformity[34]. Ferrick *et al*[35] suggest performing permanent hemiepiphysiodesis if there are 1 or 2 years of growth remaining and stress the importance of close follow-up. If correction is achieved before maturity, epiphysiodesis should be completed with or without contralateral epiphysiodesis to control leg length equality.

Temporary (or reversible) hemiepiphysiodesis (growth plate modulation)

The longitudinal growth of long bones occurs at the level of the growth plates, which are affected by mechanical loading as a result of the Hueter-Volkmann law. Summarizing, the tensile forces that increase growth rate and compression decrease activity in the growth plate[36,37]. Growth plate modulation is induced by a surgical device tethered to one side of a growing physis, thereby allowing differential growth[36].

Staples: Haas[38] was the first to describe a reversible epiphysiodesis technique using wires over the growth plate. However, this technique became more popular after the studies of Blount and Clarke[39], who controlled growth by epiphyseal stapling (Figure 3). Satisfactory results with correction of the deformity are reported in 80%-85% of cases. Implant failure with staple extrusion or breakage is



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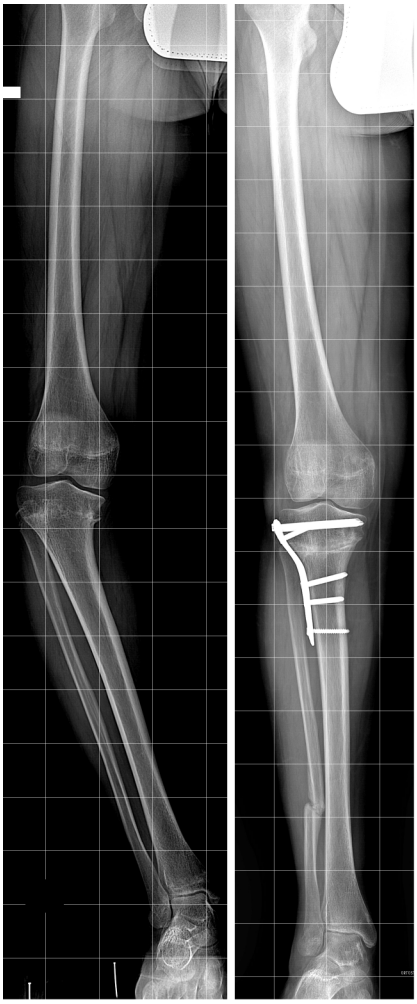
Figure 5 Radiographic measurement of Drennan's metaphyseal-diaphyseal angle. The metaphyseal-diaphyseal angle (MDA) is measured from a perpendicular line to the tibial diaphyseal axis and a line passing through the axial plane of the proximal tibial metaphysis. An MDA > 10 degrees associated with a tibiofemoral angle > 20 degrees indicates a toddler at risk. MDA: Metaphyseal-diaphyseal angle.

observed in approximately 10% of treated physes.

Tension band plate (guided growth): Stevens[40] coined the term "guided growth" and proposed an alternate device consisting of a small, non-rigid extraperiosteal plate locked by two screws - one proximal and one distal to the physis - serving as a focal hinge at the perimeter of the physis (Figure 4). The critical difference between Blount's staple and Stevens' plate is that the former is rigid and compresses the physis, whereas the latter is a non-rigid device and acts as a tension band plate (TBP) [40]. This difference means a lower risk of plate extrusion and the need to insert only one plate.

Stevens' classic TBP, known as the 8-plate, consists of a non-locking plate and two screws. Owing to the high cost of these classic plates, particularly in developing countries, some authors report good results using 2-hole 3.5 mm stainless steel reconstruction plates and 4 mm non-cannulated cancellous screws[41].

Steven[40] reports a faster correction rate using the TBP instead of staples. However, several other studies show faster correction with staples, suggesting that the latter implant causes immediate compression to the physis, whereas the tension plate becomes effective a few months after insertion[42]. There is some debate in the literature about the angle of the screws during implantation. In a recent clinical study, Eltayeby *et al*[43] show that the initial screw angle (0-30 degrees) does not significantly affect the rate of correction, and they recommend inserting screws taking account of anatomical restrictions to avoid the physis, rather than favoring parallel, divergent or widely divergent configurations.



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Figure 6 High tibial osteotomy for genu varum correction.

Some authors report a modified surgical technique called the "sleeper plate"[44,45]. In this modified TBP, when the deformity is corrected, the metaphyseal screw is removed and the plate with the epiphyseal screw is left in place. If the deformity recurs, only the metaphyseal screw needs to be reinserted.

Outcomes and complications of reversible hemiepiphysiodesis

The success rate of growth plate modulation in the literature is reported to be close to 100% in idiopathic cases with a low complication rate[11,19,46]. Pathological cases have a slightly lower success rate and a higher complication rate[19,46]. Adverse events can be divided into: (1) Failure to achieve the correction: This is defined as the failure of the screws to diverge during treatment and to correct the deformity. The risk factors for failure are related to body mass index (BMI), age, and underlying etiology[46]. The rate of this complication differs in the studies present in the literature. It has been reported as being close to 0% for idiopathic cases. In pathological physes, the failure rate is reported to be as high as 45% in patients with pseudoachondroplasia and 36.8% in those with Blount disease[47]. Boero *et al*[19] reported no correction failure in the idiopathic deformity group, while in the non-idiopathic deformity group the complete correction rate was 78.5%, the partial correction rate 17.9%, and the no correction rate 3.6%. Joeris *et al*[48] published an international multicenter study in which a 66% success rate was reported for varus/valgus deformity correction using TBPs. In this paper, patients with idiopathic and secondary deformities were not analyzed separately; (2) Overcorrection: Precise timing of implant or hardware removal and routine post-operative follow-up is essential for avoiding this complication. Overcorrection is usually associated with low patient compliance and failure to attend clinical or radiological monitoring after implantation[49]; (3) Hardware failure: Implant breakage, loosening, migration or extrusion were reported for both staples and TBPs[50,51]. The original TBP technique involves the use of cannulated screws. Several reports describe broken screws in this type of implant, particularly in obese patients. The use of solid screws should be considered in patients with a high BMI in order to increase the strength and resistance of the implants[52]; (4) Premature epiphyseal closure: This is a theoretical complication, but an extremely rare one as long as the hardware is removed within 2 or 3 years of

insertion[19,46]. To avoid this complication, the entire procedure should be extraperiosteal and care must be taken to preserve the physis, the zone of Ranvier, and the perichondrial ring of LaCroix during hardware implantation[11,44]. This complication is reported to be higher in cases using the sleeper plate technique[45]; and (5) Rebound: This is defined as a recurrence of malalignment (at least 5 degrees of varus or valgus) after the restoration of physeal growth on removal of the implanted hardware and is caused by growth acceleration on the previously tethered physis[4,11,13,46]. This phenomenon is theoretically possible in all patients, but is not always present and cannot be predicted with certainty. Leveille *et al*[53] report that patients at high risk of rebound are those with severe initial deformity (> 20 degrees) who undergo early hemiepiphysiodesis (< 10 years for girls and < 12 years for boys). Some authors routinely perform an overcorrection of 5 degrees[51]. However, Leveille *et al*[53] recommend only overcorrecting patients at high risk of rebound, to avoid creating a new deformity in patients who do not experience a rebound.

Timing of hemiepiphysiodesis

When hemiepiphysiodesis is timed perfectly, the deformity is corrected in step with skeletal maturity. The timing of this procedure is therefore crucial in cases of permanent hemiepiphysiodesis. If this procedure is performed too early, it could lead to overcorrection of the deformity and require circular epiphysiodesis (with or without epiphysiodesis of the contralateral limb to counteract any potential length discrepancies). If performed too late, it may not fully correct the deformity. Temporary hemiepiphysiodesis is theoretically reversible and therefore enables growth to resume once the deformity is corrected.

Numerous methods are reported in the literature for predicting growth, particularly correction of limb-length discrepancy (LLD). Only a few articles test and report the reliability of these methods, in cases where epiphysiodesis is used to correct angular deformities of the knee.

Bowen *et al*[54] and Inan *et al*[55] chart angular deformity against remaining growth potential calculated using a formula and combining the Green-Anderson growth remaining graph. The authors summarize that, as a general rule, a correction of about 7 degrees can be estimated in cases of epiphysiodesis of the distal femur and 5 degrees in cases of epiphysiodesis of the proximal tibia. The authors also state that the prediction was accurate for normal physes but inaccurate in cases of abnormal physes[54].

Paley and Tetsworth[17], and Paley *et al*[18] introduced the Multiplier Method (MM) to predict various parameters of growth, the timing for epiphysiodesis, and timing for hemiepiphysiodesis, using both skeletal age and chronological age when calculating LLD at maturity. Some authors report greater accuracy using the skeletal age, but Eltayeby *et al*[56] report the same prediction accuracy using skeletal and chronological age. They also show that MM tends to underpredict and so suggest that guided growth procedures performed right before skeletal maturity should be started 2 to 4 mo earlier than suggested by MM[56]. In their systematic review of the literature Wu *et al*[57] report poor reliability with MM for angular deformity prediction. It is more reliable for younger patients with idiopathic deformity and shows less prediction accuracy for patients older than 10 years or with non-idiopathic deformities.

Osteotomy

The use of corrective osteotomy is indicated in patients close to or at skeletal maturity, or in those whose growth cartilages are not functional (*e.g.*, after an infection, or in the presence of a physeal bar). The specifics of realignment osteotomies are beyond the scope of this article and have been reported in articles on this theme and summarized by Paley[58]. However, it is necessary to introduce the fundamental concept of the CORA, which can be summarized as the point of maximum deformity. When a corrective osteotomy is planned, the correction should be established close to the CORA to avoid introducing translation deformity[18]. In varus and valgus deformities of the knee, the CORA is adjacent to the articular surface and the physis. For this reason, osteotomy, whether of the distal femur or the proximal tibia, is generally not feasible in skeletally immature patients. This is to avoid iatrogenic damage to the growth plate. Thus, in order to achieve realignment with corrective osteotomy, preoperative planning should take account of both the original angular deformity and any translation deformity introduced[18].

Correction through osteotomy can be acute, achieved using internal fixation devices (*e.g.*, Kirschner wires, intramedullary nail, plates) or gradual, using an external fixator and distraction osteogenesis[59]. Gradual correction is attractive in cases of multiplanar deformity and modern hexapod systems are particularly useful in these situations[60].

The different types of osteotomy used to correct a deformity acutely are[10,61]: (1) Opening wedge; (2) Closing wedge; (3) Reverse wedge; and (4) Dome osteotomy. Acute deformity correction predisposes the patient to certain risks that should be taken into consideration during planning. Non-union or delayed union should be considered in opening wedge osteotomies greater than 20 degrees[62].

Neurovascular structures risk being stretched during acute correction. It is reported that the risk of injury to neurovascular structures is related to the magnitude of correction, but the limit is not well defined. Other factors that add to this risk are the site and type of osteotomy and the direction of correction. For example, a correction of a valgus to varus deformity of the knee by osteotomy of the

distal femur or proximal tibia puts the common peroneal nerve (CPN) at risk, even if the correction is small (about 5 degrees)[63]. Conversely, a correction of a varus deformity releases the CPN. Furthermore, the deep peroneal nerve (DPN), which passes under the intermuscular septum between the lateral and anterior compartment of the leg, is more at risk of injury than the superficial peroneal nerve (SPN)[25]. For the same reason, internal or external rotation osteotomies involving tensioning of the intermuscular septum create more risk for the DPN and less for the SPN. For these reasons, some authors suggest performing prophylactic peroneal nerve decompression before acute correction[63]. Additionally, the motor branch to the extensor hallucis longus is particularly at risk during fibular osteotomy[64].

SPECIFIC CONDITIONS

Idiopathic pathological genu valgum and genu varum

It is generally established that growth plate modulation with staples or TBPs determines less morbidity than osteotomy. However, it is essential to evaluate the timing of epiphysiodesis and to schedule close clinical monitoring to avoid overcorrection.

Post-traumatic

Trauma is one of the most frequent causes of pathological coronal deformity around the knee. The deformity may be a result of inadequate reduction or injury to the growth cartilage with a consequent alteration or arrest in growth (*e.g.*, physeal bar). In the latter case, some authors report a high risk in cases of type 3 Salter-Harris (SH) fracture of the proximal tibia, whereas the type of SH fracture in the distal femur is poorly predictive[6]. In some cases, the physeal injury may be misdiagnosed if concomitant with another fracture of the femur or tibia. Therefore, some authors recommend knee X-rays in all patients with a traumatic lower limb injury[65].

Depending on the age of the patient, the location, the cause and the extent of the deformity, treatment may involve observation, physeal bar resection, epiphysiodesis, chondrodiastasis, or corrective osteotomy. Physeal bar resection consists of removing the bone bridging the metaphysis and the epiphysis and filling the gap with interposition material (*e.g.*, fat, methyl methacrylate or polymeric silicone) to prevent the bony bar from reforming. This is indicated when there are at least 1 or 2 years of remaining growth, and when the bar involves < 50% of the growth plate. If a clinically unacceptable deformity is present at the time of physeal bar resection, an osteotomy or hemiepiphysiodesis is indicated to realign the lower limb. In fact, a successful physeal bar resection alone would not be able to fully correct the deformity[66].

A frequent form of post-traumatic knee valgus is tibia valga following fracture of the proximal metaphysis of the tibia, also known as Cozen's phenomenon. The exact etiology is still under debate. In these cases, the maximum magnitude of deformity is variable, and is reached approximately 12 mo after injury. Parents should be advised of this eventuality and be informed that the deformity tends to resolve spontaneously within 2-4 years and only requires observation. Surgical treatment should be reserved for severe and symptomatic cases or for patients close to skeletal maturity with residual deformity[67]. Some authors report that, to prevent this deformity, the proximal tibial fracture should be treated with a varus-molded long-leg cast, although the efficacy of this procedure has been disputed in the literature[68]. Hemiplateau elevation (HE) is the treatment of choice for growing children with persistent deformity requiring surgery[69]. This must be performed within about three years of the trauma, since deformities tend to migrate distally at the level of the diaphysis during growth. Therefore, delayed HE could lead to a secondary "Z"-shaped deformity of the tibia (varus deformity proximal to the valgus deformity of the diaphysis)[16]. Corrective osteotomy should be avoided in growing children, as it can produce effects similar to the traumatic event itself and accentuate valgus deformity. It may be indicated in patients close to skeletal maturity with residual deformity[16].

TIBIA VARA

Introduction

Tibia vara is a developmental condition characterized by multiplanar deformities dominated by progressive genu varum malalignment caused by a growth alteration of the medial proximal metaphysis, physis and epiphysis of the tibia[70-72]. In 1937 Blount[73] published the first detailed description of this pathology, introducing the term "*osteochondrosis deformans tibiae*". He was the first to identify two forms based on the age of onset: The infantile form and the adolescent form (Table 2). These two forms of tibia vara are clinically and radiographically distinct. The infantile form is when the deformity is noted before the age of 4 and the adolescent form is when the diagnosis is made after the age of 10.

Table 2 Main differences between infantile and adolescent forms of Blount disease

	Infantile form	Adolescent form
Age (yr)	< 5	> 10
Clinical features	50% bilateral, overweight, lateral thrust during gait, possible internal rotation of the tibia	Usually unilateral, overweight/obese, male predominance
X-RAY appearance	Varus angulation at the epiphyseal-metaphyseal junction, metaphyseal beaking with apparent fragmentation, medial physeal line widening and irregularity; lateral tibial subluxation; possible compensatory distal femur valgus	Widening of the proximal medial physeal line, normal shape of the proximal tibial metaphysis; possible presence of distal femur varus and compensatory distal tibial valgus
Natural history	Depending on the stage (spontaneous resolution is possible)	Usually progressive without spontaneous resolution
Treatment options	Depending on the stage	Surgery only

Infantile tibia vara

Clinical findings: Infantile tibia vara is a developmental condition causing progressive varus deformity of the knee in young children. Its prognosis appears to be worse predominantly in the non-white population. The clinical picture of a patient with confirmed Blount disease includes a frequently bilateral (50%), though rarely symmetrical, varus, and variable internal tibial rotation[72]. A positive "cover up test" is also reported in the literature[74]. In some cases, lateral ligament instability with a "varus thrust gait" may be present[75].

Radiographic classification

On a long-leg anteroposterior radiograph, Blount disease typically appears as a varus deformity of the lower limb, presenting lack of ossification of the medial tibial plateau. In the early stages of the disease, the characteristic findings may not be present and it may be difficult to differentiate an idiopathic varus from Blount disease. Levine and Drennan[76] measured the metaphyseal-diaphyseal angle (MDA) on anteroposterior radiographs (Figure 5) for early detection of infantile tibia vara, and reported that an MDA > 10 degrees is suggestive of infantile Blount disease. Although there are discordant data in the literature regarding the usefulness of the MDA, mainly due to poor accuracy of measurement, some authors believe that a toddler may be at risk of Blount disease with a FTA > 20 degrees and an MDA greater than 10 degrees. However, the definitive diagnosis should only be made if the characteristic lesions are present[16]. Infantile tibia vara is traditionally staged using Langenskiöld's classification with six progressive stages, based on the radiographic aspects of the medial proximal tibia and epiphyseal-physeal-metaphyseal alterations[77].

Non-operative treatment

The effectiveness of full-time (23 h a day) long-leg antivarus bracing (*e.g.*, knee-ankle-foot orthosis - KAFO -, elastic KAFO and conventional hip-knee-ankle-foot orthoses) has been reported in certain patients. Patients should be ≤ 3 years old with unilateral involvement and stage ≤ II in Langenskiöld's classification. Patients with bilateral involvement may also benefit from bracing, but it is reported that there is a greater risk of progression and need for surgical correction[78]. However, the effectiveness of bracing has not been demonstrated. Indeed, some researchers advise clinical observation at stages II and III up to the age of 4[79,80].

Surgical treatment

The goals of surgical treatment can be summarized as: (1) Restoring the normal alignment of the proximal tibia by correcting the multiplanar deformity, in order to disrupt the vicious circle of proximal medial tibial alteration and prevent the onset of degenerative arthritis; (2) Preventing physeal damage; and (3) Preventing recurrence in order to limit the number of surgical procedures. It has been shown that surgical treatment in the early stages of the disease (stage II) is crucial to reduce the risk of deformity recurrence and physeal damage. There is strong consensus in the literature on not delaying surgery and on proceeding in cases of: (1) Patients < 4 years with progressive clinical and radiographic evidence of Blount disease; (2) Patients ≥ 4 years, even in stage I and II without signs of spontaneous correction, especially if the deformity exceeds 10 degrees of FTA varus; and (3) Patients in stage ≥ III in Langenskiöld's classification. The main surgical procedures for infantile Blount are as follows.

High tibial and fibular osteotomy: High tibial and fibular osteotomy (HTO) is the treatment that is generally defined as being the choice for stage I to III in Langenskiöld's classification. It is reported that, if HTO is performed in stage I and II, the risk of recurrence is significantly lower than in stage III, where recurrence is not uncommon. The goal of HTO is to fully correct or overcorrect the multiplanar deformity (varus, flexion, and internal rotation) of the proximal tibia (Figure 6). The aim is to interrupt the vicious circle caused by varus alignment and medial compartment overload, and enhance

spontaneous recovery from the local disturbance of growth. For this reason, several authors recommend an overcorrection to 5 degrees of valgus alignment, along with lateral translation of the distal segment in order to unload the medial compartment and lateralize the MA.

The correction can be achieved either acutely, using internal fixation (*e.g.*, Steinmann pins or Kirschner wires), or gradually, using an external fixator. Tibial osteotomy should be performed just distal to the insertion of the patellar tendon and in combination with fibular osteotomy of the proximal third of its diaphysis. The internal rotation deformity of the tibia may be corrected through external rotation of the distal fragment. Some authors suggest prophylactic fasciotomy of the anterior, lateral, and posterior compartments of the leg to prevent compartment syndrome, which has been reported as a complication.

Growth plate modulation: Growth modulation using a TBP is reported to be a valid alternative to HTO. The main indication is stage < II (prior to physeal bar formation) usually in patients younger than 6 years[81-83]. The internal tibial rotational deformity cannot be corrected using growth modulation. Several studies report a high rate of implant failure with breakage of titanium/cannulated screws and some authors recommend using non-cannulated stainless steel screws[84].

Physeal arrest resection: The main indication is the documented presence of a physeal bar prior to frank bony bridge formation (stage IV and V) in patients with at least 2-4 years of growth remaining. The interposition of material (*e.g.*, fat or methyl methacrylate) is a crucial step after medial epiphysiolysis to prevent rebridging. The position and size of the physeal bar should be evaluated preoperatively using advanced imaging [*e.g.*, computed tomography scan or magnetic resonance imaging (MRI)]. Physeal arrest resection is typically combined with HTO to achieve valgus alignment beyond 0 degrees. Andrade *et al*[85] report a success rate of more than 80% for physeal arrest resection in children < 7 years old. The results were less predictable in patients older than 7 years or who had previously undergone surgery, and the authors recommend alternative treatment methods for these patients.

HE: The main indication is patients older than 10 years with high-grade deformity associated with intraarticular deformity and joint incongruence caused by medial tibial plateau depression. Preoperative advanced imaging (*e.g.*, MRI) is mandatory to confirm joint incongruence. Indeed, X-ray may overestimate the intraarticular deformity, showing a severe medial ossification defect and depression, and the joint cartilage can maintain joint congruity. Intraoperative arthrography may also provide a better picture of the actual geometry of the joint surfaces. HE can be combined with metaphyseal tibial osteotomy to address the remaining long-bone deformity. Lateral proximal tibial and proximal fibular epiphysiodesis are recommended in combination with HE to prevent recurrent deformity.

Limb-length equalization procedures: LLD can be a component of the Blount deformity. Correction of the angular deformity using open-wedge HTO may equalize the LLD. In other cases, lengthening by distraction osteogenesis can be combined with gradual deformity correction using an external fixation device, performed alone as necessary, or limb-length equalization can be achieved by performing contralateral epiphysiodesis.

Adolescent tibia vara

Observation is usually considered for mild cases only and there are no data available on the use of an orthosis. Opening or closing wedge HTO is the treatment of choice in cases of severe (> 20 degrees) varus deformity or in cases of multiplanar deformity (varus, procurvatum and internal rotation). Acute deformity correction is usually suggested in uniplanar or milder cases, whereas gradual correction using an external fixator, particularly a hexapod system, is useful in cases of severe varus deformity or complex multiplanar deformity.

Lateral hemiepiphysiodesis. Good results have been reported, but patients should be carefully selected to avoid failure. The main indications are sufficient remaining growth (< 14 years old), BMI < 40 kg/m^2, body weight < 100 kg, and less than 15 degrees of varus malalignment[82].

Medial hemichondrodiastasis. This is reported to be effective in patients with moderate varus deformity (< 20 degrees) who are nearing skeletal maturity. This technique has two main advantages: It corrects the varus and the LLD simultaneously, and it entails permanent epiphysiodesis, which reduces the risk of recurrence.

CONCLUSION

Coronal plane deformities around the knee are common during childhood and are usually a cause of serious concern for parents. Physiological variations in the growth and development of children need no treatment other than observation. True deformities need proper management to avoid consequences. Treatment should be tailored to the underlying disease and associated deformities on the other axis (*e.g.*, rotation or shortening) should be ruled out. As a general rule, modulation surgery should be the treatment of choice in patients with sufficient residual growth, whereas deformities in skeletally mature

patients require osteotomy or distraction osteogenesis.

FOOTNOTES

Author contributions: Coppa V and Gigante A wrote the paper; Marinelli M, Procaccini R, Falcioni D and Farinelli L collected the data.

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REFERENCES

1 **Paley D**. Principles of Deformity Correction. In: Paley D. Normal Lower Limb Alignment and Joint Orientation. Heidelberg: Springer, 2002: 1-18
2 **Salenius P**, Vankka E. The development of the tibiofemoral angle in children. *J Bone Joint Surg Am* 1975; **57**: 259-261 [PMID: 1112851]
3 **Sabharwal S**, Zhao C, Edgar M. Lower limb alignment in children: reference values based on a full-length standing radiograph. *J Pediatr Orthop* 2008; **28**: 740-746 [PMID: 18812900 DOI: 10.1097/BPO.0b013e318186eb79]
4 **Moreland JR**, Bassett LW, Hanker GJ. Radiographic analysis of the axial alignment of the lower extremity. *J Bone Joint Surg Am* 1987; **69**: 745-749 [PMID: 3597474]
5 **Brooks WC**, Gross RH. Genu Varum in Children: Diagnosis and Treatment. *J Am Acad Orthop Surg* 1995; **3**: 326-335 [PMID: 10790671 DOI: 10.5435/00124635-199511000-00003]
6 **White GR**, Mencio GA. Genu Valgum in Children: Diagnostic and Therapeutic Alternatives. *J Am Acad Orthop Surg* 1995; **3**: 275-283 [PMID: 10795033 DOI: 10.5435/00124635-199509000-00003]
7 **Staheli LT**. Practice of Pediatric Orthopaedic. In: Mosca V. Lower Limb. Seattle: Lippincott Williams & Wilkins, 2006: 77-104
8 **Hsu RW**, Himeno S, Coventry MB, Chao EY. Normal axial alignment of the lower extremity and load-bearing distribution at the knee. *Clin Orthop Relat Res* 1990; 215-227 [PMID: 2347155]
9 **Cahuzac JP**, Vardon D, Sales de Gauzy J. Development of the clinical tibiofemoral angle in normal adolescents. A study of 427 normal subjects from 10 to 16 years of age. *J Bone Joint Surg Br* 1995; **77**: 729-732 [PMID: 7559698]
10 **Gupta P**, Gupta V, Patil B, Verma V. Angular deformities of lower limb in children: Correction for whom, when and how? *J Clin Orthop Trauma* 2020; **11**: 196-201 [PMID: 32099279 DOI: 10.1016/j.jcot.2020.01.008]
11 **Saran N**, Rathjen KE. Guided growth for the correction of pediatric lower limb angular deformity. *J Am Acad Orthop Surg* 2010; **18**: 528-536 [PMID: 20810934 DOI: 10.5435/00124635-201009000-00004]
12 **Heath CH**, Staheli LT. Normal limits of knee angle in white children--genu varum and genu valgum. *J Pediatr Orthop* 1993; **13**: 259-262 [PMID: 8459023]
13 **Engel GM**, Staheli LT. The natural history of torsion and other factors influencing gait in childhood. A study of the angle of gait, tibial torsion, knee angle, hip rotation, and development of the arch in normal children. *Clin Orthop Relat Res* 1974; 12-17 [PMID: 4825705 DOI: 10.1097/00003086-197403000-00002]
14 **Yeo A**, James K, Ramachandran M. Normal lower limb variants in children. *BMJ* 2015; **350**: h3394 [PMID: 26152216 DOI: 10.1136/bmj.h3394]
15 **Kaspiris A**, Zaphiropoulou C, Vasiliadis E. Range of variation of genu valgum and association with anthropometric characteristics and physical activity: comparison between children aged 3-9 years. *J Pediatr Orthop B* 2013; **22**: 296-305 [PMID: 23563283 DOI: 10.1097/BPB.0b013e328360f9a5]
16 **Herring JA**. Tachdjian's Pediatric Orthopaedics: From the Texas Scottish Rite Hospital for Children. 5th ed. In: Johnston CE, Young M. Disorders of the Leg. Philadelphia: Elsevier, 2013: 713-761
17 **Paley D**, Tetsworth K. Mechanical axis deviation of the lower limbs. Preoperative planning of uniapical angular deformities of the tibia or femur. *Clin Orthop Relat Res* 1992; 48-64 [PMID: 1611764]
18 **Paley D**, Herzenberg JE, Tetsworth K, McKie J, Bhave A. Deformity planning for frontal and sagittal plane corrective

osteotomies. *Orthop Clin North Am* 1994; **25**: 425-465 [PMID: 8028886]
19 **Boero S**, Michelis MB, Riganti S. Use of the eight-Plate for angular correction of knee deformities due to idiopathic and pathologic physis: initiating treatment according to etiology. *J Child Orthop* 2011; **5**: 209-216 [PMID: 22654982 DOI: 10.1007/s11832-011-0344-4]
20 **Felson DT**, Niu J, Gross KD, Englund M, Sharma L, Cooke TD, Guermazi A, Roemer FW, Segal N, Goggins JM, Lewis CE, Eaton C, Nevitt MC. Valgus malalignment is a risk factor for lateral knee osteoarthritis incidence and progression: findings from the Multicenter Osteoarthritis Study and the Osteoarthritis Initiative. *Arthritis Rheum* 2013; **65**: 355-362 [PMID: 23203672 DOI: 10.1002/art.37726]
21 **Janakiramanan N**, Teichtahl AJ, Wluka AE, Ding C, Jones G, Davis SR, Cicuttini FM. Static knee alignment is associated with the risk of unicompartmental knee cartilage defects. *J Orthop Res* 2008; **26**: 225-230 [PMID: 17763451 DOI: 10.1002/jor.20465]
22 **Tetsworth K**, Paley D. Malalignment and degenerative arthropathy. *Orthop Clin North Am* 1994; **25**: 367-377
23 **Stevens PM**, Maguire M, Dales MD, Robins AJ. Physeal stapling for idiopathic genu valgum. *J Pediatr Orthop* 1999; **19**: 645-649 [PMID: 10488868]
24 **HierholzerK G**, Müller H. Corrective Osteotomies of the Lower Extremity after Trauma. In: Müller KH, Müller-Färber J. Indications, Localization and Planning of Posttraumatic Osteotomies about the Knee. Heidelberg: Springer, 1985: 195-223
25 **Paley D**. Principles of Deformity Correction. Heidelberg: Springer, 2002 [DOI: 10.1007/978-3-642-59373-4]
26 **Wright JG**, Treble N, Feinstein AR. Measurement of lower limb alignment using long radiographs. *J Bone Joint Surg Br* 1991; **73**: 721-723 [PMID: 1894657 DOI: 10.1302/0301-620X.73B5.1894657]
27 **Sabharwal S**. Pediatric Lower Limb Deformities. In: Miller ML, Eric Gordon J. Decision making in lower extremity deformity correction. New York: Springer, 2016: 37-50
28 **Ghanem I**, Karam JA, Widmann RF. Surgical epiphysiodesis indications and techniques: update. *Curr Opin Pediatr* 2011; **23**: 53-59 [PMID: 21169837 DOI: 10.1097/MOP.0b013e32834231b3]
29 **Phemister DB**. Operative arrestment of longitudinal growth of bones in the treatment of deformities. *J Bone Joint Surg Br* 1933; **15**: 1-15
30 **Terry Canale S**. Percutaneous epiphysiodesis. *Oper Tech Orthop* 1993; **3**: 161-165 [DOI: 10.1016/S1048-6666(06)80036-4]
31 **Métaizeau JP**, Wong-Chung J, Bertrand H, Pasquier P. Percutaneous epiphysiodesis using transphyseal screws (PETS). *J Pediatr Orthop* 1998; **18**: 363-369 [PMID: 9600565]
32 **Dodwell ER**, Garner MR, Bixby E, Luderowski EM, Green DW, Blanco JS, Widmann RF. Percutaneous Epiphysiodesis Using Transphyseal Screws: a Case Series Demonstrating High Efficacy. *HSS J* 2017; **13**: 255-262 [PMID: 28983218 DOI: 10.1007/s11420-017-9549-5]
33 **Ruzbarsky JJ**, Goodbody C, Dodwell E. Closing the growth plate: a review of indications and surgical options. *Curr Opin Pediatr* 2017; **29**: 80-86 [PMID: 27845969 DOI: 10.1097/MOP.0000000000000438]
34 **Woo K**, Lee YS, Lee WY, Shim JS. The Efficacy of Percutaneous Lateral Hemiepiphysiodesis on Angular Correction in Idiopathic Adolescent Genu Varum. *Clin Orthop Surg* 2016; **8**: 92-98 [PMID: 26929805 DOI: 10.4055/cios.2016.8.1.92]
35 **Ferrick MR**, Birch JG, Albright M. Correction of non-Blount's angular knee deformity by permanent hemiepiphyseodesis. *J Pediatr Orthop* 2004; **24**: 397-402 [PMID: 15205622 DOI: 10.1097/00004694-200407000-00010]
36 **Gottliebsen M**, Shiguetomi-Medina JM, Rahbek O, Møller-Madsen B. Guided growth: mechanism and reversibility of modulation. *J Child Orthop* 2016; **10**: 471-477 [PMID: 27826908 DOI: 10.1007/s11832-016-0778-9]
37 **Frost HM**. A chondral modeling theory. *Calcif Tissue Int* 1979; **28**: 181-200 [PMID: 92358 DOI: 10.1007/BF02441236]
38 **Haas SL**. Retardation of bone growth by a wire loop. *J Bone Jt Surg - Am Vol* 1945; **27**: 25-36
39 **Blount WP**, Clarke GR. Control of bone growth by epiphyseal stapling; a preliminary report. *J Bone Joint Surg Am* 1949; **31A**: 464-478 [PMID: 18153890]
40 **Stevens PM**. Guided growth for angular correction: a preliminary series using a tension band plate. *J Pediatr Orthop* 2007; **27**: 253-259 [PMID: 17414005 DOI: 10.1097/BPO.0b013e31803433a1]
41 **Narayana Kurup JK**, Shah HH. Hemiepiphysiodesis using 2-holed reconstruction plate for correction of angular deformity of the knee in children. *J Orthop* 2020; **20**: 54-59 [PMID: 32042230 DOI: 10.1016/j.jor.2020.01.001]
42 **Goyeneche RA**, Primomo CE, Lambert N, Miscione H. Correction of bone angular deformities: experimental analysis of staples versus 8-plate. *J Pediatr Orthop* 2009; **29**: 736-740 [PMID: 20104155 DOI: 10.1097/BPO.0b013e3181b529fc]
43 **Eltayeby HH**, Iobst CA, Herzenberg JE. Hemiepiphysiodesis using tension band plates: does the initial screw angle influence the rate of correction? *J Child Orthop* 2019; **13**: 62-66 [PMID: 30838077 DOI: 10.1302/1863-2548.13.180086]
44 **Kadhim M**, Hammouda AI, Herzenberg JE. The "Sleeper" plate: A technical note. *J Limb Lengthen Reconstr* 2019; **5**: 27-32 [DOI: 10.4103/jllr.jllr_2_19]
45 **Keshet D**, Katzman A, Zaidman M, Eidelman M. Removal of Metaphyseal Screw Only After Hemiepiphysiodesis Correction of Coronal Plane Deformities Around the Knee Joint: Is This a Safe and Advisable Strategy? *J Pediatr Orthop* 2019; **39**: e236-e239 [PMID: 30222639 DOI: 10.1097/BPO.0000000000001257]
46 **Shabtai L**, Herzenberg JE. Limits of Growth Modulation Using Tension Band Plates in the Lower Extremities. *J Am Acad Orthop Surg* 2016; **24**: 691-701 [PMID: 27564792 DOI: 10.5435/JAAOS-D-14-00234]
47 **Oto M**, Yılmaz G, Bowen JR, Thacker M, Kruse R. Adolescent Blount disease in obese children treated by eight-plate hemiepiphysiodesis. *Eklem Hastalik Cerrahisi* 2012; **23**: 20-24 [PMID: 22448825]
48 **Joeris A**, Ramseier L, Langendörfer M, von Knobloch M, Patwardhan S, Dwyer J, Slongo T. Paediatric lower limb deformity correction with the Eight Plate: adverse events and correction outcomes of 126 patients from an international multicentre study. *J Pediatr Orthop B* 2017; **26**: 441-448 [PMID: 27832012 DOI: 10.1097/BPB.0000000000000397]
49 **Jelinek EM**, Bittersohl B, Martiny F, Scharfstädt A, Krauspe R, Westhoff B. The 8-plate versus physeal stapling for temporary hemiepiphyseodesis correcting genu valgum and genu varum: a retrospective analysis of thirty five patients. *Int Orthop* 2012; **36**: 599-605 [PMID: 21983939 DOI: 10.1007/s00264-011-1369-5]
50 **Hosseinzadeh P**, Ross DR, Walker JL, Talwalkar VR, Iwinski HJ, Milbrandt TA. Three Methods Of Guided Growth For

Pediatric Lower Extremity Angular Deformity Correction. *Iowa Orthop J* 2016; **36**: 123-127 [PMID: 27528848]
51 **Zuege RC**, Kempken TG, Blount WP. Epiphyseal stapling for angular deformity at the knee. *J Bone Joint Surg Am* 1979; **61**: 320-329 [PMID: 429399]
52 **Kadhim M**, Hammouda AI, Herzenberg JE. Solid screw insertion for tension band plates: a surgical technique tip. *J Child Orthop* 2016; **10**: 307-311 [PMID: 27312797 DOI: 10.1007/s11832-016-0748-2]
53 **Leveille LA**, Razi O, Johnston CE. Rebound Deformity After Growth Modulation in Patients With Coronal Plane Angular Deformities About the Knee: Who Gets It and How Much? *J Pediatr Orthop* 2019; **39**: 353-358 [PMID: 31305378 DOI: 10.1097/BPO.0000000000000935]
54 **Bowen JR**, Leahey JL, Zhang ZH, MacEwen GD. Partial epiphysiodesis at the knee to correct angular deformity. *Clin Orthop Relat Res* 1985; 184-190 [PMID: 4028549]
55 **Inan M**, Chan G, Bowen JR. Correction of angular deformities of the knee by percutaneous hemiepiphysiodesis. *Clin Orthop Relat Res* 2007; **456**: 164-169 [PMID: 17065845 DOI: 10.1097/01.blo.0000246560.65714.c8]
56 **Eltayeby HH**, Gwam CU, Frederick MM, Herzenberg JE. How Accurate is the Multiplier Method in Predicting the Timing of Angular Correction After Hemiepiphysiodesis? *J Pediatr Orthop* 2019; **39**: e91-e94 [PMID: 30376494 DOI: 10.1097/BPO.0000000000001278]
57 **Wu Z**, Ding J, Zhao D, Zhao L, Li H, Liu J. Multiplier method may be unreliable to predict the timing of temporary hemiepiphysiodesis for coronal angular deformity. *J Orthop Surg Res* 2017; **12**: 104 [PMID: 28693513 DOI: 10.1186/s13018-017-0604-1]
58 **Paley D**. Principles of Deformity Correction. In: Osteotomy Concepts and Frontal Plane Realignment. Heidelberg: Springer, 2002: 99-154 [DOI: 10.1007/978-3-642-59373-4_5]
59 **Paley D**. Principles of Deformity Correction. In: Length Considerations: Gradual Versus Acute Correction of Deformities. Heidelberg: Springer, 2002: 269-289 [DOI: 10.1007/978-3-642-59373-4_10]
60 **Riganti S**, Nasto LA, Mannino S, Marrè Brunenghi G, Boero S. Correction of complex lower limb angular deformities with or without length discrepancy in children using the TL-HEX hexapod system: comparison of clinical and radiographical results. *J Pediatr Orthop B* 2019; **28**: 214-220 [PMID: 30531204 DOI: 10.1097/BPB.0000000000000573]
61 **Smith JO**, Wilson AJ, Thomas NP. Osteotomy around the knee: evolution, principles and results. *Knee Surg Sports Traumatol Arthrosc* 2013; **21**: 3-22 [PMID: 23052110 DOI: 10.1007/s00167-012-2206-0]
62 **Kamegaya M**, Shinohara Y, Shinada Y. Limb lengthening and correction of angulation deformity: immediate correction by using a unilateral fixator. *J Pediatr Orthop* 1996; **16**: 477-479 [PMID: 8784700 DOI: 10.1097/00004694-199607000-00010]
63 **Nogueira MP**, Paley D. Prophylactic and Therapeutic Peroneal Nerve Decompression for Deformity Correction and Lengthening. *Oper Tech Orthop* 2011; **21**: 180-183 [DOI: 10.1053/j.oto.2011.01.001]
64 **Tunggal JA**, Higgins GA, Waddell JP. Complications of closing wedge high tibial osteotomy. *Int Orthop* 2010; **34**: 255-261 [PMID: 19547973 DOI: 10.1007/s00264-009-0819-9]
65 **Hresko MT**, Kasser JR. Physeal arrest about the knee associated with non-physeal fractures in the lower extremity. *J Bone Joint Surg Am* 1989; **71**: 698-703 [PMID: 2732259]
66 **Dabash S**, Prabhakar G, Potter E, Thabet AM, Abdelgawad A, Heinrich S. Management of growth arrest: Current practice and future directions. *J Clin Orthop Trauma* 2018; **9**: S58-S66 [PMID: 29628701 DOI: 10.1016/j.jcot.2018.01.001]
67 **Papamerkouriou YM**, Tsoumpos P, Tagaris G, Christodoulou G. Does Cozen's phenomenon warrant surgical intervention? *J Child Orthop* 2020; **14**: 213-220 [PMID: 32582389 DOI: 10.1302/1863-2548.14.190147]
68 **Burton A**, Hennrikus W. Cozen's phenomenon revisited. *J Pediatr Orthop B* 2016; **25**: 551-555 [PMID: 27182753 DOI: 10.1097/BPB.0000000000000327]
69 **Morin M**, Klatt J, Stevens PM. Cozen's deformity: resolved by guided growth. *Strategies Trauma Limb Reconstr* 2018; **13**: 87-93 [PMID: 29549568 DOI: 10.1007/s11751-018-0309-y]
70 **Sabharwal S**. Blount disease. *J Bone Joint Surg Am* 2009; **91**: 1758-1776 [PMID: 19571101 DOI: 10.2106/JBJS.H.01348]
71 **Sabharwal S**. Blount disease: an update. *Orthop Clin North Am* 2015; **46**: 37-47 [PMID: 25435033 DOI: 10.1016/j.ocl.2014.09.002]
72 **Janoyer M**. Blount disease. *Orthop Traumatol Surg Res* 2019; **105**: S111-S121 [PMID: 29481866 DOI: 10.1016/j.otsr.2018.01.009]
73 **Blount WP**. Tibia Vara. *J Bone Joint Surg* 1937; **19**: 1-29
74 **Davids JR**, Blackhurst DW, Allen BL Jr. Clinical evaluation of bowed legs in children. *J Pediatr Orthop B* 2000; **9**: 278-284 [PMID: 11143472 DOI: 10.1097/01202412-200010000-00012]
75 **Birch JG**. Blount disease. *J Am Acad Orthop Surg* 2013; **21**: 408-418 [PMID: 23818028 DOI: 10.5435/JAAOS-21-07-408]
76 **Levine AM**, Drennan JC. Physiological bowing and tibia vara. The metaphyseal-diaphyseal angle in the measurement of bowleg deformities. *J Bone Joint Surg Am* 1982; **64**: 1158-1163 [PMID: 7130229]
77 **Langenskiold A**. Tibia vara; (osteochondrosis deformans tibiae); a survey of 23 cases. *Acta Chir Scand* 1952; **103**: 1-22 [PMID: 14923172]
78 **Richards BS**, Katz DE, Sims JB. Effectiveness of brace treatment in early infantile Blount's disease. *J Pediatr Orthop* 1998; **18**: 374-380 [PMID: 9600567]
79 **Shinohara Y**, Kamegaya M, Kuniyoshi K, Moriya H. Natural history of infantile tibia vara. *J Bone Joint Surg Br* 2002; **84**: 263-268 [PMID: 11922370 DOI: 10.1302/0301-620x.84b2.11821]
80 **Vasiliadis AV**, Maris A, Gadikoppula S. Tibia vara or Blount's disease: Why an early diagnosis and treatment are important? *Clin Pract* 2020; **10**: 1222 [PMID: 32419907 DOI: 10.4081/cp.2020.1222]
81 **Heflin JA**, Ford S, Stevens P. Guided growth for tibia vara (Blount's disease). *Medicine (Baltimore)* 2016; **95**: e4951 [PMID: 27741108 DOI: 10.1097/MD.0000000000004951]
82 **Danino B**, Rödl R, Herzenberg JE, Shabtai L, Grill F, Narayanan U, Gigi R, Segev E, Wientroub S. The efficacy of guided growth as an initial strategy for Blount disease treatment. *J Child Orthop* 2020; **14**: 312-317 [PMID: 32874365 DOI: 10.1302/1863-2548.14.200070]
83 **Griswold BG**, Shaw KA, Houston H, Bertrand S, Cearley D. Guided growth for the Treatment of Infantile Blount's

disease: Is it a viable option? *J Orthop* 2020; **20**: 41-45 [PMID: 32042227 DOI: 10.1016/j.jor.2020.01.007]

84 **Burghardt RD**, Specht SC, Herzenberg JE. Mechanical failures of eight-plateguided growth system for temporary hemiepiphysiodesis. *J Pediatr Orthop* 2010; **30**: 594-597 [PMID: 20733426 DOI: 10.1097/BPO.0b013e3181e4f591]

85 **Andrade N**, Johnston CE. Medial epiphysiolysis in severe infantile tibia vara. *J Pediatr Orthop* 2006; **26**: 652-658 [PMID: 16932107 DOI: 10.1097/01.bpo.0000230338.03782.75]

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ORIGINAL ARTICLE

Retrospective Study

Insufficient lateral stem contact is an influencing factor for significant subsidence in cementless short stem total hip arthroplasty

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Abstract

BACKGROUND

Subsidence is one of the concerning early complications in cementless femoral stem. Few publications have studied the influencing factors for subsidence in short cementless stems, due to their metaphyseal anchoring without diaphyseal invasion, they might demonstrate different subsidence patterns than with the conventional stems.

AIM

To analyze the factors associated with significant subsidence in short stems, including any radiographic parameters.

METHODS

The digitized radiographs of 274 consecutive short stem total hip arthroplasties were retrospectively reviewed. Subsidence, neck-filling ratio (NFR), seating height and lateral stem contact were evaluated after a minimum of two years follow-up. A threshold of subsidence > 3 mm was considered a clinically significant migration.

RESULTS

For the entire cohort, subsidence occurred in 75 cases (27.4%) with the mean stem subsidence of 0.5 mm. (0-12.7, 1.68). Twelve hips (4.4%) had significant subsidence (> 3 mm). The univariate regression analysis demonstrated that age, diagnosis, BMI, Dorr's type B, NFR, and seating height had no significant influence on significant subsidence, whereas insufficient lateral stem contact (≥ 1 mm) did have a statistically significant influence [Odds ratio (OR) = 5.02; 95%CI: 1.3-18.9; P = 0.017]. The multivariate regression analysis also demonstrated that insufficient lateral stem contact was a statistically significant influencing factor (OR = 5.5;

95%CI: 1.4-21.4; P = 0.014). There was no femoral stem revision for aseptic loosening in our cohort.

CONCLUSION

This study demonstrated that insufficient lateral stem contact was a statistically significant influencing factor on significant subsidence. Therefore, it is a particularly important step to create proper lateral cortical contact when performing the short stem total hip arthroplasty.

Key Words: Total hip arthroplasty; Short stem; Subsidence; Metaphyseal anchorage; Metha

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Core Tip: Short stem total hip arthroplasties (THAs) are commonly used in young and active patients. The advantages of these stems include more proximal load transfer which reduces stress shielding and, thigh pain, and they provide better options should revision surgery become necessary. Subsidence is one of the concerning complications in cementless femoral fixation. It is particularly important to identify the key intraoperative decision criteria to predict post-implantation subsidence of the short stem, which should be useful for choosing the proper size and position of the short stem and for allowance of early weight bearing post-operatively. This study demonstrated that insufficient lateral stem contact was a statistically significant influencing factor on significant subsidence. Therefore, it is a particularly important step to create proper lateral cortical contact when performing the short stem THA.

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INTRODUCTION

Cementless femoral stem in total hip arthroplasty (THA) is one of the most successful procedures in orthopaedic surgery[1]. Short stem THAs are commonly used in young and active patients. The advantages of these stems include more proximal load transfer which reduces stress shielding and, thigh pain, and they provide better options should revision surgery become necessary[2]. Short stem THA has shown excellent results in patients with primary osteoarthritis[3-5], osteonecrosis of the femoral head (ONFH)[6-9] and developmental dysplasia of the hip (DDH)[10,11] in many previous studies.

Subsidence is one of the concerning complications in cementless femoral fixation. It can lead to limb length discrepancy, decreased hip stability, or even implant failure. In conventional cementless stems, several previous studies have revealed the relationship between subsidence and stem survivorship[12, 13], and some studies demonstrated the relationship between percentage of canal fill and subsidence[14, 15]. However, few publications have studied the influencing factors for subsidence in short cementless stems, due to their metaphyseal anchoring without diaphyseal invasion, they might demonstrate different subsidence patterns than with the conventional stems. The purpose of this study is to analyze the factors associated with subsidence in short stems, including any radiographic parameters after a minimum of two years follow-up.

MATERIALS AND METHODS

This research has been approved by the IRB of the authors' affiliated institutions. The digitized radiographs of patients who had undergone short stem THA in our institute between January 2011 and December 2018 were retrospectively reviewed. According to previous study showed that the short stem subsided at the initial phase of about 3-6 mo after implantation and then no further subsidence was observed at two years follow-up[16]. Therefore, the inclusion criteria in this study were patients aged > 18 years with complete radiographic data at a minimum of two years follow-up. Because the Metha stem was designed for metaphyseal fitting without diaphyseal anchorage which suitable for patients with good bone quality, therefore, we excluded patients with osteoporotic bone. Patients with history of previous surgical treatment on the hip was also excluded.

All THAs in this study were performed using Metha short stem by two experienced surgeons (Suksathien Y, Sueajui J), through a modified Hardinge approach. The Metha short stem is cementless, tapered, collarless, and made of titanium forged alloy (Ti6A14V) with suggested metaphyseal anchorage within the closed ring of the femoral neck. This stem is available in 5 sizes (0, 1, 2, 3 and 4) and 3 caput-column-diaphysis angles (120°, 130° and 135°). The Metha short stem is round coated with Plasmapore, a calcium phosphate layer, for osseointegration (Figure 1). In all cases the femoral neck was cut above the notch of the femoral neck at an angle of 50° to the femoral axis to create a closed cortical ring[17]. Intra-operative calcar cracks that occurred incidentally were routinely treated with cerclage wire. The Metha short stem was classified as type IIA according to Khanuja *et al*[18]; type I is femoral neck only, type II is calcar loading, type III is calcar loading with lateral flare, and type IV is shortened tapered stem. Additionally, type 2 stems are categorized into 4 subtypes: A, trapezoidal; B, round; C, threaded; and D, thrust plate. The cementless acetabular cup (Plasmafit, B.Braun Aesculap, Tuttlingen, Germany) with polyethelene liner (Vitelene, Vit E Stabilized Highly Crosslinked Polyethelene, B.Braun Aesculap, Tuttlingen, Germany) and metal head was used in all cases with the target angles for acetabular cup abduction and anteversion were 40° and 15° respectively. The femoral head diameter depended on cup size, 32 mm for cup diameter 50 mm or less, and 36 mm for cup diameter 52 mm or more.

Patients were allowed to stand and progress to full weight-bearing using crutches on the second post-operative day. The standard protocol for anteroposterior (AP) digital radiograph of both hips with both legs at 15° internal rotation and lateral cross-table, to control femoral stem rotation, was taken on the first post-operative day and at each follow-up radiograph. Patients were routinely contacted every three months in the first post-operative year and then every six months thereafter.

Pre-operative radiographs were assessed by using mediolateral cortical index as per Dorr *et al*[19]. Post-operative AP digital radiographs were calibrated with known femoral head size to minimize magnification error. The line from upper border of lessor trochanter to the notch of the femoral neck was defined as the base of femoral neck level. The Metha stem is designed for metaphyseal anchorage within the cortical ring of the femoral neck[17]; therefore, the neck-filling ratio (NFR) at the base of femoral neck level was defined, as the implant width divided by the distance from the inner cortex of the medial femoral neck to the inner cortex of the notch of the femoral neck. The distance from the shoulder point of the stem perpendicular to the base of the femoral neck level in millimeters was defined as the seating height of the femoral stem. Stem subsidence was calculated as the different distance from the shoulder point of the stem to the most prominent point of the greater trochanter between the first post-operative day and at two years follow-up by AP radiograph[20]. The subsidence threshold of more than 3 mm was considered as clinically significant subsidence[21,22]. A lateral stem contact was defined as the distance between the most lateral point of the stem and the inner lateral femoral cortex; a distance of less than 1 mm was defined as sufficient contact[23] (Figure 2).

Two independent observers (Tippimanchai T, Chuvanichanon P) measured each radiograph, and measurements were averaged into one final value after confirming that data reliability between the observers was sufficient. For the intra-observer reliability, the intraclass correlation coefficients (ICCs) for NFR were 0.85 (95%CI: 0.72-0.93) and 0.83 (95%CI: 0.68-0.91), for seating height they were 0.99 (95%CI: 0.99-0.99) and 0.98 (95%CI: 0.98-0.99), for lateral stem contact they were 0.98 (95%CI: 0.97-0.99) and 0.97 (95%CI: 0.95-0.99) and for subsidence they were 0.99 (95%CI: 0.99-0.99) and 0.99 (95%CI: 0.99-1.0) for observer 1 and observer 2, respectively. For the inter-observer reliability, the ICC for NFR was 0.77 (95%CI: 0.71-0.81), for seating height it was 0.99 (95%CI: 0.99-0.99), lateral stem contact was 0.97 (95%CI: 0.96-0.98), and subsidence was 0.99 (95%CI: 0.98-0.99) (Table 1).

Statistical analysis

The mean, SD, lowest and highest values, and ratio were used in the descriptive statistics of data. Mean subsidence between NFR < 0.8 and ≥ 0.8, seating height < 5 and ≥ 5 mm and lateral stem contact < 1 and ≥ 1 mm groups were compared using unpaired *t*-test. Univariate regression analysis was used to identify the factors related to significant subsidence including age (≥ 60 yr), diagnosis, body mass index (BMI) (≥ 30 kg/m^2), Dorr's type B, NFR (< 0.8)[24], seating height (< 5 mm)[17], and insufficient lateral stem contact (≥ 1 mm)[23]. Multivariate regression analysis was also conducted to assess the effect of insufficient lateral stem contact on significant subsidence. SPSS version 25.0 (SPSS Inc., Chicago, IL) was used for all statistical analyses with $P < 0.05$ defined as statistically significant.

RESULTS

There were 322 Metha stem THAs in the study period, 1 case died 1 year after surgery from a condition unrelated to the arthroplasty, 47 cases were lost before a minimum of two years follow-up, leaving 274 cases which including 186 males (67.9%) and 88 females (32.1%) to study. Their mean age was 48.1 years (range, 18-73 years) with a mean BMI of 23.8 (range, 14.7-40.9). There were 223 cases (81.4%) of Dorr's type A and 51 cases (18.6%) of type B. The diagnoses included 213 cases (77.7%) of ONFH, 33 cases (12.1%) of DDH, 19 cases (6.9%) of primary osteoarthritis of the hip and 9 cases (3.3%) of femoral neck

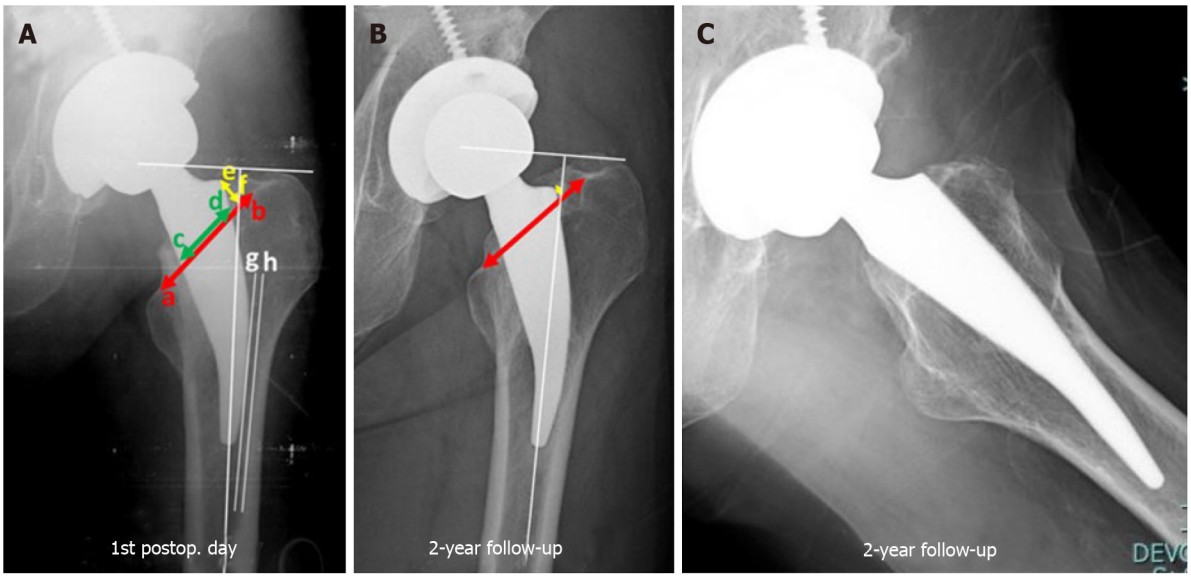
Table 1 Intraclass correlation coefficients

	Neck-filling ratio	Seating height	Lateral stem contact	Subsidence
Intra-observer				
Observer 1	0.85 (95%CI: 0.72-0.93)	0.99 (95%CI: 0.99-0.99)	0.98 (95%CI: 0.97-0.99)	0.99 (95%CI: 0.99-0.99)
Observer 2	0.83 (95%CI: 0.68-0.91)	0.98 (95%CI: 0.98-0.99)	0.97 (95%CI: 0.95-0.99)	0.99 (95%CI: 0.99-1.0)
Inter-observer	0.77 (95%CI: 0.71-0.81)	0.99 (95%CI: 0.99-0.99)	0.97 (95%CI: 0.96-0.98)	0.99 (95%CI: 0.98-0.99)



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Figure 1 Photograph shows the Metha short stem.



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Figure 2 Radiograph images. A: The 1st post-operative day; B: 2-year follow-up anteroposterior; C: Lateral radiographs. Neck-filling ratio is distance from c to d divided by a to b. Seating height is distance from e to f. Lateral stem contact is distance between line g and h.

fractures (Table 2).

For the entire cohort, subsidence occurred in 75 cases (27.4%) with the mean stem subsidence of 0.5 mm. (0-12.7, 1.68). In most subsided cases the subsidence was occurred at the initial phase of about 3-6 mo after surgery and then no further subsidence was observed at two years follow-up. For the radiographic parameters, the mean subsidence of NFR < 0.8 and ≥ 0.8 groups were 0.5 mm. (0-11.89, 1.44) and 0.5 mm. (0-12.7, 2.02), of seating height < 5 and ≥ 5 mm groups were 0.51 mm. (0-12.7, 0.16) and 0.50 mm. (0-11.89, 0.11) respectively, there was no statistically significant difference with $P = 0.99$ in both compared groups. The mean subsidence of lateral stem contact < 1 and ≥ 1 mm groups were 0.39 mm. (0-11.89, 1.26) and 0.71 mm. (0-12.7, 1.94) respectively, there was no statistically significant difference ($P = 0.09$) (Table 3). Lateral cortical hypertrophy was detected on two years follow-up AP

Table 2 Demographic data

Parameters	Values
No. of hips	274
Gender (male/female)	186/88
mean age (yr) (range, SD)	48.1 (18-73, 11.2)
mean BMI (range, SD) (kg/m^2)	23.8 (14.7-40.9, 4.3)
Dorr's classification, *n* (%)	
Dorr's type A	223 (81.4)
Dorr's type B	51 (18.6)
Diagnosis, *n* (%)	
ONFH	213 (77.7)
DDH	33 (12.1)
Primary osteoarthritis of the hip	19 (6.9)
Femoral neck fracture	9 (3.3)

BMI: Body mass index; ONFH: Osteonecrosis of the femoral head; DDH: Developmental dysplasia of the hip.

Table 3 Results of subsidence of any radiographic parameters in the entire cohort

Parameters (*n*)	Value, mean (mm) (range, SD)	*P* value
Subsidence of the entire cohort (75/274)	0.5 (0-12.7, 1.68)	
Subsidence of any radiographic parameters		
Neck-filling ratio < 0.8 (232)	0.51 (0-11.89, 1.44)	0.99
Neck-filling ratio ≥ 0.8 (42)	0.5 (0-12.7, 2.02)	
Seating height < 5 mm (110)	0.51 (0-12.7, 0.16)	0.99
Seating height ≥ 5 mm (164)	0.5 (0-11.89, 0.11)	
Lateral stem contact < 1 mm (178)	0.39 (0-11.89, 1.26)	0.09
Lateral stem contact ≥ 1 mm (96)	0.71 (0-12.7, 1.94)	

radiograph in 10 cases (5.03%) of non-subsided group and 3 cases (4%) in subsided group.

Twelve hips (4.4%) had significant subsidence (> 3 mm) with the mean of 6.7 mm. (3.21-12.7), including 7 cases of Dorr's type A and 5 cases of Dorr's type B, 11 cases of ONFH and 1 case of DDH. The univariate regression analysis demonstrated that age, diagnosis, BMI, Dorr's type B, NFR, and seating height had no significant influence on significant subsidence, whereas insufficient lateral stem contact did have a statistically significant influence [Odds ratio (OR) = 5.02; 95%CI: 1.3-18.9; P = 0.017] (Table 4). The multivariate regression analysis also demonstrated that insufficient lateral stem contact was a statistically significant influencing factor (OR = 5.5; 95%CI: 1.4-21.4; P = 0.014). The intra-operative calcar crack incidence was 6.6% (18/274) and all were treated with cerclage wire with no further subsidence.

At the latest follow-up, there were 3 cases of revision. One case of femoral stem revision due to periprosthetic fracture, 4 years after index surgery from trauma, we revised using conventional stem with plate and screws and there were 2 cases of cup revision due to aseptic loosening, 2 and 5 years after index surgery. There was 1 case of significant subsidence (5.6 mm) with posterior dislocation, 5 years after index surgery from minor trauma, which was successfully treated with closed reduction. There was no femoral stem revision for aseptic loosening in our cohort.

DISCUSSION

Subsidence is one of the concerning early complications when using the cementless short stem. In this study we found subsidence occurred in 75 cases (27.4%) with the mean stem subsidence for the entire

Table 4 Results of univariate regression analysis of 12 cases with significant subsidence

Variables	Univariate analysis		
	OR	95%CI	*P* value
Age (≥ 60 yr)	0.96	0.2-4.6	0.96
DDH	0.65	0.1-5.2	0.69
ONFH	3.3	0.4-25.8	0.26
BMI (≥ 30 kg/m^2)	0.95	0.1-7.6	0.96
Dorr's type B	2.29	0.6-7.9	0.19
Seating height (< 5 mm)	0.91	0.3-2.9	0.87
NFR (< 0.8)	1.98	0.2-15.7	0.52
Insufficient lateral stem contact (≥ 1 mm)	5.02	1.3-18.9	0.017[1]

[1]Significant value.

DDH: Developmental dysplasia of the hip; ONFH: Osteonecrosis of the femoral head; BMI: Body mass index; OA: Osteoarthritis; NFR: Neck filling ratio; OR: Odds ratio.

cohort of 0.5 mm, (0-12.7, 1.68), a finding consistent with Jahnke *et al*[24], who demonstrated mean subsidence of 1.01 ± 1.27 mm (0.05-8.23) at two years follow-up. Schwarze *et al*[25] also showed the mean subsidence of 0.86 mm with two years follow-up using Metha stem. Different results of subsidence at two years follow-up were reported from many previous studies[23-30] using different types of short stem according to Khanuja *et al*[18]. Klein *et al*[31] who studied short stem with collar, CFP stem (LINK, Germany) (type IIB), demonstrated that the mean subsidence was 0.3 mm (0.2-0.4) at two years follow-up (Table 5).

It is particularly important to identify the key intraoperative decision criteria to predict post-implantation subsidence of the short stem, which should be useful for choosing the proper size and position of the short stem and for allowance of early weight bearing post-operatively. In this study we demonstrated that the insufficient lateral stem contact group (≥ 1 mm) seemed to have higher subsidence than the sufficient lateral stem contact group (< 1 mm) in the entire cohort, but did not reach statistical significance (P = 0.09). For significant subsidence cohort, the only significant influencing factor was insufficient lateral stem contact, the univariate and multivariate regression analyses showed statistical significance, (OR = 5.02; 95%CI: 1.3-18.9; P = 0.017) and (OR = 5.5; 95%CI: 1.4-21.4; P = 0.014) respectively. This is consistent with Kutzner *et al*[23], whose study using Optimys stem (type IIB according to Khanuja *et al*[18]), demonstrated that the mean subsidence was significantly higher in the no-contact group (≥ 1 mm) (2.07 mm, range -7.7 to 1.7) than in the sufficient lateral contact group (< 1 mm) (1.23 mm, range -4.5 to 1.8) at five years follow-up. According to our findings, sufficient lateral contact should always be the intra-operative aim when using Metha short stem. It is a particularly important step that when starting to prepare the femoral stem with a curved awl, the surgeon should carefully check that it be in contact with the lateral cortical bone, then followed by rasping in the same direction until reaching the designed femoral size (Figure 3). Therefore, intra-operative fluoroscopy might be considered mandatory in some cases with doubtful lateral contact. Nevertheless, if post-operative radiographs show that the patient has insufficient lateral contact, initial partial weight bearing should be recommended for preventing stem subsidence.

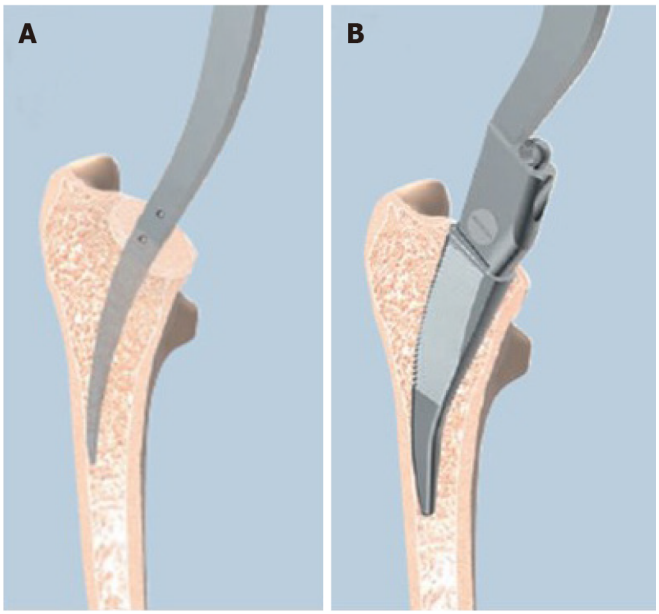
Some studies have demonstrated the relationship between percentage of canal fill and subsidence in conventional cementless stems[14,15]. In short stems, Jahnke *et al*[24] studied fit and fill ratios in 40 patients using Metha stem with one year follow-up. They found 100% of cases had a tight fit and fill ratio (≥ 0.8) at the proximal level, and the mean subsidence in the whole cohort of their study was 1.28 ± 2.24 mm. In our own study, we could not find a significant correlation between NFR (< 0.8) and significant subsidence (OR = 1.98; 95%CI: 0.2-15.7; P = 0.52). One possible explanation might be that we found the cortical ring of the femoral neck in some patients had a flat oval shape, with the result that the proximal stem had stable fixation with the anterior and posterior neck, instead of mediolateral.

The seating height was also not a significant influencing factor for significant subsidence in this study (OR = 0.91; 95%CI: 0.3-2.9; P = 0.87). Consistent with Floerkemeier *et al*[17], who studied synthetic bone using Metha stem and demonstrated that the deeper the resection, the more similar the strain patterns when compared to a non-implanted synthetic bone.

In our cohort, age (≥ 60 yrs.), diagnosis, BMI (≥ 30 kg/m^2), and Dorr's type B had no statistically significant influence on significant subsidence. Interestingly, patients with ONFH and Dorr's type B seemed to have higher chance of having significant subsidence, but did not reach statistical significance, (OR = 3.3; 95%CI: 0.4-25.8; P = 0.26) and (OR = 2.29; 95%CI: 0.6-7.9; P = 0.19) respectively. Similar to Schaer *et al*[32] who studied Optimys stem (type IIB according to Khanuja *et al*[18]) with subsidence of

Table 5 Summary of stem subsidence at two years follow-up for different types of short stems

Ref.	Femoral stem	Khanuja *et al*[18] classification	Follow-up (mo)	Subsidence(mm)	*n*
Christiansen *et al*[26]	Primoris, Biomed, UK	1	24	0.38	50
Schwarze *et al*[25]	Metha, Aesculap, Germany	2A	24	0.86	39
Jahnke *et al*[24]	Metha, Aesculap, Germany	2A	24	1.28 ± 2.24	71
This study	Metha, Aesculap, Germany	2A	24	0.5	274
Budde *et al*[27]	Nanos, Smith + nephew, Germany	2A	24	0.46 ± 0.31	18
Ferguson *et al*[28]	MiniHip, Corin, UK	2A	24	0.26	20
Kutzner *et al*[23]	Optimys, Mathys AG, Switzerland	2B	24	1.23 (contact); 2.07 (non-contact)	191
Klein *et al*[31]	CFP, Link, Germany	2B	24	0.3 (0.2-0.4)	39
Mahmoud *et al*[29]	Proxima, DePuy, UK	3	24	0.22	28
Acklin *et al*[30]	Fitmore, Zimmer, Switzerland	4	24	0.39	24



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Figure 3 Starting step with curved awl and rasping in the same direction. A: Pictures show the starting step with curved awl, which it must be in contact with the lateral cortex; B: Then rasping in the same direction.

2.04 ± 1.42 mm at five years follow-up, reported that age (≥ 65 yrs.), BMI (≥ 30 kg/m^2), and Dorr's type B did not have a statistically significant impact on the amount of stem subsidence.

Press-fit is one of the key factors for stability of cementless stems. The surgeon is guided by visual, sensory, and auditory clues during insertion of the short stem; a good balance between perfect press-fit level and not fracturing the calcar remains challenging. In this study, the incidence of intra-operative calcar crack was 6.6% (18/274) and all cases were treated with cerclage wire with no further subsidence. We believe this was because of the relatively narrow neck diameter of patients in our country. As in our previous mid-term study of Metha short stem in patients with ONFH, Suksathien *et al*[9] reported 4.8% of intra-operative calcar crack treated with cerclage wire without any complication. Lateral cortical hypertrophy was detected in both non-subsided and subsided groups at two yeas follow-up, 10 cases (5.03%) and 3 cases (4%) respectively. This finding demonstrated that lateral cortical hypertrophy had no influence for stem subsidence. In most subsided cases the subsidence was occurred at the initial phase of about 3-6 mo after surgery and then no further subsidence was observed at two years follow-up.

This study had some limitations. First, we used digital radiographs to measure all radiographic parameters, which is less accurate than radiostereometric analysis. Nevertheless, the aim of this study was to describe intraoperative key decision criteria with respect to proper positioning of short stems, that are suitable for intraoperative use by all surgeons, solely by performing intraoperative fluoroscopy, and post-operative radiographic evaluation of influencing factors to prevent stem subsidence. Second,

our cohort was a consecutive study of Metha stem, which was classified as type IIA according to Khanuja *et al*[18], the surgical technique for femoral preparation might be different from type I, III and IV. Third, there were many patients which loss before two years follow-up in our cohort, most of them were young workers, after fully recovery from THAs they moved to work in any remote area which unable to contact. However, there was no record of any complication at their last follow-up. Fourth, our cohort was relatively small which we had only 12 cases with significant subsidence to analyze, resulting in a relatively low power to detect statistically significant difference. Finally, this study was a single institute experience; different outcomes might have been obtained by different surgeons with varying levels of experience in any type of short stem THA.

CONCLUSION

In the entire cohort, we found higher subsidence in insufficient lateral stem contact group than in sufficient group, but did not reach statistical significance. In significant subsidence cohort, the only statistically significant influencing factor for significant subsidence was insufficient lateral stem contact. Therefore, it is a particularly important step to create proper lateral cortical contact when performing the Metha stem THA and intra-operative fluoroscopy should be considered mandatory in some cases with doubtful lateral contact. Initial partial weight bearing should be recommended in patients whose post-operative radiographs demonstrate insufficient lateral cortical contact for preventing stem subsidence.

ARTICLE HIGHLIGHTS

Research background

Many previous studies have shown satisfactory results using conventional total hip arthroplasty (THA), there may have some clinical problems related to proximodistal dimensional mismatch, thigh pain, stress shielding, periprosthetic fracture and difficulty during removal when revision is necessary. In an effort to reduce these problems, short-stem THA was developed, because the short stem has a metaphyseal fitting and no diaphyseal anchoring, so these problems may be minimized.

Research motivation

Few publications have studied the influencing factors for subsidence in short cementless stems, due to their metaphyseal fitting without diaphyseal anchoring, they might demonstrate different subsidence patterns than with the conventional stems.

Research objectives

This study aimed to analyze the influencing factors with subsidence in short stems.

Research methods

Retrospectively reviewed the digitized radiographs of 274 consecutive short stem total hip arthroplasties. Subsidence, neck-filling ratio, seating height and lateral stem contact were evaluated after a minimum of two years follow-up. A threshold of subsidence > 3 mm was considered a clinically significant subsidence.

Research results

In this study we demonstrated that the insufficient lateral stem contact group (≥ 1 mm) seemed to have higher subsidence than the sufficient lateral stem contact group (< 1 mm) in the entire cohort, but did not reach statistical significance. For significant subsidence cohort, the only significant influencing factor was insufficient lateral stem contact, the univariate and multivariate regression analyses showed statistical significance.

Research conclusions

Insufficient lateral stem contact was a statistically significant influencing factor on significant subsidence when using short stem. Therefore, it is a particularly important step to create proper lateral cortical contact when performing the Metha stem THA.

Research perspectives

Long term follow-up for this study group will be the next study.

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FOOTNOTES

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REFERENCES

1 **Learmonth ID**, Young C, Rorabeck C. The operation of the century: total hip replacement. *Lancet* 2007; **370**: 1508-1519 [PMID: 17964352 DOI: 10.1016/S0140-6736(07)60457-7]
2 **Floerkemeier T**, Schwarze M, Hurschler C, Gronewold J, Windhagen H, von Lewinski G, Budde S. The Influence of Tribological Pairings and Other Factors on Migration Patterns of Short Stems in Total Hip Arthroplasty. *Biomed Res Int* 2017; **2017**: 8756432 [PMID: 28497067 DOI: 10.1155/2017/8756432]
3 **Kamada S**, Naito M, Nakamura Y, Shitama T. Total hip arthroplasty using a short stem, stem design, position and size influence the development of bone trabeculae and appearance of radiolucent lines around the stem. *Curr Orthop Pract* 2011; **22**: 52-58 [DOI: 10.1097/BCO.0b013e3181f4b2bb]
4 **Simank HG**, Greiner R. Clinical and radiographic short to midterm results with the short hip stem prosthesis "Metha" in 120 cases. *J Orthopaedics* 2010; **7**: e8
5 **Wittenberg RH**, Steffen R, Windhagen H, Bücking P, Wilcke A. Five-year results of a cementless short-hip-stem prosthesis. *Orthop Rev (Pavia)* 2013; **5**: e4 [PMID: 23705062 DOI: 10.4081/or.2013.e4]
6 **Capone A**, Bienati F, Torchia S, Podda D, Marongiu G. Short stem total hip arthroplasty for osteonecrosis of the femoral head in patients 60 years or younger: a 3- to 10-year follow-up study. *BMC Musculoskelet Disord* 2017; **18**: 301 [PMID: 28716026 DOI: 10.1186/s12891-017-1662-6]
7 **Floerkemeier T**, Tscheuschner N, Calliess T, Ezechieli M, Floerkemeier S, Budde S, Windhagen H, von Lewinski G. Cementless short stem hip arthroplasty METHA® as an encouraging option in adults with osteonecrosis of the femoral head. *Arch Orthop Trauma Surg* 2012; **132**: 1125-1131 [PMID: 22546932 DOI: 10.1007/s00402-012-1524-5]
8 **Kim YH**, Park JW. Ultra-Short Anatomic Uncemented Femoral Stem and Ceramic-on-Ceramic Bearing in Patients With Idiopathic or Ethanol-Induced Femoral Head Osteonecrosis. *J Arthroplasty* 2020; **35**: 212-218 [PMID: 31542265 DOI: 10.1016/j.arth.2019.08.047]
9 **Suksathien Y**, Sueajui J. Mid-term results of short stem total hip arthroplasty in patients with osteonecrosis of the femoral head. *Hip Int* 2019; **29**: 603-608 [PMID: 30526072 DOI: 10.1177/1120700018816011]
10 **Buttaro MA**, Slullitel PA, Zanotti G, Comba FM, Piccaluga F. Is a short stem suitable for patients with hip dysplasia? *Hip*

Int 2018; **28**: 315-323 [PMID: 29048691 DOI: 10.5301/hipint.5000562]
11 **Suksathien Y**, Tippimanchai T, Akkrasaeng T, Ruangboon C. Mid-term results of short-stem total hip arthroplasty in patients with Crowe type I and II developmental dysplasia of the hip. *Eur J Orthop Surg Traumatol* 2021; **31**: 319-325 [PMID: 32875473 DOI: 10.1007/s00590-020-02777-1]
12 **Grant TW**, Lovro LR, Licini DJ, Warth LC, Ziemba-Davis M, Meneghini RM. Cementless Tapered Wedge Femoral Stems Decrease Subsidence in Obese Patients Compared to Traditional Fit-and-Fill Stems. *J Arthroplasty* 2017; **32**: 891-897 [PMID: 27793497 DOI: 10.1016/j.arth.2016.09.023]
13 **Ries C**, Boese CK, Dietrich F, Miehlke W, Heisel C. Femoral stem subsidence in cementless total hip arthroplasty: a retrospective single-centre study. *Int Orthop* 2019; **43**: 307-314 [PMID: 29916001 DOI: 10.1007/s00264-018-4020-x]
14 **Streit MR**, Haeussler D, Bruckner T, Proctor T, Innmann MM, Merle C, Gotterbarm T, Weiss S. Early Migration Predicts Aseptic Loosening of Cementless Femoral Stems: A Long-term Study. *Clin Orthop Relat Res* 2016; **474**: 1697-1706 [PMID: 27130649 DOI: 10.1007/s11999-016-4857-5]
15 **Warth LC**, Grant TW, Naveen NB, Deckard ER, Ziemba-Davis M, Meneghini RM. Inadequate Metadiaphyseal Fill of a Modern Taper-Wedge Stem Increases Subsidence and Risk of Aseptic Loosening: Technique and Distal Canal Fill Matter! *J Arthroplasty* 2020; **35**: 1868-1876 [PMID: 32147340 DOI: 10.1016/j.arth.2020.02.024]
16 **Kutzner KP**, Pfeil D, Kovacevic MP, Rehbein P, Mai S, Siebert W, Pfeil J. Radiographic alterations in short-stem total hip arthroplasty: a 2-year follow-up study of 216 cases. *Hip Int* 2016; **26**: 278-283 [PMID: 27102556 DOI: 10.5301/hipint.5000339]
17 **Floerkemeier T**, Gronewold J, Berner S, Olender G, Hurschler C, Windhagen H, von Lewinski G. The influence of resection height on proximal femoral strain patterns after Metha short stem hip arthroplasty: an experimental study on composite femora. *Int Orthop* 2013; **37**: 369-377 [PMID: 23271689 DOI: 10.1007/s00264-012-1725-0]
18 **Khanuja HS**, Banerjee S, Jain D, Pivec R, Mont MA. Short bone-conserving stems in cementless hip arthroplasty. *J Bone Joint Surg Am* 2014; **96**: 1742-1752 [PMID: 25320202 DOI: 10.2106/JBJS.M.00780]
19 **Dorr LD**, Faugere MC, Mackel AM, Gruen TA, Bognar B, Malluche HH. Structural and cellular assessment of bone quality of proximal femur. *Bone* 1993; **14**: 231-242 [PMID: 8363862]
20 **Jahnke A**, Wiesmair AK, Fonseca Ulloa CA, Ahmed GA, Rickert M, Ishaque BA. Outcome of short- to medium-term migration analysis of a cementless short stem total hip arthroplasty using EBRA-FCA: a radiological and clinical study. *Arch Orthop Trauma Surg* 2020; **140**: 247-253 [PMID: 31786645 DOI: 10.1007/s00402-019-03315-3]
21 **Kim YH**, Kim JS, Joo JH, Park JW. A prospective short-term outcome study of a short metaphyseal fitting total hip arthroplasty. *J Arthroplasty* 2012; **27**: 88-94 [PMID: 21435826 DOI: 10.1016/j.arth.2011.02.008]
22 **Albers A**, Aoude AA, Zukor DJ, Huk OL, Antoniou J, Tanzer M. Favorable Results of a Short, Tapered, Highly Porous, Proximally Coated Cementless Femoral Stem at a Minimum 4-Year Follow-Up. *J Arthroplasty* 2016; **31**: 824-829 [PMID: 26411395 DOI: 10.1016/j.arth.2015.08.020]
23 **Kutzner KP**, Freitag T, Bieger R. Defining 'undersizing' in short-stem total hip arthroplasty: the importance of sufficient contact with the lateral femoral cortex. *Hip Int* 2022; **32**: 160-165 [PMID: 32644828 DOI: 10.1177/1120700020940276]
24 **Jahnke A**, Engl S, Seeger JB, Basad E, Rickert M, Ishaque BA. Influences of fit and fill following hip arthroplasty using a cementless short-stem prosthesis. *Arch Orthop Trauma Surg* 2015; **135**: 1609-1614 [PMID: 26272583 DOI: 10.1007/s00402-015-2302-y]
25 **Schwarze M**, Budde S, von Lewinski G, Windhagen H, Keller MC, Seehaus F, Hurschler C, Floerkemeier T. No effect of conventional vs. minimally invasive surgical approach on clinical outcome and migration of a short stem total hip prosthesis at 2-year follow-up: A randomized controlled study. *Clin Biomech (Bristol, Avon)* 2018; **51**: 105-112 [PMID: 29287171 DOI: 10.1016/j.clinbiomech.2017.12.004]
26 **Christiansen JD**, Ejaz A, Nielsen PT, Laursen M. An Ultra-Short Femoral Neck-Preserving Hip Prosthesis: A 2-Year Follow-up Study with Radiostereometric Analysis and Dual X-Ray Absorptiometry in a Stepwise Introduction. *J Bone Joint Surg Am* 2020; **102**: 128-136 [PMID: 31596796 DOI: 10.2106/JBJS.19.00104]
27 **Budde S**, Seehaus F, Schwarze M, Hurschler C, Floerkemeier T, Windhagen H, Noll Y, Ettinger M, Thorey F. Analysis of migration of the Nanos® short-stem hip implant within two years after surgery. *Int Orthop* 2016; **40**: 1607-1614 [PMID: 26404094 DOI: 10.1007/s00264-015-2999-9]
28 **Ferguson RJ**, Broomfield JA, Malak TT, Palmer AJR, Whitwell D, Kendrick B, Taylor A, Glyn-Jones S. Primary stability of a short bone-conserving femoral stem: a two-year randomized controlled trial using radiostereometric analysis. *Bone Joint J* 2018; **100-B**: 1148-1156 [PMID: 30168759 DOI: 10.1302/0301-620X.100B9.BJJ-2017-1403.R1]
29 **Mahmoud AN**, Kesteris U, Flivik G. Stable migration pattern of an ultra-short anatomical uncemented hip stem: a prospective study with 2 years radiostereometric analysis follow-up. *Hip Int* 2017; **27**: 259-266 [PMID: 28165591 DOI: 10.5301/hipint.5000458]
30 **Acklin YP**, Jenni R, Bereiter H, Thalmann C, Stoffel K. Prospective clinical and radiostereometric analysis of the Fitmore short-stem total hip arthroplasty. *Arch Orthop Trauma Surg* 2016; **136**: 277-284 [PMID: 26739137 DOI: 10.1007/s00402-015-2401-9]
31 **Klein LJ**, Puretic G, Mohaddes M, Kärrholm J. Similar clinical results and early subsidence between the Collum Femoris Preserving and the Corail stem: a randomized radiostereometric study of 77 hips with 2 years' follow-up. *Acta Orthop* 2019; **90**: 202-208 [PMID: 30739560 DOI: 10.1080/17453674.2019.1577344]
32 **Schaer MO**, Finsterwald M, Holweg I, Dimitriou D, Antoniadis A, Helmy N. Migration analysis of a metaphyseal-anchored short femoral stem in cementless THA and factors affecting the stem subsidence. *BMC Musculoskelet Disord* 2019; **20**: 604 [PMID: 31831070 DOI: 10.1186/s12891-019-2980-7]

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ORIGINAL ARTICLE

Retrospective Study

Distal femur complex fractures in elderly patients treated with megaprosthesis: Results in a case series of 11 patients

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Abstract

BACKGROUND

Surgical treatment of complex fractures of the distal femur in the elderly is controversial. Osteoporosis and pre-existent osteoarthritis are common comorbidities in the elderly which add to the need for early walking and rapid restoration of function and also pose significant obstacles to achievement of satisfactory results with standard fixation techniques. Recently, several authors have suggested that primary arthroplasty could be a viable alternative option to standard fixation techniques in selected patients with complex distal femur fractures.

AIM

To present our experience with 11 cases of distal femur fractures treated with knee arthroplasty and large femoral resection in a population of patients over the age of 85.

METHODS

Data from 11 consecutive patients (10 females, 1 male) presenting with acute intra-articular supracondylar or intercondylar distal femur fractures and with pre-existent primary osteoarthritis who were treated with primary knee arthroplasty were recorded. We collected standard demographic data, comorbidities and patient reported outcomes including Visual Analogical Scale (VAS), Oxford Knee Score (OKS) and Barthel's Index. Post-operative joint range of motion (ROM) and standard radiographic data were also collected.

RESULTS

At a mean follow-up of 23.2 mo, all of the implants were well-positioned and osteointegrated. Furthermore, all the patients were alive and walking either independently or with walking aids. There was a marked improvement in pain (VAS 4.5 postop *vs* 1.9 at the last follow-up), OKS score (29.5 postop *vs* 36.81 at the last follow-up), ROM (96.2° postop *vs* 102° at the last follow-up) and restoration of pre-injury ambulatory status (average Barthel Index 77.3). The radiographic evaluations showed good restoration of the articular geometry. No deaths and no complications were recorded.

CONCLUSION

In conclusion, we believe that knee megaprosthesis in the case of complex fractures of the distal femur is a valid surgical choice. This is particularly true in elderly patients with severe osteoporosis and pre-existing osteoarthritis. It is important to note that this surgery should be performed by surgeons with proven experience in prosthetic hip and knee surgery and that a scrupulous selection of the cases is completed.

Key Words: Knee; Joint replacement; Megaprosthesis; Elderly; Distal femur fracture

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Core Tip: We evaluated safety and efficacy of a knee megaprosthesis in the setting of complex fractures of the distal femur in elderly patients with a short-term follow-up. We retrospectively evaluated 11 patients over the age of 85 treated with distal femoral replacement with a fully porous coated metaphyseal sleeve for acute fractures of the distal femur with a minimum follow-up of 2 years. During our study period we observed stability of the implants and improvement in the Visual Analogical Scale, Oxford Knee Score, range of motion, Barthel Index, quality of life and survival.

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INTRODUCTION

Fractures of the distal femur account for 0.4% of all bone fractures and 4% of all femoral fractures[1]. The incidence of this type of fracture is 8.7/100000/year[2] and it is steadily increasing due to the aging population, an increase of active elderly people and fragility fractures. Lower limb fragility fractures, both at the hip and the knee joint, represent a significant cause of morbidity and mortality in the elderly population as widely reported in the literature[2]. In many institutions a general trend toward early (*i.e.* within 48 h of injury) surgical intervention has been reported in an attempt at reducing the number of complications and 1-year mortality which it is estimated at 14%-36%[3]. Distal femoral fractures are most prevalent in females with a male-to-female ratio of 1:2 and have a bimodal distribution: in young people with healthy bones following a high energy trauma and in the osteoporotic elderly population following a low energy trauma. Fifty percent of these fractures are in fact found in patients above the age of 70[4].

Treatment of distal femoral fractures in the elderly has greatly improved with the evolution of implant technology, geriatric care, nursing assistance and physiotherapy. Historically, these fractures were managed in a conservative manner with trans-skeletal traction combined with bracing and followed by a prolonged period of immobilization. Nowadays, several surgical options exist for distal femur fractures including: retrograde intramedullary nailing, open reduction and internal fixation with plates and screws, variable angle locking compression plate, closed reduction and internal fixation with

plates and screws, less invasive stabilization systems using minimally invasive plate osteosynthesis technique and external fixation. Other available techniques include arthroplasty in the acute setting or arthrodesis[5].

Although open reduction and internal fixation with locking plates is perhaps the most common method for treatment of these fractures, it retains a high rate of synthesis failure and loss of reduction in the elderly (*i.e.* up to 30% to 79% of cases)[6]. The osteoporotic bone is indeed less resistant to axial and torsional loading regardless of the internal fixation method used to stabilize the fracture. Furthermore, another important factor to take into account in these fractures is the presence of preexisting arthritis which may lead to an unsatisfactory outcome. Currently, the most popular technique to overcome these limitations is a staged total knee arthroplasty (TKA) procedure in which the fracture is repaired first, then a prosthetic implant is fitted after fracture healing. However, this method shows a high rate of arthrofibrosis, progressive reduction of the post-operative range of motion (ROM) as well as a modification of the anatomical and mechanical axis of the femur. An alternative approach is the primary TKA in the acute setting with the use of implants such as constrained prosthesis[7].

Currently, the use of distal femur replacement (DFR) in distal femur fractures can be considered for low-activity elderly patients with one or several of the following: severely comminuted intra-articular fracture patterns, osteoporosis, concomitant knee osteoarthritis and low pre-injury functional status. The goal of DFR is to resect the fracture and to allow full weight bearing as soon as possible to reduce hospital stay and to prevent complications such as deep vein thrombosis, pulmonary complications and other sequelae of post-operative decreased mobility. The aim of this study was to present our experience with treatment of complex fractures of the distal femur in an elderly osteoporotic cohort of eleven patients treated with acute knee megaprosthesis.

MATERIALS AND METHODS

Following Institutional Review Board approval, we retrospectively reviewed a total of 11 patients who underwent total knee arthroplasty for acute fractures of the distal femur at our institution between 2014 and 2019. The inclusion criteria for the surgical procedure were: age of 85 or older, the presence of an acute (treated within 1 mo of the injury) traumatic low or high energy comminuted fracture, intra-articular supracondylar or intercondylar distal femur fracture (AO/OTA classification 33C), pre-existent primary or post-traumatic osteoarthritis Kallgren-Lawrence stage 3 or higher[8], pre-fracture walking distance > 200 m and a body mass index (BMI) < 35 kg/m^2. The reason to restrict our study to patients over the age of 85 was based on the clinical finding of the overall bad outcomes reported for these patients following complex, comminuted articular fractures of the distal femur[6]. The same senior surgeon performed all surgical procedures. Patients with pathological fractures of the distal femur, dementia, inability to ambulate before the injury, infections, periprosthetic fractures, the presence of bilateral injuries, patients suffering from inflammatory diseases (rheumatoid arthritis) and/or neurological diseases (neurovascular event, chronic diseases) were not included.

To assess the presence of significant osteopenia or osteoporosis, standard radiographs were used to search for cortical thinning and hyper-transparency of the bone[7,9]. At the same time, the severity of degenerative disease was determined by the presence of subchondral sclerosis, subchondral cysts formation and periarticular osteophyte formation. Clinical data, radiological exams and outcome scores were evaluated by an independent researcher not involved in the care of the patients.

Surgical technique

In all cases, a total cemented knee arthroplasty system was used (LPS™ Limb Preservation System, De Puy Synthes, Raynham, Massachusetts, United States). This is a megaprosthesis with modular distal femoral components, a cemented femoral and tibial stem with a fully porous coated metaphyseal sleeve, modular tibial component and a rotating hinge articulation. All surgical procedures were performed under spinal anesthesia; 2 g of cefazolin was administered before surgery and at 8, 16, 24 and 48 h after the surgery. Tranexamic acid was used for bleeding control, administered preoperatively, intraoperatively and 3 h after surgery. An intraoperative blood loss recovery system was used in all cases. Deep vein thrombosis prophylaxis with a daily dose of low molecular weight heparins was used during the first 35 d after surgery in all cases, starting from 24 h after the procedure. The procedure was performed using a standard medial parapatellar approach, the distal femoral fractures fragments were removed by subperiosteal dissection within a minimum distance of 8 cm from the joint line and retained on the operating room back table to allow for approximate sizing of components. Any other fragments proximal to the resection line were stabilized with metal wires (Orthopaedic Cable System, De Puy Synthes Trauma, NJ, United States). Placement of a "prophylactic" banding wire using a 1.7 mm De Puy Synthes Trauma Cable around the proximal end of the remaining diaphysis may potentially decrease the risk of intra-operative fracture during press-fit insertion of a porous femoral sleeve particularly with fragile bone. Furthermore, the crimp may be used as a landmark to help set femoral rotation throughout the operation. After a 1 cm proximal tibial cut, the tibial canal was sequentially reamed and broached to the appropriate size, followed by assembling of the final components. The tibial components were

placed in a press-fit fashion with a small amount of cement beneath the tibial tray. The femoral canal was sequentially reamed and broached and trial components were assembled in the femur. Trialing was performed to assess rotation and patellar tracking. A canal plug was placed and the femoral canal was cleaned with a bottle brush followed by pulse lavage. The canal was filled in a retrograde manner using pressurized gentamicin bone cement and final components were cemented in place. SmartSet MV bone cement was used to fix the distal femoral stem extension to host bone. The wound was closed in layers with absorbable sutures. The second day, the drain was removed and the patients started the rehabilitation protocol consisting of continuous passive motion, active exercises and assisted loading with two crutches. All patients started to walk between 2 and 6 d after the surgery using crutches or a four-wheeled walker. All patients except one underwent rehabilitation in a specialized physical medicine unit.

Our cohort was clinically evaluated using numerous scales and indexes including: Visual Analogical Scale (VAS), Oxford Knee Score (OKS), ROM, mobilization and functional autonomy (Barthel's Index), knee flexion deformity, muscle strength and joint stability. Patients were followed-up in our outpatient clinic at 45 d, 3, 6 and 12 mo and after the last visit a yearly follow-up was executed after a median period of 23 mo.

We also collected data regarding the operative duration, blood transfusions, blood intra-operative losses, type of implant, range of motion, stability, perioperative and postoperative complications, mortality rate at the 1-year follow-up, length of hospital and rehabilitation stays, preoperative ambulatory status and the presence of pre-existent implants or osteosynthesis. In all patients, standard antero-posterior (AP) and lateral x-ray and computed tomography scan of the knee, and subsequently long-leg x-ray, AP and lateral x-rays of the knee, Rosenberg and axial patella x-rays, AP x-ray of the pelvis and frog-leg view were taken after the procedure and at the last follow-up visit.

We also searched for subsidence on the last radiograph. Early non-progressive horizontal radiolucent lines under the tibial component were also analyzed and considered non-significant if < 2 mm. These evaluations were carried out on an AP x-ray of the knee (1, 2 medial zones and 3, 4 lateral zones) and on lateral x-ray of the knee (1, anterior zone and 2, posterior zone)[1]. Location, size, and progression of all radiolucent lines under the femoral component were also assessed on lateral knee x-ray. Location was determined using the Knee Society total knee arthroplasty radiographic evaluation and scoring system [10].

Mean mortality rate was calculated at 30 d and 1 year of follow-up in concordance with the majority of published literature assessing hip fracture mortality. Major and minor complications after surgery were monitored. Major complications included deep infection, pulmonary embolism, neurovascular accident, myocardial infarction, death or removal or revision of the implants. All other complications were considered minor.

RESULTS

A total of eleven patients, 10 women and 1 man, underwent DFR with a fully porous coated metaphyseal sleeve for acute fracture of the distal femur at our institution between 2014 and 2019. The mean age was 87 (range of 85-90 years), no patient died nor was lost to follow-up during the study period. Average BMI was 29.36 (min 24.3, max 35.5), with a slight left sided fractures prevalence (63.3%). Due to the relative older age of our cohort, the prevalent cause of fractures was accidental fall at home (9 patients), while 2 of them were caused by road accidents. The distribution of fractures, according to AO/OTA classification, was the following: 4 patients C1, 3 patients C2, 4 patients C3. Every patient showed radiological evidence of osteoarthritis and a history of knee pain prior to trauma. Furthermore, we noticed a large amount of osteoporosis around the knee despite all patients having a good degree of preoperative functional autonomy. None of the patients used walking aids prior to the accident (Table 1).

In our cohort we observed that the majority of patients had a pre-existent orthopaedic implant or osteosynthesis: 2 patients with elective total hip arthroplasty and 1 patient with contralateral TKA, while 1 patient with proximal femoral trochanteric nail ipsilateral to the fractures of the knee. Comorbidities of our cohort of patients are listed in Table 2. Five patients were affected by diabetes (45.5%), while 4 patients suffered from cardiovascular disease (36.4%). Only one patient had a low-grade form of Parkinson syndrome with no impact on his functional autonomy.

The average hospitalization time in the orthopedic ward was 8.3 d for all patients, except in 2 cases (min 6, max 10) where they were transferred to an orthogeriatric rehabilitation unit. The mean surgical time was 112.9 min (min 96.6, max 130.7). The mean blood intra-operative loss was 280 mL (min 200, max 420); four patients required one blood transfusion, whereas two patients needed two transfusions.

A mild improvement was recorded in the patient's clinical course, pain and quality of life. Using the values of OKS and VAS obtained immediately after surgery and at the last follow-up visit, we observed an improvement in the values of both scales (post-op OKS score 29.5, range 30-43; OKS at 3 mo 32.3 (+9.5%); OKS at 6 mo 34 (+15.2%); OKS at 12 mo 35.8 (+23.3%); OKS at last follow-up 36.8, range 30-43 (+24.8%); post-op VAS 4.5, range 1.5-7.5; VAS at 3 mo 3.5 (-22.2%); VAS at 6 mo 2.7 (-40%); VAS at 12 mo

Table 1 Demographics of the study population, *n* = 11

Demographics of the study population	
Sex	10 female; 1 male
Mean age in yr	86 (84-90)
BMI	29.36 (24.3-35.5)
Affected side, *n* (%)	4 right-sided (36); 7 left-sided (63)
ASA score, *n* (%)	8 grade II (72); 3 grade III (27)
Etiology, *n*	2 traffic incidents 9 mechanical falls
Classification, *n*	4 C1; 3 C2; 4 C3
Type of implant	LPS^{TM}Limb Preservation System De Puy Synthes
Prophylactic banding using a 1.7 mm DePuy Synthes trauma cable, *n* (%)	7 (63)
Preoperative functionality level	All patients walked without walking aids
Prior implants/osteosynthesis, *n* (%)	2 ipsilateral THA (18), 1 contralateral TKA (9), 1 ipsilateral intramedullary femoral nail (9)
Osteoporosis/prior osteoarthritis, *n* (%)	11 (100)
Follow-up in mo	23.2 (11-26)

Data are expressed as average (min-max), unless stated otherwise. BMI: Body mass index; THA: Total hip arthroplasty; TKA: Total knee arthroplasty.

Table 2 List of the comorbidities of the patients included in the study

Comorbidities of the patients	
Cancer	0
Diabetes	5 (45%)
Chronic kidney disease	1 (9%)
Steroidal use	0
Rheumatological disease	0
Immunosuppressants	0
Venous insufficiency	1 (9%)
Liver cirrhosis	0
Cardiopathies	4 (36%)
Neurological conditions	1 (9%)

Data are expressed as *n* (%), unless stated otherwise.

2.3 (-48.9%); VAS at last follow-up 1.9, range 1.5-7.5 (-57.8%) (Figures 1 and 2). We also used the Barthel Index Score to evaluate the mean functional activity and daily living autonomy score at the time of the last follow-up: 77.3 (range 70-85). At the time of the last follow-up 4 patients could walk without any walking aid (36.4%), 6 patients required a wheeled walker for mobilization (54.5%), and 1 patient used a wheelchair (9.1%). Due to the lack of pre-operative clinical scores, no formal statistical analysis was performed. At the mean follow-up of 23.2 mo, all implants appeared well positioned and osteointegrated with a mean knee score of 34.81 (range 30-41). Mean knee postoperative flexion was 96.2° (range 80-105) and 102° (range 90-106) at the time of last follow-up. No patient showed signs of fixed deformity, extension lag or hyper-extension of the involved leg. In 7 patients, prophylactic cerclage of the femur was needed due to fractures extending to the metadiaphyseal region, with important comminution (C2.1-C2.2; C3.2-C3.3) and a severe grade of osteoporosis requiring a more proximal resection of the distal femur with the use of a longer stem to permit a greater stability of the implant.

The radiological study showed excellent osteointegration of the cemented femoral stems, according to the criteria of the Knee Society Rating System[11] (Figures 3 and 4). No radiolucent line or osteolysis

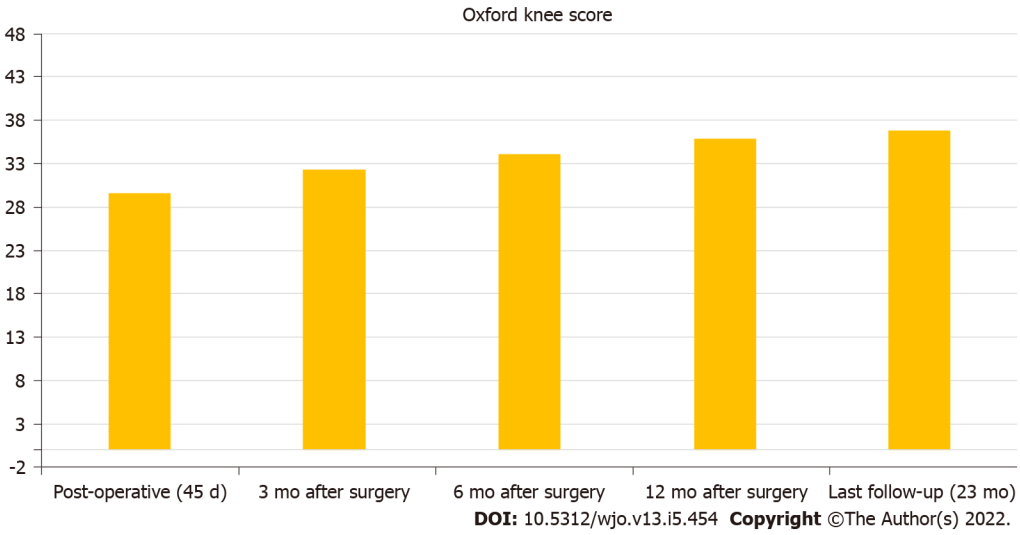


Figure 1 Post-treatment Oxford Knee Scores (*n* = 2 years follow-up) are shown at 45 d postoperative, 3, 6, 12, mo, last follow-up (average 2 years post-surgery) after surgical treatment with distal femur replacement for acute fractures of the distal femur.

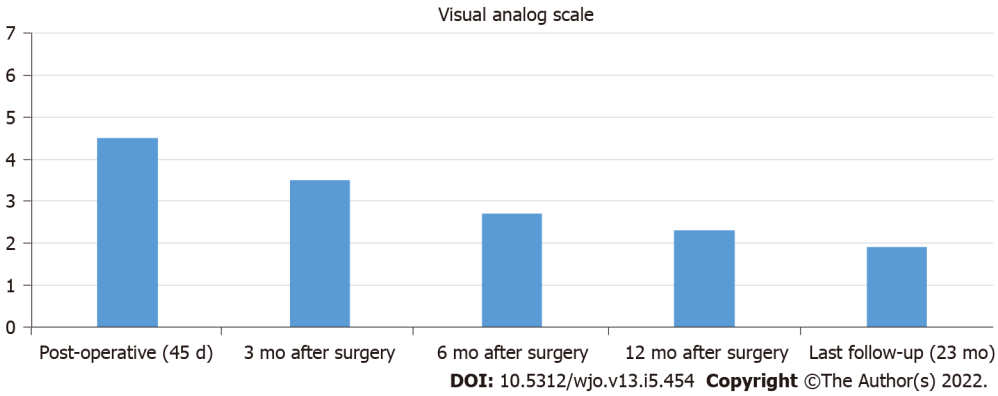


Figure 2 Post-treatment Visual Analogical Scale (*n* = 2 years follow-up) are shown at 45 d postoperative, 3, 6, 12 mo, last follow-up (average 2 years post-surgery) after surgical treatment with distal femur replacement for acute fractures of the distal femur.

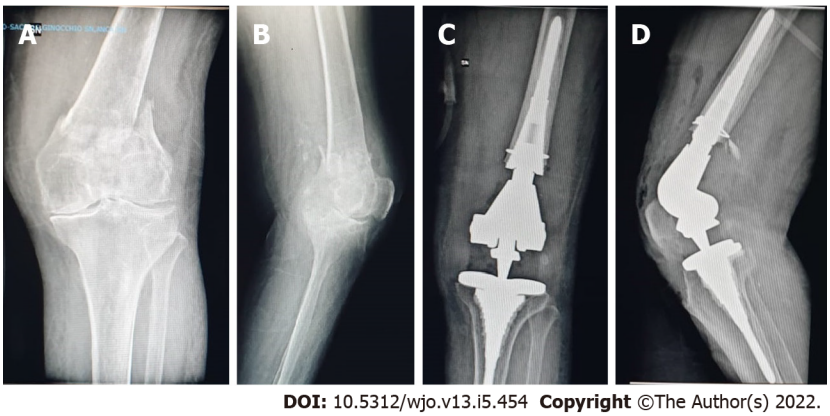
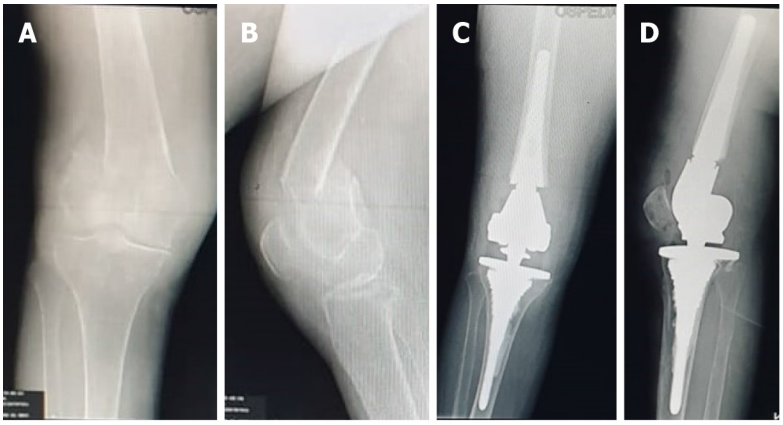


Figure 3 Case example 1. A and B: 87-year-old female patient with distal femur fracture; C and D: Pre-existing osteoarthritis of the knee treated with a knee megaprosthesis.

around the surface of the femoral and tibial stems were observed. There were no signs of angular deformity or malunion. Stress-shielding in zone 6 of the tibial stems was physiologically represented in 60% of the analyzed stems. No progressive axial subsidence > 5 mm was observed. No leg length discrepancy > 1 cm was observed. There was, however, a suspected radiolucent line under the tibial



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Figure 4 Case example 2. A-D: 85-year-old male patient treated with distal femoral resection and implantation of fully porous coated metaphyseal sleeve (C and D) for acute fracture of the distal femur (A and B).

(zone 3) in 4 patients but < 1 mm and 1 patient < 2 mm, but both were not progressive. The measurements performed on the radiographs showed a good restoration of the joint geometry of the knee. There were no major or minor peri-operative complications. No revisions were needed during the follow-up period (Table 3).

DISCUSSION

Prosthetic surgery is one of the greatest achievements of orthopaedics of the last century. Clinical results are excellent in the medium and long term. In addition, the research for better materials has improved the safety and reliability of the implants. In the late decades, an important topic has been debated in international literature: synthesis *vs* arthroplasty as a treatment of choice to be used in the lateral fractures of the proximal femur. Multi-fragmentary fractures burdened by intrinsic instability, poor bone quality and associated comorbidities that require early recovery, are the elements that tip the scale in favor of arthroplasty. The same thought process was used regarding fractures of the distal femur. Fracture patterns that are difficult to classify (fracture pattern AO/OTA 33C), osteoporosis and important associated degenerative changes (osteoarthritis) and advanced age, are the elements that led the choice towards the use of prosthetics. Metaphyseal comminution complicates the reconstruction of the native alignment and a solid fixation is extremely difficult to achieve and consequently often leads to malunion and/or non-union. Similarly, severe osteoporosis and profound condylar destruction can cause inadequate reduction, secondary loss of reduction and osteosynthesis failure with implant cut-out due to the poor bone stock[12-15]. For these reasons, in elderly, arthroplasty might be the first choice of treatment in case of complete destruction of the distal femur and/or the proximal tibia.

In our study, all patients were over the age of 85 and suffered from supracondylar or intercondylar displaced femoral fractures. All patients had a diagnosis of osteoporosis and a certain grade of pre-existing knee osteoarthritis. A cemented femoral stem with porous coated Metaphyseal Sleeve was used in every patient because of the complex and unstable fracture patterns, the fragile osteoporotic bone, the lack of pre-existent implant (except 1 patient with proximal ipsilateral femoral osteosynthesis) and the low BMI of our population. This allowed reaching the main objective of DFR: The early restoration of a stable limb which guaranteed early mobilization or transfers, depending on the previous level of mobility. The use of a megaprosthesis satisfies both of these requirements.

Mega-implants were originally designed to meet the needs of cancer surgery after extensive resections of bone segments[16]. Over the years, large resection prostheses have been used both in trauma surgery for complex fractures and periarticular pseudarthrosis and in revision surgery[17-19]. The modern modular mega-implants have replaced monoliths, while making the surgical technique simpler and more versatile. Recently, several authors documented that in selected patients, this procedure is better than arthroplasty secondary to failure of open reduction and internal fixation, and shows excellent results and great patient-satisfaction. However, there have been limited reports regarding the use of arthroplasty with mega-prostheses in the acute setting for distal femoral fractures in the elderly and all of them are small retrospective case studies.

The most pivotal paper was published by Appleton *et al*[20] in 2006. The authors analyzed a population of 52 patients, aged between 55 and 98, who underwent a primary cemented hinged total knee replacement for distal femoral fracture with a metaphyseal extension and reported a 1-year mortality rate of 41%[21,22], a revision rate of 13.6% and an implant survival rate of 4.6% at 1 year. Similar results were obtained by Rosen *et al*[9] with a 1-year implant survival rate of 100% and a 71%

Table 3 Operative data and observed complications, *n* = 11

Operative data and observed complications	
OR time in min	112.9 (96.6-130.7)
Blood loss in mL	280 (200-420)
Blood transfusion, *n* (%)	1 (9)
1-yr mortality rate (for every cause), *n* (%)	0 (0)
Length of stay in d	8.3 (6-10)
Postoperative ROM in degrees	96 (80-105) at 3 mo
	102 (90-106) at 2 yr
Functional autonomy at 1 yr (Barthel Index)	77.3 (70-85)
	6 patients using a walker
	1 patients using a wheelchair
	4 patients walking without any walking aid
Early (< 1 mo) post-operative complications, *n*	0
Late (> 1 mo) post-operative complications, *n*	4 patients with radiolucent lines < 1 mm
	1 patient with radiolucent lines < 2 mm

Data are expressed as mean (min-max), unless stated otherwise.

rate of return to the pre-operative ambulation capacities in a cohort of 24 patients with non-union fractures of the distal femur.

Our study showed better results in terms of mortality as compared to what it is found in the literature, with a low 1-year mortality rate (0%). This can be explained by our study population which had few comorbidities, only 3 out of 11 patients with an American Society of Anesthesiologists (ASA) level 3, and the fact that all the patients had a favorable family history and a good level of mobility prior to the intervention. Streubel *et al*[23] observed a 23% mortality rate following distal (native) and proximal femoral fractures. Similarly, Boureau *et al*[24] found a 1-year mortality rate of 14% because the studied population included 62% of patients with an ASA score of 3.

In our study, all surgeries were performed by the same surgeon, leading to a standardization of the technique. Our results are comparable with those found in the literature. The most important parameters we have taken into consideration are: blood loss and related transfusions, surgical time, functional and radiographical results, hospitalization time and complications. Regarding blood loss, we had an average Hbg loss of 2.8 g/dL (280 mL). Wang *et al*[7] reported a mean Hgb loss of 3.8 g/dL (380 mL). In our series we observed lower blood transfusion rates of 9.9% (1 unit of blood transfused postoperatively) than those observed by Pearse *et al*[25] (24%) (2.5 units of blood transfused postoperatively). On the other hand, Wang *et al*[7] did not mention blood transfusions in their study.

In terms of functional results, we evaluated our population using validated questionnaires during the follow-up period at 45 d, 3, 6, 12, and 18 mo after surgery (VAS, OKS) and assessed the ROM. Our results were slightly inferior in terms of short-term ROM and 1-year post-operative mobility (Barthel Index) than those reported by Parratte *et al*[26]. The functional results reported by Sarzaeem *et al*[14] and Boureau *et al*[24] were not comparable because of the use of different clinical scores (Knee society score, Parker score, Tegner activity scale).

These studies conclusions have some limitations: data was retrospectively collected from a registry, so there could be coding errors; procedures were performed by different surgeons with different levels of experience, directly influencing the results. A total of 30 patients with proximal tibial fractures who underwent knee replacements using different implants were analyzed. Our operative times were higher than those reported by Pearse *et al*[25] (112.9 min for our study against 97 min) but lower than those reported by Rosen *et al*[9] (170 min).

In terms of average hospital stay, our average stay was of 8.3 d (not including orthogeriatric and rehabilitation unit), against 11 d in the study by Bettin *et al*[4] and 15 d for Appleton *et al*[20] No major or minor complications were recorded in our study. The French Hip and Knee Society multicenter series of TKA reported 1 death from cardiovascular etiology (major complications) and 3 patients with deep vein thrombosis, including 1 complicated by a pulmonary embolism[26].

The results further confirm that major complications are predominant in patients over the age of 75, which underlines the need for a geriatric oriented-management[12,26]. In addition, Parratte *et al*[26] found a revision rate of 11.5%, similar to the one found by Boureau *et al*[24] at 9.5%. However, both of

these results seemed inferior than patients treated by osteosynthesis for this type of fracture. Radiolucent lines, based on the radiographic and Hospital for Special Surgery Knee Score, on the femoral side were not seen while they were found on the tibial side in 4 patients with < 1 radiolucent line and 1 patient with less than 2. Our imaging results analyses revealed favorable outcomes and all knee implants were stable.

Our study shows that this surgical procedure is equally safe and effective. In fact, hospitalization times and intra-operative blood losses were not higher than expected and the surgical procedure was well tolerated by patients. This last data is relevant because it shows that if performed by an experienced surgeon, distal femoral replacement can be done rapidly without increasing the risk of malrotation, implant instability, infections and blood loss. The excellent osteointegration of the implants and the absence of revisions, albeit limited by our short follow-up, demonstrate that DFR surgery is safe and effective. Our case series is certainly more recent because it goes from 2015 to 2020 and it is clear that surgical techniques and perioperative management of patients have changed during the years. For example, the use of tranexamic acid and blood loss recovery protocol has limited the intraoperative need for transfusions. The implementation of an outpatient physiotherapy protocol has encouraged early discharge: two patients did not undergo inpatient rehabilitation and were directly discharged.

The authors believe that the most important factors determining the success of DFR is the possibility of immediate unrestricted weight-bearing, intensive physical rehabilitation and early discharge[27]. A stable and quickly cemented fixation with megaprosthesis is indeed an undemanding technique in elderly, osteoporotic, low-demand or sedentary patients which allows a rapid mobilization and prevents prolonged bed rest[28].

This study has several limitations: the small size of the study group, the type of retrospective series and the biases created by it, the inhomogeneous etiology and multiple missing data (anthropometrics data, surgery related factor, no pre-operative functional scores). Furthermore, we noticed other clear limitations: the extreme age of our patients, disfavoring long-term follow-up, the absence of a control group and the short follow-up period. Nevertheless, our data are still one of the most recent and largest cohorts available in the literature.

In the osteoporotic elderly patient with severe arthritis, DFR using a fully porous coated Metaphyseal Sleeve for acute fractures of the distal femur can be a valid option. However, this type of surgery should only be performed in centers specializing in prosthetic hip and knee revision and failure surgery[29]. It is important to note that in order to achieve the best functional outcomes it is necessary to operate on only carefully selected patients and as quickly as possible. Carefully selected patients have a higher chance of prolonged implant survival because of a diminished risk of non-union, implant failure, mal-union and infection, especially in the absence of an ipsilateral total hip arthroplasty.

CONCLUSION

In conclusion, complex fractures of the distal femur in elderly osteoporotic patients treated with megaprosthesis have shown good functional outcomes and low complication rates similar to other studies with a short-term follow-up. We recommend this procedure in selected patients without relevant comorbidities. Patient selection is of paramount importance and parameters to consider include: age (with age > 90 being a contraindication), comorbidities, ASA score, good previous functional status, physical-mental compliance and the absence of an ipsilateral implant. Acute distal femoral replacement surgery of the knee can reduce the length of hospital stays, hospitalization-related complications and costs. However, in order to achieve statistically relevant evidence, more randomized controlled studies are needed.

ARTICLE HIGHLIGHTS

Research background

Treatment of complex distal femur fractures in the elderly is debated. Currently available techniques (*i.e.* retrograde nailing, plate and screws fixation, delayed knee replacement surgery) are plagued by poor outcomes. More recently, megaprosthesis have been used for treatment of major trauma and their use has been investigated in treatment of distal femur fractures as well.

Research motivation

There is a lack of short to long term outcomes studies on the use of megaprosthesis for treatment of complex distal femur fractures in the elderly.

Research objectives

The aim of this study is to critically review our clinical experience with usage of megaprosthesis for treatment of complex distal femur fractures in a series of 11 elderly patients.

Research methods

We conducted a retrospective review of 11 consecutive patients older than 85-years-old for treatment with knee megaprosthesis at our institution. Patients were followed-up on an average for 23 mo after surgery. Clinical and radiographical outcome measures were assessed. Mortality was also recorded.

Research results

No deaths were recorded in our case series. At the time of the last follow-up all patients were walking either independently or with walking aids. The average Oxford Knee Score at the time of the last follow-up was 36.8 points. The average Visual Analogical Scale score at the time of the last follow-up was 1.9 points.

Research conclusions

Knee megaprosthesis in the setting of complex distal femur fractures in elderly patients is a valid solution which is able to offer short operative times and hospital stays.

Research perspectives

Longer follow-up studies will be needed to further validate our results. Furthermore, case-controlled studies (*i.e.* magaprosthesis *vs* standard plate fixation) would be useful to compare clinical outcomes between these two techniques.

FOOTNOTES

Author contributions: Pola E and Zanchini F participated in the conceptualization; Piscopo A participated in surgical technique development; Cipolloni V and Nasto LA participated in methodology and writing-original preparation; Pola E participated in validation; Cipolloni V and Piscopo D participated in formal analysis and investigation; Cipolloni V and Pripp C participated in data curation; Nasto LA participated in writing–review and editing; Pola E, Piscopo A and Cacciapuoti S participated in supervision; All authors have read and agreed to the published version of the manuscript.

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REFERENCES

1 **Loosen A**, Fritz Y, Dietrich M. Surgical Treatment of Distal Femur Fractures in Geriatric Patients. *Geriatr Orthop Surg Rehabil* 2019; **10**: 2151459319860723 [PMID: 31308992 DOI: 10.1177/2151459319860723]
2 **Larsen P**, Ceccotti AA, Elsoe R. High mortality following distal femur fractures: a cohort study including three hundred and two distal femur fractures. *Int Orthop* 2020; **44**: 173-177 [PMID: 31081515 DOI: 10.1007/s00264-019-04343-9]
3 **Myers P**, Laboe P, Johnson KJ, Fredericks PD, Crichlow RJ, Maar DC, Weber TG. Patient Mortality in Geriatric Distal Femur Fractures. *J Orthop Trauma* 2018; **32**: 111-115 [PMID: 29462121 DOI: 10.1097/BOT.0000000000001078]

4 **Bettin CC**, Weinlein JC, Toy PC, Heck RK. Distal Femoral Replacement for Acute Distal Femoral Fractures in Elderly Patients. *J Orthop Trauma* 2016; **30**: 503-509 [PMID: 27078131 DOI: 10.1097/BOT.0000000000000600]

5 **Hake ME**, Davis ME, Perdue AM, Goulet JA. Modern Implant Options for the Treatment of Distal Femur Fractures. *J Am Acad Orthop Surg* 2019; **27**: e867-e875 [PMID: 30939565 DOI: 10.5435/JAAOS-D-17-00706]

6 **Tampere T**, Ollivier M, Jacquet C, Fabre-Aubrespy M, Parratte S. Knee arthroplasty for acute fractures around the knee. *EFORT Open Rev* 2020; **5**: 713-723 [PMID: 33204515 DOI: 10.1302/2058-5241.5.190059]

7 **Wang W**, Yang K, Yang P, Song D, Wang C, Song J, Li X, Wang K. Primary total knee arthroplasty for complex supracondylar femoral fractures in patients with knee arthritis: A retrospective study of a patient cohort. *Medicine (Baltimore)* 2018; **97**: e12700 [PMID: 30290668 DOI: 10.1097/MD.0000000000012700]

8 **Kohn MD**, Sassoon AA, Fernando ND. Classifications in Brief: Kellgren-Lawrence Classification of Osteoarthritis. *Clin Orthop Relat Res* 2016; **474**: 1886-1893 [PMID: 26872913 DOI: 10.1007/s11999-016-4732-4]

9 **Rosen AL**, Strauss E. Primary total knee arthroplasty for complex distal femur fractures in elderly patients. *Clin Orthop Relat Res* 2004; 101-105 [PMID: 15292794 DOI: 10.1097/01.blo.0000132466.65220.62]

10 **Huddleston JI**, Wiley JW, Scott RD. Zone 4 femoral radiolucent lines in hybrid *vs* cemented total knee arthroplasties: are they clinically significant? *Clin Orthop Relat Res* 2005; **441**: 334-339 [PMID: 16331023 DOI: 10.1097/01.blo.0000180452.11048.b8]

11 **Ewald FC**. The Knee Society total knee arthroplasty roentgenographic evaluation and scoring system. *Clin Orthop Relat Res* 1989; 9-12 [PMID: 2805502]

12 **Bohm ER**, Tufescu TV, Marsh JP. The operative management of osteoporotic fractures of the knee: to fix or replace? *J Bone Joint Surg Br* 2012; **94**: 1160-1169 [PMID: 22933485 DOI: 10.1302/0301-620X.94B9.28130]

13 **Campana V**, Ciolli G, Cazzato G, Giovannetti De Sanctis E, Vitiello C, Leone A, Liuzza F, Maccauro G. Treatment of distal femur fractures with VA-LCP condylar plate: A single trauma centre experience. *Injury* 2020; **51** Suppl 3: S39-S44 [PMID: 31703959 DOI: 10.1016/j.injury.2019.10.078]

14 **Sarzaeem MM**, Omidian MM, Kazemian G, Manafi A. Acute Primary Total Knee Arthroplasty for Proximal Tibial Fractures in Elderly. *Arch Bone Jt Surg* 2017; **5**: 302-307 [PMID: 29226201]

15 **Caliogna L**, Medetti M, Bina V, Brancato AM, Castelli A, Jannelli E, Ivone A, Gastaldi G, Annunziata S, Mosconi M, Pasta G. Pulsed Electromagnetic Fields in Bone Healing: Molecular Pathways and Clinical Applications. *Int J Mol Sci* 2021; **22** [PMID: 34299021 DOI: 10.3390/ijms22147403]

16 **Donati F**, Di Giacomo G, D'Adamio S, Ziranu A, Careri S, Rosa M, Maccauro G. Silver-Coated Hip Megaprosthesis in Oncological Limb Savage Surgery. *Biomed Res Int* 2016; **2016**: 9079041 [PMID: 27642605 DOI: 10.1155/2016/9079041]

17 **Parvizi J**, Tarity TD, Slenker N, Wade F, Trappler R, Hozack WJ, Sim FH. Proximal femoral replacement in patients with non-neoplastic conditions. *J Bone Joint Surg Am* 2007; **89**: 1036-1043 [PMID: 17473141 DOI: 10.2106/JBJS.F.00241]

18 **Perticarini L**, Rossi SMP, Fioruzzi A, Jannelli E, Mosconi M, Benazzo F. Modular tapered conical revision stem in hip revision surgery: mid- term results. *BMC Musculoskelet Disord* 2021; **22**: 29 [PMID: 33407327 DOI: 10.1186/s12891-020-03886-y]

19 **Rossi SMP**, Ivone A, Ghiara M, Jannelli E, Sangaletti R, Perticarini L, Benazzo F. A ligament tensor-guided extramedullary alignment technique for distal femoral cut in total knee replacement: results at a minimum 3 years follow-up. *Arch Orthop Trauma Surg* 2021; **141**: 2295-2302 [PMID: 34386837 DOI: 10.1007/s00402-021-04115-4]

20 **Appleton P**, Moran M, Houshian S, Robinson CM. Distal femoral fractures treated by hinged total knee replacement in elderly patients. *J Bone Joint Surg Br* 2006; **88**: 1065-1070 [PMID: 16877607 DOI: 10.1302/0301-620X.88B8.17878]

21 **Moran CG**, Wenn RT, Sikand M, Taylor AM. Early mortality after hip fracture: is delay before surgery important? *J Bone Joint Surg Am* 2005; **87**: 483-489 [PMID: 15741611 DOI: 10.2106/JBJS.D.01796]

22 **Shortt NL**, Robinson CM. Mortality after low-energy fractures in patients aged at least 45 years old. *J Orthop Trauma* 2005; **19**: 396-400 [PMID: 16003199 DOI: 10.1097/01.bot.0000155311.04886.7e]

23 **Streubel PN**, Ricci WM, Wong A, Gardner MJ. Mortality after distal femur fractures in elderly patients. *Clin Orthop Relat Res* 2011; **469**: 1188-1196 [PMID: 20830542 DOI: 10.1007/s11999-010-1530-2]

24 **Boureau F**, Benad K, Putman S, Dereudre G, Kern G, Chantelot C. Does primary total knee arthroplasty for acute knee joint fracture maintain autonomy in the elderly? *Orthop Traumatol Surg Res* 2015; **101**: 947-951 [PMID: 26589193 DOI: 10.1016/j.otsr.2015.09.021]

25 **Pearse EO**, Klass B, Bendall SP, Railton GT. Stanmore total knee replacement *vs* internal fixation for supracondylar fractures of the distal femur in elderly patients. *Injury* 2005; **36**: 163-168 [PMID: 15589936 DOI: 10.1016/j.injury.2004.04.007]

26 **Parratte S**, Ollivier M, Argenson JN. Primary total knee arthroplasty for acute fracture around the knee. *Orthop Traumatol Surg Res* 2018; **104**: S71-S80 [PMID: 29199087 DOI: 10.1016/j.otsr.2017.05.029]

27 **Bell KM**, Johnstone AJ, Court-Brown CM, Hughes SP. Primary knee arthroplasty for distal femoral fractures in elderly patients. *J Bone Joint Surg Br* 1992; **74**: 400-402 [PMID: 1587887 DOI: 10.1302/0301-620X.74B3.1587887]

28 **Oliva MS**, Vitiello R, Cauteruccio M, Pesare E, Rovere G, Meschini C, Liuzza F, Maccauro G, Ziranu A. Cemented *versus* cementless megaprosthesis in proximal femur metastatic disease: A systematic review. *Orthop Rev (Pavia)* 2020; **12**: 8689 [PMID: 32913616 DOI: 10.4081/or.2020.8689]

29 **Ebied A**, Zayda A, Marei S, Elsayed H. Medium term results of total knee arthroplasty as a primary treatment for knee fractures. *SICOT J* 2018; **4**: 6 [PMID: 29547115 DOI: 10.1051/sicotj/2017060]

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ORIGINAL ARTICLE

Observational Study

Prevalence and factors of work-related musculoskeletal disorders among hand surgeons

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Abstract

BACKGROUND

The nature of tasks required by hand surgeons require both forceful and repetitive maneuvers, thus subjecting these surgeons to the risk of musculoskeletal (MSK) injuries during their years in practice.

AIM

To assess the prevalence, characteristics and impact of MSK disorders among hand surgeons.

METHODS

A modified version of the physical discomfort survey was sent to surgeons who were members of the American Society for Surgery of the Hand *via* e-mail. The collected data were analyzed using descriptive statistics, one-way analysis of variance, and Fisher's exact test. P values of < 0.05 were considered statistically significant.

RESULTS

Of the 578 respondents, 60.4% reported that they had sustained a work-related MSK injury, of which the most common diagnoses were lateral elbow epicondylitis (18.7%), low back pain (17.1%) and carpal tunnel syndrome (15.6%). Among those that reported an injury, 73.1 % required treatment and 29.2 % needed time off work as a direct result of their injury. The number of work-related injuries incurred by a surgeon increased significantly with increasing age ($P < 0.003$), increasing years in practice ($P < 0.001$) and higher case load ($P < 0.05$).

CONCLUSION

To our knowledge this study is the first of its kind to assess MSK injuries

sustained by Hand surgeons with a high incidence. These results should increase awareness on this aspect and fuel future studies directed at preventing these types of work-related injuries, thus minimizing the financial and psychological burden on these surgeons and the healthcare system.

Key Words: Hand; Surgeon; Prevalence; Musculoskeletal disorders; Occupational injuries

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Core Tip: Work-related musculoskeletal injuries are a common occurrence during the years of practice of hand surgeons. The most common diagnoses were lateral elbow epicondylitis, low back pain and carpal tunnel syndrome. Awareness and knowledge of these injuries can minimize the financial and psychological burden on both surgeons and the healthcare system.

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INTRODUCTION

Occupational injuries have gained recent attention in the medical literature, with studies exploring the prevalence of these injuries and possible predisposing factors. While all physicians are at risk of sustaining these injuries, surgeons have been identified as a high-risk group[1-6].

Musculoskeletal (MSK) disorders have been identified as a common occupational risk for surgeons, which has been referred to as "an impending epidemic"[1]. Their risk of occurrence increases especially when the surgeon in involved in tasks requiring repetitive and forceful movements, as it has been found that the prevalence of these injuries was more than 60% in practicing orthopaedic surgeons of different subspecialties[3-5,7-9]. These injuries involved multiple MSK regions, including the lower back, elbow and wrist, thus requiring a large cohort of these injured surgeons to take time off work as a direct result of their sustained injuries.

Awareness of these MSK disorders and improvements in operative room ergonomics may have a substantial effect on the prevention of their occurrence[10-12]. Unfortunately, this effect isn't evident from the most recent literature, possibly due to the difficulty in applying some of the proposed ergonomical alterations and recommendations in the operative field[10,13,14].

We conducted a study exploring prevalence of work-related MSK disorders among hand surgeons, with a goal to identify specific factors predisposing to these injuries and their impact on the surgeon's practice. Also, we aimed from this study to increase awareness of these types of injuries both to the practicing surgeon and members of the healthcare system in general.

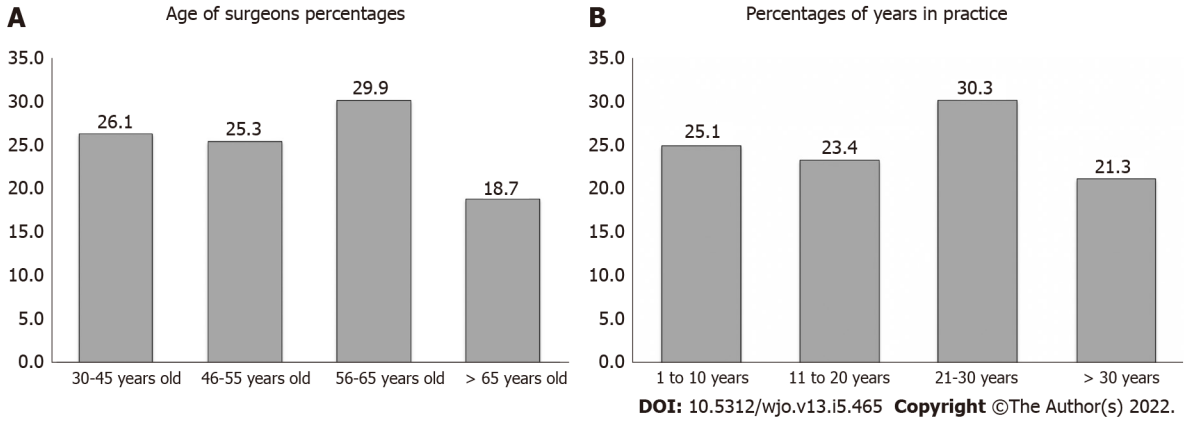
MATERIALS AND METHODS

Members of the American Society for Surgery of the Hand were sent a modified version of the physical discomfort survey *via* e-mail. The initial email was sent in June 2016, followed by a reminder email in December 2017, and survey collection was closed by June 2017.

Questions pertaining to the surgeons general demographics (*e.g.*, age, gender, hand-dominance, type of practice, number of years in practice and annual caseload), in addition to questions exploring work related MSK injuries were included in the survey. The explored MSK injuries were divided into anatomical regions, including neck, shoulder, elbow/forearm, wrist/hand, hip, knee, foot and ankle, low back. In addition, participants were asked about both treatment required and time off work required due to the reported injuries, if any.

Statistical analyses

The collected data was analyzed using descriptive statistics, one-way analysis of variance, and Fisher's exact test using SPSS statistical package version 24 (SPSS Inc., Chicago, IL). P values of < 0.05 were considered statistically significant.



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Figure 1 Age distribution, distribution of years in practice among survey participants. A: Age distribution; B: Distribution of years in practice.

RESULTS

Five hundred and seventy-eight surgeons completed the survey, with a respondent rate of 16.5%. The majority of respondents were males (84.8%), while 15.2% were females. More than half of the responding surgeons were younger than 55 years, while most have been in practice less than 30 years (Figure 1A and B). The vast majority of surgeons were practicing in an academic, community or private institute.

Concerning work related injuries, 60.4% reported that they had sustained a work-related MSK injury (Table 1), of which the most common diagnoses were lateral elbow epicondylitis (18.7%), low back pain (17.1%) and carpal tunnel syndrome (15.6%) (Figure 2). The number of work-related injuries incurred by a surgeon increased significantly with increasing age ($P < 0.003$), increasing years in practice ($P < 0.001$) and higher case load ($P < 0.05$). No association was found between sustained injuries and sex, hand dominance, nor type of practice.

Among those that reported an injury, 73.1 % required treatment, of which 11.8% required surgical management only, while 31.5% required both surgical and medical management for their injuries (Table 2). The need to undergo treatment or take time off due to the injury was associated with increased number of injuries ($P < 0.001$). In addition, surgeons were more likely to receive surgical treatment when they were > 56 years of age ($P < 0.001$) or had been in practice for > 30 years ($P < 0.001$).

Of the respondents, 29.2% needed time off work as a direct result of their injury (Table 2). We also found that surgeons were more likely to require time off work when they were > 56 years of age ($P < 0.001$) or had been in practice for > 21 years ($P < 0.001$).

DISCUSSION

We assessed the prevalence of work-related musculoskeletal injuries sustained by hand surgeons during their career. We found that of those responding to a survey, a high proportion of these surgeons (60.4%) reported a musculoskeletal injury sustained during work. A number of previous studies have assessed this prevalence in different specialties, as Davis *et al*[3] reported a 44% prevalence of these work-related injuries in the general orthopaedic surgeon cohort. Specifically, Alqahtani *et al*[4,5] surveyed both the orthopaedic adult reconstructive and the orthopaedic trauma surgeon cohorts and found a similar prevalence of 66% in both studies. Alzahrani *et al*[7] found that 67% of the 402 orthopaedic pediatric surgeon respondents reported that they sustained a work-related MSK injury.

The most common injuries reported by the surveyed hand surgeons in our cohort were lateral epicondylitis (18.7%) and low back pain (17.1%). We also found a high prevalence of carpal tunnel syndrome which was reported by more than 15% of the respondents. These common pathologies were similar to the previously published studies in different specialities, as low back pain and elbow injuries were the most common reported injuries by the surveyed surgeons.

Increasing age and years in practice were associated with the number of reported injuries in our cohort. We also found that surgeons with a higher case load were more likely to report a work-related MSK injury. Alqahtani *et al*[5] and Alzahrani *et al*[7] also found that increasing age and number of years in practice were independently associated with the number of reported MSK injuries in both the orthopaedic trauma and pediatric surgeon populations. In a study of 183 orthopaedic adult reconstruction surgeons, age > 55, practicing for > 20 years and increased case load were found to be associated with requiring time off work due to the sustained injury, but they found that these variables were not associated with the number of reported injuries[4]. In our cohort we found similar results, as time off work was more likely in surgeons older than 56 years and surgeons who have been in practice

Table 1 Percentage of surveyed hand surgeons with disorders and their requirement of time off work according to sex, age, hand dominance, type of practice, number of institutes, years in practice and annual caseload, *n* (%)

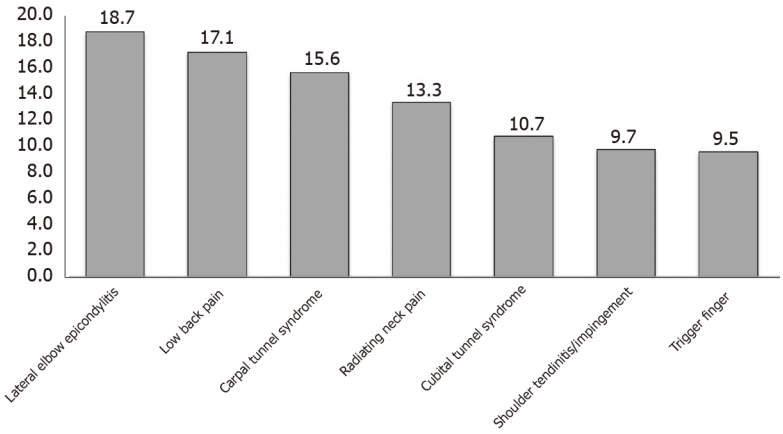
	Number of respondents	Number of respondents with injuries	Number of Injured requiring time off work
Age (yr)			
≤ 45	151	91 (60.3)	10 (6.6)
46-55	146	90 (61.6)	20 (13.7)
56-65	173	102 (59)	42 (24.3)
> 65	108	66 (61.1)	30 (27.8)
Sex			
Male	490	292 (59.6)	87 (17.8)
Female	88	57 (64.8)	15 (17)
Hand dominance			
Right	518	316 (61)	92 (17.8)
Left	60	33 (55)	10 (16.7)
Type of practice			
Academic	171	111 (64.9)	33 (19.3)
Community	186	114 (61.3)	38 (20.4)
Private	182	99 (54,4)	27 (14.8)
Other	39	25 (64.1)	4 (10.3)
Number of institutes			
1	544	329 (60.5)	98 (18.1)
> 1	34	20 (58.8)	4 (11.8)
Years in practice			
≤ 10	145	86 (59.3)	9 (6.2)
11-20	135	85 (63)	20 (14.8)
21-30	175	103 (58.9)	38 (21.7)
> 30	123	75 (61)	35 (28.5)
Annual caseload			
≤ 250	110	55 (50)	19 (17.3)
251-500	273	179 (65.6)	52 (19)
501-750	117	65 (55.6)	19 (16.2)
> 750	78	50 (64.1)	12 (15.4)

for more than 21 years.

Identifying this high prevalence of MSK-injuries in practicing surgeons (who responded to the survey) is the first step in exploring factors that can be implemented to aid in reducing the risk of sustaining such injuries. Operative room ergonomics has been identified in recent studies as an area that requires significant improvement, especially in surgeon postures and movements[10,14,15]. These include the use of specific body supports to improve posture and lower extremity compressive stockings to decrease the edema especially in long anticipated cases[13,16]. In addition, making use of certain power tools for screw insertions can help decrease the burden of the repetitive forceful movements required in this this surgeon population[8]. As these factors have been found to possibly improve the surgeons experience in the operating room and decrease the risk of sustaining injuries, we believe that increased focus should be directed to exploring the true effect of these recommendations, in addition to identifying other modifications that may be of benefit to the surgeon and the healthcare system in general in preventing the occurrence of such work-related MSK injuries.

Table 2 Percentage of surveyed hand surgeons with diagnosed disorders per region and number of respondents requiring treatment, requiring surgical treatment and requiring time-off work due to their musculoskeletal disorders

Region	Percentage of respondents with injuries	Percentage of injured respondents requiring treatment	Percentage of treated respondents requiring surgical treatment	Percentage of treated respondents requiring time-off work
Neck	30.4	13.9	3.6	4.0
Shoulder	23.1	15.0	4.9	4.0
Elbow	26.0	13.3	2.1	1.5
Forearm, wrist and hand	52.0	27.3	10.0	6.6
Hip and thigh	6.5	3.8	1.4	1.2
Knee and lower leg	12.3	8.1	5.2	3.4
Foot and ankle	9.5	6.7	1.2	1.2
Lower back	34.5	19.4	4.2	5.7



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Figure 2 Musculoskeletal disorders and complaints among survey participants.

We believe that our study has some limitations that are common with these types of prevalence studies. Recall bias is always a risk in surveys that depend on the respondents ability to recall events or factors that occurred in the past. In addition, while the majority of the surgeons identify their injuries as work-related, other factors that may have come into effect cannot be ruled out. Another weakness is that the survey used was not assessed for validity or reliability, especially the included self-reported measures. It is possible that some deficiency can be identified is such types of surveys, but a validation study would be required to explore these possible missed indicators and can be an area for future research.

CONCLUSION

Our current study has shown a high occurrence of work-related MSK injuries sustained by hand surgeons. Increased awareness and preventative measures are key to minimize the financial and psychological burden on these surgeons and the healthcare system. To our knowledge this study is the first of its kind to assess these types of injuries is this surgeon sub-specialty.

ARTICLE HIGHLIGHTS

Research background

Common tasks required by hand surgeons need both forceful and repetitive maneuvers, which can

subject these surgeons to the risk of musculoskeletal injuries during their years in practice.

Research motivation

These injuries can place a physical and psychological burden on the surgeon, which can in turn affect the healthcare system. Therefore, attention should be directed at studying their prevalence and associated factors.

Research objectives

The objective of the study was to assess the prevalence, characteristics and impact of musculoskeletal disorders among hand surgeons.

Research methods

A modified version of the physical discomfort survey was sent to surgeons who were members of the American Society for Surgery of the Hand *via* e-mail. The collected data were analyzed using descriptive statistics, one-way analysis of variance, and Fisher's exact test. P values of < 0.05 were considered statistically significant.

Research results

Of the 578 respondents, 60.4% reported that they had sustained a work-related musculoskeletal injury, of which the most common diagnoses were lateral elbow epicondylitis, low back pain and carpal tunnel syndrome.

Research conclusions

We have shown a high prevalence of musculoskeletal disorders among hand surgeons, with more than half of the surveyed surgeons reporting a sustained injury.

Research perspectives

These results should increase awareness on this aspect and fuel future studies directed at preventing these types of work-related injuries, thus minimizing the financial and psychological burden on these surgeons and the healthcare system.

FOOTNOTES

Author contributions: Alqahtani SM and Alzahrani MM contributed to the concept, design, study execution, manuscript writing and review; Bicknell R and Pichora D contributed to the concept, design, manuscript writing and review.

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REFERENCES

1 **Epstein S**, Sparer EH, Tran BN, Ruan QZ, Dennerlein JT, Singhal D, Lee BT. Prevalence of Work-Related Musculoskeletal Disorders Among Surgeons and Interventionalists: A Systematic Review and Meta-analysis. *JAMA Surg* 2018; **153**: e174947 [PMID: 29282463 DOI: 10.1001/jamasurg.2017.4947]

2 **Vijendren A**, Yung M. An overview of occupational hazards amongst UK Otolaryngologists. *Eur Arch Otorhinolaryngol* 2016; **273**: 2825-2832 [PMID: 27048520 DOI: 10.1007/s00405-016-4024-3]

3 **Davis WT**, Sathiyakumar V, Jahangir AA, Obremskey WT, Sethi MK. Occupational injury among orthopaedic surgeons. *J Bone Joint Surg Am* 2013; **95**: e107 [PMID: 23925752 DOI: 10.2106/JBJS.L.01427]

4 **Alqahtani SM**, Alzahrani MM, Tanzer M. Adult Reconstructive Surgery: A High-Risk Profession for Work-Related Injuries. *J Arthroplasty* 2016; **31**: 1194-1198 [PMID: 26791046 DOI: 10.1016/j.arth.2015.12.025]

5 **AlQahtani SM**, Alzahrani MM, Harvey EJ. Prevalence of musculoskeletal disorders among orthopedic trauma surgeons: an OTA survey. *Can J Surg* 2016; **59**: 42-47 [PMID: 26812408 DOI: 10.1503/cjs.014415]

6 **Vajapey SP**, Li M, Glassman AH. Occupational hazards of orthopaedic surgery and adult reconstruction: A cross-sectional study. *J Orthop* 2021; **25**: 23-30 [PMID: 33897136 DOI: 10.1016/j.jor.2021.03.026]

7 **Alzahrani MM**, Alqahtani SM, Tanzer M, Hamdy RC. Musculoskeletal disorders among orthopedic pediatric surgeons: an overlooked entity. *J Child Orthop* 2016; **10**: 461-466 [PMID: 27538942 DOI: 10.1007/s11832-016-0767-z]

8 **Auerbach JD**, Weidner ZD, Milby AH, Diab M, Lonner BS. Musculoskeletal disorders among spine surgeons: results of a survey of the Scoliosis Research Society membership. *Spine (Phila Pa 1976)* 2011; **36**: E1715-E1721 [PMID: 21508887 DOI: 10.1097/BRS.0b013e31821cd140]

9 **Wyatt RW**, Lin CC, Norheim EP, Przepiorski D, Navarro RA. Occupation-related Cervical Spine Disease in Orthopaedic Surgeons. *J Am Acad Orthop Surg* 2020; **28**: 730-736 [PMID: 32324708 DOI: 10.5435/JAAOS-D-19-00834]

10 **Esser AC**, Koshy JG, Randle HW. Ergonomics in office-based surgery: a survey-guided observational study. *Dermatol Surg* 2007; **33**: 1304-13; discussion 1313 [PMID: 17958581 DOI: 10.1111/j.1524-4725.2007.33281.x]

11 **van Veelen MA**, Kazemier G, Koopman J, Goossens RH, Meijer DW. Assessment of the ergonomically optimal operating surface height for laparoscopic surgery. *J Laparoendosc Adv Surg Tech A* 2002; **12**: 47-52 [PMID: 11908485 DOI: 10.1089/109264202753486920]

12 **Alaqeel M**, Tanzer M. Improving ergonomics in the operating room for orthopaedic surgeons in order to reduce work-related musculoskeletal injuries. *Ann Med Surg (Lond)* 2020; **56**: 133-138 [PMID: 32637088 DOI: 10.1016/j.amsu.2020.06.020]

13 **Albayrak A**, van Veelen MA, Prins JF, Snijders CJ, de Ridder H, Kazemier G. A newly designed ergonomic body support for surgeons. *Surg Endosc* 2007; **21**: 1835-1840 [PMID: 17356937 DOI: 10.1007/s00464-007-9249-1]

14 **Lin DW**, Bush RW, Earle DB, Seymour NE. Performance and ergonomic characteristics of expert surgeons using a face-mounted display during virtual reality-simulated laparoscopic surgery: an electromyographically based study. *Surg Endosc* 2007; **21**: 1135-1141 [PMID: 17180274 DOI: 10.1007/s00464-006-9063-1]

15 **Park A**, Lee G, Seagull FJ, Meenaghan N, Dexter D. Patients benefit while surgeons suffer: an impending epidemic. *J Am Coll Surg* 2010; **210**: 306-313 [PMID: 20193893 DOI: 10.1016/j.jamcollsurg.2009.10.017]

16 **Lester JD**, Hsu S, Ahmad CS. Occupational hazards facing orthopedic surgeons. *Am J Orthop (Belle Mead NJ)* 2012; **41**: 132-139 [PMID: 22530210]

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ORIGINAL ARTICLE

Observational Study

What factors are important to new patients when selecting an orthopedic oncologist?

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Abstract

BACKGROUND

Understanding how patients choose a provider may improve the overall experience by identifying ways to tailor a clinical practice.

AIM

To identify factors that patients consider important when choosing an orthopedic oncologist.

METHODS

New patients presenting to an orthopedic oncology clinic within a tertiary academic medical center from January 2019 to August 2020 were invited to complete an anonymous survey. The questionnaire consisted of 27 items including a Likert-type assessment of the importance of selection factors.

RESULTS

A total of 101 new patients with a median age of 66 years (range, 14 years to 91 years) responded. Most were referred by another doctor (n = 63, 62.4%), and of the referring providers, the most frequent specialty was orthopedic surgery (n = 32, 51%). Using a Likert-type scale with 1 representing 'least important' and 5 representing 'most important', the most important factor was the hospital reputation (mean, 4.65; SD, 0.85). Additional factors of importance were the number of years in practice (3.87 ± 1.3) and a primary care provider referral (3.71 ± 1.6). Patients younger than 40 years old found social media (P = 0.016) and internet presence (P = 0.035) of their surgeon to be more important than older patients. In contrast, older patients considered care within an academic center to be of greater importance than younger patients (P = 0.014).

CONCLUSION

This investigation suggests a primary care referral, as well as hospital and physician reputation, are among the most important factors when selecting an

orthopedic oncologist. Furthermore, social media utilization appears to be more important for younger patients.

Key Words: Advertising; Patient choice; Selection; Patient selection; Questionnaire; Practice management; Orthopedic oncologist

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Core Tip: The most important factor for orthopedic oncologist selection was the reputation of the hospital, followed by a primary care provider referral and the number of years in practice of the oncologist. Patients under the age of 40 found social media and internet presence of the oncologist to be more important than older patients. Patients over the age of 60 considered care within an academic center to be of greater importance than younger patients.

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INTRODUCTION

Consumer-driven health plans have increased the demand for transparency in the quality of care[1]. As the quality of care influences patient satisfaction, understanding how patients choose a provider may improve the overall experience by identifying ways to tailor a clinical practice.

There are few data to inform how patients choose a physician, and these studies are largely focused in primary care or medicine specialties[2-5]. In medical oncology, it appears most patients utilize the Internet when researching a condition, though it is unclear whether such resources are used when subsequently selecting a provider[6]. In orthopedic surgery, the physician manner and ease of scheduling availability appear to impact the decision of where to establish care, though factors such as age, race, and sex of the provider are less important[7-11]. While there is evidence to inform how a patient chooses an orthopedist, however, these data largely pertain to elective surgery where the underlying condition does not carry the same magnitude as an orthopedic oncologic diagnosis.

This study sought to identify factors that new patients consider important when choosing an orthopaedic oncologist. We hypothesize younger patients would utilize social media and the Internet when choosing a surgeon, whereas older patients would identify a primary care referral and physician reputation as highly important.

MATERIALS AND METHODS

Design

Following Institutional Review Board approval, all new patients presenting to an orthopedic oncology clinic between January 2019 and August 2020 were invited to complete an anonymous survey. The clinic is located within a tertiary academic institution in major metropolitan area. Within three to five miles there are several oncologic choices each with an equivalent reputation. Inclusion criteria were new patients who initiated oncologic care with the senior author in the aforementioned time frame. There was no exclusion by age. Prior to completion of the survey, each eligible patient received a short cover letter describing the study. The subsequent questionnaire was designed using REDCap and consisted of 27 survey items[12]. The first category included demographic questions regarding age, sex, health insurance provider, referral status, and highest level of schooling. Age was also converted to a categorical variable considered conceptually meaningful based off a consistent pattern of ages seen in our clinic. The second category assessed utilization of social media (Facebook, Instagram, and/or Twitter) and the Internet (Healthgrades.com, RateMDs.com, Vitals.com, WebMD.com). The final category was a five-point Likert-type scale evaluation of various factors considered to be of importance in choosing an orthopedic oncologist[4]. The importance of each factor was scaled from least important (1) to unimportant (2); somewhat important (3); very important (4); and most important (5).

Statistical analyses

Continuous and categorical data were analyzed using descriptive statistics and reported as the median and range or mean and SD. Each Likert-type response was converted to a numerical variable and represented as the mean and SD. Mean responses to each factor from the Likert scale were compared between those less than 40 years of age and those older than 60 years of age using a two-sample *t*-test. *P* values were not corrected for multiple hypotheses as the analyses were primarily exploratory in nature. When possible, all available data were included for analyses. Statistical significance was set to a *P* value of less than 0.05, and all analyses were performed using SPSS version 26.0 (IBM Corp., Armonk, NY, USA).

RESULTS

Demographics

The response rate was 24% (n = 101/426). Demographics are listed in Table 1. The median age was 66 years (range, 14 years to 91 years) and the majority were female (n = 61, 60.4%). With respect to health insurance, 45.5% (n = 46) had governmental insurance, 38.6% (n = 39) had employee insurance, 13.9% (n = 14) had private insurance.

Visit details

The majority of new patients were referred by another doctor (n = 63, 62.4%), and of the referring providers the most frequent specialty was orthopedic surgery (n = 32, 51%), followed by family practice (n = 16, 25%), 'Other' (n = 20, 32%), and medical oncology (n = 7, 11%). The majority of new patients (n = 72, 71.3%) did not utilize social media or the Internet prior to their encounter (Table 2).

Selection factors

Among all responders, the most important selection factor was the hospital having a good reputation from other patients or doctors (mean, 4.65; SD, 0.85) (Figure 1A). Additional factors of importance were the number of years the orthopedic oncologist has been in practice (3.87 ± 1.3), how other patients or friends of patients rated the surgeon (3.73 ± 1.5), ease of scheduling availability (3.83 ± 1.3) and an in-network provider (3.84 ± 1.4), and whether the patient's primary care provider referred the patient (3.71 ± 1.6).

Factors by age group

Age was then categorically grouped into those younger than 40 years of age (Figure 1B; n = 20), 40 years to 60 years (n = 16), or older than 60 years of age (Figure 1C; n = 50) (Table 3). Patients younger than age 40 identified social media (P = 0.016) and Internet (P = 0.035) presence of their provider as more important compared to patients older than age 60. In contrast, older patients considered working within an academic center to be of greater importance when selecting an orthopedic oncologist (P = 0.014).

DISCUSSION

The findings of the current study suggest a primary care provider referral is one of the most important factors that new patients consider when choosing an orthopedic oncologist. Additionally, a good hospital reputation, locating an in-network provider, and the number of years in practice were important selection factors.

This study also found the individual physician reputation to be a strong selection factor, which is consistent with how outpatients choose other orthopedic specialists[13]. Though in contrast, the orthopedic oncologist sees new patients of a variety of different ages, often with morbid diagnoses. The presenting demographic consists of children and young adults, as well as parents of those children, in addition to the middle aged and elderly. In an era where use of the Internet and social media has become ubiquitous, the potential to reach patients *via* these platforms has increased tremendously. Chen *et al*[6] note the media and Internet offer a profound means of medical information dissemination in cancer care, though they caution strategic efforts are needed to improve the quality of reporting and transparency of certain diseases. Additionally, social media and internet advertisement and outreach may closely be intertwined with profit-driven incentivization; therefore, further care should be taken by patients when selecting physicians. In the current study, we sought to determine whether the Internet presence was an important selection factor when choosing an orthopedic oncologist, and it appears the majority of patients neither utilize these resources nor consider it to be highly important.

When grouped by age, however, new patients younger than 40 years old identified social media and Internet presence of their surgeon to be of greater importance than older patients. While this finding is no surprise given the trends in social media utilization by younger generations, the implications for practice expansion are worth noting. For example, children and adolescents seen by orthopedic

Table 1 Demographics of all responders

	n (%)
Age (yr), median (range)	66 (14-91)
Female	61 (60.4)
Male	39 (39.0)
Health insurance	
Governmental	46 (45.5)
Employee	39 (38.6)
Private	14 (13.9)
Other	2 (2.0)
Highest schooling	
Graduate or professional degree	39 (38.6)
College degree	36 (35.6)
Some college, no degree	15 (14.9)
Highschool or GED	7 (6.9)
No degree	3 (3.0)
Referral	
Yes	63 (62.4)
No	38 (37.6)

Sum may not represent total cumulative count (n = 101).

Table 2 Utilization of social media and the Internet among all responders, *n* (%)

	Yes	No
Social media		
Facebook	6 (5.9)	88 (87.1)
Twitter	4 (4.0)	90 (89.1)
Instagram	4 (4.0)	90 (89.1)
Internet		
HealthGrades.com	13 (12.9)	80 (79.2)
RateMDs.com	9 (8.9)	84 (83.2)
Vitals.com	4 (4.0)	86 (85.1)
WebMD.com	13 (12.9)	80 (79.2)

Sum may not represent total cumulative count (n = 101).

oncologists typically undergo surgery for primary tumors of bone. One such procedure, the rotationplasty, is at first sight a cosmetically unappealing option for new patients and their families. However, some studies demonstrate favorable long-term functional outcomes and a high quality of life after this procedure[14]. In this instance, social media may allow the public (including young patients who use social media) to see the positive outcomes of rotationplasty. This tactic can certainly increase the transparency of cancer care, though also help a new patient and their family make a decision regarding where to pursue care. If appropriate, the orthopedic oncologist might utilize individual patient testimony to further promote these and other procedures with demonstrated efficacy, and social media may provide an outlet to do so given the importance of this selection factor in younger patients.

For clinics within a large metropolitan area such as the one in the current study, physician outreach is essential to a growing practice. The orthopedic oncologist and hospital alike must place an emphasis on

Table 3 Comparison of selection factors between patients younger than 40 years of age and those older than 60 years of age

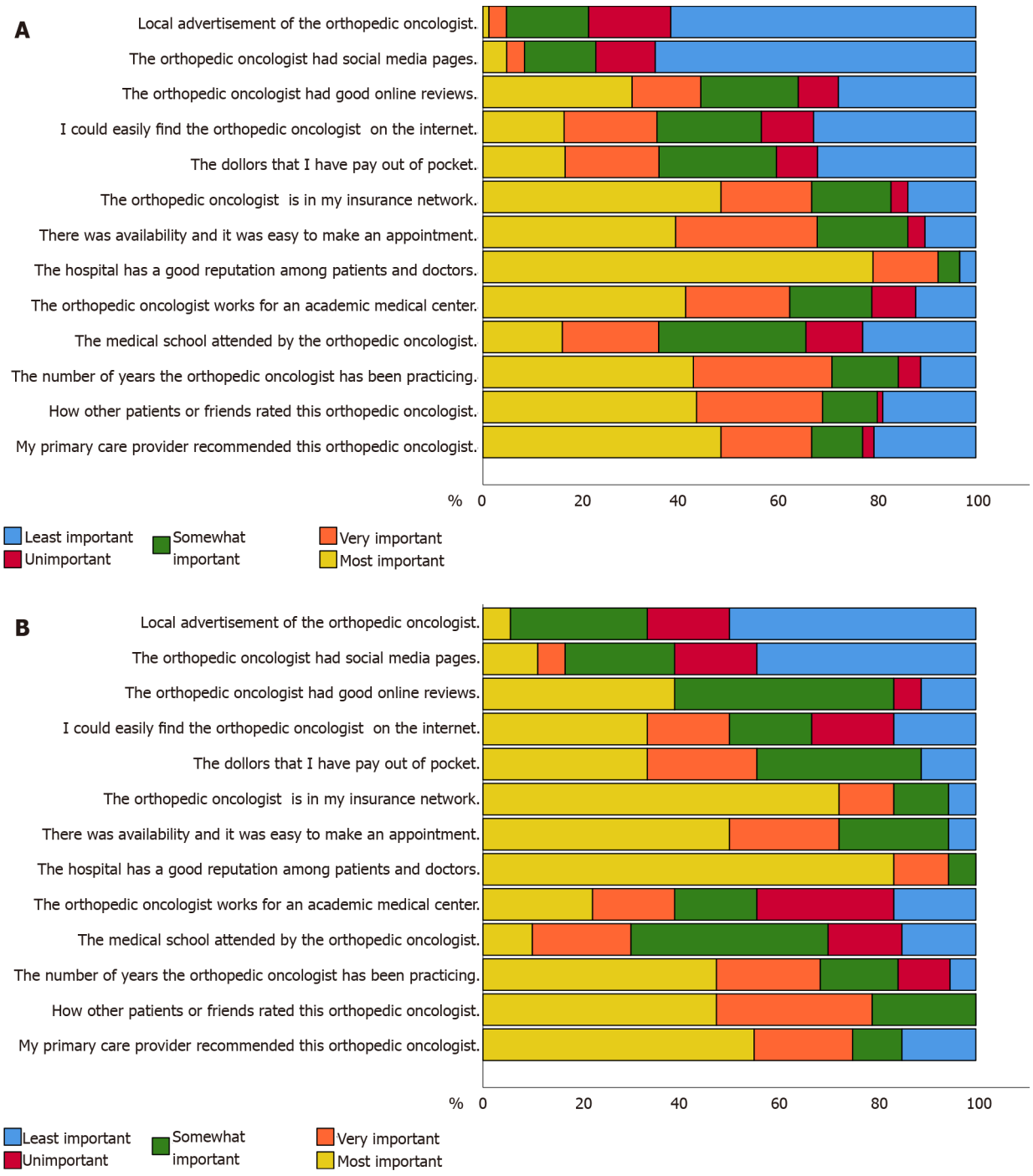
Selection factor	< 40 yr, mean (SD)	> 60 yr, mean (SD)	*P* value
Recommended by primary care provider	4.0 (1.5)	3.5 (1.7)	0.25
How other patients or friends rated the physician	4.26 (0.8)	3.48 (1.7)	0.056
Number of years of practice	3.95 (1.3)	3.8 (1.4)	0.745
The medical school attended	2.95 (1.2)	3.1 (1.4)	0.669
Works in an academic medical center	3.0 (1.5)	3.96 (1.4)	0.014[1]
The hospital has a good reputation	4.78 (0.5)	4.56 (1.0)	0.396
It was easy to make an appointment	4.11 (1.1)	3.81 (1.4)	0.402
They were in my insurance network	4.44 (1.1)	3.48 (1.6)	0.019[1]
The amount of dollars I have to pay out of pocket	3.67 (1.3)	2.24 (1.4)	< 0.001[1]
I could easily find the doctor on the Internet	3.33 (1.5)	2.44 (1.5)	0.035[1]
They had good online reviews	3.5 (1.4)	2.84 (1.7)	0.143
They had accessible social media pages	2.22 (1.4)	1.48 (0.9)	0.016[1]
They were locally advertised	1.94 (1.2)	1.57 (0.9)	0.167

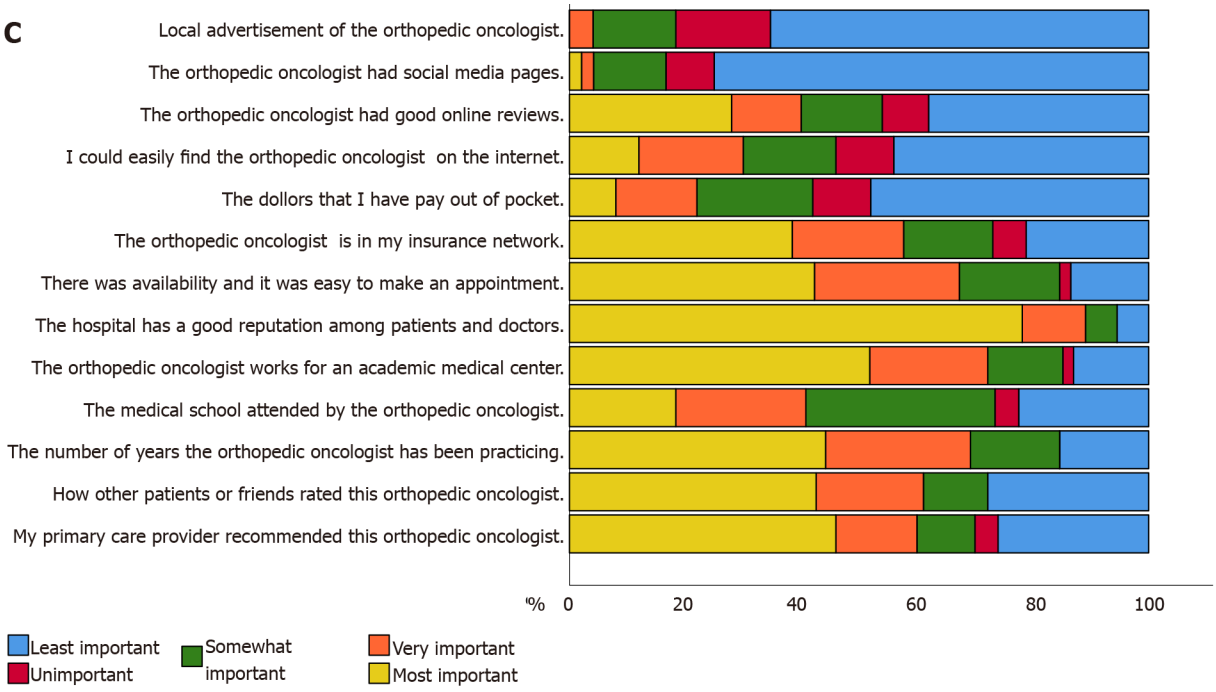
[1]Significant.
A mean value close to '5' is considered most important.

the importance of being readily available to patients. Additionally, the hospital and surgeon must also make the practice attractive to new patients by highlighting instances of outstanding care and favorable outcomes. Bozic *et al*[7] found orthopedic patients express desire to seek information regarding the quality of the provider, though note accessible and actionable information sources are often lacking. While this can be overcome with more frequent advertisement, the current study also found a majority of patients regardless of age chose an orthopedic oncologist based on the recommendation of their primary care provider. In total, 62% were referred, most commonly from an orthopedic surgeon or family doctor. Thus, with respect to expanding the practice or maintaining a favorable reputation, these data imply it may be beneficial to for an orthopedic oncologist to contact referring providers, which not only expands the practice, but contributes to the continuity of patient care. Such an interaction may certainly impact the reputation of the orthopedic oncologist as well.

One unique finding of the current study is that older patients placed a higher emphasis on the importance of seeking care within an academic medical center compared to younger patients. It is difficult to draw conclusions regarding this discrepancy by age, though one explanation is that older patients may have been treated in the same academic center and are simply new to the orthopedic oncology section itself. Another explanation is the perceived association of a higher quality of care with larger, higher volume centers. This may be in contrast to decisions made when choosing a hospital for other orthopedic procedures such as primary arthroplasty. Moser *et al*[15] found that selecting a hospital for arthroplasty is extremely complex, and often an individualized process with no real discernable preference towards higher volume centers in their cohort. For orthopedic cancer diagnoses, the magnitude of the underlying condition is often greater, and a higher volume center may indicate a more experienced multidisciplinary team which may motivate a new patient to seek care at one of these facilities. Furthermore, the current responders chose years in practice as a strong selection factor, and such providers may be located within these high volume centers. However, it is also likely that new patients are generally unaware of the multidisciplinary effort, and simply choose a hospital on familiarity of the name or proximity to the facility.

As this study was a survey design, the findings may not be applicable to orthopedic oncologists in a different practice setting. Second, the overall response rate was 24%, which is low, though appears to be consistent with response rates from other survey studies used to identify selection factors[4,8,16]. Third, the question items of this survey were not validated, and in certain instances, patients omitted answers. As a large amount of the surveyed patients were of an advanced age, we believe that administering a survey *via* REDCap (electronic mailed survey) resulted in a lower yield than would be expected if they were approached in a clinical setting. Last, the patients seen in this practice are of a heterogenous group of diagnoses, ranging from incidental findings to aggressive malignancies, and the factors that influence choosing an orthopedic oncologist may vary by diagnosis. However, given the potential for recall bias, we did not inquire about any underlying diagnoses.


A
Local advertisement of the orthopedic oncologist.
The orthopedic oncologist had social media pages.
The orthopedic oncologist had good online reviews.
I could easily find the orthopedic oncologist on the internet.
The dollors that I have pay out of pocket.
The orthopedic oncologist is in my insurance network.
There was availability and it was easy to make an appointment.
The hospital has a good reputation among patients and doctors.
The orthopedic oncologist works for an academic medical center.
The medical school attended by the orthopedic oncologist.
The number of years the orthopedic oncologist has been practicing.
How other patients or friends rated this orthopedic oncologist.
My primary care provider recommended this orthopedic oncologist.
% 0 20 40 60 80 100
Least important
Unimportant
Somewhat important
Very important
Most important
B
Local advertisement of the orthopedic oncologist.
The orthopedic oncologist had social media pages.
The orthopedic oncologist had good online reviews.
I could easily find the orthopedic oncologist on the internet.
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The number of years the orthopedic oncologist has been practicing.
How other patients or friends rated this orthopedic oncologist.
My primary care provider recommended this orthopedic oncologist.
% 0 20 40 60 80 100
Least important
Unimportant
Somewhat important
Very important
Most important



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Figure 1 Importance of selection factors among new patients. A: Importance of selection factors among all new patients; B: Importance of selection factors among new patients younger than 40 years of age; C: Importance of selection factors among new patients older than 60 years of age.

CONCLUSION

The findings of this investigation suggest a primary care referral, a good hospital reputation, and a good physician reputation are among the most important factors when selecting an orthopedic oncologist. Furthermore, younger patients found social media and Internet presence of their surgeon to be more important than older patients, which may highlight an area for practice expansion when advertising to this group.

ARTICLE HIGHLIGHTS

Research background

There have been efforts to elucidate what factors patients use to select medical oncologists and orthopedic surgeons, but no studies have specifically investigated the patient selection factors for orthopedic oncologists.

Research motivation

Better understanding what factors patients deem important in their process of selecting a physician may allow for better tailoring of a clinical practice.

Research objectives

This study aimed to identify the factors that patients deem important in selecting an orthopedic oncologist with whom to establish care.

Research methods

All new patients presenting to an orthopedic oncology clinic were invited to complete an anonymous survey consisting of 27 questions that identified patient demographic factors, patient social media utilization, and patient identified factors on a Likert scale that are important to selecting an orthopedic oncologist.

Research results

The most important factor for patient selection overall was a good reputation of the hospital. Other important factors were the number of years in practice of the orthopedic oncologist, referral from the patient's primary care provider, and how other patients rated the surgeon. Social media and Internet

presence of the surgeon was more important to patients under the age of 40 and those over the age of 60 felt it more important that the surgeon work in an academic center.

Research conclusions

Strong hospital reputation, primary care referral, and physician reputation were among the strongest selection factors among patients. While hospital reputation may not be adjustable by the individual orthopedic oncologist, it appears important for surgeons to network with primary care providers to increase referrals in order to grow one's practice.

Research perspectives

Future studies could investigate selection factors for patients who come to orthopedic oncology for second opinions after having been evaluated elsewhere.

FOOTNOTES

Author contributions: Gusho CA and Patel V contributed to the data collection, analysis, interpretation, drafting, editing, and revision; Lee L contributed to the interpretation, drafting, editing, and revisions; Blank AT contributed to the conception, oversight, editing, and revision.

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REFERENCES

1 **Porter ME**, Teisberg EO. Redefining Health Care: Creating Value-Based Competition on Results. Cambridge: Harvard Business Publishing, 2006: 25
2 **Harris KM**. How do patients choose physicians? *Health Serv Res* 2003; **38**: 711-732 [PMID: 12785569 DOI: 10.1111/1475-6773.00141]
3 **Kim K**, Ahn S, Lee B, Lee K, Yoo S, Suh DH, No JH, Kim YB. Factors associated with patients' choice of physician in the Korean population: Database analyses of a tertiary hospital. *PLoS One* 2018; **13**: e0190472 [PMID: 29293614 DOI: 10.1371/journal.pone.0190472]
4 **Berger GK**, Medairos R, Regala P, Jacobsohn K, Langenstroer P, See WA, Johnson SC. Factors Influencing Patient Selection of Urologists. *Urology* 2020; **137**: 19-25 [PMID: 31809771 DOI: 10.1016/j.urology.2019.08.066]
5 **Mercado F**, Mercado M, Myers N, Hewit M, Haller NA. Patient preferences in choosing a primary care physician. *J Prim Care Community Health* 2012; **3**: 125-131 [PMID: 23803456 DOI: 10.1177/2150131911421802]

6 **Chen X**, Siu LL. Impact of the media and the internet on oncology: survey of cancer patients and oncologists in Canada. *J Clin Oncol* 2001; **19**: 4291-4297 [PMID: 11731511 DOI: 10.1200/JCO.2001.19.23.4291]

7 **Bozic KJ**, Kaufman D, Chan VC, Caminiti S, Lewis C. Factors that influence provider selection for elective total joint arthroplasty. *Clin Orthop Relat Res* 2013; **471**: 1865-1872 [PMID: 23065331 DOI: 10.1007/s11999-012-2640-9]

8 **Manning BT**, Ahn J, Bohl DD, Mayo BC, Louie PK, Singh K. Spine Surgeon Selection Criteria: Factors Influencing Patient Choice. *Spine (Phila Pa 1976)* 2016; **41**: E814-E819 [PMID: 26656051 DOI: 10.1097/BRS.0000000000001385]

9 **Abghari MS**, Takemoto R, Sadiq A, Karia R, Phillips D, Egol KA. Patient perceptions and preferences when choosing an orthopaedic surgeon. *Iowa Orthop J* 2014; **34**: 204-208 [PMID: 25328483]

10 **Conner-Spady BL**, Marshall DA, Bohm E, Dunbar MJ, Loucks L, Hennigar AW, Frank C, Noseworthy TW. Patient factors in referral choice for total joint replacement surgery. *Med Care* 2014; **52**: 300-306 [PMID: 24848204 DOI: 10.1097/MLR.0000000000000087]

11 **Blank AT**, Shaw S, Wakefield CJ, Zhang Y, Liu WJ, Jones KB, Randall RL. What factors influence patient experience in orthopedic oncology office visits? *World J Clin Oncol* 2020; **11**: 136-142 [PMID: 32257844 DOI: 10.5306/wjco.v11.i3.136]

12 **Harris PA**, Taylor R, Thielke R, Payne J, Gonzalez N, Conde JG. Research electronic data capture (REDCap)--a metadata-driven methodology and workflow process for providing translational research informatics support. *J Biomed Inform* 2009; **42**: 377-381 [PMID: 18929686 DOI: 10.1016/j.jbi.2008.08.010]

13 **Fraval A**, Ming Chong Y, Holcdorf D, Plunkett V, Tran P. Internet use by orthopaedic outpatients - current trends and practices. *Australas Med J* 2012; **5**: 633-638 [PMID: 23382767 DOI: 10.4066/AMJ.2012.1530]

14 **Gradl G**, Postl LK, Lenze U, Stolberg-Stolberg J, Pohlig F, Rechl H, Schmitt-Sody M, von Eisenhart-Rothe R, Kirchhoff C. Long-term functional outcome and quality of life following rotationplasty for treatment of malignant tumors. *BMC Musculoskelet Disord* 2015; **16**: 262 [PMID: 26403306 DOI: 10.1186/s12891-015-0721-0]

15 **Moser A**, Korstjens I, van der Weijden T, Tange H. Patient's decision making in selecting a hospital for elective orthopaedic surgery. *J Eval Clin Pract* 2010; **16**: 1262-1268 [PMID: 20727062 DOI: 10.1111/j.1365-2753.2009.01311.x]

16 **Manning BT**, Bohl DD, Wang KC, Hamid KS, Holmes GB, Lee S. Factors Influencing Patient Selection of a Foot and Ankle Surgeon. *Foot Ankle Spec* 2018; **11**: 315-321 [PMID: 28874071 DOI: 10.1177/1938640017729499]

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SYSTEMATIC REVIEWS

Anterior vertebral body tethering for idiopathic scoliosis in growing children: A systematic review

Davide Bizzoca, Andrea Piazzolla, Lorenzo Moretti, Giovanni Vicenti, Biagio Moretti, Giuseppe Solarino

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Abstract

BACKGROUND

The management of idiopathic scoliosis (IS) in skeletally immature patients should aim at three-dimensional deformity correction, without compromising spinal and chest growth. In 2019, the US Food and Drug Administration approved the first instrumentation system for anterior vertebral body tethering (AVBT), under a Humanitarian Device Exception, for skeletally immature patients with curves having a Cobb angle between 35° and 65°.

AIM

To summarize current evidence about the efficacy and safety of AVBT in the management of IS in skeletally immature patients.

METHODS

From January 2014 to January 2021, Ovid Medline, Embase, Cochrane Library, Scopus, Web of Science, Google Scholar and PubMed were searched to identify relevant studies. The methodological quality of the studies was evaluated and relevant data were extracted.

RESULTS

Seven clinical trials recruiting 163 patients were included in the present review.

Five studies out of seven were classified as high quality, whereas the remaining two studies were classified as moderate quality. A total of 151 of 163 AVBT procedures were performed in the thoracic spine, and the remaining 12 tethering in the lumbar spine. Only 117 of 163 (71.8%) patients had a nonprogressive curve at skeletal maturity. Twenty-three of 163 (14.11%) patients required unplanned revision surgery within the follow-up period. Conversion to posterior spinal fusion (PSF) was performed in 18 of 163 (11%) patients.

CONCLUSION

AVBT is a promising growth-friendly technique for treatment of IS in growing patients. However, it has moderate success and perioperative complications, revision and conversion to PSF.

Key Words: Idiopathic scoliosis; Spinal growth modulation; Anterior spinal instrumentation; Curve correction; Anterior vertebral body tethering; Paediatric spine; Growing spine; Skeletally immature patients; Growth-friendly spinal implants

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Core tip: Although anterior vertebral body tethering is a promising growth-friendly technique for treatment of idiopathic scoliosis in growing patients, it has a moderate success rate and has perioperative complications, revision and conversion to posterior spinal fusion. Future level I studies, with long-term follow-up, are needed to best define the limits and potentials of this emerging surgical technique.

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INTRODUCTION

The management of idiopathic scoliosis (IS) in skeletally immature patients should aim at three-dimensional (3D) deformity correction, without compromising the spinal and chest growth and complete lung development[1-3]. In order to achieve all these goals, besides the classic conservative treatments for IS in growing children - *i.e.,* bracing[4-6] and serial casting - several growth-friendly surgical procedures have been introduced in clinical practice in recent years[7]. These include growing rods[8,9], Shilla procedure[10], vertebral body stapling[11], posterior dynamic deformity correction device[12] and anterior vertebral body tethering (AVBT)[11-16].

AVBT for IS correction, in skeletally immature patients, relies on the asymmetric inhibition of vertebral growth, by applying the Hueter-Volkmann principle[17-21]. Each vertebral body grows both in length, *via* endochondral ossification, and in circumference, by appositional growth[22-25]. The subsequent compression of the growth plate on the curve convexity inhibits vertebral body growth, while the concomitant distraction on the curve concavity promotes vertebral body growth[15]. This dynamic phenomenon finally limits the curve progression and, ideally, reduces deformity without affecting spinal growth and mobility.

After preclinical studies performed in animal models[26-28], in 2010 Crawford and Lenke[16] reported the first case of an 8-year-old child, with a 40° right thoracic curve successfully managed through AVBT. In the following years, based on these encouraging results, different spinal surgeons started the use of off-label devices and the first case series describing the use of AVBT were published by Samdani *et al*[24,29].

In 2019, the US Food and Drug Administration (FDA) approved the first instrumentation system for AVBT, under a Humanitarian Device Exception, for skeletally immature patients with curves having a Cobb angle between 35° and 65°[30]. Since then, several clinical trials focusing on AVBT have been published[8-12]. However, some controversies still exist about this emerging surgical technique and few data are available about the long-term results.

This systematic review aimed to summarize the current evidence about the efficacy and safety of AVBT in the management of IS in skeletally immature patients. Particular attention was given to surgical indications, clinical and radiological outcomes, postoperative complications, re-intervention rates and conversion rates to posterior spinal fusion (PSF).

MATERIALS AND METHODS

The study was conducted with methods described in PRISMA[31]. It was registered in PROSPERO (ID: CRD42020183915) before the data extraction and analysis.

Literature search and study eligibility

Scopus, Web of Science, Springer Link, Ovid Medline, Embase, Cochrane Library, Google Scholar and PubMed were searched from January 2014 to January 2021 to identify relevant papers for further analysis. The main keywords were: "anterior vertebral body tethering (AVBT)" or "tethering" and "scoliosis" and "growing spine" or "growing child" or "immature patients". A manual search of the reference lists of the selected publications was also performed to identify additional studies for potential inclusion. Due to the paucity of studies on AVBT, both retrospective and prospective studies were included in the present systematic review. The following exclusion criteria were applied: (1) < 24 mo of follow-up; (2) Lack of surgical intervention description; and (3) Dropout > 20% at the final follow-up. The review was restricted to articles published in English. When multiple papers from the same centre or trial were depicted, the most thorough publication was selected. Two review authors (Bizzoca D and Piazzolla A) analysed the titles and abstracts. Potentially relevant articles were acquired for full-length text and authors were contacted when the full text was not available.

Data extraction

Information was extracted from each study by two review authors (Bizzoca D and Piazzolla A) and finally checked by two other authors (Moretti B and Solarino G), including: (1) Characteristics of study participants (age, gender, preoperative Cobb angle); (2) Study inclusion; (3) Surgical approach; (4) Clinical outcome; (5) Radiological outcome; (6) Percentage of successful AVBT procedures; (7) Perioperative complication rate and type; (8) Re-intervention rate; and (9) Number of conversions to PSF. Disagreements were resolved by discussion between them.

Study quality assessment and bias risk of the included studies

The quality of the analysed papers was evaluated following the American Academy of Orthopedic Surgeons (AAOS) clinical practice guidelines and review methodology version 2[32]. We assessed the following features: Inclusion and exclusion criteria description; sample size and features; number of patients lost to follow-up; prognostic factors evaluation; outcome evaluation; appropriate statistical analysis; references of the study; data evaluation; presence of bias; presence of confounding factors; and follow-up duration. Based on the study design and the depicted flaws, the quality of each study included in this systematic review was defined as follows: High (< 2 flaws); moderate (≥ 2 and < 4 flaws); low (≥ 4 and < 6 flaws) and very low (≥ 6 flaws). Two authors (Bizzoca D and Piazzolla A) independently evaluated all the studies. In case of disagreement between them, a new combined evaluation was performed. Two senior authors (Moretti B and Solarino G) finally approved the quality assessment procedure. Publication bias could not be assessed by a funnel plot considering the low number of patients in each study.

Primary, secondary and tertiary outcomes

The primary outcome was to assess the success of AVBT at skeletal maturity, with a minimum 24-mo follow-up, in patients managed with this growth-friendly technique. The secondary outcome was to identify the rate of perioperative complications, re-interventions and conversions to PSF, in patients who underwent AVBT. The tertiary outcome was to depict the correct indications for AVBT and the correct preoperative workup, as well as to describe the main feature of the surgical procedure.

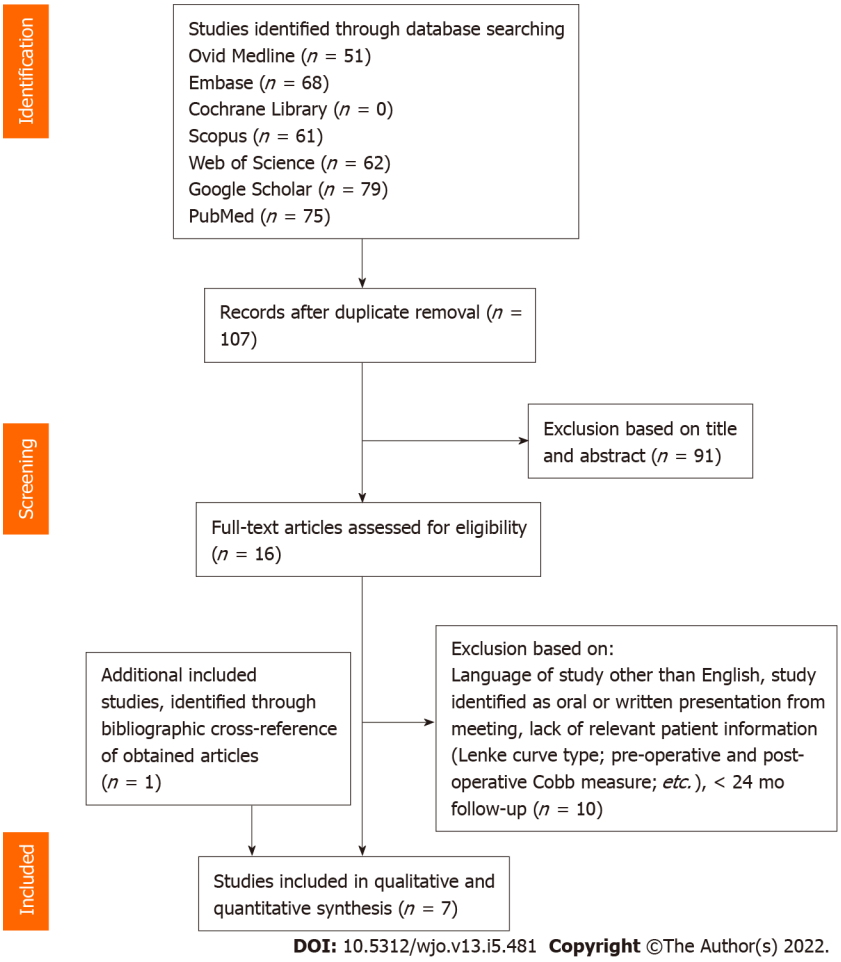
RESULTS

Study selection

The Scopus, Springer Link, Web of Science, Ovid Medline, Embase, Cochrane Library, Google Scholar and PubMed database searches provided a total of 396 studies for potential inclusion in the review (Figure 1). After adjusting for duplicates, 107 studies remained. Of these, 91 studies were discarded after reading titles and reviewing abstracts. The full text of the remaining 16 studies was examined in greater detail. Of these, 10 studies did not meet the inclusion criteria. One additional study was identified through a bibliographic cross-reference of obtained articles. A total of seven articles were finally included in this systematic review.

Study quality

The process of quality assessment, performed according to the AAOS clinical practice guidelines and review methodology version 2, gave the following results: Five[14,20-23] studies out of seven (71.43%) were classified as high quality, whereas the remaining two[17,24] studies out of 10 (28.57%) were



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Figure 1 PRISMA flow diagram.

classified as moderate quality (Table 1).

Study characteristics

The features of the included papers are summarised in Table 1. Seven clinical trials, *i.e.*, one retrospective comparative study (level III)[22], two prospective observational studies (level IV)[21,23] and four retrospective studies[14,17,20,24], recruiting 163 patients were included in the present review. Only one of the included studies (14.3%) compared the outcomes between patients managed with AVBT and a matched cohort of patients treated with PSF and instrumentation[22]. The number of patients, gender, age, minimum follow-up length, clinical and radiological outcomes at the final follow-up and the successful AVBT rate are reported in Table 1. The patients undergoing AVBT had the following scoliosis pattern distribution, according to Lenke's classification: Lenke 1 (n = 140; 85.9%), Lenke 2 (n = 10; 6.13%), Lenke 3 (n = 3; 1.84%), Lenke 5 (n = 9; 5.52%), Lenke 6 (n = 1; 0.61%). A total of 151 of 163 AVBT procedures were performed in the thoracic spine, whereas the remaining 12 were in the lumbar spine. Perioperative complications, number of tether revisions and conversion to PSF of the AVBT procedures are reported in Table 2.

Main indications for AVBT

Currently, there is still not a universal consensus on AVBT indications, about Lenke type, curve size and remaining skeletal growth at the time of surgery. Clinical trials showed the features of the ideal patient for vertebral tethering, but the rate of postoperative complications and the lack of long-term results should be carefully considered when recommending AVBT. Krakow *et al*[30], in a retrospective analysis of 359 patients treated between 2016 and 2019 at a large paediatric centre, showed 75 patients (20.9%) could have been tethered in the years preceding approval FDA approval of AVBT device, by applying the FDA IDE criteria. Nonetheless, all the following points should be carefully assessed before considering this growth-friendly surgical procedure.

Age and skeletal maturity

AVBT has been used in boys and girls aged mainly from 8 to 16 years. Besides biological age, however, skeletal maturity should be carefully evaluated, to estimate the potential curve progression entity, as

Table 1 Study, design, inclusion criteria, study groups feature, follow-up, outcome measures and results of the included trials

Ref.	Design (level of evidence)	Study quality according to AAOS methodology	Inclusion criteria for AVBT	Study group	Control group	AVBT surgical approach	Follow-up	Outcomes at the final FU	Preoperative main features	Results at the final FU
Miyanji *et al*[14], 2020	Retrospective study (level IV)	High-quality study	Major main T or L curves ≥ 40°. Risser score ≤ 3. Sanders score < 5	AVBTs (*n* = 57). Female: 54 (94.74%). Mean age: 12.7 yr (8-16). Curves: Lenke 1: 48; Lenke 2: 6; Lenke 3: 1; Lenke 4: 0; Lenke 5: 1; Lenke 6: 1. Tether location: Thoracic (*n* = 55); lumbar (*n* = 2)	None	VATS plus mini-open for TL/L curves	Minimum 24 mo	Clinical and radiological assessment (success: Residual curve < 35° at maturity)	Tethered curve mean Cobb: 51°. Tethered curve flexibility: 41.8%. Untethered minor curve Cobb: 31.5°. TK (T5-T12): 18°. LL (L1-S1): -55.4°. Rib hump: 14.9 mm. Lumbar prominence: 3.9 mm	Tethered curve Cobb: 23°[a]. Tethered curve correction: 42.9%. Untethered minor curve Cobb: 22.3°[a]. TK (T5-T12): 22°[a]. LL (L1-S1): -56.5°. Rib hump: 10.3 mm[a]. Lumbar prominence: 2.3 mm[a]. Successful AVBT: 44 (77.19%)
Baker *et al*[17], 2021	Retrospective study (level IV)	Moderate quality study	N/A	AVBTs (*n* = 19 in 17 pts). Female: 12 (70.6%). Mean age: 12.9 yr. Curves: Lenke 1: 9 pts; Lenke 2: 3 pts; Lenke 3: 1 pts; Lenke 4: 0; Lenke 5: 4 pts; Lenke 6: 0. Tether location: Thoracic (*n* = 13); lumbar (*n* = 6)	None	VATS plus mini-open for TL/L curves	Minimum 24 mo (2 to 4 yr)	Radiological assessment (success: Residual curve < 35° at maturity)	Tethered curve Cobb: 45°. Tethered curve flexibility: 63%. Untethered minor curve Cobb: 28°. TK (T5-T12): 20°. LL (L1-S1): -59°. Rib hump: N/A. Lumbar prominence: N/A	Tethered curve Cobb: 20°[a]. Tethered curve correction: 73%. Untethered minor curve Cobb: 26°. TK (T5-T12): N/A. LL (L1-S1): -52°. Rib hump: N/A. Lumbar prominence: N/A. Successful AVBT: 9 (52.94%)
Hoernschemeyer *et al*[20], 2020	Retrospective study (level IV)	High-quality study	N/A	AVBTs (*n* = 29). Female: 26 (89.65%). Mean age: 12.7 yr (10-16). Curves: Lenke 1: 23; Lenke 2: 1; Lenke 3: 1; Lenke 4: 0; Lenke 5: 4; Lenke 6: 0. Tether location: Thoracic (*n* = 22); TL (*n* = 3); lumbar (*n* = 4)	None	VATS plus mini-open for TL/L curves	Minimum 24 mo (2 to 5 yr)	Radiological assessment (success: Residual curve ≤ 30° at maturity)	Tethered curve Cobb: MT: 40°. Long thoracic: MT = 56°; L = 22°; Left TL: L = 49°. Tether top, brace bottom: MT = 48°; L=38°. Tether top & bottom: MT = 48°; L = 42°; TK: 36.2°; LL: -60.83°. Rib hump: N/A. Lumbar prominence: N/A	Tethered curve Cobb: MT: 9°[b]. Long thoracic: MT = 21°; L = -1°. Left TL: L = 21°[b]. Tether top, brace bottom: MT = 23°[a]; L = 24°[a]. Tether top & bottom: MT = 24°[a]; L = 15°[a]; TK: 34.48°; LL: -57°. Rib hump: N/A. Lumbar prominence: N/A. Successful AVBT: 20 (74%)
Pehlivanoglu *et al* [21], 2020	Prospective cohort study (level IV)	High-quality study	Age: 9-14 yr. Risser ≤ 2. Sanders ≤ 4). Curve progression after at least 6 mo of brace (> 40°). MT curve > 35°. Curve flexibility > 30%	AVBTs (*n* = 21). Female: 15 (71.43%). Mean age: 11.1 yr (9-14). Curves: Lenke 1: 21. Tether location: Thoracic (*n* = 21)	None	VATS	Minimum 24 mo	Radiological assessment	Tethered curve Cobb: 48.2°. Tethered curve flexibility: N/A. Untethered minor curve Cobb: 24.8°. TK (T5-T12): 26.8°; LL (L1-S1): -51.3°. Rib hump: N/A. Lumbar prominence: N/A	Tethered curve Cobb: 10.1°[a]. Tethered curve flexibility: N/A. Untethered minor curve Cobb: 9.6°[a]. TK (T5-T12): 26°; LL (L1-S1): -51.8°. Rib hump: N/A. Lumbar prominence: N/A.

										Successful AVBT: 20 (95.24%)
Newton *et al*[22], 2020	Retrospective case-control study (level III)	High-quality study	Age: 9-15 yr. Primary thoracic idiopathic scoliosis. Cobb angle: 40°-67°. Risser ≤ 1. No prior spine surgery	AVBTs (*n* = 23). Female: 16 (69.56%). Mean age: 12 yr (9-15). Curves: Lenke 1: 23. Tether location: Thoracic (*n* = 23)	PSF (*n* = 26). Female: 23 (88.46%). Mean age: 13 yr (10-14). Curves: Lenke 1: 26. Tether location: Thoracic (*n* = 26)	VATS	Minimum 24 mo (2 to 5 yr)	Clinical and radiological assessment (success: Residual curve < 35° at maturity)	AVBT group: Tethered curve Cobb: 53°. Untethered curve Cobb: 34°. TK (T2-T12): 25°. LL (L1-S1): N/A. Rib hump: N/A. Lumbar prominence: N/A. PSF group: MT: 54°; LT: 34°; TK (T2-T12): 25°	AVBT group: Tethered curve Cobb: 33°[a]. Untethered minor curve Cobb: 29°. TK (T2-T12): 12°; LL (L1-S1): N/A. Rib hump: N/A. Lumbar prominence: N/A. Successful AVBT: 12 (52%). PSF group: MT: 16°[a]; LT: 12°[a]; TK (T2-T12): 29°
Wong *et al*[23], 2019	Prospective cohort study; a single-centre, Phase-2A pilot study (level IV)	High-quality study	Juvenile or adolescent IS. Age: ≥ 8 and < 15 yr. Risser stage = 0. Bone age of ≤ 13 yr (hand/wrist X-ray). Major right thoracic scoliosis with a Cobb angle of 35°-55° and Lenke-1 curve pattern. TK (T5-T12) < 40°. Instrumentation to be applied no more cephalad than T4 and no more caudal than L2 (inclusive). Menses < 4 mo	AVBTs (*n* = 5). Female: All. Mean age: 11 yr (9-12). Curves: Lenke 1: All. Tether location: Thoracic (all)	None	VATS	Minimum 4 yr	Clinical and radiological assessment	Tethered curve mean Cobb: 40°. Tethered curve flexibility: 63.7%. Untethered curve Cobb: 20.6°. TK (T5-T12): N/A; LL (L1-S1): N/A; Rib hump: N/A. Lumbar prominence: N/A	Tethered curve Cobb: 18.9°[a]. Tethered curve correction: 53.8%. Untethered minor curve Cobb: 5°. Successful AVBT: 3 (60%)
Samdani *et al* [24], 2014	Retrospective study (level IV)	Moderate quality study	N/A	AVBTs (*n* = 11). Female: 8 (73%). Mean age: 12.3 yr. Curves: Lenke 1: All. Tether location: Thoracic (all)	None	VATS	Minimum 24 mo	Clinical and radiological assessment	Tethered curve Cobb: 44°. Tethered curve flexibility: 57%. Untethered curve Cobb: 25.1°. TK (T5-T12): 20.8°; LL (L1-S1): -47.5°. Rib hump: N/A. Lumbar prominence: N/A	Tethered curve Cobb: 13.5°[a]. Tethered curve correction: 70%. Untethered curve Cobb: 7.2°. TK (T5-T12): 21.6°; LL (L1-S1): -54.9°. Successful AVBT: 9 (81.8%)

[a]*P* < 0.001.

[b]*P* > 0.05.

AVBT: Anterior vertebral body tethering; PSF: Posterior spinal fusion; pts: Patients; VATS: Video-Assisted Thoracoscopic Surgery; N/A: Not available; TL: Thoracolumbar; L: Lumbar; FU: Follow-up; IS: Idiopathic scoliosis; AAOS: American Academy of Orthopedic Surgeons.

well as to allow the asymmetrical modulation of the spinal growth *via* the Hueter-Volkmann principle. The ideal skeletal age for AVBT is defined by a Risser score[33] of ≤ 2 and a Sanders score[34] of 3-4. It is important to note Sanders score has shown a strong correlation with the probability of curve progression[35], hence it should be always performed in children eligible for AVBT. Indeed, if the vertebral tethering is performed too early, a higher risk of curve overcorrection should be considered. If it is performed in an almost skeletal mature patient, there will not be enough remaining growth, thus leading to the lack of a relevant curve correction and relevant risk of tethering rupture[36].

Table 2 Perioperative complications, number of tether revisions and conversion to posterior spinal fusion and instrumentation of anterior vertebral body tethering procedures in the included studies

Ref.	Patients (*n*)	Perioperative complications		Tether revision			Conversion to PSF	
		Type of complication	*n* of cases (%)	Causes	*n* of cases (%)	*n* of revisions (%)	Causes	*n* of cases (%)
Miyanji *et al*[14], 2020	57	Pulmonary. Atelectasis. Pneumonia. Superficial wound infection. Hip and shoulder pain. Numbness in the arm and breast	3 (5.26). 1 (1.75). 1 (1.75). 1 (1.75). 1 (1.75)	Overcorrection (loosening tether). Tether breakage (replaced). Adding on (extension of tether)	1 (1.75). 1 (1.75). 1 (1.75)	1 (1.75). 1 (1.75). 1 (1.75)	Insufficient correction of tethered curve and progression of the deformity. Adding on	5 (8.77). 1 (1.75)
Baker *et al*[17], 2020	17	N/A	N/A	Broken tether. Other complications	9 (52.94). 3 (17.7)	1 (5.88). 3 (17.7)	Overcorrection. Progression of the untethered thoracic curve in a patient with lumbar AVBT	1 (5.88). 1 (5.88)
Hoernschemeyer *et al*[20], 2020	29	Recurrent pneumothorax. Syncopal episodes (decompression of a Chiari 1 malformation, diagnosed after AVBT)	1 (3.45). 1 (3.45)	Broken tether. Overcorrection. Adding on	14 (48.275). 2 (6.9). 1 (3.45)	3 (10.3): 1 revisio. 2 PSF. 2 (6.9). 1 (3.45)	Progression of the tethered curve after broken tether	2 (6.9)
Pehlivanoglu *et al*[21], 2020	21	Chylothorax (conservatively managed)	1 (4.76)	Broken tether	1 (4.76)	1 (4.76)	-	-
Newton *et al*[22], 2020	23	Atelectasis with pulmonary oedema (treated with positive airway pressure that resolved by postoperative day 6). Pain radiating down the leg (3 yr postop resolved with physical therapy). Horner syndrome (withasymmetric pupils remaining)	1 (4.35). 1 (4.35). 1 (4.35)	Broken tether (revision for curve progression). Overcorrection (tether removal, tether replaced with less tension). Progression of the untethered curve. Second revision (broken tether with progression, progression)	12. 3. 2. 2	2 (8.7). 2 (8.7). 1 (4.35). 2 (8.7). 1 (4.35). 1 (4.35)	Curve progression (converted to PSF, indication to PSF, but not yet undergone)	3 (13). 3 (13)
Wong *et al*[23], 2019	5	Fever. Postop. Nausea. Postop. Vomiting. Postop. Haematuria. Reactive airways. Right pneumothorax. Left/dependent lung pleural effusion. Pneumonia. Conjunctivitis. Trunk listing	5 (100). 1 (20). 1 (20). 1 (20). 1 (20). 2 (40). 1 (20). 1 (20). 1 (20). 1 (20)	-	-	-	Overcorrection. Curve progression/distal decompensation	1 (20). 1 (20)
Samdani *et al*[24], 2014	11	Persistent atelectasis (bronchoscopy)	1 (9.1)	Overcorrection	2 (18.2)	2 (18.2)	-	-

AVBT: Anterior vertebral body tethering; PSF: Posterior spinal fusion.

Curve aetiology

AVBT has been proposed for idiopathic curves only, since patients with syndromic scoliosis may not respond as predictably, compared with IS. In this kind of patient, the growth of the untethered portion of the spine may be unpredictable, thus potentially increasing the re-intervention rate. Similarly, left-sided thoracic curves are not an absolute contraindication for AVBT, but the surgeon must rule out the presence of a syndromic condition, before recommending AVBT. Finally, the surgeon should be aware the left-sided approach might be high-demanding, from a technical point of view, since segmentary vessels lie closer to the aorta, compared with the right side, thus ligation could be more difficult.

Curve location, size, flexibility and 3D features

AVBT has been largely studied in idiopathic flexible thoracic curves, Lenke type 1, with a Cobb angle between 35° and 65°, according to FDA IDE criteria[37]. Published and ongoing clinical trials have also focused on other Lenke types, *i.e.*, types 2, 3C and 5[38]; the Cobb angle for lumbar curves should be < 35°. Although lumbar curves are not contraindications for AVBT, this technique has been described for thoracic curves; consequently, particular caution should be taken when performing surgery of the lumbar spine (*i.e.*, open laparotomy or mini-laparotomy could be needed to access the lumbar spine)[39]. Furthermore, as suggested by Newton *et al*[15], tethering more than one curve potentially reduces the predictability of the outcome. Curve flexibility should be preoperatively assessed on supine bending radiographs; a curve showing a 50% flexibility is an ideal candidate for AVBT[15]. Thoracic kyphosis > 40°[29] is a relative contraindication for AVBT, since this growing-friendly technique, by involving the tethering of the most anterior portion of the spine, could improve the patient's kyphosis[39]. Finally, a careful preoperative evaluation of the patient's sagittal profile, spinopelvic and 3D parameters can help reduce the risk of flat back or decreased lordosis[39].

Preoperative planning

The preoperative workup for patients undergoing AVBT includes upstanding and supine full spine films in anteroposterior and lateral projections, supine bending films and full spine and brain magnetic resonance imaging. Buyuk *et al*[13], in a retrospective study recruiting 51 patients, confirmed preoperative bending radiographs provide a reasonable estimate of postoperative correction for patients undergoing AVBT. An increase of the major Cobb angle, however, is expected on first upstanding spine radiographs, compared to intraoperative X-rays. Spine levels are typically instrumented from upper to lower vertebra; tension should be applied on the tether, to bring the tilted discs into neutral alignment where possible[14].

Surgical technique

AVBT should be carried out using a strict lateral decubitus position, with the convex side of the thoracic deformity facing upward, on a radiolucent table. The patient is induced under general anaesthesia, using a double-lumen endotracheal tube, thus allowing the anaesthetist to deflate the right lung (or left lung, in presence of left-sided thoracic curves) during the procedure, to access the anterior thoracic vertebral bodies. Care should be taken to protect the brachial plexus by placing a soft gel roll under the axilla[39]. The right arm should be placed on an armrest, and a soft gel pad should be used to protect the ulnar nerve. The patient is finally secured with tape. Intraoperative neuromonitoring, with somatosensory evoked potential and transcranial motor evoked potentials should be used to monitor spinal cord function during surgery and assess upper and lower extremities. All the vertebral bodies to be instrumented should be identified under fluoroscopic guidance and marked on the skin. The right lung (left lung in left-sided thoracic curves) should be deflated by the anaesthetist before starting surgery. After standard skin preparation and draping, anterior surgical access is performed; thoracoscopic, mini-open and traditional open access have been described.

Although video-assisted thoracoscopy surgery (VATS) usually allows vertebral instrumentation from T4 to L2, in some cases, the diaphragmatic attachments may make the instrumentation of the vertebrae distally to T12 more technically demanding. An additional open or mini-open retroperitoneal approach is usually needed to instrument the vertebrae distally to L2. VATS is generally performed using two anterior viewing portals of 1 cm in length, placed on the anterior axillary line, and two/three posterior instrumentation portals of about 3 cm in length, placed on the posterior axillary line, overlying the vertebral bodies.

In deep dissection, the parietal pleura is opened over the spine and segmental vessels should be ligated on the convex side. Once vertebral dissection and exposure are completed, under fluoroscopic guidance, a staple and a bicortical screw are implanted in each instrumented vertebra. The entry point for the staple and the screw is just anterior to the rib head in the vertebral body. After completing all levels of instrumentation, the polyethylene cable is installed. Tension on the cable is applied on each instrumented level; care should be taken to maximally tighten the tether at the curve apex, while minimal tension should be applied at the upper and lower instrumented vertebrae, to avoid screw plough and adding-on. However, there is no consensus about the exact amount of tension to be applied.

Before wound closure, the thoracic cavity should be irrigated with saline and accurate haemostasis should be performed. The lung is reinflated, and a chest drainage tube is typically placed and set to suction. All wounds finally undergo layered sutures. The chest tube should be put on suction for 48 h with daily radiographic control; on postoperative day 3, if there is no residual pneumothorax, the tube should be put off suction and then removed on postoperative day four.

Clinical outcome and complication rates

The clinical success of AVBT is defined as the achievement of a nonprogressive scoliosis curve - *i.e.*, Cobb angle < 35° - at skeletal maturity, avoiding PSF. Patients who needed one or more revision procedures were considered successful if they finally presented a stable curve at skeletal maturity. Only 117 of 163 (71.8%) patients carried out a nonprogressive curve at skeletal maturity. The success rate of

AVBT also showed a wide heterogeneity in the analysed studies, ranging from 52%[22] to 95.24%[21].

A postoperative complication rate of 17.8% was observed, and complications were also observed in patients that achieved a successful outcome at skeletal maturity. Postoperative complications included pulmonary complications (n = 12; 7.4%), including atelectasis (n = 5; 3.07%), pneumonia (n = 2; 1.23 %), pneumothorax (n = 4; 2.45%) and chylothorax (n = 1; 0.6%). All these complications were successfully managed conservatively.

Twenty-three of 163 (14.11%) patients required unplanned revision surgery within the follow-up period. The main indications for AVBT revision were: Curve overcorrection (n = 11; 6.75%); broken tether with curve progression (n = 8; 4.9%); adding-on (n = 2; 1.23%); and progression of the untethered curve (n = 2; 1.23%). Overcorrection was defined by a reduction of the preoperative Cobb angle progressing beyond the neutral axis, and was recorded as a negative number. Broken tethers, identified as a change in screw angulation > 5° on consecutive standing spine radiographs, were not an indication for revision surgery. A re-intervention was needed when curve progression was detected because of the tether breakage. Adding-on, *i.e.*, postoperative loss of correction due to curve progression, was managed with tether extension.

Untethered curve progression is another concern of AVBT. Hoernschemeyer *et al*[20] described the combined use of thoracic tether and lumbar brace in eight patients with larger main thoracic curves and smaller lumbar curves. In this subset of patients, a significant decrease in all the three measured curves, from preoperatively to the latest postoperative follow-up was observed[20]. This therapeutic strategy, combining thoracic AVBT with a lumbar brace, could be useful in the management of scoliosis in growing children.

Conversion to PSF was performed in 18 of 163 (11%) patients during follow-up. In these patients, AVBT gave no significant advantages, since the patients could not avoid PSF surgery, within 24-mo after tethering.

AVBT versus PSF

PSF and instrumentation is the gold standard for the treatment of patients with scoliotic curves > 45°[40, 41]. Newton *et al*[22] in a retrospective comparative study, have recently compared outcomes of patients with immature IS, who underwent AVBT, with those of a matched cohort of patients treated with PSF, at a minimum 24-mo follow-up. Although the post-intervention patient-reported outcomes (PROMs) were similar in both groups, at the final follow-up, the AVBT group had a significantly higher residual deformity, compared with patients receiving PSF (P < 0.001). In the AVBT cohort, only 52% of patients were successful in having curves of < 35° at skeletal maturity. In the PSF cohort, no patient needed revision surgery, whereas in the AVBT group, five of 23 (21.74%) patients underwent one AVBT revision and the other two patients (8.7%) needed two AVBT revisions procedures. A broken tether was observed in 12 of 23 (52%) patients. Three of 23 patients needed surgical conversion to PSF and an additional three were indicated for PSF, but they had not yet undergone PSF within the study period (overall conversion rate to PSF: 26%). Finally, the proposed advantages of tethering, including progressive postoperative curve correction and maintenance of spinal motion, were not demonstrated in the AVBT group.

DISCUSSION

AVBT is a promising emerging technique for the surgical treatment of IS in growing patients[36]. It mainly aims for 3D correction of the scoliotic deformity, without reverting to spinal fusion or delaying the need for PSF[15,36]. In 2019, the first instrumentation system for AVBT received FDA clearance, under a Humanitarian Device Exemption, based on the results of a Phase 2A pilot study, performed by Wong *et al*[23]. Although AVBT has shown encouraging results in the treatment of IS in growing patients, there is a paucity of published data about this growth-friendly procedure and long-term results are not yet available. This systematic review aimed to summarise current evidence about the efficacy and safety of AVBT in the management of IS in skeletally immature patients.

Although there is still not a universal consensus on AVBT indications, clinical trials have shown the features of the ideal patient for vertebral tethering, *i.e.*, a skeletally immature patient, with a primary and flexible idiopathic thoracic curve. More recent clinical studies[14,17,20] have also investigated the role of AVBT in scoliosis patterns other than Lenke 1. Baker *et al*[17] in a retrospective study analysing the results of 19 AVBT procedures performed in 17 patients, compared 13 thoracic AVBT procedures to lumbar ones. The two groups had comparable demographic features in terms of gender, body mass index and skeletal age. These authors observed in lumbar AVBTs a greater immediate percentage correction and a higher correction rate per level per month compared with the thoracic cohort. Nonetheless, one revision procedure only (8%) was performed in the thoracic group, whereas three revision surgical procedures were needed in lumbar AVBT (50%).

Hoernschemeyer *et al*[20] in a retrospective study recruiting 29 patients, identified five distinct subgroups of skeletally immature patients, each receiving different treatments. Patients with a single, main thoracic curve received thoracic AVBT only. In these patients, the structural curve and both

compensatory curves demonstrated continued postoperative improvement and achieved good control at the final follow-up[20]. Patients receiving thoracic AVBT and a lumbar brace also showed postoperative improvement of both curves[20]. Similar findings were observed in patients with left thoracolumbar curves and those with large main thoracic and lumbar curves treated with a combined thoracic and lumbar AVBT[20]. Finally, patients with a long thoracic curve received a single tether and exhibited a decrease in the main thoracic curve at the latest follow-up[20]. The last subgroup of patients, however, should be monitored over time since they have the largest number of consecutive levels tethered[20].

The anterior approach to the spine needed in the vertebral tethering could be another concern. In the last decades, posterior approaches have largely replaced the anterior access to the spine, therefore several surgeons have not been trained to perform an anterior approach to the spine. However, Baroncini *et al*[18] in a retrospective study that recruited 90 patients, have recently observed that AVBT has a rapid learning curve. These authors showed intubation time and surgical time per screw decrease by > 50% for each treated patient; the estimated blood loss per screw decreased by 66% for each surgical procedure; and intubation and hospitalization decreased by 32%.

Despite AVBT being a promising growth-friendly surgical procedure, endowed with several potential advantages, it has still a lower success rate and a higher complication rate compared with PSF. Hence, the gathered data of the studies included showed AVBT was successful only in 117 of 163 (71.8%) patients. Moreover, 23 of 163 (14.11%) patients required unplanned revision surgery and 18 of 163 (11%) patients needed conversion to PSF within the follow-up period. A postoperative complication rate of 17.8% was also observed in the studies included in the present review.

This is, to the best of our knowledge, the first systematic review to investigate the effectiveness and safety of AVBT in the management of IS in growing children. The main limitation of the present study was the low level of evidence of the included studies, since no randomised clinical trials have been published on AVBT. Currently, six ongoing clinical trials are available on Clinicaltrials.gov[42]: Four prospective clinical trials focusing on AVBT and one prospective comparative nonrandomised and one randomised clinical trial are aiming to compare AVBT to PSF. The ongoing and future studies should confirm the surgical criteria for AVBT, prove tethering long-term effectiveness and safeness, focus on PROMs, and propose strategies to avoid perioperative complications and long-term implant failures. A more durable, fatigue-resistant cable should be also developed to prevent the high number of broken tethers observed in the published studies.

CONCLUSION

The analysis of the literature included in this systematic review showed that AVBT is a promising growth-friendly technique for the treatment of IS in growing patients. However, AVBT has a moderate success rate and has perioperative complications, revision and conversion to PSF. Future level I studies, with long-term follow-up, are needed to define the limits and potentials of this emerging surgical technique.

ARTICLE HIGHLIGHTS

Research background

Anterior vertebral body tethering (AVBT) was originally described in 2010 by Crawford and Lenke[16], who reported the first case of an 8-year-old child, with a 40° right thoracic curve successfully managed with this growth-friendly technique. In 2019, the US Food and Drug Administration approved the first instrumentation system for AVBT, under a Humanitarian Device Exception, for skeletally immature patients with curves having a Cobb angle between 35° and 65°. However, some controversies still exist in this emerging surgical technique.

Research motivation

This systematic review was designed to summarise current evidence about the efficacy and safety of AVBT in the management of idiopathic scoliosis in skeletally immature patients.

Research objectives

The objectives of this systematic review were: (1) To assess the success of AVBT at a minimum 24-mo follow-up; (2) To identify the rate of perioperative complications, re-interventions and conversions to posterior spinal fusion (PSF), in patients who underwent AVBT; and (3) To identify the correct indications for AVBT.

Research methods

The search of electronic databases was performed to identify relevant clinical studies, dealing with AVBT, for further analysis. A total of 107 studies were identified, but only seven of these were included in the present review.

Research results

The pooled data of seven studies with 163 patients showed that AVBT was successful only in 117 patients (71.8%). Moreover, 23 patients (14.11%) required unplanned revision surgery and 18 (11%) needed conversion to PSF within the follow-up period. A postoperative complication rate of 17.8% was also observed.

Research conclusions

AVBT is a promising growth-friendly technique for the treatment of idiopathic scoliosis in growing patients. However, AVBT has a moderate success rate has perioperative complications, revision and conversion to PSF.

Research perspectives

Future studies should confirm the surgical criteria for AVBT, prove tethering long-term effectiveness and safety, focus on patient-reported outcomes measures, and propose strategies to avoid perioperative complications and long-term implant failures. A more durable, fatigue-resistant cable should be developed to prevent the high number of broken tethers observed in the published studies.

FOOTNOTES

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REFERENCES

1 **Akbarnia BA**. Management themes in early onset scoliosis. *J Bone Joint Surg Am* 2007; **89** Suppl 1: 42-54 [PMID: 17272422 DOI: 10.2106/jbjs.f.01256]

2 **Williams BA**, Matsumoto H, McCalla DJ, Akbarnia BA, Blakemore LC, Betz RR, Flynn JM, Johnston CE, McCarthy RE, Roye DP Jr, Skaggs DL, Smith JT, Snyder BD, Sponseller PD, Sturm PF, Thompson GH, Yazici M, Vitale MG. Development and initial validation of the Classification of Early-Onset Scoliosis (C-EOS). *J Bone Joint Surg Am* 2014; **96**: 1359-1367 [PMID: 25143496 DOI: 10.2106/JBJS.M.00253]

3 **Ruf M**, Drumm J, Jeszenszky D. Anterior instrumented fusion for adolescent idiopathic scoliosis. *Ann Transl Med* 2020; **8**: 31 [PMID: 32055622 DOI: 10.21037/atm.2019.11.84]

4 **Piazzolla A**, Bizzoca D, Solarino G, Brayda-Bruno M, Tombolini G, Ariagno A, Moretti B. Maria Adelaide brace in the management of Scheuermann's Kyphosis. *Spine Deform* 2021; **9**: 549-557 [PMID: 33206353 DOI: 10.1007/s43390-020-00225-y]

5 **Hawary RE**, Zaaroor-Regev D, Floman Y, Lonner BS, Alkhalife YI, Betz RR. Brace treatment in adolescent idiopathic scoliosis: risk factors for failure-a literature review. *Spine J* 2019; **19**: 1917-1925 [PMID: 31325626 DOI: 10.1016/j.spinee.2019.07.008]

6 **Halsey M**, Dolan LA, Hostin RA, Adobor RD, Dayer R, Dema E, Letaif OB. Scoliosis Research Society survey: brace management in adolescent idiopathic scoliosis. *Spine Deform* 2021; **9**: 697-702 [PMID: 33580371 DOI: 10.1007/s43390-020-00265-4]

7 **Dimeglio A**, Canavese F. The immature spine: growth and idiopathic scoliosis. *Ann Transl Med* 2020; **8**: 22 [PMID: 32055613 DOI: 10.21037/atm.2019.11.134]

8 **Skaggs DL**, Akbarnia BA, Flynn JM, Myung KS, Sponseller PD, Vitale MG; Chest Wall and Spine Deformity Study Group; Growing Spine Study Group; Pediatric Orthopaedic Society of North America; Scoliosis Research Society Growing Spine Study Committee. A classification of growth friendly spine implants. *J Pediatr Orthop* 2014; **34**: 260-274 [PMID: 23995146 DOI: 10.1097/BPO.0000000000000073]

9 **Jeszenszky D**, Kaiser B, Meuli M, Fekete TF, Haschtmann D. Surgical growth guidance with non-fused anchoring segments in early-onset scoliosis. *Eur Spine J* 2019; **28**: 1301-1313 [PMID: 30848364 DOI: 10.1007/s00586-019-05934-1]

10 **McCarthy RE**, Luhmann S, Lenke L, McCullough FL. The Shilla growth guidance technique for early-onset spinal deformities at 2-year follow-up: a preliminary report. *J Pediatr Orthop* 2014; **34**: 1-7 [PMID: 23934092 DOI: 10.1097/BPO.0b013e31829f92dc]

11 **Cuddihy L**, Danielsson AJ, Cahill PJ, Samdani AF, Grewal H, Richmond JM, Mulcahey MJ, Gaughan JP, Antonacci MD, Betz RR. Vertebral Body Stapling versus Bracing for Patients with High-Risk Moderate Idiopathic Scoliosis. *Biomed Res Int* 2015; **2015**: 438452 [PMID: 26618169 DOI: 10.1155/2015/438452]

12 **Floman Y**, El-Hawary R, Lonner BS, Betz RR, Arnin U. Vertebral growth modulation by posterior dynamic deformity correction device in skeletally immature patients with moderate adolescent idiopathic scoliosis. *Spine Deform* 2021; **9**: 149-153 [PMID: 32827087 DOI: 10.1007/s43390-020-00189-z]

13 **Buyuk AF**, Milbrandt TA, Mathew SE, Potter DD, Larson AN. Does preoperative and intraoperative imaging for anterior vertebral body tethering predict postoperative correction? *Spine Deform* 2021; **9**: 743-750 [PMID: 33481215 DOI: 10.1007/s43390-020-00267-2]

14 **Miyanji F**, Pawelek J, Nasto LA, Rushton P, Simmonds A, Parent S. Safety and efficacy of anterior vertebral body tethering in the treatment of idiopathic scoliosis. *Bone Joint J* 2020; **102-B**: 1703-1708 [PMID: 33249889 DOI: 10.1302/0301-620X.102B12.BJJ-2020-0426.R1]

15 **Newton PO**. Spinal growth tethering: indications and limits. *Ann Transl Med* 2020; **8**: 27 [PMID: 32055618 DOI: 10.21037/atm.2019.12.159]

16 **Crawford CH 3rd**, Lenke LG. Growth modulation by means of anterior tethering resulting in progressive correction of juvenile idiopathic scoliosis: a case report. *J Bone Joint Surg Am* 2010; **92**: 202-209 [PMID: 20048114 DOI: 10.2106/JBJS.H.01728]

17 **Baker CE**, Kiebzak GM, Neal KM. Anterior vertebral body tethering shows mixed results at 2-year follow-up. *Spine Deform* 2021; **9**: 481-489 [PMID: 33113121 DOI: 10.1007/s43390-020-00226-x]

18 **Baroncini A**, Trobisch PD, Migliorini F. Learning curve for vertebral body tethering: analysis on 90 consecutive patients. *Spine Deform* 2021; **9**: 141-147 [PMID: 32827085 DOI: 10.1007/s43390-020-00191-5]

19 **Baroncini A**, Rodriguez L, Verma K, Trobisch PD. Feasibility of Single-Staged Bilateral Anterior Scoliosis Correction in Growing Patients. *Global Spine J* 2021; **11**: 76-80 [PMID: 32875858 DOI: 10.1177/2192568219892904]

20 **Hoernschemeyer DG**, Boeyer ME, Robertson ME, Loftis CM, Worley JR, Tweedy NM, Gupta SU, Duren DL, Holzhauser CM, Ramachandran VM. Anterior Vertebral Body Tethering for Adolescent Scoliosis with Growth Remaining: A Retrospective Review of 2 to 5-Year Postoperative Results. *J Bone Joint Surg Am* 2020; **102**: 1169-1176 [PMID: 32618924 DOI: 10.2106/JBJS.19.00980]

21 **Pehlivanoglu T**, Oltulu I, Ofluoglu E, Sarioglu E, Altun G, Korkmaz M, Yildirim K, Aydogan M. Thoracoscopic Vertebral Body Tethering for Adolescent Idiopathic Scoliosis: A Minimum of 2 Years' Results of 21 Patients. *J Pediatr Orthop* 2020; **40**: 575-580 [PMID: 32427800 DOI: 10.1097/BPO.0000000000001590]

22 **Newton PO**, Bartley CE, Bastrom TP, Kluck DG, Saito W, Yaszay B. Anterior Spinal Growth Modulation in Skeletally Immature Patients with Idiopathic Scoliosis: A Comparison with Posterior Spinal Fusion at 2 to 5 Years Postoperatively. *J Bone Joint Surg Am* 2020; **102**: 769-777 [PMID: 32379117 DOI: 10.2106/JBJS.19.01176]

23 **Wong HK**, Ruiz JNM, Newton PO, Gabriel Liu KP. Non-Fusion Surgical Correction of Thoracic Idiopathic Scoliosis Using a Novel, Braided Vertebral Body Tethering Device: Minimum Follow-up of 4 Years. *JB JS Open Access* 2019; **4**: e0026 [PMID: 32043058 DOI: 10.2106/JBJS.OA.19.00026]

24 **Samdani AF**, Ames RJ, Kimball JS, Pahys JM, Grewal H, Pelletier GJ, Betz RR. Anterior vertebral body tethering for idiopathic scoliosis: two-year results. *Spine (Phila Pa 1976)* 2014; **39**: 1688-1693 [PMID: 24921854 DOI: 10.1097/BRS.0000000000000472]

25 **ROAF R**. Vertebral growth and its mechanical control. *J Bone Joint Surg Br* 1960; **42-B**: 40-59 [PMID: 13854527 DOI: 10.1302/0301-620x.42b1.40]

26 **Newton PO**, Upasani VV, Farnsworth CL, Oka R, Chambers RC, Dwek J, Kim JR, Perry A, Mahar AT. Spinal growth modulation with use of a tether in an immature porcine model. *J Bone Joint Surg Am* 2008; **90**: 2695-2706 [PMID: 19047716 DOI: 10.2106/JBJS.G.01424]

27 **Newton PO**, Farnsworth CL, Faro FD, Mahar AT, Odell TR, Mohamad F, Breisch E, Fricka K, Upasani VV, Amiel D. Spinal growth modulation with an anterolateral flexible tether in an immature bovine model: disc health and motion preservation. *Spine (Phila Pa 1976)* 2008; **33**: 724-733 [PMID: 18379398 DOI: 10.1097/BRS.0b013e31816950a0]

28 **Newton PO**, Fricka KB, Lee SS, Farnsworth CL, Cox TG, Mahar AT. Asymmetrical flexible tethering of spine growth in an immature bovine model. *Spine (Phila Pa 1976)* 2002; **27**: 689-693 [PMID: 11923660 DOI: 10.1097/00007632-200204010-00004]

29 **Samdani AF**, Ames RJ, Kimball JS, Pahys JM, Grewal H, Pelletier GJ, Betz RR. Anterior vertebral body tethering for immature adolescent idiopathic scoliosis: one-year results on the first 32 patients. *Eur Spine J* 2015; **24**: 1533-1539 [PMID:

25510515 DOI: 10.1007/s00586-014-3706-z]
30 **Krakow AR**, Magee LC, Cahill PJ, Flynn JM. Could have tethered: predicting the proportion of scoliosis patients most appropriate for thoracic anterior spinal tethering. *Spine Deform* 2021; **9**: 1005-1012 [PMID: 33534123 DOI: 10.1007/s43390-021-00296-5]
31 **Liberati A**, Altman DG, Tetzlaff J, Mulrow C, Gøtzsche PC, Ioannidis JP, Clarke M, Devereaux PJ, Kleijnen J, Moher D. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate healthcare interventions: explanation and elaboration. *BMJ* 2009; **339**: b2700 [PMID: 19622552 DOI: 10.1136/bmj.b2700]
32 **AAOS**. AAOS Clinical Practice Guideline and Systematic Review Methodology. [cited 20 January 2021]. Available from: https://aaos-app-prod-aaoswww01.azurewebsites.net/uploadedFiles/PreProduction/Quality/Guidelines_and_Reviews/Guideline%20and%20Systematic%20Review%20Processes_v4.0_Final8cd7.pdf?_ga=2.244485197.938110896.1540216238-29030028.1531151248
33 **Risser JC**, Brand RA. The iliac apophysis: An invaluable sign in the management of scoliosis. *Clinical Orthopaedics and Related Research* 2010; **468**: 646-653
34 **Sanders JO**, Khoury JG, Kishan S, Browne RH, Mooney JF 3rd, Arnold KD, McConnell SJ, Bauman JA, Finegold DN. Predicting scoliosis progression from skeletal maturity: a simplified classification during adolescence. *J Bone Joint Surg Am* 2008; **90**: 540-553 [PMID: 18310704 DOI: 10.2106/JBJS.G.00004]
35 **Sitoula P**, Verma K, Holmes L Jr, Gabos PG, Sanders JO, Yorgova P, Neiss G, Rogers K, Shah SA. Prediction of Curve Progression in Idiopathic Scoliosis: Validation of the Sanders Skeletal Maturity Staging System. *Spine (Phila Pa 1976)* 2015; **40**: 1006-1013 [PMID: 26356067 DOI: 10.1097/BRS.0000000000000952]
36 **Senkoylu A**, Riise RB, Acaroglu E, Helenius I. Diverse approaches to scoliosis in young children. *EFORT Open Rev* 2020; **5**: 753-762 [PMID: 33204519 DOI: 10.1302/2058-5241.5.190087]
37 **Cahill P**. Vertebral Body Tethering Outcomes for Pediatric Idiopathic Scoliosis. In: ClinicalTrials.gov. [accessed 2021 Jan 20]. In: ClinicalTrials.gov [Internet]. Bethesda (MD): U.S. National Library of Medicine. Available from: https://clinicaltrials.gov/ct2/show/NCT03194568 ClinicalTrials.gov Identifier: NCT03194568
38 **Larson NA**. Anterior Vertebral Body Tethering (AVBT) Using Zimmer Biomet Tether System or Dynesys System Components to Treat Pediatric Scoliosis. Available from: https://clinicaltrials.gov/ct2/show/NCT03506334 ClinicalTrials.gov Identifier: NCT03506334
39 **Parent S**, Shen J. Anterior Vertebral Body Growth-Modulation Tethering in Idiopathic Scoliosis: Surgical Technique. *J Am Acad Orthop Surg* 2020; **28**: 693-699 [PMID: 32618681 DOI: 10.5435/JAAOS-D-19-00849]
40 **Piazzolla A**, Montemurro V, Bizzoca D, Parato C, Carlucci S, Moretti B. Accuracy of plain radiographs to identify wrong positioned free hand pedicle screw in the deformed spine. *J Neurosurg Sci* 2019; **63**: 372-378 [PMID: 27167472 DOI: 10.23736/S0390-5616.16.03670-5]
41 **Piazzolla A**, Bizzoca D, Solarino G, Parato C, Moretti B. Plasma Technology Reduces Blood Loss in Adolescent Idiopathic Scoliosis Surgery: A Prospective Randomized Clinical Trial. *Global Spine J* 2021; **11**: 874-880 [PMID: 32677514 DOI: 10.1177/2192568220928344]
42 **Clinicaltrials.gov**. Clinicaltrials.org: search for "Anterior Vertebral Body Tethering" [cited 20 January 2021]. Available from: https://www.clinicaltrials.gov/ct2/results?cond=tethering+scoliosis&term=&cntry=&state=&city=&dist=

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SYSTEMATIC REVIEWS

Effect of non-steroidal anti-inflammatory drugs on fracture healing in children: A systematic review

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Abstract

BACKGROUND

Non-steroidal anti-inflammatory drugs (NSAIDs) are among the most commonly prescribed medications in the United States. Although they are safe and effective means of analgesia for children with broken bones, there is considerable variation in their clinical use due to persistent concerns about their potentially adverse effect on fracture healing.

AIM

To assess whether NSAID exposure is a risk factor for fracture nonunion in children.

METHODS

We systematically reviewed the literature reporting the effect of NSAIDs on bone healing. We included all clinical studies that reported on adverse bone healing complications in children with respect to NSAID exposure. The outcomes of interest were delayed union or nonunion. Study quality was assessed using the Newcastle-Ottawa scale for non-randomized studies. A final table was constructed summarizing the available evidence.

RESULTS

A total of 120 articles were identified and screened, of which 6 articles were included for final review. Nonunion in children is extremely rare; among the studies included, there were 2011 nonunions among 238822 fractures (0.84%). None of the included studies documented an increased risk of nonunion or delayed bone healing in those children who are treated with NSAIDs in the

immediate post-injury or peri-operative time period. Additionally, children are likely to take these medications for only a few days after injury or surgery, further decreasing their risk of adverse side-effects.

CONCLUSION

This systematic review suggests that NSAIDS can be safely prescribed to pediatric orthopaedic patients absent other contraindications without concern for increased risk of fracture non-union or delayed bone healing. Additional prospective studies are needed focusing on higher risk fractures and elective orthopaedic procedures such as osteotomies and spinal fusion.

Key Words: Non-steroidal anti-inflammatory drug; Nonunion; Complication; Pediatric fractures; Pain management; Bone healing

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Core Tip: Non-steroidal anti-inflammatory drugs (NSAIDs) are among the most commonly prescribed medications in the United States. To assess whether NSAID exposure is a risk factor for fracture nonunion in children. We systematically reviewed the literature reporting the effect of NSAIDs on bone healing. This systematic review suggests that NSAIDS can be safely prescribed to pediatric orthopaedic patients absent other contraindications without concern for increased risk of fracture non-union or delayed bone healing.

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INTRODUCTION

Non-steroidal anti-inflammatory drugs (NSAIDs) are among the most commonly prescribed medications in the United States as well as some of the most frequently purchased over-the-counter analgesics. They work *via* inhibition of cyclooxygenase (COX) isoforms, including COX-1 and COX-2, to decrease downstream production of pro-inflammatory prostaglandins and thromboxane, a mediator of thrombogenesis and platelet function. COX-2 is involved in chondrocyte differentiation and is expressed in both osteoblasts and fracture callus[1,2]. Relating to fracture healing, a study of human callus found a thirteen-fold decrease in COX-2 expression in the callus of nonunions as compared to that of healed fractures[3].

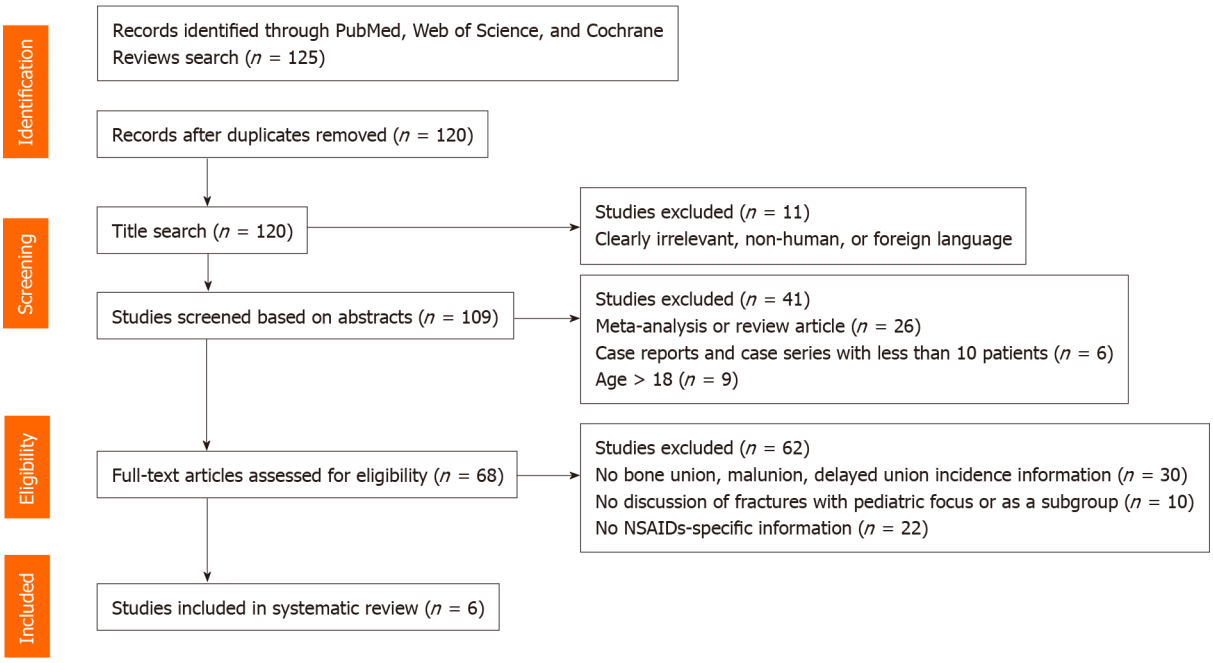
As a result of these findings, the effects of NSAIDs on bone healing are an active area of study. Although eight animal studies suggest decreased callus formation and quality in animals exposed to NSAIDs[4-11], other investigations have found no difference in callus quality or healing rates[12-15]. One possible explanation for these discordant findings is a lack of standardization of agent, COX enzyme specificity, duration of therapy, and dose. Across the adult fracture nonunion literature, NSAIDs have both been associated with nonunion and found to have no effect on nonunion rates[16-20]. Nevertheless, despite these contradictory findings, a recent survey of orthopaedic surgeons found that 86% believe NSAIDs to be a risk factor for nonunion[21].

Additionally, very little is known about the effects of NSAID use on bone healing in children. Notably, nonunions in pediatric patients are exceedingly rare, with one epidemiological study suggesting that only 1 in 500 pediatric fractures goes on to nonunion[22]. This is an order of magnitude lower than the nonunion rate across all fractures in adults, which is estimated at 1.9%-6.8%[23,24]. The biological underpinnings of this difference in risk are theorized to include a robust periosteum which provides centripetal blood flow, greater innate regenerative potential, ongoing osteogenesis, and increased vascularity with greater fracture hematoma formation[25]. Further supporting their use, evidence has arisen indicating that NSAIDs are equally or more effective for post-fracture pain control than opiates while also leading to fewer side effects[22,26-29]. Reported side effects include bleeding complications due to inhibition of thromboxane formation and gastritis, which are common in adults but rare in children.

Clinically, there is considerable variation in the use of NSAIDs in pediatric fractures, likely due to varying reports in the literature and extrapolation of results from studies in other populations. There have been recent publications focusing on the use of NSAIDs for pediatric fractures and the goal of this systematic review was to assess whether NSAID exposure is a risk factor for fracture nonunion in

Table 1 Newcastle-Ottawa scale for assessing the quality of nonrandomized studys

Ref.	Representativeness of the exposed cohort	Selection of the non-exposed cohort	Ascertainment of exposure	Demonstration that outcome of interest was not present at start of study	Comparability of cohorts on the basis of the design or analysis	Assessment of outcome	Was follow-up long enough for outcomes to occur?	Adequacy of follow up of cohorts	Total, *n*
Zura *et al*[30], 2018	1	1	1	1	1	1			6
Kay *et al*[31], 2010	1	1	1	1	1	1			6
Kay *et al*[32], 2011	1	1	1	1	1	1			6
DePeter *et al* [33], 2017	1	1	1	1	2	1			7



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Figure 1 PRISMA diagram. NSAIDs: Non-steroidal anti-inflammatory drugs.

children. In doing so, we hope to clarify the safety profile of NSAIDs in order to optimize their use in standard, multimodal analgesic regimens across pediatric orthopaedic fracture care.

MATERIALS AND METHODS

We performed a computerized search using MEDLINE (PubMed platform), Cochrane Database, and Web of Science. The author (Katyal T) identified and utilized a combination of keywords and MeSH terms for "fracture", "bone healing", and "pediatric" patient population. The searches were performed in November 2020. Results were limited by language, English, but not by publication date. We included all English language, full-text articles of human subjects focusing on pediatric patients with fractures, post-fracture NSAID exposure, and control cohorts without NSAID exposure. Outcomes of interest were the reported rates of delayed unions, malunion, growth disturbance, and nonunions. Case reports

Table 2 Evidence table

Study	Ref.	Level of evidence
Risk factors for nonunion of bone fracture in pediatric patients: An inception cohort study of 237033 fractures	Zura *et al*[30], 2018	Level II
Perioperative ketorolac use in children undergoing lower extremity osteotomies	Kay *et al*[31], 2010	Level III
Complications of ketorolac use in children undergoing operative fracture care	Kay *et al*[32], 2011	Level III
Does the use of ibuprofen in Children with extremity fractures increase their risk for bone healing complications?	DePeter *et al*[33], 2017	Level I
A randomized clinical trial of ibuprofen versus acetaminophen with codeine for acute pediatric arm fracture pain	Drendel *et al*[34], 2009	Level I
Effect of NSAID use on bone healing in pediatric fractures: A preliminary, prospective, randomized, blinded study	Nuelle *et al*[35], 2020	Level I

NSAIDs: Non-steroidal anti-inflammatory drugs.

and case series with less than 10 patients were excluded. All relevant randomized controlled trials, retrospective reviews, cohort, and case-control studies were included.

Each title from the performed search was assessed for inclusion based on the specified criteria described above (Figure 1). The relevant abstracts were then independently reviewed by two authors (Katyal T and Stroud S) for inclusion, and if there was any doubt regarding the relevance and applicability, the full-text article was obtained. Full-text articles of the selected abstracts were then appraised by two authors (Katyal T and Stroud S) for inclusion in the systematic review. Any conflicts in screening were resolved by a third author (Gornitzky AL). Two authors (Stroud S and Gornitzky AL) then independently extracted relevant data including age, number of patients in sample size, NSAID class, comparison group, rate of delayed healing and/or nonunion rate, results specific to NSAID type, and details concerning duration of exposure, length of follow-up, and definition of delayed union or nonunion. Study quality was assessed independently using the Newcastle-Ottawa scale (NOS) for the nonrandomized studies from the final list of articles (Table 1). Nonrandomized studies with an NOS score of five or greater on the nine-point scale were included.

RESULTS

In total, 120 unique articles were identified. As demonstrated in the PRISMA flow diagram (Figure 1), 114 articles were excluded from final analysis, including 11 articles after review of titles, 41 studies after screening of abstracts and 62 studies after assessment of full-text articles. Six studies were included for final analysis review (Table 2).

Analyzing an insurance claims database including more than 237000 pediatric fractures, Zura *et al*[30] reported a cumulative pediatric nonunion rate of less than 1%, which was 80% lower than adults. Specifically, age was directly related to risk of nonunion, increasing from 0.20% in those 0-6 years old to 0.26% in those 7-11 years and 1.63% in those 12-17 years old. With respect to NSAIDs, the authors found that prescription NSAID use alone did not increase the risk of nonunion [odds ratio (OR) = 1.05; 95% confidence interval (CI): 0.81-1.35; Table 3]. In comparison, the risk of nonunion did increase when NSAIDs were combined with opioids (OR = 2.52; 95%CI: 2.18-2.91), including a more than two-fold increase for those using opioids alone (OR = 2.47; 95%CI: 2.18-2.78)[1].

In a series of retrospective studies looking at NSAID use in children, some studies concluded that routine perioperative ketorolac use after orthopaedic surgery is not associated with an increased risk of delayed bone healing or nonunion[31,32]. This included both routine operative fracture care (0% nonunion rate after ketorolac use)[31] and lower extremity deformity correction[32]. Looking further at the high-risk osteotomy cohort, only 5 out of 682 osteotomies (0.7%) were complicated by delayed union or nonunion, with all 4 delayed unions in the ketorolac group (4/625; 0.6%) going on to heal completely without surgery[32]. Similarly, DePeter *et al*[33] retrospectively analyzed all children who presented to their emergency department with a fracture of the tibia, femur, humerus, scaphoid or fifth metatarsal. Comparing those who received ibuprofen to those who did not, the authors found no differences in the rate of nonunion, delayed union or fracture re-displacement on follow-up radiographs, leading them to conclude that ibuprofen administration is not associated with an increased risk for clinically important bone healing complications following traumatic fractures in kids.

There have been two prospective, randomized clinical trials in children looking at fracture healing following ibuprofen administration. First, Drendel *et al*[34] reported no instances of nonunion at minimum 1-year follow-up in 244 children managed nonoperatively with either ibuprofen or

Table 3 Summary of evidence of non-steroidal anti-inflammatory drugs use and nonunions in children

Ref.	Study population	Age	Number of patients	NSAID studied	Comparison group	Delayed healing/nonunion rate (%)	NSAID specific results	Notes
Zura *et al*[30], 2018	18 most commonly fractures	< 18 yr	237033	All prescription NSAIDs	No analgesics	0.85	Multivariate OR for nonunion was 1.05 (95% CI: 0.81-1.35) for 'NSAID' *vs* 'No analgesic' group	Data from a large, private insurance database in the United States from 2011. Included both operative and nonoperatively managed fractures
Kay *et al*[31], 2010	Operative fracture care	Mean = 6.7 yr	221	Ketorolac	No ketorolac	0	There were no cases of delayed union or nonunion in either group	Included 169 patients who received ketorolac *vs* 52 who did not. Only accounted for NSAID use in the immediate post-operative period. Fractures were predominantly in the upper extremity
Kay *et al*[32], 2011	Lower extremity osteotomies	Mean = 8.5 yr	327 patients (682 osteotomies)	Ketorolac	No ketorolac	0.70	Delayed healing in 0.6% in the ketorolac group (4/625) *vs* 1.8% in the control group (1/57; $P = 0.89$)	Included osteotomies of the pelvis, femur, tibia and foot. Only accounted for NSAID use in the immediate post-operative period
DePeter *et al* [33], 2017	Fractures of the tibia, femur, humerus, scaphoid or fifth metatarsal	Median = 7 yr	808	Ibuprofen	No ibuprofen	1.4	3% (10/338) of ibuprofen group developed a bone healing complication *vs* 4% (17/470) of controls (OR = 0.8, 95%CI: 0.4-1.8)	Exposure to ibuprofen included either administration during hospitalization or a prescription for ibuprofen at discharge. A bone healing complication was defined as radiographic evidence of nonunion, delayed union or future re-displacement as determined by a pediatric radiologist. Total complications (27/808; 3.5%) included 1% ($n = 8$) with nonunion, 0.4% ($n = 3$) with delayed union and 2% ($n = 16$) with re-displacement
Drendel *et al* [34], 2009	Upper extremity fractures (non-op)	Mean = 7.8 yr	244 patients	Ibuprofen	Acetaminophen with codeine	0	No documented fracture nonunions	Excluded fractures that required reduction/manipulation or surgery. Four (1.6%) children had another fracture at the same site within 1 yr of the original fracture, including 3 who had received acetaminophen and 1 received ibuprofen
Nuelle *et al* [35], 2020	Skeletally immature patients with long-bone fractures	Mean = 7.7 yr	95 patients (97 fractures)	Ibuprofen	Acetaminophen	0	At 6 wk, there was radiographic healing in 92% of the NSAID group *vs* 82% of the control group ($P = 0.22$). This increased to 100% and 98%, respectively, at 10-12 wk post-injury ($P = 0.48$)	Included females < 16 and males < 14 with open physes. Fractures managed both operatively and nonoperatively. Healing was documented at a mean of 41 d in the control group and 40 d in the NSAID group ($P = 0.76$). No cases of nonunion were documented in either group

NSAIDs: Non-steroidal anti-inflammatory drugs; CI: Confidence interval; OR: Odds ratio.

acetaminophen with codeine for pediatric upper extremity fractures. Of those who did have a refracture at the same site within 1 year of the original injury ($n = 4$; 1.6%), only 1 had received ibuprofen. Finally, Nuelle *et al*[35] compared ibuprofen to acetaminophen administration following long-bone fractures in 95 skeletally immature children. Overall, they reported no difference in radiographic healing at 6- or 12-wk post-injury, including 100% healing in the NSAID group by 12 wk post-fracture.

Overall, the included studies show that nonunion in children is extremely rare, and no published study to date has documented an increased risk of nonunion or delayed bone healing in those children who are treated with NSAIDs in the immediate post-injury or peri-operative time period.

DISCUSSION

The present review identified six studies that examined the effects of NSAID exposure on nonunion or delayed union in pediatric patients. Among the studies included, there were 2011 nonunions among 238822 fractures (0.84%). Of these studies, three examined the effects of ibuprofen in the acute post-fracture period, three studied ketorolac in the same time frame, and one was a database study that did not capture the specific agent or the timing of NSAID exposure. None of the six studies found NSAID exposure to be a risk factor for nonunion or delayed union in children, including a retrospective review that focused on bones with an innately higher risk for nonunion[33]. In contrast, in their large database study, Zura *et al*[30] found age (especially over 11 years), bone (*e.g.*, scaphoid, femoral neck, tibia or fibula), male sex, higher body mass index, open fracture, or multiple concomitant fractures to be risk factors for pediatric nonunion.

From a clinical perspective, NSAID exposure is not associated with increased risk of bleeding, blood transfusions, or wound complications[31,32,35]. Specifically, of the six studies included, four did not examine the rate of wound complications and the two studies that did found no difference between the NSAID and non-NSAID groups[31,32]. In fact, NSAIDs are associated with both a lower risk of adverse effects and a lower rate of functional impairment[34]. Furthermore, NSAIDs are safe, cheap and effective opioid-sparing analgesics[22,26,27,34]. Unfortunately, due in part to persistent concerns regarding delayed fracture healing, they are a frequently underutilized medication[36].

Of note, most of the included studies have methodological limitations. First, Zura *et al*[30] did not capture whether NSAID exposure was acute or chronic and was focused only on a specific cohort whose parents had employer-supplied health insurance, which may not be generalizable to all patients. Next, while two of the three retrospective reviews were able to report a standardized dose of ketorolac, the third did not. Additionally, none of the three were able to control for concomitant opioid use or medications that may have been purchased over the counter and administered by parents after discharge[31-33]. In one of the two randomized controlled trials, each experimental group was sent home with both drugs and instructed to take the other group's medication if they experienced breakthrough pain, thus making it difficult to exclude potential cross-over effect[34]. Third, none of the included studies examined COX-2 specific inhibitors or the effects of longer-term NSAID exposure on pediatric nonunion risk. For this reason, conclusions are limited to ibuprofen and ketorolac use in the acute period. Finally, nonunion in children is very rare, and many of the included studies reported zero nonunions, thus suggesting an overall limitation in study power.

Despite these limitations, however, it is still possible to draw several meaningful conclusions. First, nonunion in children is extremely rare across most age groups and fracture types, including those deemed 'high risk'. Second, at standard doses in the acute post-injury/surgery period, both ibuprofen and ketorolac do not appear to be associated with an increased risk for nonunion or delayed union in pediatric patients. These findings are specific to upper extremity and long bone fractures. Moreover, children are likely to take these medications for only a few days after injury, another factor which decreases their exposure to any potential deleterious effects on osteogenesis. For example, Nuelle *et al*[35] reported that ibuprofen was used for only 4 d on average in their prospective cohort.

CONCLUSION

Finally, NSAIDs are safe in children and are associated with a decreased risk of adverse effects and equivalent analgesia to opioid-containing agents. Taken together, this systematic review suggests that NSAIDS can be safely prescribed to pediatric orthopaedic patients absent other contraindications without concern for increased risk of fracture non-union or delayed healing. Additional prospective studies are needed focusing on higher risk fractures and elective orthopaedic procedures such as osteotomies and spinal fusion.

ARTICLE HIGHLIGHTS

Research background

Non-steroidal anti-inflammatory drugs (NSAIDs) are among the most commonly prescribed medications in the United States. Although they are safe and effective means of analgesia for children with broken bones, there is considerable variation in their clinical use due to persistent concerns about

their potentially adverse effect on fracture healing.

Research motivation

The goal of this systematic review was to assess whether NSAID exposure is a risk factor for fracture nonunion in children.

Research objectives

The goal of this systematic review was to assess whether NSAID exposure is a risk factor for fracture nonunion in children.

Research methods

We systematically reviewed the literature reporting the effect of NSAIDs on bone healing. We included all clinical studies that reported on adverse bone healing complications in children with respect to NSAID exposure. The outcomes of interest were delayed union or nonunion. Study quality was assessed using the Newcastle-Ottawa scale for non-randomized studies. A final table was constructed summarizing the available evidence.

Research results

A total of 120 articles were identified and screened, of which 6 articles were included for final review. Nonunion in children is extremely rare; among the studies included, there were 2011 nonunions among 238822 fractures (0.84%). None of the included studies documented an increased risk of nonunion or delayed bone healing in those children who are treated with NSAIDs in the immediate post-injury or peri-operative time period. Additionally, children are likely to take these medications for only a few days after injury or surgery, further decreasing their risk of adverse side-effects.

Research conclusions

This systematic review suggests that NSAIDS can be safely prescribed to pediatric orthopaedic patients absent other contraindications without concern for increased risk of fracture non-union or delayed bone healing. Additional prospective studies are needed focusing on higher risk fractures and elective orthopaedic procedures such as osteotomies and spinal fusion.

Research perspectives

Additional prospective studies are needed focusing on higher risk fractures and elective orthopaedic procedures such as osteotomies and spinal fusion.

FOOTNOTES

Author contributions: Katyal T performed the literature search for the systematic review; Stroud S and Katyal T reviewed the articles using the inclusion and exclusion criteria; Stroud S, Katyal T, and Gornitzky AL collected and analyzed the data and wrote the paper; Swarup I supervised and contributed to the report.

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REFERENCES

1 **Vuolteenaho K**, Moilanen T, Moilanen E. Non-steroidal anti-inflammatory drugs, cyclooxygenase-2 and the bone healing process. *Basic Clin Pharmacol Toxicol* 2008; **102**: 10-14 [PMID: 17973900 DOI: 10.1111/j.1742-7843.2007.00149.x]
2 **Spiro AS**, Beil FT, Baranowsky A, Barvencik F, Schilling AF, Nguyen K, Khadem S, Seitz S, Rueger JM, Schinke T, Amling M. BMP-7-induced ectopic bone formation and fracture healing is impaired by systemic NSAID application in C57BL/6-mice. *J Orthop Res* 2010; **28**: 785-791 [PMID: 20063306 DOI: 10.1002/jor.21044]
3 **Daluiski A**, Ramsey KE, Shi Y, Bostrom MP, Nestor BJ, Martin G, Hotchkiss R, Stephan DA. Cyclooxygenase-2 inhibitors in human skeletal fracture healing. *Orthopedics* 2006; **29**: 259-261 [PMID: 16539205 DOI: 10.3928/01477447-20060301-02]
4 **Inal S**, Kabay S, Cayci MK, Kuru HI, Altikat S, Akkas G, Deger A. Comparison of the effects of dexketoprofen trometamol, meloxicam and diclofenac sodium on fibular fracture healing, kidney and liver: an experimental rat model. *Injury* 2014; **45**: 494-500 [PMID: 24246878 DOI: 10.1016/j.injury.2013.10.002]
5 **Janssen MP**, Caron MM, van Rietbergen B, Surtel DA, van Rhijn LW, Welting TJ, Emans PJ. Impairment of the chondrogenic phase of endochondral ossification in vivo by inhibition of cyclooxygenase-2. *Eur Cell Mater* 2017; **34**: 202-216 [PMID: 29039630 DOI: 10.22203/eCM.v034a13]
6 **O'Connor JP**, Capo JT, Tan V, Cottrell JA, Manigrasso MB, Bontempo N, Parsons JR. A comparison of the effects of ibuprofen and rofecoxib on rabbit fibula osteotomy healing. *Acta Orthop* 2009; **80**: 597-605 [PMID: 19916696 DOI: 10.3109/17453670903316769]
7 **Lu C**, Xing Z, Wang X, Mao J, Marcucio RS, Miclau T. Anti-inflammatory treatment increases angiogenesis during early fracture healing. *Arch Orthop Trauma Surg* 2012; **132**: 1205-1213 [PMID: 22622792 DOI: 10.1007/s00402-012-1525-4]
8 **Ochi H**, Hara Y, Asou Y, Harada Y, Nezu Y, Yogo T, Shinomiya K, Tagawa M. Effects of long-term administration of carprofen on healing of a tibial osteotomy in dogs. *Am J Vet Res* 2011; **72**: 634-641 [PMID: 21529215 DOI: 10.2460/ajvr.72.5.634]
9 **Bergenstock M**, Min W, Simon AM, Sabatino C, O'Connor JP. A comparison between the effects of acetaminophen and celecoxib on bone fracture healing in rats. *J Orthop Trauma* 2005; **19**: 717-723 [PMID: 16314720 DOI: 10.1097/01.bot.0000184144.98071.5d]
10 **Endo K**, Sairyo K, Komatsubara S, Sasa T, Egawa H, Ogawa T, Yonekura D, Murakami R, Yasui N. Cyclooxygenase-2 inhibitor delays fracture healing in rats. *Acta Orthop* 2005; **76**: 470-474 [PMID: 16195060 DOI: 10.1080/17453670510041439]
11 **Bissinger O**, Kreutzer K, Götz C, Hapfelmeier A, Pautke C, Vogt S, Wexel G, Wolff KD, Tischer T, Prodinger PM. A biomechanical, micro-computertomographic and histological analysis of the influence of diclofenac and prednisolone on fracture healing in vivo. *BMC Musculoskelet Disord* 2016; **17**: 383 [PMID: 27596101 DOI: 10.1186/s12891-016-1241-2]
12 **Brown KM**, Saunders MM, Kirsch T, Donahue HJ, Reid JS. Effect of COX-2-specific inhibition on fracture-healing in the rat femur. *J Bone Joint Surg Am* 2004; **86**: 116-123 [PMID: 14711953 DOI: 10.2106/00004623-200401000-00017]
13 **Utvåg SE**, Fuskevåg OM, Shegarfi H, Reikerås O. Short-term treatment with COX-2 inhibitors does not impair fracture healing. *J Invest Surg* 2010; **23**: 257-261 [PMID: 20874480 DOI: 10.3109/08941939.2010.481009]
14 **Hak DJ**, Schulz KS, Khoie B, Hazelwood SJ. The effect of Cox-2 specific inhibition on direct fracture healing in the rabbit tibia. *J Orthop Sci* 2011; **16**: 93-98 [PMID: 21264481 DOI: 10.1007/s00776-010-0016-0]
15 **Sevimli R**, Uzel M, Sayar H, Kalender AM, Dökmeci O. The effect of dexketoprofen trometamol on the healing of diaphysis fractures of rat tibia. *Acta Orthop Traumatol Turc* 2013; **47**: 423-429 [PMID: 24509223 DOI: 10.3944/aott.2013.3093]
16 **Jeffcoach DR**, Sams VG, Lawson CM, Enderson BL, Smith ST, Kline H, Barlow PB, Wylie DR, Krumenacker LA, McMillen JC, Pyda J, Daley BJ; University of Tennessee Medical Center, Department of Surgery. Nonsteroidal anti-inflammatory drugs' impact on nonunion and infection rates in long-bone fractures. *J Trauma Acute Care Surg* 2014; **76**: 779-783 [PMID: 24553548 DOI: 10.1097/TA.0b013e3182aafe0d]
17 **Sagi HC**, Jordan CJ, Barei DP, Serrano-Riera R, Steverson B. Indomethacin prophylaxis for heterotopic ossification after acetabular fracture surgery increases the risk for nonunion of the posterior wall. *J Orthop Trauma* 2014; **28**: 377-383 [PMID: 24625922 DOI: 10.1097/BOT.0000000000000049]
18 **Donohue D**, Sanders D, Serrano-Riera R, Jordan C, Gaskins R, Sanders R, Sagi HC. Ketorolac Administered in the Recovery Room for Acute Pain Management Does Not Affect Healing Rates of Femoral and Tibial Fractures. *J Orthop Trauma* 2016; **30**: 479-482 [PMID: 27124828 DOI: 10.1097/BOT.0000000000000620]
19 **Fader L**, Whitaker J, Lopez M, Vivace B, Parra M, Carlson J, Zamora R. Tibia fractures and NSAIDs. Does it make a difference? *Injury* 2018; **49**: 2290-2294 [PMID: 30270011 DOI: 10.1016/j.injury.2018.09.024]
20 **Dodwell ER**, Latorre JG, Parisini E, Zwettler E, Chandra D, Mulpuri K, Snyder B. NSAID exposure and risk of nonunion: a meta-analysis of case-control and cohort studies. *Calcif Tissue Int* 2010; **87**: 193-202 [PMID: 20552333 DOI: 10.1007/s00223-010-9379-7]
21 **Bhandari M**, Fong K, Sprague S, Williams D, Petrisor B. Variability in the definition and perceived causes of delayed unions and nonunions: a cross-sectional, multinational survey of orthopaedic surgeons. *J Bone Joint Surg Am* 2012; **94**: e1091-e1096 [PMID: 22854998 DOI: 10.2106/JBJS.K.01344]
22 **Mills LA**, Simpson AH. The risk of non-union per fracture in children. *J Child Orthop* 2013; **7**: 317-322 [PMID: 24432093 DOI: 10.1007/s11832-013-0521-8]
23 **Ekegren CL**, Edwards ER, de Steiger R, Gabbe BJ. Incidence, Costs and Predictors of Non-Union, Delayed Union and

Mal-Union Following Long Bone Fracture. *Int J Environ Res Public Health* 2018; **15** [PMID: 30551632 DOI: 10.3390/ijerph15122845]

24 **Schmal H**, Brix M, Bue M, Ekman A, Ferreira N, Gottlieb H, Kold S, Taylor A, Toft Tengberg P, Ban I; Danish Orthopaedic Trauma Society. Nonunion - consensus from the 4th annual meeting of the Danish Orthopaedic Trauma Society. *EFORT Open Rev* 2020; **5**: 46-57 [PMID: 32071773 DOI: 10.1302/2058-5241.5.190037]

25 **Lindaman LM**. Bone healing in children. *Clin Podiatr Med Surg* 2001; **18**: 97-108 [PMID: 11344982]

26 **Poonai N**, Datoo N, Ali S, Cashin M, Drendel AL, Zhu R, Lepore N, Greff M, Rieder M, Bartley D. Oral morphine versus ibuprofen administered at home for postoperative orthopedic pain in children: a randomized controlled trial. *CMAJ* 2017; **189**: E1252-E1258 [PMID: 29018084 DOI: 10.1503/cmaj.170017]

27 **Koller DM**, Myers AB, Lorenz D, Godambe SA. Effectiveness of oxycodone, ibuprofen, or the combination in the initial management of orthopedic injury-related pain in children. *Pediatr Emerg Care* 2007; **23**: 627-633 [PMID: 17876251 DOI: 10.1097/PEC.0b013e31814a6a39]

28 **Neri E**, Maestro A, Minen F, Montico M, Ronfani L, Zanon D, Favret A, Messi G, Barbi E. Sublingual ketorolac versus sublingual tramadol for moderate to severe post-traumatic bone pain in children: a double-blind, randomised, controlled trial. *Arch Dis Child* 2013; **98**: 721-724 [PMID: 23702435 DOI: 10.1136/archdischild-2012-303527]

29 **Friday JH**, Kanegaye JT, McCaslin I, Zheng A, Harley JR. Ibuprofen provides analgesia equivalent to acetaminophen-codeine in the treatment of acute pain in children with extremity injuries: a randomized clinical trial. *Acad Emerg Med* 2009; **16**: 711-716 [PMID: 19624576 DOI: 10.1111/j.1553-2712.2009.00471.x]

30 **Zura R**, Kaste SC, Heffernan MJ, Accousti WK, Gargiulo D, Wang Z, Steen RG. Risk factors for nonunion of bone fracture in pediatric patients: An inception cohort study of 237,033 fractures. *Medicine (Baltimore)* 2018; **97**: e11691 [PMID: 30075567 DOI: 10.1097/MD.0000000000011691]

31 **Kay RM**, Directo MP, Leathers M, Myung K, Skaggs DL. Complications of ketorolac use in children undergoing operative fracture care. *J Pediatr Orthop* 2010; **30**: 655-658 [PMID: 20864848 DOI: 10.1097/BPO.0b013e3181efb8b4]

32 **Kay RM**, Leathers M, Directo MP, Myung K, Skaggs DL. Perioperative ketorolac use in children undergoing lower extremity osteotomies. *J Pediatr Orthop* 2011; **31**: 783-786 [PMID: 21926877 DOI: 10.1097/BPO.0b013e31822ed33a]

33 **DePeter KC**, Blumberg SM, Dienstag Becker S, Meltzer JA. Does the Use of Ibuprofen in Children with Extremity Fractures Increase their Risk for Bone Healing Complications? *J Emerg Med* 2017; **52**: 426-432 [PMID: 27751698 DOI: 10.1016/j.jemermed.2016.09.027]

34 **Drendel AL**, Gorelick MH, Weisman SJ, Lyon R, Brousseau DC, Kim MK. A randomized clinical trial of ibuprofen versus acetaminophen with codeine for acute pediatric arm fracture pain. *Ann Emerg Med* 2009; **54**: 553-560 [PMID: 19692147 DOI: 10.1016/j.annemergmed.2009.06.005]

35 **Nuelle JAV**, Coe KM, Oliver HA, Cook JL, Hoernschemeyer DG, Gupta SK. Effect of NSAID Use on Bone Healing in Pediatric Fractures: A Preliminary, Prospective, Randomized, Blinded Study. *J Pediatr Orthop* 2020; **40**: e683-e689 [PMID: 32555047 DOI: 10.1097/BPO.0000000000001603]

36 **Rajput K**, Vadivelu N. Acute Pain Management of Chronic Pain Patients in Ambulatory Surgery Centers. *Curr Pain Headache Rep* 2021; **25**: 1 [PMID: 33443656 DOI: 10.1007/s11916-020-00922-3]

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SYSTEMATIC REVIEWS

Prosthetic joint infection of the hip and knee due to *Mycobacterium species*: A systematic review

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Abstract

BACKGROUND

Mycobacterium species (*Mycobacterium sp*) is an emerging cause of hip and knee prosthetic joint infection (PJI), and different species of this organism may be responsible for the same.

AIM

To evaluate the profile of hip and knee *Mycobacterium* PJI cases as published in the past 30 years.

METHODS

A literature search was performed in PubMed using the MeSH terms "Prosthesis joint infection" AND "Mycobacterium" for studies with publication dates from January 1, 1990, to May 30, 2021. To avoid missing any study, another search was performed with the terms "Arthroplasty infection" AND "Mycobacterium" in the same period as the previous search. The Preferred Reporting Items for Systematic Reviews and Meta-Analyses chart was used to evaluate the included studies for further review. In total, 51 studies were included for further evaluation of the

cases, type of pathogen, and treatment of PJI caused by *Mycobacterium sp*.

RESULTS

Seventeen identified *Mycobacterium sp* were reportedly responsible for hip/knee PJI in 115 hip/knee PJI cases, whereas in two cases there was no mention of any specific *Mycobacterium sp*. *Mycobacterium tuberculosis* (*M. tuberculosis*) was detected in 50/115 (43.3%) of the cases. Nontuberculous mycobacteria (NTM) included *M. fortuitum* (26/115, 22.6%), *M. abscessus* (10/115, 8.6%), *M. chelonae* (8/115, 6.9%), and *M. bovis* (8/115, 6.9%). Majority of the cases (82/114, 71.9%) had an onset of infection > 3 mo after the index surgery, while in 24.6% (28/114) the disease had an onset in ≤ 3 mo. Incidental intraoperative PJI diagnosis was made in 4 cases (3.5%). Overall, prosthesis removal was needed in 77.8% (84/108) of the cases to treat the infection. Overall infection rate was controlled in 88/102 (86.3%) patients with *Mycobacterium* PJI. Persistent infection occurred in 10/108 (9.8%) patients, while 4/108 (3.9%) patients died due to the infection.

CONCLUSION

At least 17 *Mycobacterium sp* can be responsible for hip/knee PJI. Although *M. tuberculosis* is the most common causal pathogen, NTM should be considered as an emerging cause of hip/knee PJI.

Key Words: *Mycobacterium species*; Prosthetic joint infection; Hip; Knee; Systematic review

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Core Tip: Prosthetic joint infection (PJI) is a difficult complication after total hip/knee arthroplasty. *Mycobacterium species* (*Mycobacterium sp*) is one of the emerging causes of hip and knee PJI, and various species could be responsible for it. This study aimed to evaluate the profile of hip and knee *Mycobacterium* PJI cases published in the past 30 years. This study resulted the information regarding the distribution of *Mycobacterium sp* that related to PJI hip/knee. This paper also evaluated the disease course, treatment and outcome of *Mycobacterium* PJI.

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INTRODUCTION

The incidence of prosthetic joint infection (PJI) has increased with an increase in the number of patients undergoing total joint arthroplasty, particularly hip and knee arthroplasties[1]. The cumulative incidence of PJI after total hip arthroplasty (THA) and total knee arthroplasty remains unclear; however, it is believed to range between 2.05% and 2.18%. The majority of PJI cases are caused by gram-positive cocci such as *Staphylococcus aureus* and coagulase-negative *Staphylococci* (60%); however, sometimes they can also be caused by gram-negative bacteria, such as *Mycobacteria* or *fungi*[2,3]. *Mycobacterial* infections account for approximately 2% of all PJI cases[4]. *Mycobacterium tuberculosis* (*M. tuberculosis*) is an infrequent cause of PJI, accounting for only 7 cases (0.3%) as reported during a 22-year period at one center[5]. However, in tuberculosis-endemic countries, patients undergoing joint arthroplasty with previous tuberculous septic arthritis are at an increased risk of developing *M. tuberculosis* complex PJI [1]. Some other *Mycobacteria* (rapidly growing *Mycobacteria*) are reported to grow rapidly, and they spread in various environments worldwide[4].

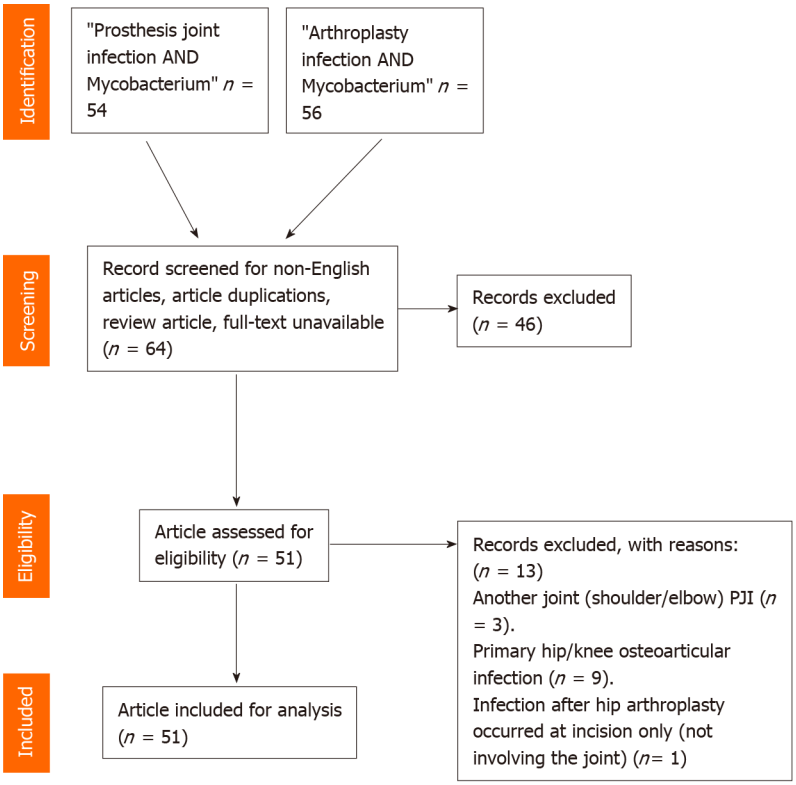
Appropriate management is mandatory to prevent complications that arise from PJI. Successful management of PJI is achieved by a combination of surgical intervention and appropriate medical therapeutic strategies to eradicate infection, reduce pain, restore function, and prevent prolonged antimicrobial therapy in patients[1,2,6]. The diagnosis of mycobacterial infections is often delayed due to the low index of suspicion, clinical and laboratory presentation that mimics bacterial infections, and low yield of smears and culture for acid-fast bacilli. Moreover, mycobacterial infections are often known to occur together with other bacteria, such as coinfection or superinfection[2,6]. Delayed diagnosis and prevention of PJI can lead to prolonged illness with various dangerous manifestations that can threaten the patient's life. Although *Mycobacteria* are not among the common causative agents of PJI, it is important to recognize and treat them differently from non-mycobacterial infections. The aim of this study was to identify and evaluate the profile of PJI cases due to mycobacterial infection in the hip and knee as published over the past 30 years.

Table 1 Articles included in the systematic review

No	Ref.	Joint involvement (No. of cases)	Pathogens	Onset of disease (early: ≤ 3 mo; late: > 3 mo)	Treatment	Outcome
1	Ribeiro *et al*[7], 2020	Hip (1)	*M. tuberculosis*	Early	Removal of prosthesis	Controlled
2	Patel *et al*[8], 2019	Hip (1)	*M. bovis*	Late	Removal of prosthesis	Controlled
3	Sixt *et al*[9], 2020	Hip (1)	*M. avium*	Late	Removal of prosthesis	Controlled
4	Barry *et al*[10], 2019	Knee (1)	*M. tuberculosis*	Late	Antimicrobials only	Controlled
5	Goldstein *et al* [11], 2019	Hip (2), knee (4)	*M. intracellulare* (1), *M. abscessus* (1), *M. fortuitum* (1), *M. gordonae* (1), NA (2)	Early (1), kate (4), NA (1)	Removal prosthesis (5), amputation (1)	Controlled
6	Buser *et al*[12], 2019	Hip (5), knee (4)	*M. fortuitum* (7), *M. goodii* (2)	Early (1), late (8)	NA	NA
7	Spanyer *et al* [13], 2018	Knee (1)	*M. abscesus*	NA	Removal of prosthesis	Controlled
8	Meyssonnier *et al* [14], 2019	Hip (9)	*M. tuberculosis* (9)	Late (5), intraoperative (4)	Antimicrobials only (5), removal of prosthesis (4)	Controlled
9	Chang *et al*[15], 2018	Hip (7), knee (6)	*M. tuberculosis* (13), mixed infection (6)	Early (2), late (11)	Removal of prosthesis (11), debridement (2)	Controlled (8), persistent (3), dead (2)
10	Metayer *et al* [16], 2018	Hip (1)	*M. bovis*	Late	Removal of prosthesis	Controlled
11	Elzein *et al*[5], 2017	Knee (1)	*M. tuberculosis*	Late	Removal of prosthesis	Controlled
12	Kim *et al*[17], 2017	Knee (2)	*M. abscessus*	Early (1), late (1)	Removal of prosthesis (2)	Controlled
13	Henry *et al*[18], 2016	Hip (1), knee (1)	*M. abscessus*	Late	Removal of prosthesis (2)	Controlled
14	Jeong *et al*[19], 2012	Knee (1)	*M. wolinskyi*	NA	Debridement	NA
15	Lee *et al*[20], 2012	Knee (1)	*M. chelonae*	Late	Removal of prosthesis	Controlled
16	Wang *et al*[21], 2011	Knee (1)	*M. abscessus, M. fortuitum*	Early	Removal of prosthesis	NA
17	Ahmad *et al*[22], 2010	Knee (1)	*M. goodii*	Early	Removal of prosthesis	Controlled
18	Gupta *et al*[23], 2009	Hip (1)	*M. avium* complex	Late	Removal of prosthesis	Controlled
19	Porat *et al*[24], 2008	Knee (2) bilateral	*M. fortuitum*	Late	Antimicrobials only	Persistent
20	Reigstad *et al* [25], 2008	Hip (1)	*M. bovis*	Late	Removal of prosthesis	Controlled
21	Brown *et al*[26], 2008	Hip (1)	*M. tuberculosis, M. chelonae*	Late	Removal of prosthesis	Controlled
22	Cheung *et al*[27], 2008	Knee (1)	*M. fortuitum*	Early	Removal of prosthesis	Controlled
23	Eid *et al*[28], 2007	Knee (7), hip (1)	*M. chelonae* (3), *M. abscessus* (2), *M. fortuitum* (3), *M. smegmatis* (1)	Early (3), late (5)	Removal of prosthesis	Controlled (7), persistent (1)
24	Segal *et al*[29], 2007	Hip (1)	*M. bovis*	Late	Removal of prosthesis	Controlled
25	Khater *et al*[30], 2007	Knee (1)	*M. tuberculosis*	Early	Removal of prosthesis	Controlled
26	Pulcini *et al*[31],	Hip (1)	*M. wolinskyi*	Late	Removal of prosthesis	Controlled

	2006					
27	Neuberger *et al* [32], 2006	Knee (1)	*M. kansasii*	Late	Removal of prosthesis	Controlled
28	Wong *et al*[33], 2005	Hip (1)	*M. farcinogenes*	Late	Removal of prosthesis	Controlled
29	Yim *et al*[34], 2004	Hip (10)	*M. xenopi*	Late	Removal of prosthesis	Controlled
30	Spinner *et al*[35], 1996	Knee (1)	*M. tuberculosis*	Early	Debridement	Controlled
31	Pring *et al*[36], 1996	Knee (1)	*M. chelonae*	Early	Removal of prosthesis	Controlled
32	Kreder *et al*[37], 1996	Hip (1)	*M. tuberculosis*	Late	Removal of prosthesis	Controlled
33	Lusk *et al*[38], 1995	Knee (1)	*M. tuberculosis*	Late	Removal of prosthesis	Dead
34	Tokumoto *et al* [39], 1995	Knee (2), hip (1)	*M. tuberculosis*	Late	Removal of prosthesis (3)	Controlled
35	Ueng *et al*[40], 1995	Hip (2)	*M. tuberculosis*	Late	Removal of prosthesis (2)	Controlled
36	Heathcock *et al* [41], 1994	Hip (1)	*M. chelonae*	Late	Removal of prosthesis	Controlled
37	Leach *et al*[42], 1993	Hip (1)	*M. bovis*	Late	Removal of prosthesis	Controlled
38	Guerra *et al*[43], 1998	Hip (1)	*M. bovis*	Late	Removal of prosthesis	Controlled
39	LaBombardi *et al* [44], 2005	Knee (1)	*M. thermoresistibile*	Early	Removal of prosthesis	Controlled
40	Saccente[45], 2006	Knee (1)	*M. fortuitum*	Early	Removal of prosthesis	Controlled
41	Wang *et al*[46], 2007	Knee (1)	*M. tuberculosis*	Late	Debridement	Dead
42	Klein *et al*[47], 2012	Knee (1)	*M. tuberculosis*	Late	Removal of prosthesis	Controlled
43	Srivastava *et al* [48], 2011	Hip (1)	*M. bovis*	Late	Removal of prosthesis	Controlled
44	Rispler *et al*[49], 2015	Knee (1)	*M. bovis*	Late	Debridement	Controlled
45	Vutescu and Koenig[50], 2017	Knee (1)	*M. cosmeticum*	Late	Removal of prosthesis	Controlled
46	Jitmuang *et al*[4], 2017	Knee (10), hip (1)	*M. fortuitum* (9), *M. abscessus* (1), *M. peregrinum* (1) (mixed cases 2)	Early (9), late (2)	Removal of prosthesis (10), debridement (1)	Controlled (6), persistent (1), NA (4)
47	Mannelli *et al* [51], 2018	Hip (1)	*M. chelonae*	Late	Antimicrobials only	Persistent
48	Uhel *et al*[52], 2019	Hip (6), knee (6)	*M. tuberculosis*	Late (12)	Antimicrobials only (4), removal of prosthesis (5), debridement (3)	Controlled (8), persistent (3), dead (1)
49	Rodari *et al*[53], 2020	Hip (1)	*M. xenopi*	Late	Removal prosthesis	Controlled
50	Congia *et al*[54], 2020	Knee (1)	*M. tuberculosis*	Early	Debridement	Controlled
51	Fix *et al*[55], 2020	Hip (1)	*M. fortuitum*	Early	Removal prosthesis	Controlled

Removal of prosthesis: With or without revision. *M.*: *Mycobacteria*; NA: Not available.



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Figure 1 Flow diagram of the study. PJI: Prosthetic joint infection.

Search strategy

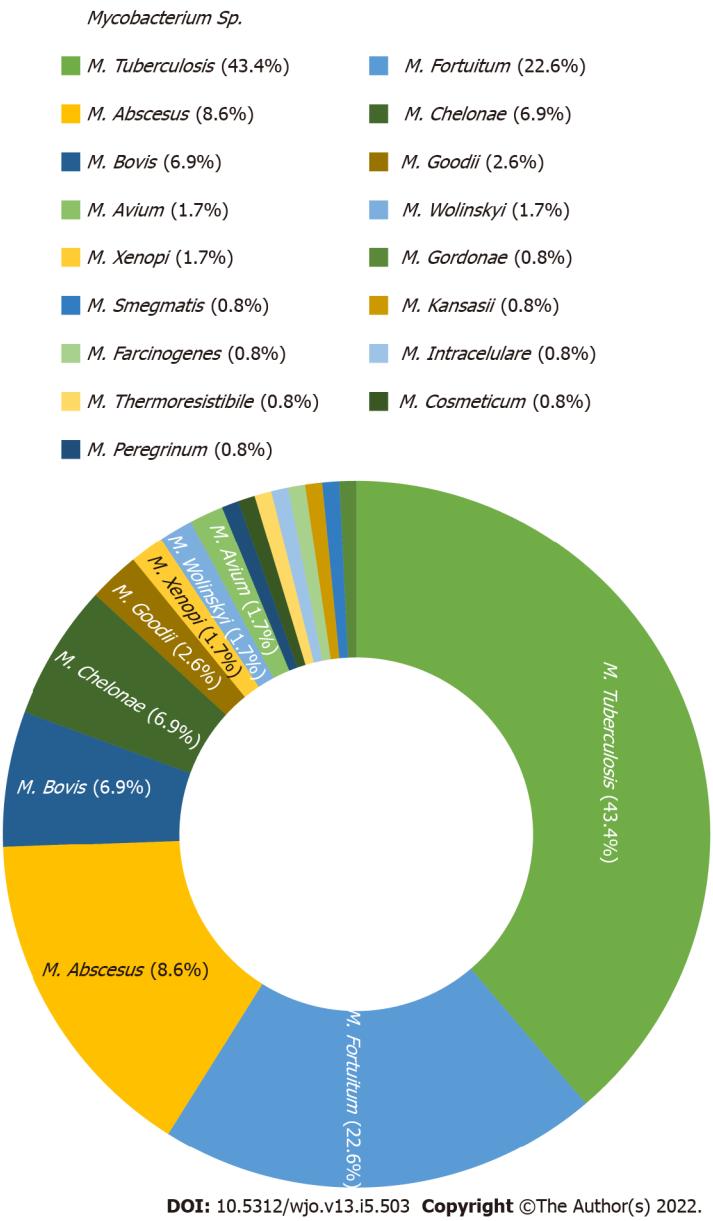
A literature search was performed using MeSH terms on PubMed from January 1, 1990, to May 30, 2021. The following two search scenarios were used accordingly: "Prosthesis joint infection AND Mycobacterium" and "Arthroplasty infection AND Mycobacterium". The articles were screened based on the Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement.

Inclusion and exclusion criteria

The following inclusion criteria were used in our systematic review: (1) Clinical studies; (2) All levels of evidence; and (3) PJI of the hip or knee due to any *Mycobacterium species* (*Mycobacterium sp*). Studies were excluded if they met any of the following criteria: (1) Non-English articles; (2) PJI not involving the hip or knee joint; (3) Primary *Mycobacterium* hip/knee osteoarticular infection prior to arthroplasty; (4) Articles published in abstract form only; (5) Review articles; and (6) Technique articles.

Data collection/extraction

Three authors (Santoso A, Phatama KY, and Rhatomy S) independently screened the titles and abstracts of the included studies. The first search with the terms "Prosthetic joint infection AND Mycobacterium" revealed 54 records. Of these, 6 records were excluded for not being in English, 5 for presenting primary osteoarticular hip/knee infection, 2 for presenting shoulder/elbow PJI, 1 for presenting wound infection after THA without involvement of the joint, and 3 for unavailability of the full-text articles. The remaining 37 records were included in the further analysis. The second search method was performed with the words "Arthroplasty infection AND Mycobacterium", which revealed 56 records. Of these, 33 records were excluded for duplicating previous search results, 4 for presenting primary hip/knee osteoarticular infection, 1 for presenting shoulder PJI, 1 for being a non-English article, 2 for being review articles, and 1 for unavailability of the full-text article. Thus, 14 records were finally included from the second search in the analysis. Considering the 37 records from the first search and 14 from the second search, a total of 51 records were included in the final analysis (Figure 1). The analysis included type of study, demographics, number of patients, hip or knee PJI cases, *Mycobacterium sp* strain, treatment, and outcomes of the mycobacterial PJI cases (Table 1). Furthermore, we performed a descriptive comparison between PJI caused by *M. tuberculous* (*n* = 43) and *nontuberculous mycobacteria* (NTM) (*n* = 63). This comparative evaluation excluded all cases of mixed infections of *M. tuberculous* and NTM (*n* = 1), NTM and *Staphylococcus species* (*Staphylococcus sp*) (*n* = 2), and *M. tuberculous* and *Staphylococcus sp* (*n* = 6). Two cases with no data 5 regarding the specific species of *Mycobacteria* were also excluded at this stage (Table 2). Comparative analysis of categorical data was performed using the chi-square test.



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Figure 2 Distribution of *Mycobacterium* strains as the cause of hip/knee prosthetic joint infection (*n* = 115). *M.*: *Mycobacteria*.

RESULTS

Of the 51 included studies, 40 (80.3%) were case reports and 11 (19.6%) studies were of the retrospective series type. There were studies from America (27/51, 52.9%), Europe (12/51, 23.5%), and Asia-Pacific (12/51, 23.5%) included in the analysis. In total, 117 *Mycobacterium* hip/knee PJI cases were reported across 51 studies. There were 46.15% (54/117) cases of knee PJI and 53.85% (63/117) of hip PJI, and the age range of the patients was 17-101 years. In total, 17 types of *Mycobacteria sp* recorded in this review were responsible for PJI in 115 hip/knee PJI cases, whereas in 2 cases there was no mention of any specific *Mycobacterium sp*. *M. tuberculosis* was detected in 50/115 (43.3%) of the cases. The NTM included *M. fortuitum* (26/115, 22.6%), *M. abscessus* (10/115, 8.6%), *M. chelonae* (8/115, 6.9%), and *M. bovis* (8/115, 6.9%). Other strains with a smaller number of cases were also isolated as the causes of hip/knee PJI (Figure 2). Mixed infections in mycobacterial PJI cases were noted in 8 cases caused by *M. abscessus* and *M. fortuitum* (all NTM) in 1 case and by *M. tuberculosis* and *M. chelonae* in another. The other six cases showed co infection with *Staphylococcus sp*. The majority of the cases (82/114, 71.9%) showed an onset of infection > 3 mo after the index surgery, whereas 24.6% (28/114) of patients showed disease onset in ≤ 3 mo. Incidental intraoperative PJI diagnosis was reported in 4 cases (3.5%) (Figure 3A), and it was not specified in 9 cases. Removal of the prosthesis (with or without revision) was needed in 77.8% (84/108) of cases to treat the infection (Figure 3B). While debridement was needed in 11/108 (10.2%) cases, antimicrobial therapy was needed in 12/108 (11.1%), and amputation was performed in 1 case. The overall infection rate was controlled in 88/102 (86.3%) *mycobacterial* PJI cases. Persistent infection occurred in 10/102 (9.8%) patients, and 4/102 (3.9%) patients died due to the infection (Figure 4).

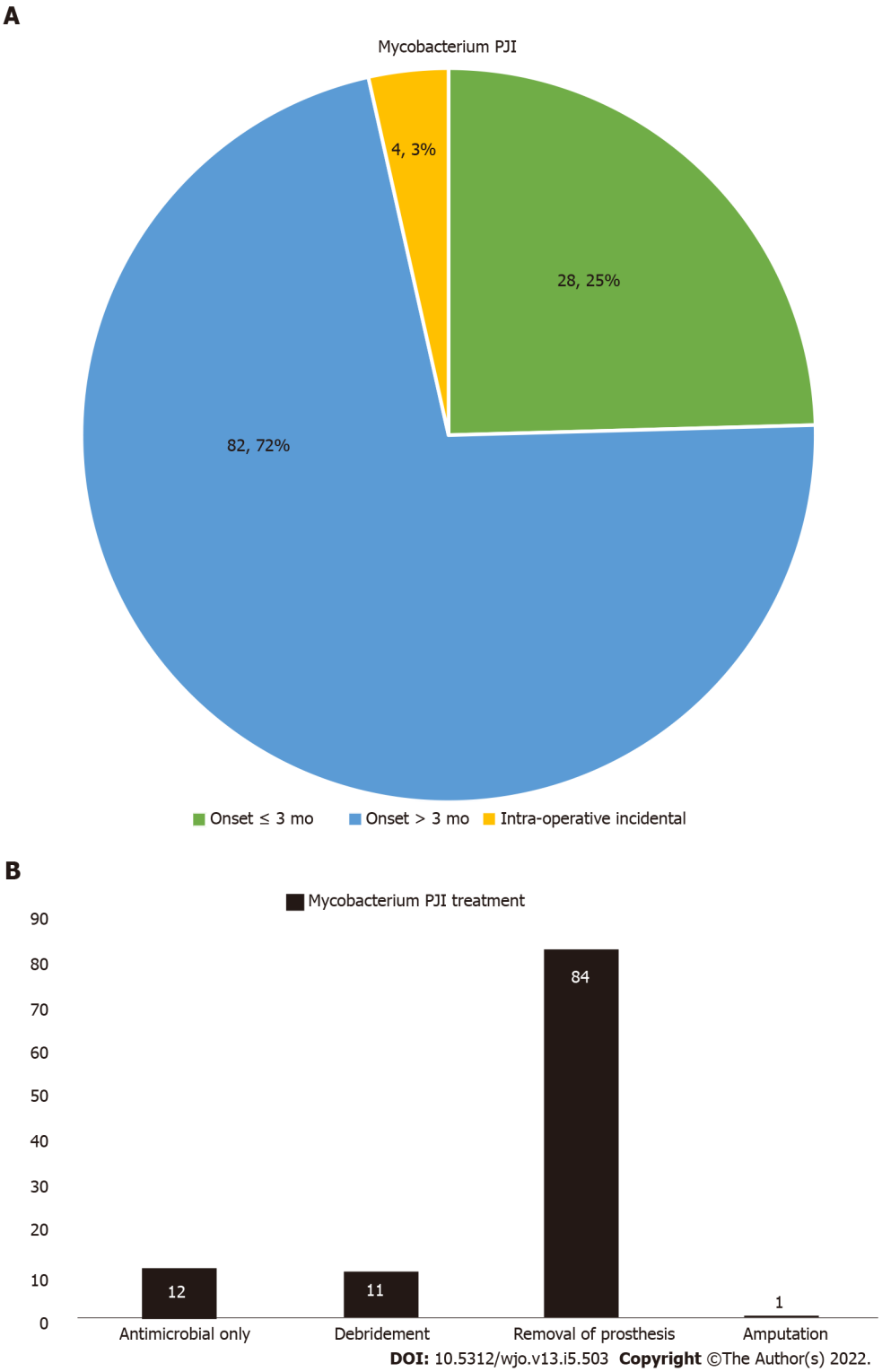


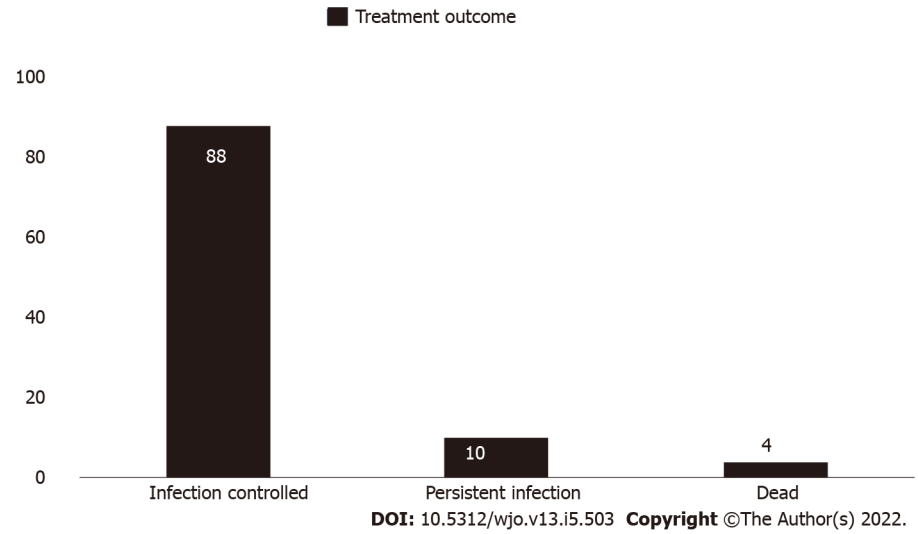
Figure 3 Distribution of overall *Mycobacterium* prosthetic joint infection cases. A: By onset of infection after index surgery (*n* = 114); B: By treatment (*n* = 108). PJI: Prosthetic joint infection.

Comparative analysis showed no difference in the rate of hip or knee involvement in PJI with *M. tuberculous* or NTM ($P > 0.05$). Both *tuberculous* and *nontuberculous* PJI cases predominantly showed disease onset of > 3 mo (79.1% and 63.3%, respectively). However, *nontuberculous* PJI cases showed a higher rate of early onset (< 3 mo) of disease than those cases with tuberculous PJI (36.7% *vs* 11.6%). Removal of the prosthesis was needed in more cases of nontuberculous PJI than in cases of tuberculous PJI (88.9% *vs* 58.1%). The infection control rates were comparable between the tuberculous and nontuberculous PJI cases (81.4% and 91.7%, respectively) (Table 2).

Table 2 Descriptive comparison between tuberculous and nontuberculous *Mycobacteria* prosthetic joint infection cases (excluding mixed-infection cases)

	Tuberculous PJI (*n* = 43)	Nontuberculous PJI (*n* = 63)	*P* value
Joint involvement			
Hip	22/43 (55.1%)	22/63 (34.9%)	0.096
Knee	21/43 (44.9%)	41/63 (65.1%)	
Onset of disease after index surgery			
≤ 3 mo	5/43 (11.6%)	22/60 (36.7%)	0.002
> 3 mo	34/43 (79.1%)	38/60 (63.3%)	
Intraoperative	4/43 (9.3%)	0	
NA	0	3	
Treatment			
Antimicrobial therapy only	10/43 (23.3%)	2/54 (3.7%)	0.002
Debridement	8 /43(18.6%)	3/54 (5.5%)	
Removal of prosthesis	25/43 (58.1%)	48/54 (88.9%)	
Amputation	0	1/54 (1.8%)	
NA	0	9	
Outcome			
Infection controlled	35/43 (81.4%)	44/48 (91.7%)	0.092
Persistent infection	4/43 (9.3%)	4/48 (8.3%)	
Dead	4/43 (9.3%)	0	
NA	0	15	

P < 0.05: Significant. NA: Data not available; PJI: Prosthetic joint infection.



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Figure 4 Distribution of overall final outcome of *Mycobacterium* prosthetic joint infection treatments (*n* = 102).

DISCUSSION

More than 150 *Mycobacterium sp* have been officially recognized until now, in literature which consist of tuberculous mycobacteria and NTM[56]. One of the purposes of this systematic review was to evaluate the various *Mycobacteria sp* that can cause hip/knee PJI, and at least 17 *Mycobacterium sp* were identified accordingly. They comprised of *M. tuberculosis* and 16 NTM. The NTM was further divided into rapidly

growing and slowly growing mycobacteria[56]. Several studies have reported rapidly growing NTM as the cause of early hip/knee PJI[4,17,18,28]. Early PJI (≤ 3 mo) was noted in 36% of the NTM cases in this review, which was higher than that in tuberculous PJI cases (11%). The rapidly growing NTM hence needs to be considered as a differential diagnosis in cases of early hip/knee PJI. The diagnosis of *Mycobacterium* PJI is sometimes delayed, leading to delays in appropriate management[6,8]. Several treatment options were noted in this review. Removal of the prosthesis was the most commonly performed procedure, which was required in > 75% of cases. Additionally, a greater number of NTM PJI cases required removal of the prosthesis compared to the tuberculous PJI cases (88.9% *vs* 58.1%). There were no data regarding specific procedures, such as revision surgery, resection arthroplasty, or arthrodesis after the prosthesis removal procedure due to incomplete data in every published article. Another interesting finding was that conservative treatment with only antimicrobial therapy successfully controlled tuberculous hip/knee PJI in approximately 23% of the cases. This indicates that early recognition of sensitive antimicrobial agents is highly important in treating *Mycobacterium* PJI. However, the isolation of *Mycobacterium* with standard culture procedures may be sometimes difficult and more advanced techniques with gene sequencing are hence needed to isolate the *Mycobacterium sp* [19]. This could be a hindrance, especially in developing countries. Based on the pooled case analyses reported from the studies included in this systematic review, the outcome of the treatment of *Mycobacterium* PJI reportedly had an infection control rate of approximately 86%. Among the mycobacterial PJI cases, the infection control rate of nontuberculous PJI was comparable to that of tuberculous PJI (91.7% *vs* 81.4%, $P = 0.092$). This was comparable to that of PJI hip/knee associated with non-mycobacterial pathogens or even a negative-culture PJI that showed an infection control rate of 70%-90%[3,57]. *Mycobacterium* PJI has also been correlated with culture-negative PJI. A study by Palan *et al*[58] reported that fungi and mycobacteria are responsible for over 85% of negative-culture PJI. Arthroplasty surgeons need to consider *Mycobacterium* as the causal pathogen of PJI when negative culture results are obtained in clinical practice. Further diagnosis using histopathology or polymerase chain reaction assay is needed accordingly.

This study had a few limitations. First, the systematic review only included studies indexed in PubMed; therefore, some other studies may have been missed in this review. However, the wider search period (30 years) of this systematic review ensured the inclusion of several important studies from literature. Second, the studies included in this systematic review were mostly retrospective case reports or case series, which had their own limitations. It is difficult to obtain a higher level of evidence from relatively rare cases, such as those of *Mycobacterium* PJI. Third, some bias of treatment and outcome evaluation may have occurred, as every author may have used a different standard. This study also could not suggest any advisable best treatment for *Mycobacterium* PJI due to the lack of available data for evaluation. Despite these limitations, we believe that this systematic review could provide some insights into the profile of *Mycobacterium* hip/knee PJI, including its treatment options and outcomes.

CONCLUSION

At least 17 *Mycobacterium sp* can be responsible for PJI of the hip and knee. Although *M. tuberculosis* is the most common causal pathogen, NTM should be considered as an emerging cause of hip/knee PJI.

ARTICLE HIGHLIGHTS

Research background

There were many species of *Mycobacterium* that may be associated as a causal pathogens for prosthetic joint infection (PJI) of the hip and knee. However, no available literature which provides compilation data regarding this issue.

Research motivation

To do compilation data of *Mycobacterium species* (*Mycobacterium sp*) which may cause hip and knee PJI.

Research objectives

This study aimed to evaluate PJI associated with *Mycobacterium sp*.

Research methods

Systematic review of PubMed article.

Research results

Among reviewed 51 articles. We found several species of *Mycobacterium* may be associated with hip and knee PJI.

Research conclusions

We found at least 17 species of *Mycobacterium* could be responsible for hip and knee PJI.

Research perspectives

This study may open the knowledge of various species of *Myscobacterium* that can be associated with hip and knee PJI.

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FOOTNOTES

Author contributions: Santoso A, Phatama KY, and Rhatomy S contributed to the data collection and analysis; Santoso A and Phatama KY wrote the paper; Budhiparama NC contributed to the study design, analysis and finalization.

Conflict-of-interest statement: All of the author have none to disclose.

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REFERENCES

1 **Tande AJ**, Patel R. Prosthetic joint infection. *Clin Microbiol Rev* 2014; **27**: 302-345 [PMID: 24696437 DOI: 10.1128/CMR.00111-13]
2 **Aggarwal VK**, Rasouli MR, Parvizi J. Periprosthetic joint infection: Current concept. *Indian J Orthop* 2013; **47**: 10-17 [PMID: 23531512 DOI: 10.4103/0019-5413.106884]
3 **Santoso A**, Park KS, Shin YR, Yang HY, Choi IS, Yoon TR. Two-stage revision for periprosthetic joint infection of the hip: Culture-negative versus culture-positive infection. *J Orthop* 2018; **15**: 391-395 [PMID: 29881161 DOI: 10.1016/j.jor.2018.03.002]
4 **Jitmuang A**, Yuenyongviwat V, Charoencholvanich K, Chayakulkeeree M. Rapidly-growing mycobacterial infection: a recognized cause of early-onset prosthetic joint infection. *BMC Infect Dis* 2017; **17**: 802 [PMID: 29281992 DOI: 10.1186/s12879-017-2926-3]
5 **Elzein FE**, Haris M, Alolayan SS, Al Sherbini N. Total knee prosthesis infected with *Mycobacterium tuberculosis*. *BMJ Case Rep* 2017; **2017** [PMID: 28883009 DOI: 10.1136/bcr-2017-220596]
6 **Osmon DR**, Berbari EF, Berendt AR, Lew D, Zimmerli W, Steckelberg JM, Rao N, Hanssen A, Wilson WR; Infectious Diseases Society of America. Executive summary: diagnosis and management of prosthetic joint infection: clinical practice guidelines by the Infectious Diseases Society of America. *Clin Infect Dis* 2013; **56**: 1-10 [PMID: 23230301 DOI: 10.1093/cid/cis966]
7 **Ribeiro AF**, Inacio Oliveira M, Jordão P, Tavares D, Varandas L, Gouveia C. Mycobacterium tuberculosis prosthesis joint infection. *Pediatr Int* 2020; **62**: 97-99 [PMID: 31916331 DOI: 10.1111/ped.14037]
8 **Patel A**, Elzweig J. *Mycobacterium bovis* prosthetic joint infection following intravesical instillation of BCG for bladder cancer. *BMJ Case Rep* 2019; **12** [PMID: 31857290 DOI: 10.1136/bcr-2019-231830]
9 **Sixt T**, Bador J, Amoureux L, Piroth L, Blot M. Prosthetic joint infection caused by Mycobacterium avium complex. *QJM* 2020; **113**: 278-279 [PMID: 31764970 DOI: 10.1093/qjmed/hcz306]
10 **Barry M**, Akkielah L, Askar MA, Bin Nasser AS. Miliary tuberculosis with delayed-onset total knee arthroplasty Mycobacteria tuberculosis infection successfully treated with medical therapy alone: A case report and literature review.

Knee 2019; **26**: 1152-1158 [PMID: 31427242 DOI: 10.1016/j.knee.2019.07.010]
11 **Goldstein N**, St Clair JB, Kasperbauer SH, Daley CL, Lindeque B. Nontuberculous Mycobacterial Musculoskeletal Infection Cases from a Tertiary Referral Center, Colorado, USA. *Emerg Infect Dis* 2019; **25**: 1075-1083 [PMID: 31107224 DOI: 10.3201/eid2406.181041]
12 **Buser GL**, Laidler MR, Cassidy PM, Moulton-Meissner H, Beldavs ZG, Cieslak PR. Outbreak of Nontuberculous Mycobacteria Joint Prosthesis Infections, Oregon, USA, 2010-2016. *Emerg Infect Dis* 2019; **25**: 849-855 [PMID: 31002056 DOI: 10.3201/eid2505.181687]
13 **Spanyer JM**, Foster S, Thum-DiCesare JA, Kwon YM, Burke DW, Nelson SB. Mycobacterium abscessus: A Rare Cause of Periprosthetic Knee Joint Infection. *Am J Orthop (Belle Mead NJ)* 2018; **47** [PMID: 30296310 DOI: 10.12788/ajo.2018.0077]
14 **Meyssonnier V**, Zeller V, Malbos S, Heym B, Lhotellier L, Desplaces N, Marmor S, Ziza JM. Prosthetic joint infections due to Mycobacterium tuberculosis: A retrospective study. *Joint Bone Spine* 2019; **86**: 239-243 [PMID: 30266444 DOI: 10.1016/j.jbspin.2018.09.008]
15 **Chang CH**, Hu CC, Chang Y, Hsieh PH, Shih HN, Ueng SW. Two-stage revision arthroplasty for Mycobacterium Tuberculosis periprosthetic joint infection: An outcome analysis. *PLoS One* 2018; **13**: e0203585 [PMID: 30192830 DOI: 10.1371/journal.pone.0203585]
16 **Metayer B**, Menu P, Khatchatourian L, Preuss P, Dauty M, Fouasson-Chailloux A. Prosthetic joint infection with pseudo-tumoral aspect due to Mycobacterium bovis infection after Bacillus-Calmette-Guerin therapy. *Ann Phys Rehabil Med* 2018; **61**: 62-64 [PMID: 28890342 DOI: 10.1016/j.rehab.2017.08.001]
17 **Kim M**, Ha CW, Jang JW, Park YB. Rapidly growing non-tuberculous mycobacteria infection of prosthetic knee joints: A report of two cases. *Knee* 2017; **24**: 869-875 [PMID: 28551202 DOI: 10.1016/j.knee.2017.04.015]
18 **Henry MW**, Miller AO, Kahn B, Windsor RE, Brause BD. Prosthetic joint infections secondary to rapidly growing mycobacteria: Two case reports and a review of the literature. *Infect Dis (Lond)* 2016; **48**: 453-460 [PMID: 27030918 DOI: 10.3109/23744235.2016.1142673]
19 **Jeong JH**, Seo YH, Kim KH, Ahn JY, Park PH, Park YK. Mycobacterium wolinskyi infection confirmed by rpoB gene sequencing. *J Clin Lab Anal* 2012; **26**: 325-327 [PMID: 23001976 DOI: 10.1002/jcla.21526]
20 **Lee RP**, Cheung KW, Chiu KH, Tsang ML. Mycobacterium chelonae infection after total knee arthroplasty: a case report. *J Orthop Surg (Hong Kong)* 2012; **20**: 134-136 [PMID: 22535831 DOI: 10.1177/230949901202000130]
21 **Wang SX**, Yang CJ, Chen YC, Lay CJ, Tsai CC. Septic arthritis caused by Mycobacterium fortuitum and Mycobacterium abscessus in a prosthetic knee joint: case report and review of literature. *Intern Med* 2011; **50**: 2227-2232 [PMID: 21963746 DOI: 10.2169/internalmedicine.50.5610]
22 **Ahmad S**, Khakoo RA. Left knee prosthesis-related Mycobacterium goodii infection. *Int J Infect Dis* 2010; **14**: e1115-e1116 [PMID: 21071255 DOI: 10.1016/j.ijid.2010.02.2245]
23 **Gupta A**, Clauss H. Prosthetic joint infection with Mycobacterium avium complex in a solid organ transplant recipient. *Transpl Infect Dis* 2009; **11**: 537-540 [PMID: 19656344 DOI: 10.1111/j.1399-3062.2009.00433.x]
24 **Porat MD**, Austin MS. Bilateral knee periprosthetic infection with Mycobacterium fortuitum. *J Arthroplasty* 2008; **23**: 787-789 [PMID: 18534520 DOI: 10.1016/j.arth.2007.07.010]
25 **Reigstad O**, Siewers P. A total hip replacement infected with mycobacterium bovis after intravesicular treatment with Bacille-Calmette-Guérin for bladder cancer. *J Bone Joint Surg Br* 2008; **90**: 225-227 [PMID: 18256093 DOI: 10.1302/0301-620X.90B2.20038]
26 **Brown A**, Grubbs P, Mongey AB. Infection of total hip prosthesis by Mycobacterium tuberculosis and Mycobacterium chelonae in a patient with rheumatoid arthritis. *Clin Rheumatol* 2008; **27**: 543-545 [PMID: 18034202 DOI: 10.1007/s10067-007-0788-6]
27 **Cheung I**, Wilson A. Mycobacterium fortuitum infection following total knee arthroplasty: a case report and literature review. *Knee* 2008; **15**: 61-63 [PMID: 17869520 DOI: 10.1016/j.knee.2007.08.007]
28 **Eid AJ**, Berbari EF, Sia IG, Wengenack NL, Osmon DR, Razonable RR. Prosthetic joint infection due to rapidly growing mycobacteria: report of 8 cases and review of the literature. *Clin Infect Dis* 2007; **45**: 687-694 [PMID: 17712751 DOI: 10.1086/520982]
29 **Segal A**, Krauss ES. Infected total hip arthroplasty after intravesical bacillus Calmette-Guérin therapy. *J Arthroplasty* 2007; **22**: 759-762 [PMID: 17689788 DOI: 10.1016/j.arth.2006.07.010]
30 **Khater FJ**, Samnani IQ, Mehta JB, Moorman JP, Myers JW. Prosthetic joint infection by Mycobacterium tuberculosis: an unusual case report with literature review. *South Med J* 2007; **100**: 66-69 [PMID: 17269530 DOI: 10.1097/01.smj.0000232972.50186.4c]
31 **Pulcini C**, Vandenbussche E, Podglajen I, Sougakoff W, Truffot-Pernot C, Buu-Hoï A, Varon E, Mainardi JL. Hip prosthesis infection due to Mycobacterium wolinskyi. *J Clin Microbiol* 2006; **44**: 3463-3464 [PMID: 16954303 DOI: 10.1128/JCM.02685-05]
32 **Neuberger A**, Sprecher H, Oren I. Septic arthritis caused by Mycobacterium kansasii in a prosthetic knee joint. *J Clin Microbiol* 2006; **44**: 2648-2649 [PMID: 16825405 DOI: 10.1128/JCM.00087-06]
33 **Wong TC**, Chan WF, Tsang WL, Yeung SH, Ip FK. Mycobacterium farcinogenes infection after total hip arthroplasty. *J Arthroplasty* 2005; **20**: 684-687 [PMID: 16310009 DOI: 10.1016/j.arth.2005.03.001]
34 **Yim K**, Nazeer SH, Kiska D, Rose FB, Brown D, Cynamon MH. Recurrent Mycobacterium xenopi infection in a patient with rheumatoid arthritis receiving etanercept. *Scand J Infect Dis* 2004; **36**: 150-154 [PMID: 15061673 DOI: 10.1080/00365540310017474]
35 **Spinner RJ**, Sexton DJ, Goldner RD, Levin LS. Periprosthetic infections due to Mycobacterium tuberculosis in patients with no prior history of tuberculosis. *J Arthroplasty* 1996; **11**: 217-222 [PMID: 8648322 DOI: 10.1016/s0883-5403(05)80023-3]
36 **Pring M**, Eckhoff DG. Mycobacterium chelonae infection following a total knee arthroplasty. *J Arthroplasty* 1996; **11**: 115-116 [PMID: 8676110 DOI: 10.1016/s0883-5403(96)80170-7]
37 **Kreder HJ**, Davey JR. Total hip arthroplasty complicated by tuberculous infection. *J Arthroplasty* 1996; **11**: 111-114

[PMID: 8676109 DOI: 10.1016/s0883-5403(96)80169-0]
38 **Lusk RH**, Wienke EC, Milligan TW, Albus TE. Tuberculous and foreign-body granulomatous reactions involving a total knee prosthesis. *Arthritis Rheum* 1995; **38**: 1325-1327 [PMID: 7575728 DOI: 10.1002/art.1780380921]
39 **Tokumoto JI**, Follansbee SE, Jacobs RA. Prosthetic joint infection due to Mycobacterium tuberculosis: report of three cases. *Clin Infect Dis* 1995; **21**: 134-136 [PMID: 7578722 DOI: 10.1093/clinids/21.1.134]
40 **Ueng WN**, Shih CH, Hseuh S. Pulmonary tuberculosis as a source of infection after total hip arthroplasty. A report of two cases. *Int Orthop* 1995; **19**: 55-59 [PMID: 7768660 DOI: 10.1007/BF00184916]
41 **Heathcock R**, Dave J, Yates MD. Mycobacterium chelonae hip infection. *J Infect* 1994; **28**: 104-105 [PMID: 8163823 DOI: 10.1016/s0163-4453(94)94533-0]
42 **Leach WJ**, Halpin DS. Mycobacterium bovis infection of a total hip arthroplasty: a case report. *J Bone Joint Surg Br* 1993; **75**: 661-662 [PMID: 8331128 DOI: 10.1302/0301-620X.75B4.8331128]
43 **Guerra CE**, Betts RF, O'Keefe RJ, Shilling JW. Mycobacterium bovis osteomyelitis involving a hip arthroplasty after intravesicular bacille Calmette-Guérin for bladder cancer. *Clin Infect Dis* 1998; **27**: 639-640 [PMID: 9770167 DOI: 10.1086/514714]
44 **LaBombardi VJ**, Shastry L, Tischler H. Mycobacterium thermoresistibile infection following knee-replacement surgery. *J Clin Microbiol* 2005; **43**: 5393-5394 [PMID: 16208028 DOI: 10.1128/JCM.43.10.5393-5394.2005]
45 **Saccente M**. Mycobacterium fortuitum group periprosthetic joint infection. *Scand J Infect Dis* 2006; **38**: 737-739 [PMID: 16857632 DOI: 10.1080/00365540500504133]
46 **Wang PH**, Shih KS, Tsai CC, Wang HC. Pulmonary tuberculosis with delayed tuberculosis infection of total knee arthroplasty. *J Formos Med Assoc* 2007; **106**: 82-85 [PMID: 17282976 DOI: 10.1016/S0929-6646(09)60221-7]
47 **Klein GR**, Jacquette GM. Prosthetic knee infection in the young immigrant patient--do not forget tuberculosis! *J Arthroplasty* 2012; **27**: 1414.e1-4 [PMID: 22088780 DOI: 10.1016/j.arth.2011.09.020]
48 **Srivastava A**, Ostrander J, Martin S, Walter N. Mycobacterium bovis infection of total hip arthroplasty after intravesicular bacille Calmette-Guérin therapy. *Am J Orthop (Belle Mead NJ)* 2011; **40**: E226-E228 [PMID: 22263218]
49 **Rispler DT**, Stirton JW, Gilde AK, Kane KR. Mycobacterium bovid infection of total knee arthroplasty after bacille Calmette-Guérin therapy for bladder cancer. *Am J Orthop (Belle Mead NJ)* 2015; **44**: E46-E48 [PMID: 25658082]
50 **Vutescu ES**, Koenig KM. Mycobacterium cosmeticum Infection After Total Knee Arthroplasty: A Case Report. *JBJS Case Connect* 2017; **7**: e3 [PMID: 29244685 DOI: 10.2106/JBJS.CC.16.00099]
51 **Mannelli VK**, Rai MP, Nemakayala DR, Kadiri NP. *Mycobacterium Chelonae*Developing Multidrug Resistance. *BMJ Case Rep* 2018; **2018** [PMID: 29472421 DOI: 10.1136/bcr-2017-222569]
52 **Uhel F**, Corvaisier G, Poinsignon Y, Chirouze C, Beraud G, Grossi O, Varache N, Arvieux C, Berre RL, Tattevin P; Groupe d'Epidémiologie et Recherche en Infectiologie Clinique Centre-Ouest (GERICCO). Mycobacterium tuberculosis prosthetic joint infections: A case series and literature review. *J Infect* 2019; **78**: 27-34 [PMID: 30138639 DOI: 10.1016/j.jinf.2018.08.008]
53 **Rodari P**, Marocco S, Buonfrate D, Beltrame A, Piubelli C, Orza P, Fittipaldo VA, Bisoffi Z. Prosthetic joint infection due to Mycobacterium xenopi: a review of the literature with a new case report. *Infection* 2020; **48**: 165-171 [PMID: 31098926 DOI: 10.1007/s15010-019-01318-1]
54 **Congia S**, Puddu G, Sorrentino G, Dessì G, Marongiu G. Conservative treatment of early-onset tubercular periprosthetic joint infection following total knee arthroplasty. *J Infect Dev Ctries* 2020; **14**: 223-227 [PMID: 32146458 DOI: 10.3855/jidc.12053]
55 **Fix WC**, Sheth NP, Braffman MN. Mycobacterium fortuitum Prosthetic Joint Infection After Total Hip Arthroplasty: A Case Report. *JBJS Case Connect* 2020; **10**: e0343 [PMID: 32649134 DOI: 10.2106/JBJS.CC.18.00343]
56 **Tortoli E**. Microbiological features and clinical relevance of new species of the genus Mycobacterium. *Clin Microbiol Rev* 2014; **27**: 727-752 [PMID: 25278573 DOI: 10.1128/CMR.00035-14]
57 **Santoso A**, Yoon TR, Park KS, Anwar IB, Utomo P, Soetjahjo B, Sibarani T. The Results of Two-stage Revision for Methicillin-resistant Periprosthetic Joint Infection (PJI) of the Hip. *Malays Orthop J* 2020; **14**: 18-23 [PMID: 32296477 DOI: 10.5704/MOJ.2003.003]
58 **Palan J**, Nolan C, Sarantos K, Westerman R, King R, Foguet P. Culture-negative periprosthetic joint infections. *EFORT Open Rev* 2019; **4**: 585-594 [PMID: 31754464 DOI: 10.1302/2058-5241.4.180067]

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SYSTEMATIC REVIEWS

Prophylactic fixation of the unaffected contralateral side in children with slipped capital femoral epiphysis seems favorable: A systematic review

Steven J C Vink, Renée A van Stralen, Sophie Moerman, Christiaan J A van Bergen

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Abstract

BACKGROUND

Slipped capital femoral epiphysis (SCFE) occurs in adolescents and has an incidence of around 10 *per* 100000 children. Children presenting with a unilateral SCFE are 2335 times more likely to develop a contralateral SCFE than the general population. Prognostic factors that have been suggested to increase the risk of contralateral slip include a younger patient, an underlying endocrine disorder, growth hormone use and a higher radiographic posterior sloping angle. However, there is still much debate on the advantages and disadvantages of prophylactic fixation of the unaffected side in an otherwise healthy patient.

AIM

To investigate the risk rate of contralateral SCFE and assess the (dis)advantages of prophylactic fixation of the contralateral hip.

METHODS

A systematic literature search was performed in the Embase, Medline, Web of Science Core Collection and Cochrane databases. Search terms included 'slipped capital femoral epiphysis,' 'fixation,' 'contralateral,' and derivatives. The eligibility of the acquired articles was independently assessed by the authors and additional relevant articles were included through cross-referencing. Publications were considered eligible for inclusion if they presented data about otherwise healthy children with primarily unilateral SCFE and the outcomes of prophylactically pinning their unaffected side, or about the rates of contralateral slips and

complications thereof. The study quality of the included articles was assessed independently by the authors by means of the methodological index for non-randomized studies criteria.

RESULTS

Of 293 identified unique publications, we included 26 studies with a total of 12897 patients. 1762 patients (14%) developed a subsequent symptomatic contralateral slip. In addition, 38% of patients developed a subsequent slip on the contralateral side without experiencing clinical symptoms. The most outspoken advantage of prophylactic fixation of the contralateral hip in the literature is prevention of an (asymptomatic) slip, thus reducing the increased risk of avascular necrosis (AVN), cam morphology and osteoarthritis. Disadvantages include an increased risk of infection, AVN, peri-implant fractures, loss of fixation as well as migration of hardware and morphologic changes as a consequence of growth guidance. These risks, however, appeared to only occur incidentally and were usually mild compared to the risks involved with an actual SCFE.

CONCLUSION

The advantages of prophylactic pinning of the unaffected side in otherwise healthy patients with unilateral SCFE seem to outweigh the disadvantages. The final decision for treatment remains to be patient-tailored.

Key Words: Slipped capital femoral epiphysis; Primary prevention; Postoperative complications; Risk factors; Radiography

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Core Tip: The aim of this article is to provide an evidence-based review of the epidemiology, risk factors, radiographic imaging, treatment and outcomes of the unaffected contralateral side in otherwise healthy children with unilateral slipped capital femoral epiphysis. It provides a systematically reviewed comprehensive assessment of the advantages and disadvantages that should be considered when deciding on whether or not to prophylactically pin the healthy side.

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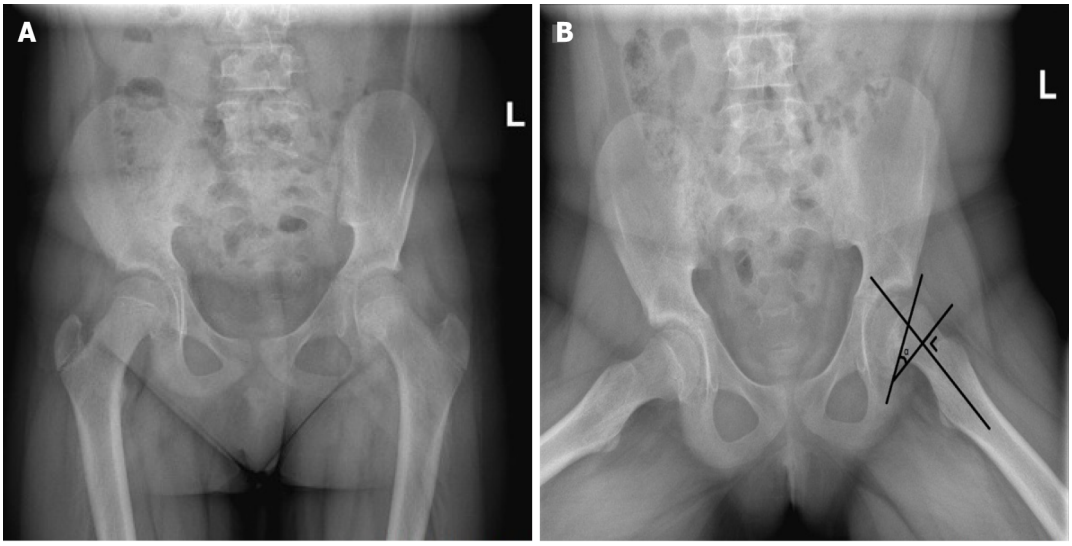
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INTRODUCTION

Slipped capital femoral epiphysis (SCFE) is a medical condition of the hip that occurs in adolescents. The name of this condition is in itself misleading, as it is rather the metaphysis that moves in relation to the epiphysis, while the latter remains in its position in the acetabulum. When suffering from SCFE, a patient will usually have intermittent pain in the groin area. The hip, thigh and knee may also be painful. If the slip is more severe, the patient might also present with a complete inability to bear weight on the affected leg, which is defined as unstable[1]. Furthermore, slips can be categorized according to the duration of symptoms; referred to as acute (< 3 wk of pain), chronic (≥ 3 wk) or acute-on-chronic (a traumatic event occurring in a chronic SCFE)[2]. For the diagnostic process, plain anteroposterior and frog-leg lateral hip or pelvic radiographs are generally used (Figure 1).

The overall incidence of SCFE is approximately 10.8 *per* 100000 children, which differs with gender, race, and seasonal variations[3,4]. The average age of onset is reported to be 12.7 years for boys and 11.2 years for girls[4]. The cause of the slip is unknown but is thought to be multifactorial and has been related to obesity, renal failure, endocrinological disorders (*e.g.*, hypothyroidism, hypogonadism, or hypopituitarism) and radiation therapy[5-8]. SCFE appears to be more apparent around the time of the growth spurt and it is more common in boys than girls[5-8].

The long-term outcome of SCFE is related to the severity of the slip. This can be classified as mild (Southwick angle ≤ 29°), moderate (30°-50°), or severe (> 50°)[2]. A higher-grade slip causes decreased range of motion and higher risk of chondrolysis, avascular necrosis (AVN) of the femoral head and osteoarthritis at a later age[9]. The overall incidence of chondrolysis in SCFE patients is estimated to be 7%[10]. AVN rates vary from 7% to 21%, depending on the stability of the slip[11-13]. The etiology of AVN in SCFE patients is not fully known, but it is suggested that it is the result of a disturbance in



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Figure 1 Plain pelvic radiographs of a left-sided slipped capital femoral epiphysis showing the posterior sloping angle of the affected side. A high posterior sloping angle of the unaffected side is considered an independent risk factor for subsequent contralateral disease. The posterior sloping angle (α), here presented on the affected side to increase visibility, is measured as the angle formed by the line along the physeal plane and the line perpendicular to the femoral neck-diaphyseal axis. A: Anteroposterior view; B: Lauenstein view.

epiphyseal blood supply and intracapsular tamponade[11]. Additionally, it has been reported that the anatomical features of a post-SCFE hip are significantly altered, even after adequate treatment, with up to 40% developing femoroacetabular impingement (FAI) and 53% developing osteoarthritis[14-16].

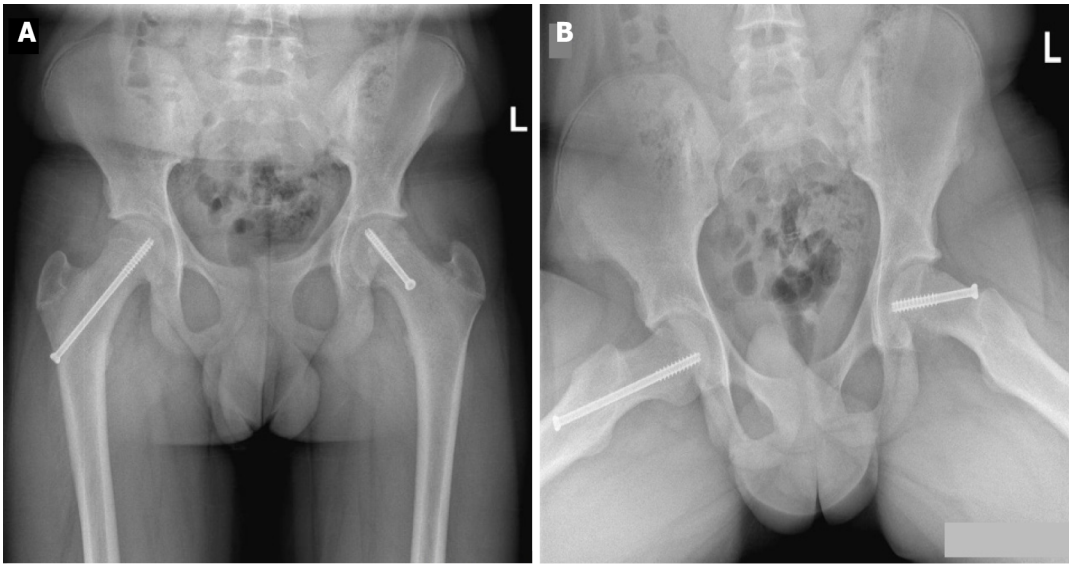
Percutaneous *in situ* fixation is the gold standard for treatment of mild and moderate grade SCFE, whereas open reduction and internal fixation is sometimes performed for severe slips[17]. Nowadays, the most commonly used surgical method is pinning with a single screw. The screw is aimed to start from the anterior aspect of the femoral neck, in order to cross to the physis perpendicularly and enter into the central portion of the femoral head (Figure 2). In severe slips, insertion may have to be relatively oblique at the intertrochanteric region in order to prevent impingement. Another reported method is by means of double screw fixation, in which screws are inserted in a similar orientation as fixation with a single screw. In bovine femurs, this was measured to yield a 33% increase in stiffness[18]. In addition, some surgeons use Kirschner wires/pins (K-wires) rather than screws for *in situ* fixation[19,20].

For years, research has been conducted on the fate of the contralateral hip, which is at an increased risk of slipping in patients with unilateral SCFE[21,22]. The exact incidence of contralateral slips is unknown, as various rates have been reported in the literature[14,23,24].

When presented with a unilateral SCFE, the attending physician has several options with regard to the contralateral side. The first is to observe the patient with regular monitoring and radiographic imaging until closure of the physis, after which the risk of developing a slip has ceased to exist. Alternatively, the surgeon may choose to prophylactically pin the contralateral side in order to prevent a potential slip. Finally, one may consider several stratifications and risk factors of the specific patient in order to estimate the risk of a contralateral slip, and decide based on this risk analysis. Recently, several risk factors have been analyzed in a systematic review and meta-analysis[25]. To this day, however, no consensus has been reached on the indication for prophylactic pinning of the contralateral side of otherwise healthy children. The present systematic review aims to provide an overall risk rate of contralateral SCFE, and a comprehensive assessment of the advantages and disadvantages that can be considered when deciding on whether or not to pin the contralateral hip of unilateral SCFE in otherwise healthy patients.

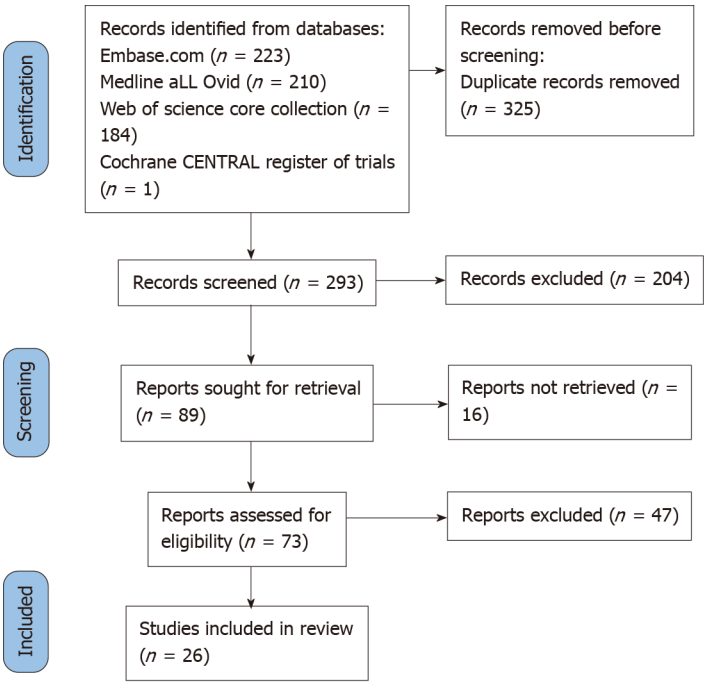
MATERIALS AND METHODS

A systematic literature search was performed on April 21, 2020, in the Embase, Medline, Web of Science Core Collection and Cochrane databases. Search terms included 'slipped capital femoral epiphysis,' 'fixation,' 'contralateral,' and derivatives thereof (Supplementary material). The searches rendered 293 unique results (Figure 3). Two authors (SV and RvS) first assessed eligibility independently by reviewing titles and abstracts, after which 89 articles remained. 73 of these were available in English and were partitioned between the four authors and again assessed independently by reviewing the full texts. Articles were considered eligible for inclusion in the current review if they reported about children with primarily unilateral SCFE that were otherwise healthy and the outcomes of prophylactically pinning the



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Figure 2 Pelvic radiographs showing *in situ* fixation of a left slipped capital femoral epiphysis and prophylactic fixation of the right proximal femur with a single screw. Note the difference in screw direction and length due to the epiphysiolysis on the left side. A: Anteroposterior view; B: Lauenstein view.



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Figure 3 PRISMA flow diagram.

unaffected contralateral side (*e.g.*, prevention of slip and perioperative and mid- to long-term complications), or about rates of contralateral slips and their complications. Cross-referencing led to a further inclusion of relevant publications. A total of 26 articles that specifically addressed the incidence and follow-up of contralateral SCFE were included (Table 1). The study quality of these 26 articles was then assessed independently by the authors by means of the methodological index for non-randomized studies (MINORS) criteria (Table 1, primary data available upon request)[26]. Considering the results of Loder *et al*[27] and Swarup *et al*[28], a follow-up period of 18 mo was deemed to be adequate, since a contralateral slip takes place in the first 18 mo in 88% of children[27,28]. In addition, 39 articles were found that described advantages or disadvantages of contralateral pinning.

Table 1 Incidence and follow-up of symptomatic contralateral slipped capital femoral epiphysis in the literature

Ref.	Incidence	Time between slips in mo	Follow-up in mo	Minors score
Greenough *et al*[57]	16 of 61 (26%)	NA[1]	NA	8 of 16
Hägglund *et al*[14]	32 of 237 (14%)	NA	NA	10 of 16
Jensen *et al*[30]	9 of 57 (16%)	NA	264 (median)	9 of 16
Segal *et al*[23]	9 of 13 (69%)	14 (mean)	37 (mean)	15 of 24
Hurley *et al*[32]	61 of 169 (36%)	NA	34 (mean)	10 of 16
Stasikelis *et al*[49]	20 of 50 (40%)	10 (mean)	34 (mean)	13 of 16
Stott and Bidwell[29]	56 of 171 (33%)	77% < 12	24 (mean)	7 of 16
MacLean and Reddy[21]	9 of 53 (17%)	13 (mean)	NA	6 of 16
Koenig *et al*[58]	12 of 71 (17%)	NA	60 (mean)	9 of 16
Lehmann *et al*[33]	15 of 62 (24%)	6 (mean)	72 (mean)	8 of 16
Baghdadi *et al*[22]	20 of 133 (15%)	12 (mean)	192 (mean)	9 of 16
Kohno *et al*[59]	11 of 65 (17%)	NA	36 (mean)	15 of 24
Phillips *et al*[60]	42 of 132 (32%)	NA	24 (mean)	11 of 16
Bhattacharjee *et al*[43]	10 of 36 (28%)	NA	36 (mean)	15 of 24
Boyle *et al*[61]	45 of 168 (27%)	NA	44 (mean)	11 of 16
Wensaas *et al*[52]	6 of 22 (27%)	NA	33 (mean)	9 of 16
Nowicki *et al*[24]	45 of 496 (9%)	NA	40 (mean)	19 of 24
Herngren *et al*[37]	43 of 201 (21%)	NA	36 (mean)	14 of 16
Balch Samora *et al*[50]	11 of 33 (33%)	NA	20 (mean)	11 of 16
Tucker *et al*[13]	11 of 40 (28%)	6 (mean)	24 (minimum)	10 of 16
Chan *et al*[62]	7 of 43 (16%)	11 (mean)	18 (mean)	9 of 16
Maranho *et al*[63]	70 of 318 (22%)	42 (median)	18 (minimum)	13 of 16
Tomaru *et al*[64]	3 of 34 (9%)	NA	58 (mean)	6 of 16
Swarup *et al*[28]	1077 of 9755 (11%)	9 (mean), 88% < 18	24 (minimum)	8 of 16
Maranho *et al*[65]	40 of 250 (28%)	NA	49 (mean)	14 of 16
Yildirim *et al*[66]	82 of 227 (36%)	7 (mean)	26 (mean)	9 of 16
Total	1762 of 12897 (14%)	Average: 9 (n = 1250)	Average: 46	Average: 63%

[1]NA: Not available.

RESULTS

This systematic review of the literature identified 26 studies including a total of 12897 healthy patients presenting with unilateral SCFE (Table 1). The included articles report on the incidence of symptomatic contralateral slips where researchers chose not to prophylactically pin the unaffected side. In general, authors had a follow-up of at least 18 mo (mean, 46 mo) after the initial slip. When evaluating the articles eligible for inclusion in this review, the mean time after which the contralateral side slipped was 9 mo, based on 1250 slips, with a range extending to 50 mo[28]. The methodological quality of the included articles was assessed by means of the MINORS criteria for non-randomized surgical studies [26]. The methodological quality was scored at an average of 63% (Table 1).

Risk rates of contralateral SCFE and advantages of prophylactic pinning

The literature provides a substantial discussion about prophylactic fixation. Prophylactically pinning the unaffected contralateral hip has been reported to be advantageous for several reasons. It is mainly aimed at preventing the potential short- and long-term adverse effects on the development of the contralateral hip.

As slipping of the epiphysis causes evident negative short- and long-term outcomes, the main purpose of prophylactic pinning is to prevent the epiphysis from slipping. To assess whether this might be an appropriate measure, it is important to better understand the magnitude of the problem. Castro *et al*[2] reported that children who present with unilateral SCFE are 2335 times more likely to develop a second SCFE than the general population[2].

The incidence of a consecutive symptomatic slip on the contralateral side in SCFE patients was reported to be between 9% and 69%, with a total of 1762 patients (14%, Table 1). In addition to symptomatic slips, several authors report on the incidence of clinically asymptomatic slips. Hägglund *et al*[14] was the first in the available literature to report on the matter and noted that 104 of 237 patients (44%) presenting with unilateral SCFE had signs of an asymptomatic contralateral slip at a follow-up of 16 years to 66 years after initial presentation[14]. Since then, several other authors have reported on patients who developed asymptomatic contralateral slips, as objectified on plain radiography[29-33]. The prevalence of an asymptomatic contralateral slip varied between 19% and 49%. The combined data from these and Hägglund's reports add up to a 174 of 456 hips, a mean incidence of 38% (Table 1).

Evidence suggests that, despite being subclinical at adolescence, patients with asymptomatic slips are also at an increased risk of developing negative outcomes in adulthood, such as a pistol-grip deformity and cam morphology. Subsequently, such patients suffer from decreased hip function, femoral acetabular impingement syndrome, and are at an increased risk of developing early osteoarthritis[21,34-37]. Specifically, Hägglund *et al*[14] reported that 28 of the 104 patients with asymptomatic slips (27%) showed osteoarthritis of that side at a later age[14]. Jensen *et al*[30] noted that 4 of 16 patients (25%) with asymptomatic slips showed signs of osteoarthritis at follow-up, merely 22 years after the primary operation for unilateral SCFE and at an average age of 36 years[30].

In addition, Hesper *et al*[38] reviewed 39 patients that had undergone computed tomography (CT) imaging of the pelvis between 2008 and 2014 after unilateral SCFE and compared the untreated contralateral hips to those of healthy age- and sex-matched controls[38]. They recorded that the unaffected hips of SCFE patients showed decreased concavity of the head-neck junction with a higher alpha angle, as well as a reduced head-neck offset. Thus they noted a lower epiphyseal extension but a more posteriorly tilted epiphysis. These resembled a mild slip deformity and subsequent cam morphology, hence also posing an increased risk of developing early osteoarthritis.

In conclusion, prophylactically pinning may prevent 14% of children with a primarily unilateral SCFE from developing a consecutive symptomatic slip, as well as another 38% from developing an asymptomatic one. Both types of consecutive slips, as well as untreated contralateral hips that do not slip, are prone to developing disadvantageous morphological and functional outcomes at a later age.

Disadvantages of prophylactic pinning

Simultaneously, prophylactic pinning poses several potential disadvantages, which have to be weighed against the advantages.

Infection

There is a small risk of postoperative infection. O'Beirne *et al*[39] reported that after inserting a single pin *via* an open lateral approach, 1 of 15 hips (7%) developed a deep wound infection which was resolved by removal of the pin[39]. Emery *et al*[40] mostly used three pins at a time to fixate 95 hips of which 5 (5%) developed a superficial wound infection[40]. These rates have decreased more recently. Seller *et al*[19] and Woelfle *et al*[20] noted that none of 94 and 1 of 65 (2%) patients, respectively, developed infections after fixation with three or four K-wires[19,20]. When using a single percutaneous screw fixation, the risk of infection seems very low; Kumm *et al*[41] (0 of 34), Dewnany and Radford[36] [1 of 65 (2%)], Sankar *et al*[42] (0 of 99) and Bhattacharjee *et al*[43] [1 of 44 (2%)] all report low rates of wound infections[36,41-43].

AVN and chondrolysis

AVN of the femoral head, although infrequent, is another risk of surgical fixation. Even though prophylactic fixation aims to prevent slip and thereby also AVN, this complication may also develop after the procedure itself. In retrospective studies, Sankar *et al*[42] reported that AVN developed in 2 of 99 patients (2%), whereas none of the 26 and 24 prophylactically pinned hips reviewed by Seller *et al*[44] and Cousins *et al*[45], respectively, developed AVN[42,44,45]. Herngren *et al*[37] reported no cases of AVN in the prophylactically treated group of their prospective cohort study[37]. Other studies report no cases of AVN[19,20,36,39-43]. Chondrolysis was also not seen by any of the referenced authors.

Implant-related problems

Peri-implant fractures may occur shortly or at a later stage after surgery. These are usually subtrochanteric fractures starting around the entrance site of the screw. Sankar *et al*[42] reported that 2 of their patients (2%) developed peri-implant fractures[42]. They suggested that there is a higher fracture rate if the screw enters distal to the level of the lesser trochanter or medial to the intertrochanteric line. Likewise, Herngren *et al*[37] noted 2 peri-implant fractures (1%) in their prospective study[37].

Several authors also report on the displacement, migration and loss of fixation of the hardware, especially with use of non-threaded pins and wires. Emery *et al*[40] reported that at the time of radiological fusion of the epiphyseal plate, the femoral head had grown off of as much as 29% of their Crawford Adams pins[40]. As such, the pins did not cross the epiphyseal plate anymore and thus only penetrated the femoral neck and trochanteric area of the shaft, rendering them useless. Additionally, in 17% of the cases of both Seller *et al*[19] and Woelfle *et al*[20], a reoperation was necessary because the K-wires did not catch the epiphysis anymore due to the physiological growth of the proximal femur, especially when it concerned very young patients[19,20].

Growth alteration and morphologic changes

Some authors argue that the surgical procedure increases the risk of the development of dysmorphology of the prophylactically pinned hip in the long term, with functional limitations as a result. Lerch *et al*[46] performed a follow-up study of 33 prophylactically pinned hips after an average of 12 years[46]. Although noting no intra- or postoperative complications, they did find radiographic evidence of cam morphology in 10 patients (30%), of whom four (12%) developed FAI syndrome as a result and required additional surgery. No patient had developed radiographic signs of osteoarthritis by then. Dodds *et al* [16] reported that 4 out of 7 prophylactically pinned hips (57%) developed a pistol grip deformity, though none of these patients experienced FAI syndrome[16]. These findings were recently supported by Kulkarni *et al*[47], who reported femoral head asphericity in 37% of their patients, rendering them at risk of developing FAI syndrome[47]. The question remains whether the secondary deformities are caused by the surgery or by the natural history of these hips.

A similar concern of pinning the unaffected hip is the possibility of premature closure of the physis. Cousins *et al*[45] compared the articulo-trochanteric distance (ATD), the trochanteric-trochanteric distance (TTD), and the neck length shortly after surgery and on average 20 mo thereafter between 24 prophylactically pinned hips and 26 observed unaffected hips[45]. The difference in TTD:ATD ratio proved to be significant, suggesting that pinning resulted in a coxa breva and relative coxa vara. It was suggested that these morphological alterations could lead to FAI syndrome and therewith osteoarthritis. Moreover, the neck length was significantly higher at follow-up in the observed group, thereby concluding that the pinned group showed less residual growth. The mean difference in final leg length between the SCFE side and the prophylactically pinned hip has been reported to be 5.7 millimeters, with a maximum of 1 centimeter[19,44]. The residual growth might be dependent on the type of fixation; Wölfle-Roos *et al*[48] reported that the residual growth was a mean of 4.4 millimeters more when using three or four K-wires, as compared to a single screw[48]. Considering the primary SCFE side, one may argue that a reduced residual growth after pinning the contralateral side is actually an advantage. The primary SCFE side also shows less residual growth as compared to healthy hips, therefore the difference in final leg length will thus decrease as compared to children who have not undergone prophylactic pinning.

Risk factors

Numerous studies have aimed to identify risk factors for developing sequential contralateral involvement in unilateral SCFE patients. Swarup *et al*[25] performed a comprehensive systematic review and meta-analysis of potential risk factors[25]. The most significant demographic factors that were reported to be associated with a contralateral slip were a body mass index (BMI) greater than the 95th percentile and a younger age at presentation. Clinically, a shorter duration of symptoms before the actual first slip was also reported to be a risk factor. When evaluating the anteroposterior and frog-leg lateral hip or pelvis radiographs, several suggested risk factors can be assessed including the posterior sloping angle (PSA, Figure 1), alpha angle and modified Oxford score (*i.e.* a measure for skeletal maturity)[25,49]. In the included studies of the meta-analysis, conflicting results were reported in regard to the slip angle, with studies showing an increased risk of contralateral slip when a lower angle was found, while other researchers reported the risk to be increased when a higher angle was present[25]. The alpha angle of the primary SCFE was reported to be a weak but significant prognostic factor. Patients with a mean angle of 51 degrees were at a higher risk of developing contralateral SCFE compared to a mean angle of 45 degrees. The PSA of the healthy side was reported to be significantly higher in patients that developed a subsequent contralateral slip. A mean of 16 degrees was related to a higher risk of subsequent slip compared to a mean of 12 degrees. According to the meta-analysis by Swarup *et al*[25], a younger age at the time of the first slip (mean difference, -0.9 years) and a higher PSA (mean difference, 4.7 degrees) remained independent significant risk factors. For other factors, such as sex, BMI, endocrine abnormality, slip stability and modified Oxford score, no significant differences were identified in the meta-analysis.

Several researchers have specifically studied additional imaging modalities to further evaluate the risk of a contralateral slip in order to detect early evidence of morphologic changes preceding symptomatic and asymptomatic slips. Balch Samora *et al*[50] assessed the use of focal or diffuse physeal widening, abnormal signal and bone marrow edema adjacent to the physis on magnetic resonance imaging (MRI) in predicting contralateral SCFE[50]. Eleven of 33 enrolled patients developed a contralateral SCFE. Overall, the sensitivity of the MRI predictors was reported to be 80%, specificity 92.9%, positive predictive value 66.7% and negative predictive value 96.3%, with an interrater reliability

of 100%. In addition, Futami *et al*[51] evaluated unilateral SCFE cases and their unaffected counterparts with MRI[51]. They scanned 10 patients for a total of 33 times. In all SCFE cases, physeal widening was observed. In 4 of the 10 patients, the unaffected side showed physeal widening without a slip. Lesions were observed in the physis which were similar to lesions in the affected hips. These were then prophylactically pinned. Neither these, nor the other observed hips that did not show physeal widening, slipped during a mean follow-up time of 36 mo. Nevertheless, the authors suggested that the physeal widening, clearly visible on MRI, may reduce epiphyseal stability and requires prophylactic pinning. Wensaas *et al*[52] also reported on MRI scans of 22 primarily unilateral SCFEs[52]. They measured the MRI slip angle, greatest focal widening of the physis, global widening of the physis measured at three locations, periphyseal bone marrow edema, the presence of pathological joint effusion and the amount of joint effusion measured from the lateral edge of the greater trochanter. These parameters were significantly altered in primarily affected hips. However, they could not discern a significant difference between the 6 hips of patients who did and the remainder who did not develop contralateral SCFE.

DISCUSSION

This article aims to provide a comprehensive review and summary of the scientific evidence regarding the prevalence of contralateral SCFE and fixation in otherwise healthy patients with unilateral SCFE. According to the reviewed data, prophylactic fixation of the contralateral side would prevent 14% of patients from developing sequential symptomatic contralateral involvement. Another 38% of asymptomatic slips may also be prevented. Because prevention of a contralateral slip may drastically reduce the possible negative outcomes, such as osteoarthritis in the long term, these rates may outweigh the small risk of complications due to the additional surgery. However, multiple patient, surgical and radiographic factors should be taken into account in the shared-decision process with the patients and their parents. The most important risk factors of a subsequent contralateral SCFE are a younger age at the time of presentation and a higher PSA on plain radiography[25].

When surgical fixation is considered, a decision with regard to the surgical technique needs to be made. K-wires as a method of fixation, may cause that the wires unintentionally migrated within the femur mostly due to physiologic growth of the proximal femur[19,20,40,53]. However, this migration rarely led to epiphysiolysis or other symptoms such as pain. Nonetheless, it can be argued that this migration does pose additional risks. On the other hand, fixation with threaded screws has a higher impact on the residual growth of the femur. One might argue that the reduced residual growth of the unaffected side can be considered an advantage, as the difference in leg length between the unaffected and affected sides at follow-up is decreased when the unaffected side is pinned as well[42]. Recently, researchers have also tested a new type of free-gliding screw, which is intended to allow growth of the physis and thereby decrease the influence of fixation on the final leg length. The first results of biomechanical studies have been reported and appear to be promising[54]. Thus, some of the possible negative effects of pinning on growth could be overcome within the foreseeable future for either side.

Opponents of prophylactic fixation argue that the patient is exposed to the risk of iatrogenic injury to an otherwise healthy hip[55]. Indeed, some of the associated complications such as AVN and chondrolysis are serious. However, they are minor in incidence, with only 0%-2% of cases developing AVN and no cases of chondrolysis reported at all in the presently reviewed literature. Other reported complications include anatomic changes such as cam morphology. However, various studies have shown that the 'unaffected' side often has dysmorphic features without having been operated on, as visualized on CT and MRI[34,50-52]. This finding questions whether the morphologic changes are a result of the surgical procedure or rather a result of the natural course of these hips.

In an attempt to be able to make a more protocolized decision, researchers have developed different decision analysis models. However, the outcomes of their respective research are contradictory. Kocher *et al*[55] described an expected-value decision analysis on the indication for strategy-prophylactic *in situ* pinning *vs* observation[55]. According to their systematic review, the expected value of prophylactic pinning remained lower than for observation. They therefore concluded that careful observation is the better strategy unless the probability of a contralateral slip exceeds 27%. In contrast, Schultz *et al*[56] concluded in a different model that prophylactic pinning of the contralateral hip is, in general, favorable for long-term outcomes[56]. Taking these conclusions to heart, the discussion on the indication for prophylactic fixation is still open, and careful education of patients and meticulous clinical and radiographic follow-up could provide an alternative to prophylactic pinning. However, one might argue that prophylactic pinning of the hip saves the time and trouble of an intensive follow-up process until physeal closure with the associated necessary additional radiographic imaging.

The present review has some limitations. Although the literature was searched systematically, there might be additional relevant research in the literature that would add to our data. Methodological quality of the included studies was quantified, but showed that the research conducted did not meet all of the MINORS criteria, averaging at 63% of the total applicable score. In addition, few authors reported about the severity of the contralateral slips that developed after initial unilateral involvement. Therefore, no definitive conclusions could be drawn as to the distribution of mild, moderate and severe

contralateral slips. Additional data on the distribution of severity within this population may prove more insightful in whether the risks of surgery outweigh the possible complications related to (severe) slips. However, with our search terms, we have sought to include a representative and comprehensive amount of data on the basis of which we present the considerations and conclusions.

CONCLUSION

The contralateral hip in otherwise healthy patients presenting with a unilateral symptomatic SCFE remains a controversial subject. Literature suggests that a substantial rate of these patients are at risk of developing a subsequent slip of the contralateral side or in fact simultaneously have an asymptomatic slip. Such slips consequently may lead to morphologic changes, decreased hip function and early osteoarthritis. Fixation of the contralateral hip may thus prevent these negative long-term outcomes.

On the other hand, fixation of the contralateral side also involves risks. However, surgical complications occur only incidentally and the clinical implications of secondary morphologic changes as a result of surgical intervention remain unclear. Hence, the disadvantages appear to be relatively infrequent and insignificant as compared to the possible advantages that can be achieved through fixation. Nonetheless, both perspectives should be taken into consideration, and the choice as to whether or not to pin the unaffected side should remain a patient-tailored one.

ARTICLE HIGHLIGHTS

Research background

Slipped capital femoral epiphysis (SCFE) is an important medical condition occurring in adolescents. It may cause severe short and long term complications. At present, there is no clear consensus on whether or not to prophylactically fixate the unaffected side in unilateral SCFE. The current review provides a comprehensive assessment of the deliberations to be made when treating this condition.

Research motivation

The risks of subsequent contralateral slipping after primary unilateral SCFE are discussed. Consequently, the advantages, but also the risks, rendered by prophylactic fixation are outlined.

Research objectives

The risk rates of subsequent contralateral slipping and its sequelae after primary unilateral SCFE are evaluated. Several imaging modalities and their interpretation in regard to the risk assessment are presented. The advantages and disadvantages of prophylactic pinning are evaluated and an overall outline is presented as to the treatment strategy.

Research methods

A systematic review of the literature was performed and the results were presented in a qualitative manner with descriptive statistics.

Research results

When presenting with unilateral SCFE, a patient has a 2335 times increased likelihood of developing a consecutive contralateral slip, with 14% developing a symptomatic and 38% asymptomatic slip. Both clinical and subclinical slips are at an increased risk of developing harmful sequelae of the hip. Prophylactic pinning of the contralateral side negates the development of such sequelae. This surgical intervention renders complications such as infection, avascular necrosis, implant related problems and morphologic changes, albeit only at very low rates. A number of methods to assess the risk of a contralateral slip have been described in the current literature, most significantly the posterior sloping angle (PSA) on plain radiographs.

Research conclusions

A substantial rate of patients presenting with unilateral SCFE develop a contralateral slip, posing an increased risk to developing harmful sequelae. The advantages of negating these developments by prophylactic pinning of the primarily unaffected side appear to be outweighing the infrequently occurring disadvantages of the surgical intervention. The decision remains to be patient-tailored and can be aided by evaluation of the PSA on plain radiographs.

Research perspectives

Additional studies evaluating a watchful waiting strategy that elaborate on the severity of subsequent slips and its sequelae may prove insightful to better weigh this against the surgery associated risks. In

addition, further research directly comparing the short and long term outcomes of watchful waiting and prophylactic pinning may aid in formulating an unambiguous treatment strategy. Also, research concerning the risks for developing a primary SCFE may further the prevention of the condition arising in the first place in the adolescent population, thereby improving their long term functioning.

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REFERENCES

1 **Loder RT**, Richards BS, Shapiro PS, Reznick LR, Aronson DD. Acute slipped capital femoral epiphysis: the importance of physeal stability. *J Bone Joint Surg Am* 1993; **75**: 1134-1140 [PMID: 8354671 DOI: 10.2106/00004623-199308000-00002]
2 **Castro FP Jr**, Bennett JT, Doulens K. Epidemiological perspective on prophylactic pinning in patients with unilateral slipped capital femoral epiphysis. *J Pediatr Orthop* 2000; **20**: 745-748 [PMID: 11097247 DOI: 10.1097/00004694-200011000-00009]
3 **Lehmann CL**, Arons RR, Loder RT, Vitale MG. The epidemiology of slipped capital femoral epiphysis: an update. *J Pediatr Orthop* 2006; **26**: 286-290 [PMID: 16670536 DOI: 10.1097/01.bpo.0000217718.10728.70]
4 **Witbreuk MM**, van Royen BJ, Van Kemenade FJ, Witte BI, van der Sluijs JA. Incidence and gender differences of slipped capital femoral epiphysis in the Netherlands from 1998-2010 combined with a review of the literature on the epidemiology of SCFE. *J Child Orthop* 2013; **7**: 99-105 [PMID: 24432066 DOI: 10.1007/s11832-012-0479-y]
5 **Loder RT**. The demographics of slipped capital femoral epiphysis. An international multicenter study. *Clin Orthop Relat Res* 1996; 8-27 [PMID: 8542716]
6 **Loder RT**, Hensinger RN. Slipped capital femoral epiphysis associated with renal failure osteodystrophy. *J Pediatr Orthop* 1997; **17**: 205-211 [PMID: 9075097 DOI: 10.1097/00004694-199703000-00013]
7 **Aronsson DD**, Loder RT, Breur GJ, Weinstein SL. Slipped capital femoral epiphysis: current concepts. *J Am Acad Orthop Surg* 2006; **14**: 666-679 [PMID: 17077339 DOI: 10.5435/00124635-200611000-00010]
8 **Witbreuk M**, van Kemenade FJ, van der Sluijs JA, Jansma EP, Rotteveel J, van Royen BJ. Slipped capital femoral epiphysis and its association with endocrine, metabolic and chronic diseases: a systematic review of the literature. *J Child Orthop* 2013; **7**: 213-223 [PMID: 24432080 DOI: 10.1007/s11832-013-0493-8]
9 **Carney BT**, Weinstein SL, Noble J. Long-term follow-up of slipped capital femoral epiphysis. *J Bone Joint Surg Am* 1991; **73**: 667-674 [PMID: 2045391]
10 **Lubicky JP**. Chondrolysis and avascular necrosis: complications of slipped capital femoral epiphysis. *J Pediatr Orthop B* 1996; **5**: 162-167 [PMID: 8866280 DOI: 10.1097/01202412-199605030-00005]

11 **Roaten J**, Spence DD. Complications Related to the Treatment of Slipped Capital Femoral Epiphysis. *Orthop Clin North Am* 2016; **47**: 405-413 [PMID: 26772949 DOI: 10.1016/j.ocl.2015.09.013]

12 **Loder RT**. What is the cause of avascular necrosis in unstable slipped capital femoral epiphysis and what can be done to lower the rate? *J Pediatr Orthop* 2013; **33** Suppl 1: S88-S91 [PMID: 23764800 DOI: 10.1097/BPO.0b013e318277172e]

13 **Tucker A**, Ballard J, Cosgrove A. Temporal changes in slipped upper femoral epiphysis at a regional level: a declining incidence and literature review. *J Child Orthop* 2019; **13**: 445-456 [PMID: 31695811 DOI: 10.1302/1863-2548.13.190037]

14 **Hägglund G**, Hansson LI, Ordeberg G, Sandström S. Bilaterality in slipped upper femoral epiphysis. *J Bone Joint Surg Br* 1988; **70**: 179-181 [PMID: 3346283 DOI: 10.1302/0301-620X.70B2.3346283]

15 **Fraitzl CR**, Käfer W, Nelitz M, Reichel H. Radiological evidence of femoroacetabular impingement in mild slipped capital femoral epiphysis: a mean follow-up of 14.4 years after pinning in situ. *J Bone Joint Surg Br* 2007; **89**: 1592-1596 [PMID: 18057358 DOI: 10.1302/0301-620X.89B12.19637]

16 **Dodds MK**, McCormack D, Mulhall KJ. Femoroacetabular impingement after slipped capital femoral epiphysis: does slip severity predict clinical symptoms? *J Pediatr Orthop* 2009; **29**: 535-539 [PMID: 19700979 DOI: 10.1097/BPO.0b013e3181b2b3a3]

17 **Loder RT**, Dietz FR. What is the best evidence for the treatment of slipped capital femoral epiphysis? *J Pediatr Orthop* 2012; **32** Suppl 2: S158-S165 [PMID: 22890456 DOI: 10.1097/BPO.0b013e318259f2d1]

18 **Karol LA**, Doane RM, Cornicelli SF, Zak PA, Haut RC, Manoli A 2nd. Single versus double screw fixation for treatment of slipped capital femoral epiphysis: a biomechanical analysis. *J Pediatr Orthop* 1992; **12**: 741-745 [PMID: 1452743 DOI: 10.1097/01241398-199211000-00008]

19 **Seller K**, Raab P, Wild A, Krauspe R. Risk-benefit analysis of prophylactic pinning in slipped capital femoral epiphysis. *J Pediatr Orthop B* 2001; **10**: 192-196 [PMID: 11497360]

20 **Woelfle JV**, Fraitzl CR, Reichel H, Nelitz M. The asymptomatic contralateral hip in unilateral slipped capital femoral epiphysis: morbidity of prophylactic fixation. *J Pediatr Orthop B* 2012; **21**: 226-229 [PMID: 22406770 DOI: 10.1097/BPB.0b013e3283524bae]

21 **MacLean JG**, Reddy SK. The contralateral slip. An avoidable complication and indication for prophylactic pinning in slipped upper femoral epiphysis. *J Bone Joint Surg Br* 2006; **88**: 1497-1501 [PMID: 17075097 DOI: 10.1302/0301-620X.88B11.17523]

22 **Baghdadi YM**, Larson AN, Sierra RJ, Peterson HA, Stans AA. The fate of hips that are not prophylactically pinned after unilateral slipped capital femoral epiphysis. *Clin Orthop Relat Res* 2013; **471**: 2124-2131 [PMID: 23283674 DOI: 10.1007/s11999-012-2762-0]

23 **Segal LS**, Davidson RS, Robertson WW Jr, Drummond DS. Growth disturbances of the proximal femur after pinning of juvenile slipped capital femoral epiphysis. *J Pediatr Orthop* 1991; **11**: 631-637 [PMID: 1918351]

24 **Nowicki PD**, Silva S, Toelle L, Strohmeyer G, Wahlquist T, Li Y, Farley FA, Caird MS. Severity of Asynchronous Slipped Capital Femoral Epiphyses in Skeletally Immature Versus More Skeletally Mature Patients. *J Pediatr Orthop* 2017; **37**: e23-e27 [PMID: 26523702 DOI: 10.1097/BPO.0000000000000678]

25 **Swarup I**, Goodbody C, Goto R, Sankar WN, Fabricant PD. Risk Factors for Contralateral Slipped Capital Femoral Epiphysis: A Meta-analysis of Cohort and Case-control Studies. *J Pediatr Orthop* 2020; **40**: e446-e453 [PMID: 32501913 DOI: 10.1097/BPO.0000000000001482]

26 **Slim K**, Nini E, Forestier D, Kwiatkowski F, Panis Y, Chipponi J. Methodological index for non-randomized studies (minors): development and validation of a new instrument. *ANZ J Surg* 2003; **73**: 712-716 [PMID: 12956787 DOI: 10.1046/j.1445-2197.2003.02748.x]

27 **Loder RT**, Aronson DD, Greenfield ML. The epidemiology of bilateral slipped capital femoral epiphysis. A study of children in Michigan. *J Bone Joint Surg Am* 1993; **75**: 1141-1147 [PMID: 8354672 DOI: 10.2106/00004623-199308000-00003]

28 **Swarup I**, Williams BA, Talwar D, Sankar WN. Rates of Contralateral SCFE in the United States: Analysis of the Pediatric Health Information System. *J Pediatr Orthop* 2020; **40**: e587-e591 [PMID: 31688819 DOI: 10.1097/BPO.0000000000001465]

29 **Stott S**, Bidwell T. Epidemiology of slipped capital femoral epiphysis in a population with a high proportion of New Zealand Maori and Pacific children. *N Z Med J* 2003; **116**: U647 [PMID: 14583805]

30 **Jensen HP**, Steinke MS, Mikkelsen SS, Thomsen PB. Hip physiolysis. Bilaterality in 62 cases followed for 20 years. *Acta Orthop Scand* 1990; **61**: 419-420 [PMID: 2239165 DOI: 10.3109/17453679008993553]

31 **Jerre R**, Billing L, Hansson G, Wallin J. The contralateral hip in patients primarily treated for unilateral slipped upper femoral epiphysis. Long-term follow-up of 61 hips. *J Bone Joint Surg Br* 1994; **76**: 563-567 [PMID: 8027141]

32 **Hurley JM**, Betz RR, Loder RT, Davidson RS, Alburger PD, Steel HH. Slipped capital femoral epiphysis. The prevalence of late contralateral slip. *J Bone Joint Surg Am* 1996; **78**: 226-230 [PMID: 8609113 DOI: 10.2106/00004623-199602000-00009]

33 **Lehmann TG**, Engesæter IØ, Laborie LB, Rosendahl K, Lie SA, Engesæter LB. In situ fixation of slipped capital femoral epiphysis with Steinmann pins. *Acta Orthop* 2011; **82**: 333-338 [PMID: 21504367 DOI: 10.3109/17453674.2011.579520]

34 **Goodman DA**, Feighan JE, Smith AD, Latimer B, Buly RL, Cooperman DR. Subclinical slipped capital femoral epiphysis. Relationship to osteoarthrosis of the hip. *J Bone Joint Surg Am* 1997; **79**: 1489-1497 [PMID: 9378734 DOI: 10.2106/00004623-199710000-00005]

35 **Hägglund G**. The contralateral hip in slipped capital femoral epiphysis. *J Pediatr Orthop B* 1996; **5**: 158-161 [PMID: 8866279 DOI: 10.1097/01202412-199605030-00004]

36 **Dewnany G**, Radford P. Prophylactic contralateral fixation in slipped upper femoral epiphysis: is it safe? *J Pediatr Orthop B* 2005; **14**: 429-433 [PMID: 16200019 DOI: 10.1097/01202412-200511000-00007]

37 **Herngren B**, Stenmarker M, Vavruch L, Hagglund G. Slipped capital femoral epiphysis: a population-based study. *BMC Musculoskelet Disord* 2017; **18**: 304 [PMID: 28720145 DOI: 10.1186/s12891-017-1665-3]

38 **Hesper T**, Bixby SD, Maranho DA, Miller P, Kim YJ, Novais EN. Morphologic Features of the Contralateral Femur in Patients With Unilateral Slipped Capital Femoral Epiphysis Resembles Mild Slip Deformity: A Matched Cohort Study.

Clin Orthop Relat Res 2018; **476**: 890-899 [PMID: 29481345 DOI: 10.1007/s11999.0000000000000127]
39 **O'Beirne J**, McLoughlin R, Dowling F, Fogarty E, Regan B. Slipped upper femoral epiphysis: internal fixation using single central pins. *J Pediatr Orthop* 1989; **9**: 304-307 [PMID: 2723049]
40 **Emery RJ**, Todd RC, Dunn DM. Prophylactic pinning in slipped upper femoral epiphysis. Prevention of complications. *J Bone Joint Surg Br* 1990; **72**: 217-219 [PMID: 2312558 DOI: 10.1302/0301-620X.72B2.2312558]
41 **Kumm DA**, Schmidt J, Eisenburger SH, Rütt J, Hackenbroch MH. Prophylactic dynamic screw fixation of the asymptomatic hip in slipped capital femoral epiphysis. *J Pediatr Orthop* 1996; **16**: 249-253 [PMID: 8742295 DOI: 10.1097/00004694-199603000-00023]
42 **Sankar WN**, Novais EN, Lee C, Al-Omari AA, Choi PD, Shore BJ. What are the risks of prophylactic pinning to prevent contralateral slipped capital femoral epiphysis? *Clin Orthop Relat Res* 2013; **471**: 2118-2123 [PMID: 23129473 DOI: 10.1007/s11999-012-2680-1]
43 **Bhattacharjee A**, Freeman R, Roberts AP, Kiely NT. Outcome of the unaffected contralateral hip in unilateral slipped capital femoral epiphysis: a report comparing prophylactic fixation with observation. *J Pediatr Orthop B* 2016; **25**: 454-458 [PMID: 27258363 DOI: 10.1097/BPB.0000000000000337]
44 **Seller K**, Wild A, Westhoff B, Raab P, Krauspe R. Radiological evaluation of unstable (acute) slipped capital femoral epiphysis treated by pinning with Kirschner wires. *J Pediatr Orthop B* 2006; **15**: 328-334 [PMID: 16891959 DOI: 10.1097/01202412-200609000-00005]
45 **Cousins GR**, Campbell DM, Wilson NI, Maclean JG. Prophylactic pinning for slipped capital femoral epiphysis: does it affect proximal femoral morphology? *J Pediatr Orthop B* 2016; **25**: 202-206 [PMID: 26588834 DOI: 10.1097/BPB.0000000000000252]
46 **Lerch TD**, Novais EN, Schmaranzer F, Ziebarth K, Steppacher SD, Tannast M, Siebenrock KA. What Is the Prevalence of Cam Deformity After Prophylactic Pinning of the Contralateral Asymptomatic Hip in Unilateral Slipped Capital Femoral Epiphysis? *Clin Orthop Relat Res* 2019; **477**: 1111-1122 [PMID: 30550402 DOI: 10.1097/CORR.0000000000000592]
47 **Kulkarni VA**, Boyles AD, Carl J, Boakes JL, Wilson B, Bagley AM, Muchow RD. Proximal Femoral Deformity Following Threaded Prophylactic Fixation for Slipped Capital Femoral Epiphysis: Risk Stratification Using the Modified Oxford Score. *J Pediatr Orthop* 2020; **40**: e592-e597 [PMID: 32218015 DOI: 10.1097/BPO.0000000000001552]
48 **Wölfle-Roos JV**, Urlaub S, Reichel H, Taurman R. Significantly lower femoral neck growth in screw fixation of the asymptomatic contralateral hip in unilateral slipped capital femoral epiphysis. *J Pediatr Orthop B* 2016; **25**: 197-201 [PMID: 26919622 DOI: 10.1097/BPB.0000000000000285]
49 **Stasikelis PJ**, Sullivan CM, Phillips WA, Polard JA. Slipped capital femoral epiphysis. Prediction of contralateral involvement. *J Bone Joint Surg Am* 1996; **78**: 1149-1155 [PMID: 8753706 DOI: 10.2106/00004623-199608000-00004]
50 **Balch Samora J**, Adler B, Druhan S, Brown SA, Erickson J, Samora WP, Klingele KE. MRI in idiopathic, stable, slipped capital femoral epiphysis: evaluation of contralateral pre-slip. *J Child Orthop* 2018; **12**: 454-460 [PMID: 30294369 DOI: 10.1302/1863-2548.12.170204]
51 **Futami T**, Suzuki S, Seto Y, Kashiwagi N. Sequential magnetic resonance imaging in slipped capital femoral epiphysis: assessment of preslip in the contralateral hip. *J Pediatr Orthop B* 2001; **10**: 298-303 [PMID: 11727372]
52 **Wensaas A**, Wiig O, Hellund JC, Khoshnewiszadeh B, Terjesen T. Magnetic resonance imaging at primary diagnosis cannot predict subsequent contralateral slip in slipped capital femoral epiphysis. *Skeletal Radiol* 2017; **46**: 1687-1694 [PMID: 28785827 DOI: 10.1007/s00256-017-2735-1]
53 **Vlachopoulos L**, Huber H, Dierauer S, Ramseier LE. Persisting growth after prophylactic single-screw epiphysiodesis in upper femoral epiphysis. *J Pediatr Orthop* 2013; **33**: 816-820 [PMID: 24096449 DOI: 10.1097/BPO.0000000000000098]
54 **Leblanc E**, Bellemore JM, Cheng T, Little DG, Birke O. Biomechanical considerations in slipped capital femoral epiphysis and insights into prophylactic fixation. *J Child Orthop* 2017; **11**: 120-127 [PMID: 28529660 DOI: 10.1302/1863-2548-11-170012]
55 **Kocher MS**, Bishop JA, Hresko MT, Millis MB, Kim YJ, Kasser JR. Prophylactic pinning of the contralateral hip after unilateral slipped capital femoral epiphysis. *J Bone Joint Surg Am* 2004; **86**: 2658-2665 [PMID: 15590850 DOI: 10.2106/00004623-200412000-00011]
56 **Schultz WR**, Weinstein JN, Weinstein SL, Smith BG. Prophylactic pinning of the contralateral hip in slipped capital femoral epiphysis : evaluation of long-term outcome for the contralateral hip with use of decision analysis. *J Bone Joint Surg Am* 2002; **84**: 1305-1314 [PMID: 12177258 DOI: 10.2106/00004623-200208000-00003]
57 **Greenough CG**, Bromage JD, Jackson AM. Pinning of the slipped upper femoral epiphysis--a trouble-free procedure? *J Pediatr Orthop* 1985; **5**: 657-660 [PMID: 4066937 DOI: 10.1097/01241398-198511000-00005]
58 **Koenig KM**, Thomson JD, Anderson KL, Carney BT. Does skeletal maturity predict sequential contralateral involvement after fixation of slipped capital femoral epiphysis? *J Pediatr Orthop* 2007; **27**: 796-800 [PMID: 17878787 DOI: 10.1097/BPO.0b013e3181558bd9]
59 **Kohno Y**, Nakashima Y, Kitano T, Nakamura T, Takamura K, Akiyama M, Hara D, Yamamoto T, Motomura G, Ohishi M, Hamai S, Yukihide I. Subclinical bilateral involvement of the hip in patients with slipped capital femoral epiphysis: a multicentre study. *Int Orthop* 2014; **38**: 477-482 [PMID: 24114248 DOI: 10.1007/s00264-013-2131-y]
60 **Phillips PM**, Phadnis J, Willoughby R, Hunt L. Posterior sloping angle as a predictor of contralateral slip in slipped capital femoral epiphysis. *J Bone Joint Surg Am* 2013; **95**: 146-150 [PMID: 23324962 DOI: 10.2106/JBJS.L.00365]
61 **Boyle MJ**, Lirola JF, Hogue GD, Yen YM, Millis MB, Kim YJ. The alpha angle as a predictor of contralateral slipped capital femoral epiphysis. *J Child Orthop* 2016; **10**: 201-207 [PMID: 27052742 DOI: 10.1007/s11832-016-0732-x]
62 **Chan CX**, Yang YO, Cheng GHM, Gera SK, Mohammad ABZ. Alpha Angle as a Predictor of Impending Contralateral Slipped Capital Femoral Epiphysis in an Asian Population. *Clin Orthop Surg* 2019; **11**: 466-473 [PMID: 31788171 DOI: 10.4055/cios.2019.11.4.466]
63 **Maranho DA**, Ferrer MG, Kim YJ, Miller PE, Novais EN. Predicting Risk of Contralateral Slip in Unilateral Slipped Capital Femoral Epiphysis: Posterior Epiphyseal Tilt Increases and Superior Epiphyseal Extension Reduces Risk. *J Bone Joint Surg Am* 2019; **101**: 209-217 [PMID: 30730480 DOI: 10.2106/JBJS.18.00440]
64 **Tomaru Y**, Kamada H, Tsukagoshi Y, Nakagawa S, Onishi M, Tanaka K, Takeuchi R, Mataki Y, Miyakawa S, Yamazaki

M. Prophylactic pinning should be considered in patients at risk for slipped capital femoral epiphysis. *J Rural Med* 2019; **14**: 191-195 [PMID: 31788141 DOI: 10.2185/jrm.3011]

65 **Maranho DA**, Miller P, Kim YJ, Novais EN. Contralateral slip after unilateral slipped capital femoral epiphysis is associated with acetabular retroversion but not increased acetabular depth and overcoverage. *J Pediatr Orthop B* 2020; **29**: 275-282 [PMID: 31305365 DOI: 10.1097/BPB.0000000000000643]

66 **Yildirim Y**, Bautista S, Davidson RS. Chondrolysis, osteonecrosis, and slip severity in patients with subsequent contralateral slipped capital femoral epiphysis. *J Bone Joint Surg Am* 2008; **90**: 485-492 [PMID: 18310697 DOI: 10.2106/JBJS.F.01027]

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CASE REPORT

Intramedullary bone pedestal formation contributing to femoral shaft fracture nonunion: A case report and review of the literature

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Abstract

BACKGROUND

Femoral shaft fracture is a commonly encountered orthopedic injury that can be treated operatively with a low overall delayed/nonunion rate. In the case of delayed union after antegrade or retrograde intramedullary nail fixation, fracture dynamization is often attempted first. Nonunion after dynamization has been shown to occur due to infection and other aseptic etiologies. We present a unique case of diaphyseal femoral shaft fracture nonunion after dynamization due to intramedullary cortical bone pedestal formation at the distal tip of the nail.

CASE SUMMARY

A 37-year-old male experienced a high-energy trauma to his left thigh after coming down hard during a motocross jump. Evaluation was consistent with an isolated, closed, left mid-shaft femur fracture. He was initially managed with reamed antegrade intramedullary nail fixation but had continued thigh pain. Radiographs at four months demonstrated no evidence of fracture union and failure of the distal locking screw, and dynamization by distal locking screw removal was performed. The patient continued to have pain eight months after the initial procedure and 4 mo after dynamization with serial radiographs continuing to demonstrate no evidence of fracture healing. The decision was made to proceed with exchange nailing for aseptic fracture nonunion. During the exchange procedure, an obstruction was encountered at the distal tip of the failed nail and was confirmed on magnified fluoroscopy to be a pedestal of cortical bone in the canal. The obstruction required further distal reaming. A longer and larger diameter exchange nail was placed without difficulty and without a distal locking screw to allow for dynamization at the fracture site. Post-operative radiographs showed proper fracture and hardware alignment. There was subsequently radiographic evidence of callus formation at one year with subsequent fracture

consolidation and resolution of thigh pain at eighteen months.

CONCLUSION
The risk of fracture nonunion caused by intramedullary bone pedestal formation can be mitigated with the use of maximum length and diameter nails and close follow up.

Key Words: Nonunion; Femoral shaft fracture; Diaphysis; Fracture fixation; Antegrade intramedullary nail; Case report

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Core Tip: Femoral shaft fracture nonunion after surgical fixation is a rare complication known to be associated with infection, anatomic abnormalities, hardware failure, and other aseptic etiologies. It is now known that intramedullary bone pedestal formation can also be a cause of nonunion after fracture dynamization. In order to prevent this complication, surgeons should elect to use a maximal length intramedullary nail during initial fixation and follow up closely if the patient is showing signs of delayed union.

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INTRODUCTION

Diaphyseal femur fractures treated with reamed intramedullary nail fixation have a low incidence of nonunion[1-5]. Nonunions have been found to occur secondary to infection and a variety of aseptic etiologies. Aseptic nonunions have been associated with fracture instability, distraction, malalignment, large bony defects, and open fractures. These procedure and fracture associated factors prevent adequate blood supply to the fracture site and impede the healing response. Patient factors have also been linked to nonunions in some series. These may be factors that lead to poor blood supply such as vascular disease, diabetes, and smoking. Others have a more direct effect on the healing process by impeding the immune response and preventing the proper balance of osteoblast/osteoclast activity. These include the use of non-steroidal anti-inflammatory drugs (NSAIDs), use of steroids, advancing age, malignancy, and diabetes mellitus[6-11].

When an aseptic fracture nonunion occurs after intramedullary nail fixation, there are multiple methods of revision that have been studied and proven to be effective. Such methods include, nail dynamization, exchange nailing, and augmentative plating[4,5]. Causes of non-union after revision have been found to be similar to that of non-union after initial fixation, though the rare incidence of repeat non-union has led to sparse data on the topic. We present a unique case of mid-shaft femur fracture nonunion after nail dynamization due to intramedullary bone pedestal formation.

CASE PRESENTATION

Chief complaints

A 37-year-old white male presented to our clinic with 5 mo of left thigh pain with activity.

History of present illness

The patient's symptoms began when he was involved in a motocross accident in which he came down hard from a jump. He remarkably was able to hop to his car and drive himself to a nearby hospital where he was found to have an obvious deformity of the left thigh. Subsequent evaluation was consistent with an isolated, closed, left mid-shaft femur fracture.

The patient underwent reamed antegrade intramedullary nail fixation of his left femur fracture at an outside hospital. Post-operative recovery was unremarkable except that he continued to have problems with left thigh pain during activity. Four months after his initial surgery, he was found to have broken his single distal locking screw, and he underwent distal locking screw removal for nail dynamization at the outside hospital. Left thigh pain with activity persisted five months post-operatively prompting presentation to our clinic.

History of past illness
The patient had no relevant previous medical history.

Personal and family history
The patient had no relevant personal or family medical history.

Physical examination
The patient had a well-healed incisions without evidence of infection. He had left thigh pain to palpation and with weight bearing.

Laboratory examinations
Baseline laboratory studies including an erythrocyte sedimentation rate were unremarkable.

Imaging examinations
Post-operative radiographs from the outside hospital showed placement of 9 mm × 380 mm Russell-Taylor Delta II antegrade intramedullary nail through a left transverse mid-shaft femur fracture with single distal interlocking screw (Figure 1A and B). Radiographs obtained four months post-operatively at the outside hospital revealed breakage of the distal interlocking screw and no evidence of fracture union (Figure 2A and B). After presentation to our clinic, the decision was made to continue with normal weight bearing activity and obtain serial radiographs. Radiographs obtained 8 mo post-operatively continued to reveal no evidence of fracture union (Figure 3A and B).

FINAL DIAGNOSIS
Aseptic nonunion of left femoral shaft fracture.

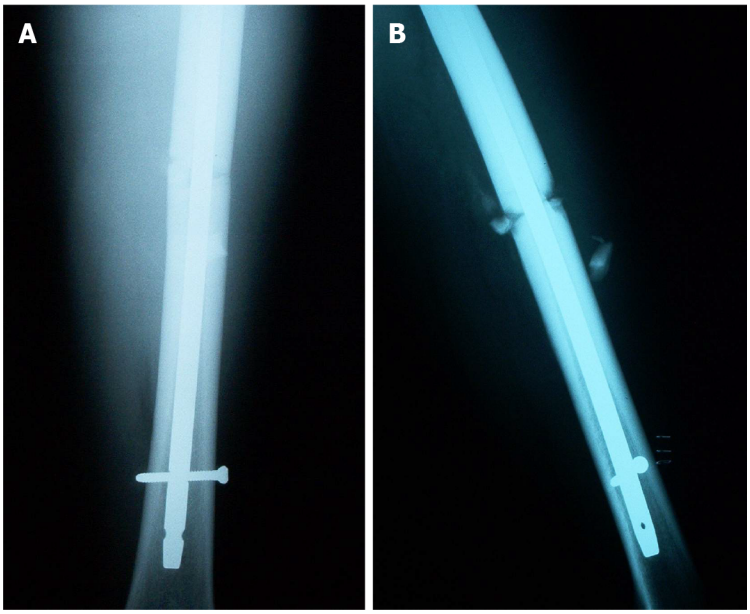
TREATMENT
The decision was made to proceed with exchange intramedullary nailing of the left femur.

Surgery
During nail extraction, attempts to pass a smooth-tip guide wire through the nail prior to removal were unsuccessful due to resistance at the nail tip (Figure 4A and B). The nail was subsequently removed with an appropriate nail extractor. Following nail removal, a standard guide wire was inserted into the canal without difficulty until it reached the point in the distal femur where the nail tip was previously seated. Again, the guide wire met resistance. Under magnified fluoroscopy, it appeared that there was a pedestal of cortical bone formation in the canal at this point (Figure 5A).

In order to breach the bony pedestal, the starting reamer was used to ream past the obstruction into the distal femoral meta-diaphyseal flare (Figure 5B). The ball-tip guide wire was then passed without difficulty to the physeal scar. The intramedullary canal was then reamed over the guide wire sequentially from 9 to 14 mm in 0.5 mm increments. The intramedullary reamings were saved for bone grafting and then inserted to the level of the fracture with the exchange tube. The bone graft was impacted using an 8 mm reamer at the fracture site. A 13 mm × 420 mm Russell-Taylor antegrade femoral nail was then inserted without difficulty. No distal locking screws were placed to allow fracture dynamization. Post-operative films showed adequate fracture reduction and placement of the intramedullary nail and proximal locking screw (Figure 6A-C). Figure 5C shows final nail placement (solid lines) compared to old, more proximal nail placement (dashed lines). Intra-operative cultures were subsequently negative.

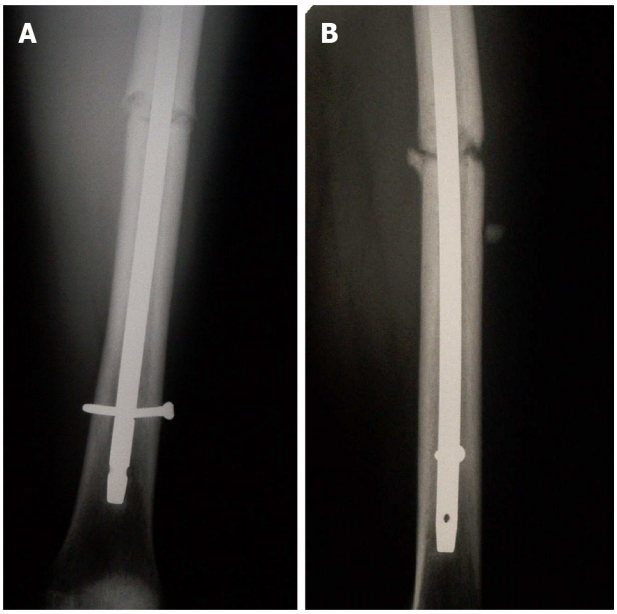
OUTCOME AND FOLLOW-UP
At 1 year follow-up there was evidence of callus formation at the fracture site but not full cortical consolidation (Figure 7A and B). By 18 mo the fracture appeared well consolidated, and the patient had resolution of his thigh pain (Figure 8A and B).

DISCUSSION
Femoral shaft fracture nonunion is uncommon and is usually the result of aseptic etiologies. Nonunion following reamed antegrade intramedullary nail is a rare complication, occurring in 1%-2.2% of cases in



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Figure 1 Post-operative radiographs of the left femur from outside hospital. A: Anterior-posterior radiograph showing transverse mid-shaft femur fracture with some comminution and Russell-Taylor Delta II 9 x 380 mm antegrade nail with single distal interlocking screw; B: Lateral radiograph showing the same.



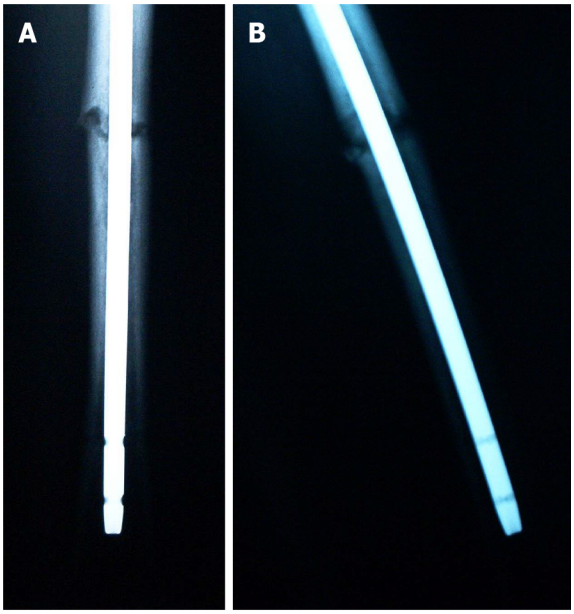
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Figure 2 Radiographs of the left femur from outside hospital obtained 4 mo post-operatively. A: Anterior-posterior radiograph showing broken distal interlocking screw and poor fracture healing; B: Lateral radiograph showing the same.

early series[1-3]. In a recent systematic review of 38 studies involving 2829 femoral shaft fractures, Koso *et al*[4] found a 3.1% rate of nonunion after antegrade nail fixation and nonunion rates of 2.9% and 6.1% for reamed *vs* unreamed nail fixation, respectively.

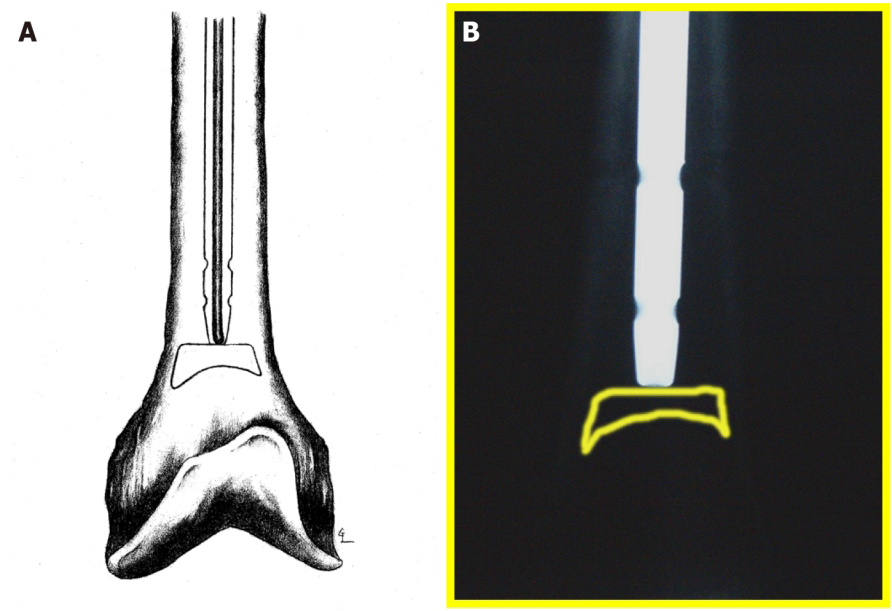
There are numerous methods that may be used in the treatment of femur fracture nonunions. With infections, exchange intramedullary nailing should be performed after appropriate irrigation and debridement of the canal followed by an appropriate 4–6-wk course of parenteral or oral antibiotics. Some surgeons advocate a two-stage approach using antibiotic-impregnated beads or rods prior to final nail insertion. Aseptic nonunions may be treated with nail dynamization, exchange nailing (EN), or plate fixation. Several adjuncts may be employed in combination with these techniques, including bone-grafting, electrical stimulation, and bone morphogenetic protein or other bone growth supplements.

Fracture dynamization by distal locking screw removal is often attempted initially for delayed unions. This method provides the advantages of short procedure time with minimal soft-tissue



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Figure 3 Radiographs of the left femur obtained 8 mo post-operatively. A: Anterior-posterior radiograph showing continued poor evidence of fracture healing despite prior distal interlocking screw removal; B: Lateral radiograph showing the same.

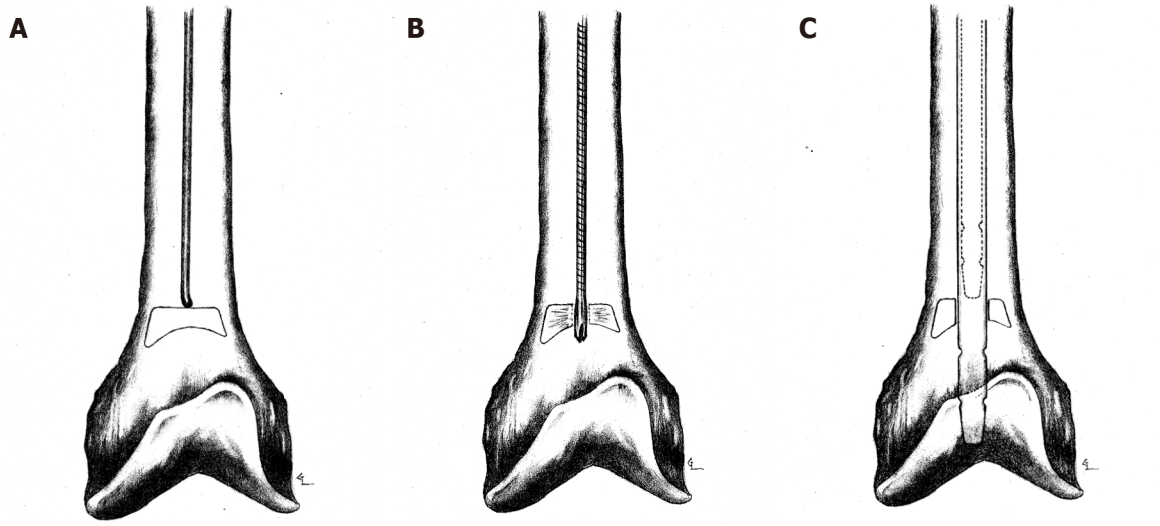


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Figure 4 Illustration and radiograph of left femur obtained intra-operatively. A: Illustration of bone pedestal at tip of intramedullary nail blocking guide rod passage; B: Radiograph showing guide rod tip (inside intramedullary nail) unable to pass intramedullary bone pedestal (outlined).

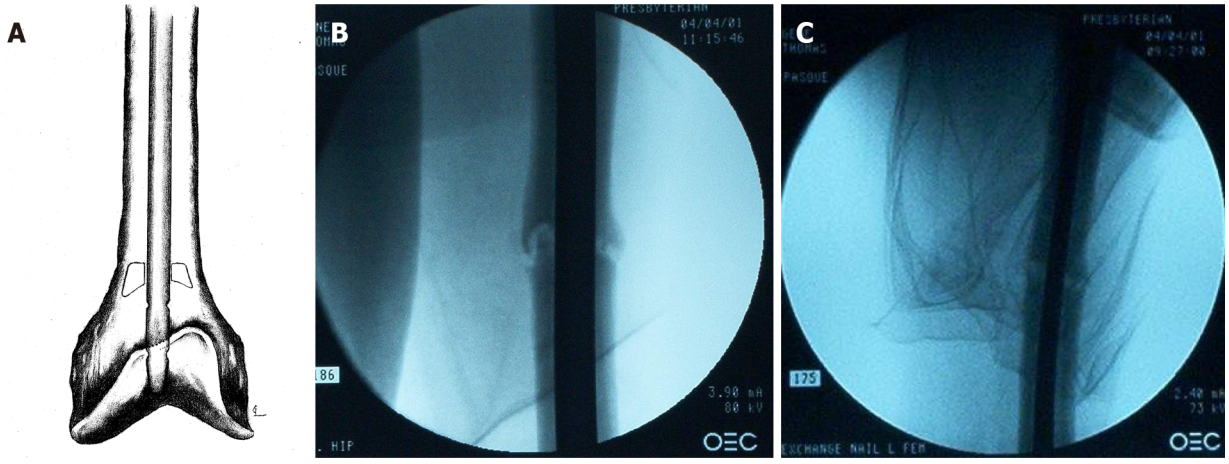
dissection. Wu showed a 58% union rate with dynamization between 4 and 12 mo, but a high rate (21%) of femoral shortening of more than 2 cm[12]. In one meta-analysis, Vaughn *et al*[13] found a 66% (84/131) union rate with dynamization after nonunion though this rate increased to 82% (45/55) when treating delayed union. This provides evidence for the importance of close follow-up after intramedullary nailing as dynamization is most effective in the earlier windows of fracture healing. A review of the literature did not yield any reports of cases of post-dynamization union failure secondary to intramedullary bone pedestal formation.

The treatment of femoral diaphyseal fracture nonunion or delayed union of any etiology has been found to have a varied (53%-100%) rate of union following exchange reamed IM nail fixation (EN)[5,14-25]. Due to the infrequency of nonunion, most case series examining outcomes of EN are of relatively small cohorts (n < 105). The largest of these series showed rates of union from 86%-100%[14-21]. Some smaller (n = 19) series have shown lower rates of union from 53%-58%[22,23]. Of note, four studies



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Figure 5 Illustration of left femur intra-operatively. A: Showing femur after intramedullary nail removal. Guide rod tip still unable to pass distally in canal due to intramedullary bone pedestal; B: Showing starting reamer used to breach intramedullary bone pedestal; C: Showing new nail (solid lines) at area of wider, more distal meta-diaphyseal bone compared to old nail (dotted lines) at area of more proximal, narrow diaphyseal bone.



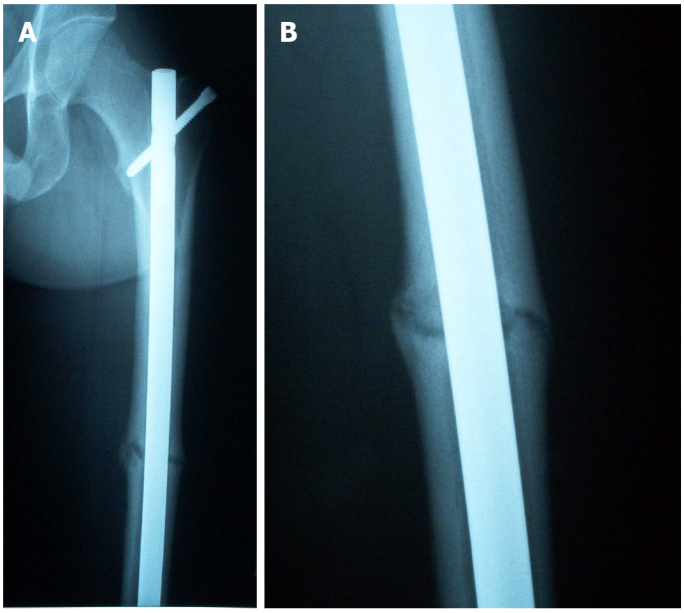
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Figure 6 Illustration and fluoroscopic radiographs of left femur obtained intra-operatively. A: Illustration showing intramedullary nail placed past bone pedestal; B: Anterior-posterior radiograph showing new, larger diameter intramedullary nail placed past bone pedestal; C: Lateral radiograph showing the same.

(including three meta-analyses) comparing EN to other methods of treatment for nonunion found rates of union from 64%-86%[5,13,24,25]. Infected nonunions have been shown to have union rates up to 90%-100% with intramedullary nail fixation[26-28]. Despite some small studies reporting poor results, the majority of the literature supports EN as an effective and safe method of fixation.

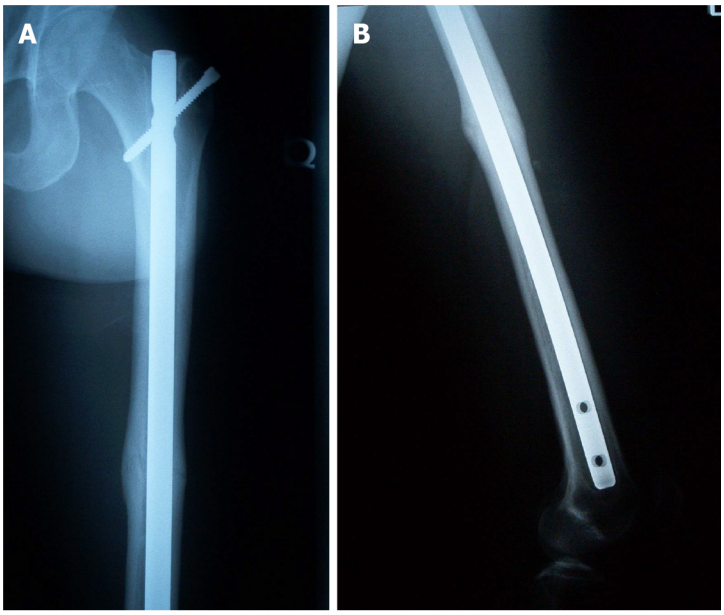
Advantages of exchange intramedullary nailing include limited soft-tissue dissection and periosteal blood supply disruption, full post-operative weight-bearing, and early active rehabilitation. Complications include persistent nonunion, infection, and hardware failure[12,21,22,26]. Current recommendations call for over-reaming the canal 1-3 mm and replacing the extracted nail with one of a larger diameter[5,7,19-21,23].

Plating techniques are sometimes employed in treating nonunions when dynamization and/or exchange nailing have failed. When large bony defects are present and open bone-grafting techniques are employed, plating techniques are often preferred for stabilization. Union rates of 91%-100% are observed with various plating techniques after removal of the failed nail[29-31]. Several case series have shown excellent results in patients treated with augmentative plating (AP) with retained IM nail after femoral shaft fracture nonunion with mean union rate of 86%-100%[24,32-36]. Two recent meta-analyses have shown a significantly higher union rate following AP with retained IM nail when compared to EN alone. In a systematic review of 21 studies involving 448 cases of nonunion after IM nailing for femoral shaft fracture, Medlock *et al*[25] reports union rates of 99.8% (190/191) and 74% (190/257) for AP and EN, respectively. In another systematic review of 3 studies involving 232 nonunions, Luo *et al*[5] found



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Figure 7 Fluoroscopic radiographs of left femur obtained intra-operatively. A: Anterior-posterior radiograph one year post-operatively showing early callous formation but incomplete fracture healing; B: Lateral radiograph showing the same but at increased magnification.



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Figure 8 Radiographs of the left femur obtained 18 mo post-operatively. A: Anterior-posterior radiograph showing evidence of good fracture healing; B: Lateral radiograph showing the same.

union rates of 100% (113/113) and 86% (102/119) for AP and EN, respectively. Indications for AP include non-isthmic nonunion or isthmic nonunion with cortical defects or IM canal widening[37]. Advantages of AP over EN include lower rates of nonunion, shorter time to union, shorter operative time, and less intra-operative blood loss. Some of the disadvantages of plating include large soft tissue dissection, increased infection rate, and increased hardware failure.

Adjuncts to nonunion surgical interventions include bone-grafting, bone morphogenetic protein, electrical stimulation, and extracorporeal shock. When treating nonunion with AP, bone grafting is recommended and has been shown to produce excellent results with union rates of 88%-100%[24,29,32,35-37]. Bone grafting can be implemented through open or closed (intramedullary over-reaming) techniques with equivalent efficacy (100% union)[38]. Closed methods have a shorter time to union[12] . Open methods require harvest from the iliac crest or the tibial condyle. General indications for open grafting include atrophic nonunions, large bony defects (> 5 mm), and fracture malalignment[33,38].

Bai *et al*[39] obtained 16/17 fracture unions using plaster of Paris and bovine BMP composite implant at an average of 6 mo for femur fracture nonunion patients. In a systematic review comparing BMP and autologous grafting, Zhou *et al*[40] found BMP to have similar healing rates, improved limb function, and lower intraoperative blood loss, but with significantly higher hospitalization costs. While the literature on treatment of femoral nonunion with electrical stimulation is limited, electrical stimulation has shown some benefit for femur fractures[41], but is more commonly used and more successful with the treatment of tibia fracture nonunions[42].

There are several causes for the development of femoral shaft fracture nonunions following IM nail fixation and a number of methods to treat these complications. We propose a new etiology of delayed union or nonunion due to intramedullary cortical bone pedestal formation at the IM nail tip leading to failure of dynamization following distal locking screw removal. This complication may have been prevented with the use of a longer IM nail during the initial fixation or earlier dynamization. With the nail tip resting more distally in an area of increased intramedullary diameter, there would theoretically be a decreased opportunity for formation of an intramedullary pedestal of bone that could bridge the distance between the femoral cortices. Earlier dynamization would have also decreased the time available for bone pedestal consolidation within the femoral canal. If exchange intramedullary nailing is required, it is important to ream past the previous nail tip region to allow appropriate dynamization/impaction of the fracture site. We also recommend not using distal interlocking screws in this situation unless the fracture pattern warrants it. Nonunion adjuncts may also be helpful such as bone graft and bone supplementation products or electrical stimulation.

The strengths of this case report include radiographs of the clinical course, a detailed description of the surgical techniques with deviations required to overcome the encountered complication, a discussion of how to clinically manage and prevent such pathology, and a review of all available literature on clinical management of femoral shaft fracture nonunion after intramedullary nail fixation. Weaknesses include limited access to some of the patient files from the outside hospital.

CONCLUSION

This case presentation and literature review covers the most recent literature on causes of femur fracture nonunion and methods of revision after intramedullary nail fixation. We propose a new etiology for femur fracture nonunion caused by intramedullary bone pedestal formation leading to failure of dynamization after distal interlocking screw removal. Through the use of intramedullary nails of maximum length and close fracture follow-up with early intervention when delayed or nonunion of a fracture is suspected, this rare complication can be prevented.

FOOTNOTES

Author contributions: Pasque CB contributed to the conceptualization, design, data collection, methodology, project administration, supervision, writing, and revising of the manuscript; Pappas AJ contributed to the initial data collection and writing of the manuscript; Cole Jr CA contributed to the data analysis, literature review, and revision of the manuscript; and all authors have read and approved the final manuscript.

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Conflict-of-interest statement: Each of the authors declare no conflict of interest.

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REFERENCES

1 **Karadimas EJ**, Papadimitriou G, Theodoratos G, Papanikolaou A, Maris J. The effectiveness of the antegrade reamed technique: the experience and complications from 415 traumatic femoral shaft fractures. *Strategies Trauma Limb Reconstr* 2009; **4**: 113-121 [PMID: 19936887 DOI: 10.1007/s11751-009-0071-2]

2 **Winquist RA**, Hansen ST Jr, Clawson DK. Closed intramedullary nailing of femoral fractures. A report of five hundred and twenty cases. *J Bone Joint Surg Am* 1984; **66**: 529-539 [PMID: 6707031 DOI: 10.2106/00004623-198466040-00006]

3 **Wolinsky PR**, McCarty E, Shyr Y, Johnson K. Reamed intramedullary nailing of the femur: 551 cases. *J Trauma* 1999; **46**: 392-399 [PMID: 10088839 DOI: 10.1097/00005373-199903000-00007]

4 **Koso RE**, Terhoeve C, Steen RG, Zura R. Healing, nonunion, and re-operation after internal fixation of diaphyseal and distal femoral fractures: a systematic review and meta-analysis. *Int Orthop* 2018; **42**: 2675-2683 [PMID: 29516238 DOI: 10.1007/s00264-018-3864-4]

5 **Luo H**, Su Y, Ding L, Xiao H, Wu M, Xue F. Exchange nailing versus augmentative plating in the treatment of femoral shaft nonunion after intramedullary nailing: a meta-analysis. *EFORT Open Rev* 2019; **4**: 513-518 [PMID: 31538001 DOI: 10.1302/2058-5241.4.180054]

6 **Giannoudis PV**, MacDonald DA, Matthews SJ, Smith RM, Furlong AJ, De Boer P. Nonunion of the femoral diaphysis. The influence of reaming and non-steroidal anti-inflammatory drugs. *J Bone Joint Surg Br* 2000; **82**: 655-658 [PMID: 10963160 DOI: 10.1302/0301-620x.82b5.9899]

7 **Hak DJ**, Lee SS, Goulet JA. Success of exchange reamed intramedullary nailing for femoral shaft nonunion or delayed union. *J Orthop Trauma* 2000; **14**: 178-182 [PMID: 10791668 DOI: 10.1097/00005131-200003000-00005]

8 **Jeffcoach DR**, Sams VG, Lawson CM, Enderson BL, Smith ST, Kline H, Barlow PB, Wylie DR, Krumenacker LA, McMillen JC, Pyda J, Daley BJ; University of Tennessee Medical Center, Department of Surgery. Nonsteroidal anti-inflammatory drugs' impact on nonunion and infection rates in long-bone fractures. *J Trauma Acute Care Surg* 2014; **76**: 779-783 [PMID: 24553548 DOI: 10.1097/TA.0b013e3182aafe0d]

9 **Wheatley BM**, Nappo KE, Christensen DL, Holman AM, Brooks DI, Potter BK. Effect of NSAIDs on Bone Healing Rates: A Meta-analysis. *J Am Acad Orthop Surg* 2019; **27**: e330-e336 [PMID: 30260913 DOI: 10.5435/JAAOS-D-17-00727]

10 **Taitsman LA**, Lynch JR, Agel J, Barei DP, Nork SE. Risk factors for femoral nonunion after femoral shaft fracture. *J Trauma* 2009; **67**: 1389-1392 [PMID: 19704386 DOI: 10.1097/TA.0b013e318182afd0]

11 **Jiao H**, Xiao E, Graves DT. Diabetes and Its Effect on Bone and Fracture Healing. *Curr Osteoporos Rep* 2015; **13**: 327-335 [PMID: 26254939 DOI: 10.1007/s11914-015-0286-8]

12 **Wu CC**. The effect of dynamization on slowing the healing of femur shaft fractures after interlocking nailing. *J Trauma* 1997; **43**: 263-267 [PMID: 9291371 DOI: 10.1097/00005373-199708000-00010]

13 **Vaughn JE**, Shah RV, Samman T, Stirton J, Liu J, Ebraheim NA. Systematic review of dynamization *vs* exchange nailing for delayed/non-union femoral fractures. *World J Orthop* 2018; **9**: 92-99 [PMID: 30079298 DOI: 10.5312/wjo.v9.i7.92]

14 **Furlong AJ**, Giannoudis PV, DeBoer P, Matthews SJ, MacDonald DA, Smith RM. Exchange nailing for femoral shaft aseptic non-union. *Injury* 1999; **30**: 245-249 [PMID: 10476292 DOI: 10.1016/s0020-1383(99)00073-x]

15 **Hierholzer C**, Glowalla C, Herrler M, von Rüden C, Hungerer S, Bühren V, Friederichs J. Reamed intramedullary exchange nailing: treatment of choice of aseptic femoral shaft nonunion. *J Orthop Surg Res* 2014; **9**: 88 [PMID: 25300373 DOI: 10.1186/s13018-014-0088-1]

16 **Naeem-ur-Razaq M**, Qasim M, Sultan S. Exchange nailing for non-union of femoral shaft fractures. *J Ayub Med Coll Abbottabad* 2010; **22**: 106-109 [PMID: 22338431 DOI: 10.2739/kurumemedj.20.125]

17 **Oh I**, Nahigian SH, Rascher JJ, Farrall JP. Closed intramedullary nailing for ununited femoral shaft fractures. *Clin Orthop Relat Res* 1975; 206-215 [PMID: 1126078 DOI: 10.1097/00003086-197501000-00032]

18 **Shroeder JE**, Mosheiff R, Khoury A, Liebergall M, Weil YA. The outcome of closed, intramedullary exchange nailing with reamed insertion in the treatment of femoral shaft nonunions. *J Orthop Trauma* 2009; **23**: 653-657 [PMID: 19897987 DOI: 10.1097/BOT.0b013e3181a2a337]

19 **Webb LX**, Winquist RA, Hansen ST. Intramedullary nailing and reaming for delayed union or nonunion of the femoral shaft. A report of 105 consecutive cases. *Clin Orthop Relat Res* 1986; 133-141 [PMID: 3769279 DOI: 10.1097/00003086-198611000-00015]

20 **Wu CC**, Chen WJ. Exchange nailing for aseptic nonunion of the femoral shaft. *Int Orthop* 2002; **26**: 80-84 [PMID: 12078882 DOI: 10.1007/s00264-001-0313-5]

21 **Swanson EA**, Garrard EC, Bernstein DT, O'Connor DP, Brinker MR. Results of a systematic approach to exchange nailing for the treatment of aseptic femoral nonunions. *J Orthop Trauma* 2015; **29**: 21-27 [PMID: 24978947 DOI: 10.1097/BOT.0000000000000166]

22 **Banaszkiewicz PA**, Sabboubeh A, McLeod I, Maffulli N. Femoral exchange nailing for aseptic non-union: not the end to all problems. *Injury* 2003; **34**: 349-356 [PMID: 12719163 DOI: 10.1016/s0020-1383(02)00191-2]

23 **Weresh MJ**, Hakanson R, Stover MD, Sims SH, Kellam JF, Bosse MJ. Failure of exchange reamed intramedullary nails for ununited femoral shaft fractures. *J Orthop Trauma* 2000; **14**: 335-338 [PMID: 10926240 DOI: 10.1097/00005131-200006000-00005]

24 **Lai PJ**, Hsu YH, Chou YC, Yeh WL, Ueng SWN, Yu YH. Augmentative antirotational plating provided a significantly higher union rate than exchanging reamed nailing in treatment for femoral shaft aseptic atrophic nonunion - retrospective cohort study. *BMC Musculoskelet Disord* 2019; **20**: 127 [PMID: 30909909 DOI: 10.1186/s12891-019-2514-3]

25 **Medlock G**, Stevenson IM, Johnstone AJ. Uniting the un-united: should established non-unions of femoral shaft fractures initially treated with IM nails be treated by plate augmentation instead of exchange IM nailing? *Strategies Trauma Limb Reconstr* 2018; **13**: 119-128 [PMID: 30426320 DOI: 10.1007/s11751-018-0323-0]

26 **Klemm KW**. Treatment of infected pseudarthrosis of the femur and tibia with an interlocking nail. *Clin Orthop Relat Res* 1986; 174-181 [PMID: 3769283 DOI: 10.1097/00003086-198611000-00019]

27 **Pradhan C**, Patil A, Puram C, Attarde D, Sancheti P, Shyam A. Can antibiotic impregnated cement nail achieve both

infection control and bony union in infected diaphyseal femoral non-unions? *Injury* 2017; **48** Suppl 2: S66-S71 [PMID: 28802424 DOI: 10.1016/S0020-1383(17)30497-7]

28 **Thonse R**, Conway J. Antibiotic cement-coated interlocking nail for the treatment of infected nonunions and segmental bone defects. *J Orthop Trauma* 2007; **21**: 258-268 [PMID: 17414554 DOI: 10.1097/BOT.0b013e31803ea9e6]

29 **Xing W**, Pan Z, Sun L, Zhang C, Zhang Z, Feng W, Liu C. Sliding bone graft combined with double locking plate fixation for the treatment of femoral shaft nonunion. *J Int Med Res* 2019; **47**: 2034-2044 [PMID: 30890016 DOI: 10.1177/0300060519835334]

30 **Peng Y**, Ji X, Zhang L, Tang P. Double locking plate fixation for femoral shaft nonunion. *Eur J Orthop Surg Traumatol* 2016; **26**: 501-507 [PMID: 27142853 DOI: 10.1007/s00590-016-1765-z]

31 **Bellabarba C**, Ricci WM, Bolhofner BR. Results of indirect reduction and plating of femoral shaft nonunions after intramedullary nailing. *J Orthop Trauma* 2001; **15**: 254-263 [PMID: 11371790 DOI: 10.1097/00005131-200105000-00004]

32 **Mittal KK**, Gupta H, Kaushik N. Reunion of post nail aseptic non-union of diaphyseal femoral fractures by augmentation plating, decortication and bone grafting - Replacement for exchange nailing. *Injury* 2021; **52**: 1529-1533 [PMID: 33059926 DOI: 10.1016/j.injury.2020.10.036]

33 **Ueng SW**, Chao EK, Lee SS, Shih CH. Augmentative plate fixation for the management of femoral nonunion after intramedullary nailing. *J Trauma* 1997; **43**: 640-644 [PMID: 9356061 DOI: 10.1097/00005373-199710000-00013]

34 **Uliana CS**, Bidolegui F, Kojima K, Giordano V. Augmentation plating leaving the nail in situ is an excellent option for treating femoral shaft nonunion after IM nailing: a multicentre study. *Eur J Trauma Emerg Surg* 2021; **47**: 1895-1901 [PMID: 32107562 DOI: 10.1007/s00068-020-01333-0]

35 **Ru JY**, Niu YF, Cong Y, Kang WB, Cang HB, Zhao JN. Exchanging reamed nailing versus augmentative compression plating with autogenous bone grafting for aseptic femoral shaft nonunion: a retrospective cohort study. *Acta Orthop Traumatol Turc* 2015; **49**: 668-675 [PMID: 26511695 DOI: 10.3944/AOTT.2015.14.0404]

36 **Choi YS**, Kim KS. Plate augmentation leaving the nail in situ and bone grafting for non-union of femoral shaft fractures. *Int Orthop* 2005; **29**: 287-290 [PMID: 16132986 DOI: 10.1007/s00264-005-0668-0]

37 **Park J**, Yang KH. Indications and outcomes of augmentation plating with decortication and autogenous bone grafting for femoral shaft nonunions. *Injury* 2013; **44**: 1820-1825 [PMID: 23510754 DOI: 10.1016/j.injury.2013.02.021]

38 **Wu CC**, Chen WJ. Treatment of femoral shaft aseptic nonunions: comparison between closed and open bone-grafting techniques. *J Trauma* 1997; **43**: 112-116 [PMID: 9253919 DOI: 10.1097/00005373-199707000-00026]

39 **Kujala S**, Raatikainen T, Ryhänen J, Kaarela O, Jalovaara P. Composite implant of native bovine bone morphogenetic protein (BMP) and biocoral in the treatment of scaphoid nonunions--a preliminary study. *Scand J Surg* 2002; **91**: 186-190 [PMID: 12164521 DOI: 10.1177/145749690209100210]

40 **Zhou YQ**, Tu HL, Duan YJ, Chen X. Comparison of bone morphogenetic protein and autologous grafting in the treatment of limb long bone nonunion: a systematic review and meta-analysis. *J Orthop Surg Res* 2020; **15**: 288 [PMID: 32727538 DOI: 10.1186/s13018-020-01805-4]

41 **Khalifeh JM**, Zohny Z, MacEwan M, Stephen M, Johnston W, Gamble P, Zeng Y, Yan Y, Ray WZ. Electrical Stimulation and Bone Healing: A Review of Current Technology and Clinical Applications. *IEEE Rev Biomed Eng* 2018; **11**: 217-232 [PMID: 29994564 DOI: 10.1109/RBME.2018.2799189]

42 **Connolly JF**. Selection, evaluation and indications for electrical stimulation of ununited fractures. *Clin Orthop Relat Res* 1981; 39-53 [PMID: 6975690 DOI: 10.1097/00003086-198111000-00007]

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CASE REPORT

Extensive adhesion formation in a total knee replacement in the setting of a gastrointestinal stromal tumor: A case report

Steven Mitchell, Anderson Lee, Ryan Stenquist, David Yatsonsky II, Megan L Mooney, Vithal B Shendge

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Abstract

BACKGROUND

Gastrointestinal stromal tumors (GISTs) are rare primary neoplasms of the gastrointestinal tract, accounting for 1% to 2% of all gastrointestinal neoplasms worldwide. GISTs are frequently discovered incidentally during workup for other diagnosis or intestinal obstruction, as they can present with few or no symptoms. Simultaneously, GISTs confer a high degree of malignant transformation, with a progression in about 10% to 30% of cases.

CASE SUMMARY

A 63-year-old healthy female presented to our institution with complaints of right knee pain and limited passive and active motion in the setting of a previous right total knee arthroplasty (TKA). One year after TKA, the patient was incidentally diagnosed with a GIST, which was successfully removed. After removal, the patient continued to have limited range of motion of the right knee and subsequently underwent revision TKA. Intraoperatively significant fibrotic adhesions were found encapsulating the femoral and tibial components. The patient's pain improved postoperatively, however, she continued to have decreased range of motion with difficulty ambulating.

CONCLUSION

We propose that this case may demonstrate a proinflammatory milieu arising from a GIST, which had a direct influence on the outcome of recent total knee arthroplasty. This proposed mechanism between neoplastic cytokinetic activity and adhesion formation could have implications on preoperative and postoperative orthopedic management of total knee arthroplasty.

Key Words: Gastrointestinal stromal tumor; Adhesion formation; Total knee arthroplasty; Inflammatory response; Decreased range of motion; Case report

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Core Tip: This case demonstrated a patient who had recurrent adhesion formation resulting in reduced clinical outcomes, hypothesized to be secondary to a gastrointestinal stromal tumor (GIST) inflammatory response. Currently, there is a paucity of literature documenting GIST tumors and potential adhesion formation and decreased clinical outcomes in patients with prosthetic joints.

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INTRODUCTION

Adhesion formation is a serious cause of adverse outcomes in the medical field. Several triggers of adhesion formation include inflammation, foreign body sensation and iatrogenic causes[1-3]. Currently, the underlying mechanisms of adhesion remain unclear but the regulation of fibrinolytic activity, leading to fibrosis, is thought to play an important role in adhesion formation[1]. Gastrointestinal stromal tumors (GISTs) are especially of interest because circulating levels of cell adhesion marker L1 Cellular Adhesion Molecule (L1CAM) which has been proposed as a prognostic marker[1,4]. Cell adhesion molecule L1CAM (CD171), a 200–220 kDa type I glycoprotein of the immunoglobulin superfamily, plays a role in development of the nervous system by regulating cell interactions, including neuronal migration[5]. L1CAM has also been shown to have other interactions with cell regulators such as integrins which play an important role in inflammation and fibrosis[6]. This case report demonstrates a patient with GIST that presented with extensive adhesion formation status-post total knee replacement, resulting in limited range of motion and need for revision surgery.

CASE PRESENTATION

Chief complaints

Our patient is a 63-year-old female with complaints of right knee osteoarthritis causing her significant discomfort.

History of present illness

The patient has had complaints of right knee osteoarthritis since 2015. The patient's other conditions included long-standing hypertension, controlled type II diabetes mellitus, and moderate obesity. Radiographs of the right knee demonstrated moderate tricompartmental osteoarthritis of the knee with notable valgus deformity. Initially, she was managed conservatively with non-steroidal anti-inflammatory drugs (NSAIDs), bracing, intra-articular cortisone injections, and physical therapy. After failing two years of conservative treatment, she elected to undergo right total knee arthroplasty in January 2017. The patient underwent right total knee arthroplasty with a Stryker Triathlon X3 implant system with posterior stabilization. The postoperative course was unremarkable; she was instructed to continue knee range of motion exercises and was referred to physical therapy.

In June 2018, the patient returned to the orthopedics clinic with pain and stiffness of the right knee. Physical exam revealed right knee range of motion at 95˚ flexion to full extension. Radiographs were unremarkable with no change of the components noted from the previous. The patient had been compliant with her physical therapy and was ambulating without assistive devices. The patient was instructed to continue strengthening exercises and was referred to physical therapy.

In February 2018, the patient presented to an outside facility for complaints of severe fatigue and melena. Subsequent computed tomography imaging and esophagogastroduodenoscopy revealed diffuse gastric wall thickening with a fungating mass and focal calcifications within the greater curvature of the stomach suspicious for neoplastic disease. Subsequent biopsy of this mass revealed a CD117-positive tumor, while being negative for pancytokeratin, CD20 (B-cell marker), and Helicobacter pylori, which was consistent with an ulcerated gastrointestinal stromal tumor. This tumor was successfully excised in April 2018 *via* open gastrectomy without complications; postoperative pathology confirmed the diagnosis of spindle-type GIST with adequate negative surgical margins. The patient was subsequently started on long-term imatinib mesylate therapy and placed on an annual surveillance

program.

In November 2018, the patient elected to undergo joint manipulation under general anesthesia due to continuing knee pain. Prior to manipulation, the patient's right knee range of motion was lacking 10-15˚ of full extension and flexion to 50˚. Post-procedure range-of-motion (ROM) demonstrated significant improvement in the ROM, with full extension to 105˚ of flexion. However, the patient quickly re-developed right knee stiffness. Two months after knee manipulation under anesthesia, clinical examination revealed a fixed flexion deformity of 25° and active flexion to 65° (Figure 1A and B). Radiographs demonstrated evidence of early polyethylene wear.

In July 2020, three-and-a-half years after her initial prosthesis implantation and after multiple attempts at physical therapy, pain management, and an unsuccessful joint manipulation, the patient elected for a single-stage revision of her right knee prosthesis. Intraoperative findings demonstrated significant adhesion formation in the suprapatellar fossa extending from the anterior aspect of the patella into the intercondylar notch and posterior capsule (Figure 2A and B). Severe calcification was noted within the posterior compartment of the knee, and significant adhesions were appreciated between the polyethylene liner and the femoral component, as well as within the lateral and medial gutters (Figure 2C and D). Multiple intraoperative specimens were sent for culture demonstrating aseptic, dense fibrous tissue with abundant fibrin and chronic inflammation. After extensive debridement, the patient underwent successful revision with a Stryker Triathlon implant system including posterior stabilization (Figure 2E).

FINAL DIAGNOSIS

The final diagnosis of the presented case is tricompartmental osteoarthritis of the knee with notable valgus deformity.

TREATMENT

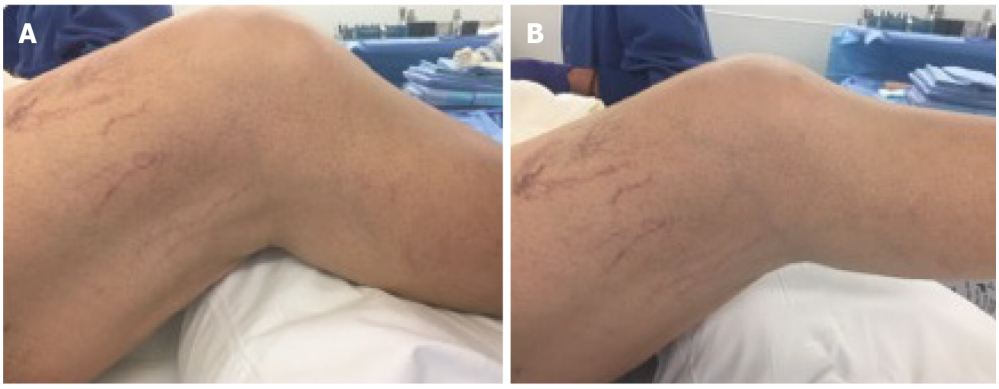
The patient was initially managed conservatively with NSAIDs, bracing, intra-articular cortisone injections, and physical therapy. After failing two years of conservative treatment, she elected to undergo right total knee arthroplasty in January 2017. The patient underwent right total knee arthroplasty with a Stryker Triathlon X3 implant system with posterior stabilization. One year post-operatively, the patient returned to the clinic with pain and stiffness of the right knee and elected to undergo joint manipulation under general anesthesia 18 mo after TKA. Three-and-a-half years after her initial prosthesis implantation and after multiple attempts at physical therapy, pain management, and an unsuccessful joint manipulation, the patient elected for a single-stage revision of her right knee prosthesis. After extensive debridement, the patient underwent successful revision with a Stryker Triathlon implant system including posterior stabilization.

OUTCOME AND FOLLOW-UP

Four months after TKA revision, the patient presented with moderate stiffness and was now utilizing a cane. On exam, the patient demonstrated 5˚ of total motion in her right knee with minimal pain. Radiographs obtained at this visit suggested a progressive scarring process in the posterior aspect of the knee. Due to this recurring scarring and limited outcome overall, this patient will be followed in a long-term setting with strengthening exercises and other conservative management constituting her primary treatment, as we discussed with this patient that she may have reached the maximal medical improvement following this revision surgery.

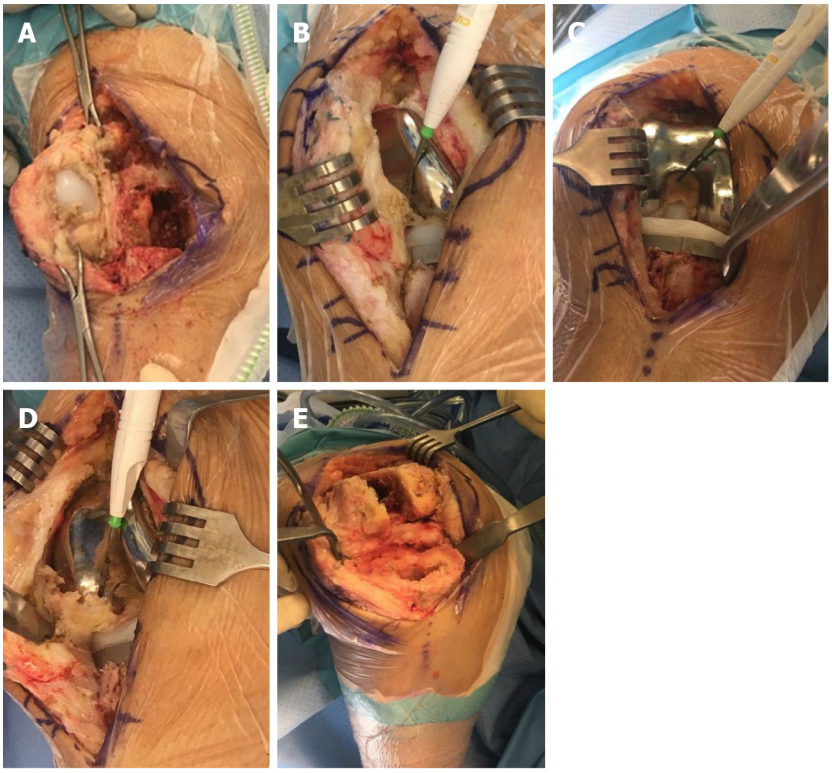
DISCUSSION

GISTs are primary neoplasms of the gastrointestinal tract that are rare, accounting for 1% to 2% of all gastrointestinal neoplasms, and are frequently discovered incidentally during workup for other diagnosis or intestinal obstruction. GISTs are often clinically silent and confer a high degree of malignant transformation, with a progression in about 10% to 30% of cases[1,7]. Søreide *et al*[6] found that the median age for GISTs was 65 with a 1:1 male to female ratio. Tumors are often 2-30 cm at time of diagnosis and cause symptoms either by mass-effect or ulcerative anemia. These tumors were not well-characterized until the 1990s, and literature suggests that GISTs have been underdiagnosed for decades[8].



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Figure 1 Preoperative flexion and extension of the right knee. A: Preoperative flexion of the right knee; B: Preoperative extension of the right knee.



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Figure 2 Images during the surgery. A: Imaging depicting parapatellar adhesions with loose patellar component; B: Intraoperative adhesions from patellar tendon into intercondylar notch; C: Intercondylar scar/fibrous tissue and tibial component; D: Tendo-notch to posterior capsular fibrous adhesions being divided with electrocautery; E: Imaging depicting femur and tibia after removal of components and subtotal synovectomy and excision of adhesions.

Most GISTs are of sporadic etiology (97%), thought to arise from an activating mutation in either KIT or platelet-derived growth factor A[7]. Typically, these tumors are composed of a nearly uniform population of spindle cells (70%), epithelioid cells (20%) or a mix of these two morphologies[1]. Over 95% of GIST tumors are associated with KIT Tyrosine activity (CD117), while over 80% of GISTs are associated with BCL2, and 70% associated with CD34[4,5,9]. Since there are a variety of presentations, this tumor is often mistaken with fibromatosis and leiomyosarcoma[10].

Key components in metastatic neoplastic lineages are mutations that either downregulate adhesion genes or upregulate motility-promoting genes. One such motility-promoting molecule is called L1CAM. L1CAM has been shown to promote angiogenesis and pro-fibrotic environments, and is associated with mediating overall cell survival[9,11,12]. Concurrently, L1CAM has been found to be expressed in at least 74% of GISTs, with higher L1CAM concentrations being associated with worse outcomes[10]. L1CAM's extracellular domains are associated with activation of integrin-dependent processes, as well as interactions with fibroblast growth factor receptor (FGFR). Prior research utilized peptides to block the L1CAM-FGFR signaling pathway, which resulted in reduced glioma cell migration and motility[13].

Double knockdown of L1CAM expression and FGFR activity in glioblastoma cells significantly reduced cellular motility (96% reduction) while knockdown of either L1CAM or FGFR displayed partially reduced cell migration[13]. These studies suggested an important relationship between L1CAM-FGFR interactions and the development of metastatic disease. Due to the role that the L1CAM-FGFR interaction plays in metastatic spread and negative outcomes in gliomas and other tumors, this patient's recurrent adhesion formation could be attributed to their underlying GIST diagnosis. Furthermore, FGFR has been shown to regulate a vast network of profibrotic mediators, including transforming growth factor beta, endothelin-1, and connective tissue growth factor amongst many other profibrotic factors[14-17]. Subsequent activation of FGFRs through the L1CAM molecule that is commonly expressed in GISTs may have led to the generation of fibrotic adhesions within this patient's prosthetic knee joint.

However, it is also possible that the multiple surgeries this patient underwent activated an inflammatory response within the knee joint, creating a fibrotic environment that resulted in the adhesions observed. While the exact underlying mechanism of intra-articular adhesions is unclear, researchers believe that many cytokines and growth factors can contribute to fibrous tissue hyperplasia which may be responsible for adhesion formation. These cytokines and growth factors are part of the inflammatory response and it is generally recognized that surgical trauma can activate this response. Additional research should clarify the exact mechanisms in which GISTs can promote adhesions in patients who undergo surgery to reduce post-operative complications as well as appropriate management and treatment of these complications. This patient demonstrates a unique case in which a GIST diagnosis may have impacted her ability to regain full motion and use of her knee after total knee arthroplasty.

CONCLUSION

Our case demonstrated a patient with extensive fibrotic scarring in a relatively new knee prosthesis in the setting of a gastrointestinal stromal tumor. This rare neoplasm has been hypothesized to induce a pro-fibrotic milieu, which has the potential to disrupt artificial devices. Further analysis of patients diagnosed with GISTs and concomitant joint arthroplasty is warranted to elucidate the exact mechanism behind the formation of these adhesions, as well as what potential therapies exist to mitigate joint complications.

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FOOTNOTES

Author contributions: Mitchell S, Lee A, Stenquist R, and Yatsonsky II D provided appreciable assistance with literature review, case reporting and management, and significant editing of the final manuscript; Mitchell S, Mooney M, and Shendge V participated in surgical appraisal of this case and were involved with orthopedic management of this case, as well as significant editing of the final manuscript.

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REFERENCES

1 **Mazur MT**, Clark HB. Gastric stromal tumors. Reappraisal of histogenesis. *Am J Surg Pathol* 1983; **7**: 507-519 [PMID: 6625048 DOI: 10.1097/00000478-198309000-00001]
2 **Daluga D**, Lombardi AV Jr, Mallory TH, Vaughn BK. Knee manipulation following total knee arthroplasty. Analysis of prognostic variables. *J Arthroplasty* 1991; **6**: 119-128 [PMID: 1875202 DOI: 10.1016/s0883-5403(11)80006-9]
3 **Yatsonsky Ii D**, Pan K, Shendge VB, Liu J, Ebraheim NA. Linkage of microbiota and osteoporosis: A mini literature review. *World J Orthop* 2019; **10**: 123-127 [PMID: 30918795 DOI: 10.5312/wjo.v10.i3.123]
4 **Zander H**, Rawnaq T, von Wedemeyer M, Tachezy M, Kunkel M, Wolters G, Bockhorn M, Schachner M, Izbicki JR, Kaifi J. Circulating levels of cell adhesion molecule L1 as a prognostic marker in gastrointestinal stromal tumor patients. *BMC Cancer* 2011; **11** 189: 1-189:7 [PMID: 21600041 DOI: 10.1186/1471-2407-11-189]
5 **Inaguma S**, Wang Z, Lasota JP, Miettinen MM. Expression of neural cell adhesion molecule L1 (CD171) in neuroectodermal and other tumors: An immunohistochemical study of 5155 tumors and critical evaluation of CD171 prognostic value in gastrointestinal stromal tumors. *Oncotarget* 2016; **7**: 55276-55289 [PMID: 27419370 DOI: 10.18632/oncotarget.10527]
6 **Corless CL**, Fletcher JA, Heinrich MC. Biology of gastrointestinal stromal tumors. *J Clin Oncol* 2004; **22**: 3813-3825 [PMID: 15365079 DOI: 10.1200/JCO.2004.05.140]
7 **Fletcher CD**, Berman JJ, Corless C, Gorstein F, Lasota J, Longley BJ, Miettinen M, O'Leary TJ, Remotti H, Rubin BP, Shmookler B, Sobin LH, Weiss SW. Diagnosis of gastrointestinal stromal tumors: A consensus approach. *Hum Pathol* 2002; **33**: 459-465 [PMID: 12094370 DOI: 10.1053/hupa.2002.123545]
8 **Søreide K**, Sandvik OM, Søreide JA, Giljaca V, Jureckova A, Bulusu VR. Global epidemiology of gastrointestinal stromal tumours (GIST): A systematic review of population-based cohort studies. *Cancer Epidemiol* 2016; **40**: 39-46 [PMID: 26618334 DOI: 10.1016/j.canep.2015.10.031]
9 **Maten MV**, Reijnen C, Pijnenborg JMA, Zegers MM. L1 Cell Adhesion Molecule in Cancer, a Systematic Review on Domain-Specific Functions. *Int J Mol Sci* 2019; **20** [PMID: 31455004 DOI: 10.3390/ijms20174180]
10 **Kaifi J**, Strelow A, Schurr P. L1 (CD171) is highly expressed in gastrointestinal stromal tumors. *Mod Pathol* 2006; **19**: 399-406 [DOI: 10.1038/modpathol.3800547]
11 **Geismann C**, Arlt A, Bauer I, Pfeifer M, Schirmer U, Altevogt P, Müerköster SS, Schäfer H. Binding of the transcription factor Slug to the L1CAM promoter is essential for transforming growth factor-β1 (TGF-β)-induced L1CAM expression in human pancreatic ductal adenocarcinoma cells. *Int J Oncol* 2011; **38**: 257-266 [PMID: 21109948]
12 **Lappegård KT**, Bergseth G, Riesenfeld J, Pharo A, Magotti P, Lambris JD, Mollnes TE. The artificial surface-induced whole blood inflammatory reaction revealed by increases in a series of chemokines and growth factors is largely complement dependent. *J Biomed Mater Res A* 2008; **87**: 129-135 [PMID: 18085644 DOI: 10.1002/jbm.a.31750]
13 **Mohanan V**, Temburni MK, Kappes JC, Galileo DS. L1CAM stimulates glioma cell motility and proliferation through the fibroblast growth factor receptor. *Clin Exp Metastasis* 2013; **30**: 507-520 [PMID: 23212305 DOI: 10.1007/s10585-012-9555-4]
14 **Sahni A**, Sahni SK, Simpson-Haidaris PJ, Francis CW. Fibrinogen binding potentiates FGF-2 but not VEGF induced expression of u-PA, u-PAR, and PAI-1 in endothelial cells. *J Thromb Haemost* 2004; **2**: 1629-1636 [PMID: 15333041 DOI: 10.1111/j.1538-7836.2004.00845.x]
15 **Arung W**, Meurisse M, Detry O. Pathophysiology and prevention of postoperative peritoneal adhesions. *World J Gastroenterol* 2011; **17**: 4545-4553 [PMID: 22147959 DOI: 10.3748/wjg.v17.i41.4545]
16 **Zhao S**, Sun Y, Li X, Wang J, Yan L, Chen H, Wang D, Dai J, He J. Reduction of intraarticular adhesion of knee by local application of rapamycin in rabbits *via* inhibition of fibroblast proliferation and collagen synthesis. *J Orthop Surg Res* 2016; **11**: 45 [PMID: 27094512 DOI: 10.1186/s13018-016-0375-0]
17 **Dees C**, Chakraborty D, Distler JHW. Cellular and molecular mechanisms in fibrosis. *Exp Dermatol* 2021; **30**: 121-131 [PMID: 32931037 DOI: 10.1111/exd.14193]



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Abstract

Given that the global population of elderly individuals is expanding and the difficulty of recovery, hip fractures will be a huge challenge and a critical health issue for all of humanity. Although people have spent more time at home during the coronavirus disease 2019 (COVID-19) pandemic, hip fractures show no sign of abating. Extensive studies have shown that patients with hip fracture and COVID-19 have a multifold increase in mortality compared to those uninfected and a more complex clinical condition. At present, no detailed research has systematically analyzed the relationship between these two conditions and proposed a comprehensive solution. This article aims to systematically review the impact of COVID-19 on hip fracture and provide practical suggestions. We found that hip fracture patients with COVID-19 have higher mortality rates and more complicated clinical outcomes. Indirectly, COVID-19 prevents hip fracture patients from receiving regular medical treatment. With regard to the problems we encounter, we provide clinical recommendations based on existing research evidence and a clinical flowchart for the management of hip fracture patients who are COVID-19 positive. Our study will help clinicians adequately prepare in advance when dealing with such patients and optimize treatment decisions.

Key Words: Hip fracture; COVID-19; Management; Adverse impact; Comorbidity; Treatment

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Core Tip: Hip fractures are common in the elderly, and in patients with hip fracture and coronavirus disease 2019 (COVID-19), multisystem clinical outcomes can be challenging for clinicians. Comprehensive identification of the COVID-19-caused impact is clinically useful in early preparation and the following intervention. Additionally, the detailed treatment options for hip fracture patients who are COVID-19 positive can provide clinicians with a credible guide for effective management.

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INTRODUCTION

Hip fracture is recognized as a worldwide health problem, and the incidence of hip fractures is on the rise due to the aging population[1]. Hip fractures are expected to increase from 258000 per year in 2010 to 458000 per year in 2050 in the United States. By 2050, the global number of hip fractures is expected to reach 4.5 million per year[2]. Older patients have more medical comorbidities, making it harder for them to recover from hip fractures[3]. Given that the global population of elderly individuals is expanding and the difficulty of recovery, hip fractures will be a huge challenge and a critical health issue for all of humanity. The new coronavirus disease-2019 (COVID-19) has posed a substantial threat to people's social lives and medical health care worldwide. The Centers for Disease Control and Prevention in the United States reported 33.8 million confirmed COVID-19 cases and 605905 related fatalities as of July 2021. COVID-19 has had a significant impact on hospital and intensive care unit (ICU) expenditures as well as the length of stay[4]. The virus is transmitted by droplets and causes a flu-like upper respiratory infection with symptoms such as cough, fever, and dyspnea in severe cases[5]. However, to control the spread of the disease, the implementation of epidemic prevention policies, lockdown of social activities, and travel restrictions have reduced traumatic injury admissions to an all-time low. The mechanism of trauma-related fractures has shifted from high energy to low energy, for example, emergency admissions due to falls from a great height and vehicle accidents have declined[6]. Most of the cases seen are due to stumbles and falls from a standing position, particularly in elderly individuals with osteoporosis. Therefore, hip fractures in the elderly are still being seen generally at an unchanged rate, especially the fragility fractures around the hip such as neck of femur and intertrochanteric fractures[7,8]. In this vulnerable group, a significant number of patients are at risk of COVID-19, as the elderly have weaker immune systems, more chronic illness, and poorer tolerance[9]. The virus (acute respiratory syndrome coronavirus 2 (SARS-CoV-2) which causes COVID-19 has been found to not only damage the respiratory system but affect multiple organ systems. Therefore, it is challenging for medical practitioners when two conditions exist in the same person, especially the elderly[10].

Hip fractures in patients defined as COVID-19 positive, whether preoperatively or postoperatively infected, have a multi-systemic impact that makes perioperative care, the course of surgery, and postoperative rehabilitation more difficult and complex. Compared to uninfected patients, they are exposed to more risks. Recent studies have identified that COVID-19 positive status is an independent predictor of mortality in hip fracture patients[11]. The data collected by Wang *et al*[12] demonstrated that the relative risk of postoperative mortality in COVID-19 positive patients compared to uninfected patients was 5.66 (95%CI: 4.01-7.98; $P < 0.001$). In a retrospective multicenter assessment, Oputa *et al*[13] discovered that the mortality of COVID-19 positive hip fracture patients at 120 d had also increased dramatically (63%:17%, $P < 0.01$). In addition, COVID-19 positive patients were associated with increased length of hospital stay, more admissions to the critical care unit, and a higher risk of perioperative complications compared with COVID negative hip fracture patients[14].

Although the prevention of COVID-19 has become a part of daily life for people all over the world and the virus does place a huge burden on both patient conditions and medical systems, the corresponding coping strategies are constantly being updated. To address these new challenges, increased attention to this comorbidity is necessary not only to gain a thorough understanding of the clinical condition of COVID-19 positive patients but also to provide optimal clinical treatment options for these patients. Here, we performed a narrative review to (1) Provide an overview of the clinical impact in COVID-19 positive hip fracture patients compared to those diagnosed as COVID-19 negative. Also to provide clinicians with predictability so that they can fully prepare in advance; and (2) Provide practical suggestions regarding existing diagnostic and care methods to overcome various difficulties caused by COVID-19.

IMPACT OF COVID-19 ON PATIENTS WITH HIP FRACTURES

The direct impact of COVID-19 itself, as well as quarantine methods against COVID-19, both have a significant influence on the diagnosis and treatment of hip fracture patients. As the age distribution of patients with hip fractures is mainly over 60 years old, most patients will experience multiple complications and cannot completely reclaim their pre-injury physical function[15]. Therefore, if they are further infected with COVID-19, the underlying medical comorbidities, severity of COVID-19 complications, corresponding treatment measures and combined morbidity and mortality of the two conditions remain unclear.

Acute respiratory distress syndrome (ARDS) with widespread alveolar damage, diffuse thrombotic alveolar microvascular occlusion, and inflammatory mediator-associated airway inflammation are three ways the virus damages the lungs histologically. The patient can present with dyspnea, decreased oxygen saturation, and even pulmonary embolism[16]. A significant increase in mortality in patients with COVID-19 and hip fractures has been extensively documented[17-20]. According to recent research, patients with hip fractures who are COVID-19 positive are more vulnerable to complex perioperative complications, such as acute sarcopenia, sepsis, pneumonia, acute respiratory failure, cardiac arrest, and acute kidney injury than patients who are COVID-19 negative[21-23], and are more likely to experience life-threatening complications, such as acute respiratory failure, cardiac arrest, and serious infections[24,25]. These perioperative complications present challenges to surgery. Some complications in certain systems may affect the long-term recovery of hip fracture patients. For example, COVID-19 can cause muscle atrophy, which can then lead to a significant decline in physical function and an increased risk of falls[23]. Following surgery, the virus can introduce a widespread hyperinflammatory state (a cytokine storm), and this condition is further exacerbated by surgery and leads to widespread organ failure. In addition, both diseases can cause a procoagulant state and increase the rate of thromboembolic events[26]. Complex clinical symptoms require extra precise therapeutic intervention and support, as well as a longer length of stay[27]. Prolonged length of stay may be due to barriers to discharge planning, including waiting for COVID-19 positive patients to become negative. COVID-19 positive patients are also more likely to be admitted to the ICU, require ventilators and other medical support equipment after surgery. As COVID-19 mainly affects the lungs, causing symptoms such as dyspnea and decreased oxygen saturation, a ventilator is a necessary auxiliary therapeutic instrument for such patients.

In addition to the acute phase, COVID-19 also causes many long-term, multi-system sequelae, which could greatly delay the rehabilitation of hip fractures. As the COVID-19 pandemic has lasted for more than a year, it is difficult to identify and investigate its long-term sequelae. However, the follow-up of patients who recovered from severe acute respiratory syndrome coronavirus 1 (SARS-COV-1) infection in 2003 reported some results that may explain the long-term prognosis of SARS-COV-2 infection. According to a follow-up study of SARS-CoV-1 survivors, pulmonary ventilation performance in all patients was affected to varying degrees, and the pulmonary diffusion function in more than one-third of patients was considerably damaged[28,29], ultimately affecting the patient's daily life. In addition to respiratory sequelae, disorders such as Alzheimer's Disease, Parkinson's Disease, and Multiple Sclerosis of the nervous system[16], acute sarcopenia of the muscular system, are all associated with COVID-19 and have detrimental effects on hip fractures.

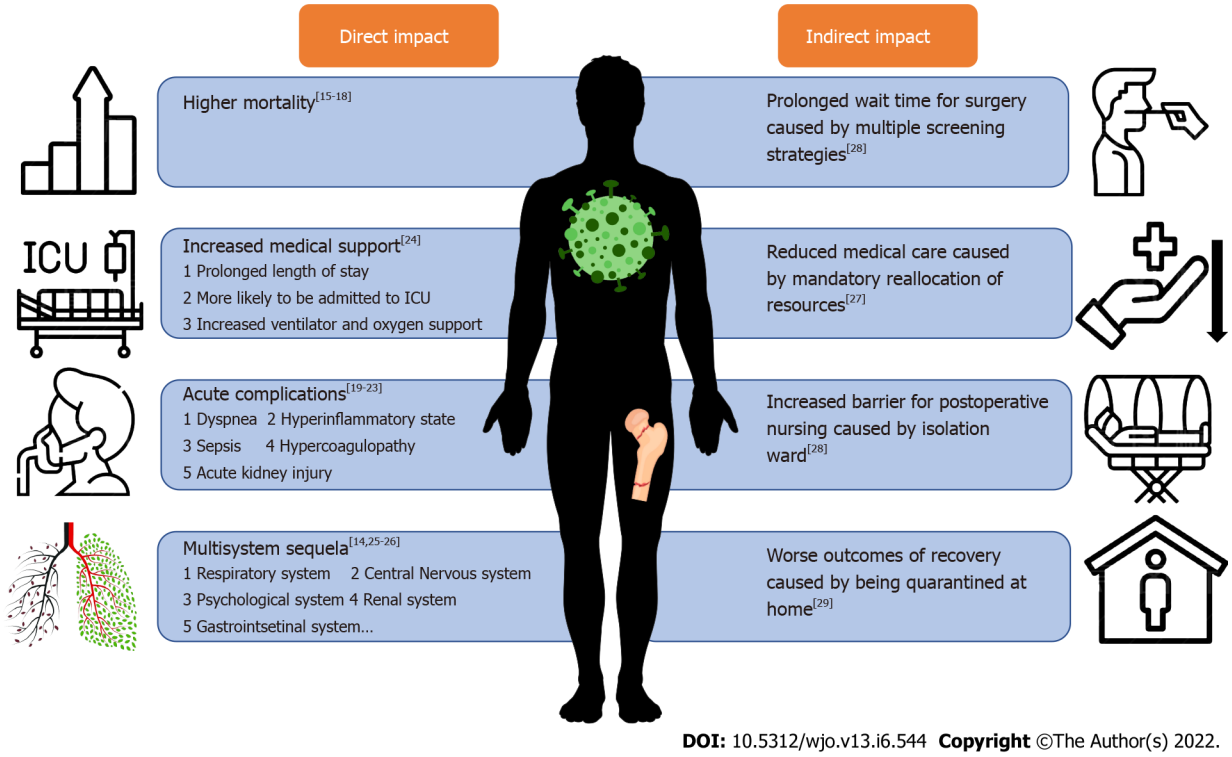
Indirectly, the COVID-19 pandemic has led to a global surge in critically ill patients, hospitals have been forced to reallocate resources to virus screening for patients' admission, setting up special isolation corridors, wards, and operating rooms (ORs), which potentially reduce patients' access to emergency care[30]. For positive or suspected positive patients requiring emergency hip surgery, multiple admission screening, and evaluation, waiting for a designated negative pressure OR will inevitably delay operation time[31]. Post-operatively, as the patient is in an isolation ward, nurses, rehabilitation therapists and physicians have less access, resulting in the absence of routine in-hospital care. After discharge, it is suggested that the patients remain at home. In order to minimize the number of visits to the hospital and reduce the risk of re-infection, frequent follow-up visits are not recommended, which increases the difficulty of long-term postoperative recovery[32].

In conclusion, not only is the virus having a severe impact on patients, but some mandatory adoptions in response to COVID-19 are also potentially having an indirect impact on patients. The effects of COVID-19 on patients with hip fractures are presented in Figure 1.

MANAGEMENT TO ADDRESS THE ISSUE

Admission screening

With no definitive treatment to date, prevention of COVID-19 is critical. To reduce infection between positive patients and other patients and hospital staff, patients admitted to the hospital and accompanying family members must be screened. Diagnosis in COVID-19 patients must be based on epidemiological history, clinical symptoms, imaging, and most importantly, a reverse-transcription PCR of nasopharyngeal and oropharyngeal swab samples[33]. An epidemiological inquiry should be made



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Figure 1 Summary of the impact of coronavirus disease 2019 on patients with hip fractures. ICU: Intensive care unit.

first to determine whether the patient has had close contact (someone who has clearly had contact with an infected person, possibly an asymptomatic carrier of the virus) with an infected person, or a high-risk community in the past 14 d.

Second, diagnostic evidence is further provided by the typical clinical features of COVID-19 infection, including fever, dry cough, and lung imaging features. Blood indicators can also be used as diagnostic indicators, such as white blood cell count, and platelet count[34].

However, 4%-18% of COVID-19 positive patients are asymptomatic carriers of the virus, and the incubation period for COVID-19 is 10 to 14 d, during which time the disease is highly contagious, but the patient may not show characteristics of systemic infection. Therefore, we strongly recommend nucleic acid testing for all hospitalized patients and multiple nucleic acid tests for patients with relevant clinical symptoms and patients with suspected epidemiology within 14 d.

Patient triage (determination of treatment)

It is widely known that early surgery should be performed in elderly patients with hip fractures[35]. If the condition does not allow surgery to be performed and the waiting time for surgery is prolonged, there are many complications associated with prolonged bed rest, such as respiratory failure, urinary and genital tract infection, stones, bedsores, body temperature disorders, deep vein thrombosis, which ultimately affect the recovery of physical functions[36]. However, COVID-19 patient status should play a role in determining the timing of surgery[37]. Recent studies have suggested that mortality in COVID-19 positive patients may be due to virus-driven high inflammation. Significantly elevated levels of multiple inflammatory markers can lead to widespread organ failure. In addition, inflammation due to acute fractures or fracture repair surgery may further exacerbate the status of patients with acute COVID-19. Therefore, surgical thresholds for positive patients should be higher than normal patients, particularly in the advanced-age group. Greater consideration should be given to the possibility of postponing non-emergency procedures and promoting non-surgical treatment. We recommend surgery only for patients with asymptomatic or mild COVID-19 symptoms. Although these patients may have temporary increased oxygen demands postoperatively, they can safely undergo early surgical intervention after appropriate medical optimization[38]. However, we still suggest that if an emergency operation is required, a comprehensive preoperative understanding of the patient's multi-system clinical data and a multidisciplinary group of experts should be established to determine the optimum time of surgery[39]. Minimally invasive surgery, which requires less surgical time and minimizes blood loss, is also recommended for older patients with hip fractures. Conservative treatment with traction may be considered for high-risk COVID-19 patients with hip fractures.

Preoperative and intraoperative matters requiring attention

Rigorous quarantine measures should be immediately followed after the admission of COVID-19 positive patients. It is necessary to rationally design the hospital passage for infected and non-infected, as well as the isolation wards. To prevent cross-infection, COVID-19 positive patients are sent to an isolation ward, where separate teams should be appointed. A channel should be set up for the transfer of COVID-19 patients, but only if the transfer is minimal in the hospital. Those with suspected COVID-19 will be assigned to a separate room until multiple nucleic acid test results are obtained before further treatment. Medical institutions with limited medical technology and resources are advised to transfer patients to special hospitals equipped to treat COVID-19 patients.

The management of special passage, ORs, and isolation wards are strict during the pandemic, which leads to a delay in the operation start time, the extension of surgery duration, difficulty in prognosis observation, and difficulty in multi-disciplinary intervention such as postoperative rehabilitation intervention. Yu *et al*[31] found that the waiting time for surgery during the outbreak period was longer due to mandatory COVID-19 screening. Early surgical intervention can improve patient outcomes. On the contrary, prolonged operation time will increase the incidence of complications. Patients who are scheduled for emergency surgery should be prepared as quickly as possible to reduce the waiting time for patients who meet surgical criteria. With regard to the choice of anesthesia and surgical procedure, there are still no guidelines for patients with hip fractures and COVID-19 to help decide which procedure is the best option. Spinal anesthesia for hip fracture surgery in older adults was not found to be superior to general anesthesia with respect to survival and recovery of ambulation[40]. In addition, the type of surgery affects the length of hospital stay. Open reduction and internal fixation, and closed reduction and percutaneous pinning lead to fewer in-patient days than total hip arthroplasty and hemiarthroplasty, which should be taken into consideration in the anesthesia and surgical method[41].

Designated isolation ORs and surgical instruments should be prepared in advance, and cancellation of elective theatres can be advocated to offset increased waiting time for surgery[42]. In addition, there should be strict standards in the OR. The majority of ORs are under positive pressure. In these circumstances, a specialized OR should be set up with negative pressure. The number of people in the OR must be reduced to a strict minimum and entering and leaving the room should be avoided as much as possible during surgery. Disposable equipment is preferred[43]. When the surgery is complete, thorough disinfection of the OR is imperative before the next operation. Whether symptoms are present or not, all patients require interval testing with further swabs following surgery[44].

Efforts should be made to coordinate intra-departmental allocation and redeployment of human resources during the pandemic. The existing model should be updated to neutralize the impact of COVID-19.

Postoperative care

Postoperative care involves multiple dimensions. Supportive and nutritional treatment should be prioritized after surgery and individualized treatment should be tailored to each patient's specific situation. A multicenter observational cohort study by Rasidovic demonstrated that male sex, smoking, and patients with two or more comorbidities (*e.g.* diabetes, dementia) were associated with higher mortality rates[45]. Extracapsular fractures are also an indicator of high mortality[46]. Smoking, alcohol consumption, and attitudes to COVID-19 may explain the higher prevalence in men than women[47]. Therefore, it is clinically meaningful to strengthen the post-operative care of males, smokers, drinkers, and patients with extracapsular fractures or multiple comorbidities. Multidisciplinary intervention in postoperative care should be provided by an expert team established preoperatively until the patient's clinical symptoms stabilize.

Despite being a respiratory illness, COVID-19 has been found to increase the risk of venous and arterial thromboembolic events[48]. The inflammatory changes in COVID-19 include a prothrombotic state with a high risk of venous thromboembolism[49]. Surgery for hip fractures may further aggravate this pathology. Therefore, postoperative use of anticoagulant drugs is necessary. Psychologically, patients under contact protection are visited less by family members and medical staff, which, together with the psychological impact of a hip fracture, leads to higher rates of anxiety, depression, and delirium[50].

Due to lockdown, people remain at home when they are discharged from the hospital. This highlights the importance of fall prevention strategies for the elderly at home. Patients at high risk of falling as indicated by the Morse Fall Scale or Berg Balance Scale before discharge are advised to wear a hip orthosis or explain the use of crutches. Indoor factors that may contribute to falls must also be corrected [51]. In addition, the unchanging living environment and facilities at home are not conducive to the progress of patients' physical function. The benefits of physical therapy should be explained to patients to avoid fragility fractures. Patients are advised to engage in low-intensity aerobic exercise (*e.g.* indoor walking for 30 min or more per day) to strengthen muscle and balance functions. Similarly, patients with muscle atrophy should be trained in a progressive manner, and patients with previous fragility fractures are at significantly increased risk of dysmotility syndrome and skeletal muscle function deficit that might presumably increase the risk of a new incident fracture[52]. Adequate daily calcium intake and regular calcium density checks should be emphasized in elderly female patients. As hospitals

remain high-risk areas for COVID-19 infection, post-surgery follow-up and rehabilitation plan updates can be consulted *via* smartphone apps and telemedicine facilities, avoiding in-person visits and sudden suspension of medical institutions[53].

With the rapid spread of COVID-19, access to safe and effective vaccines is critical in ending the COVID-19 pandemic. Studies have shown that among hospitalized patients infected with COVID-19, despite receiving only one dose of the vaccine, mortality rates are significantly lower and hospital courses are simpler in the vaccinated group[54]. Although vaccination entails certain risks for the elderly population, especially those with underlying medical conditions and frailty, studies continue to show that the benefits of vaccination far outweigh the potential risks in frail elderly (*e.g*. long-term care facilities)[55]. Thus, we believe it is necessary to vaccinate patients with hip fractures.

CONCLUSION

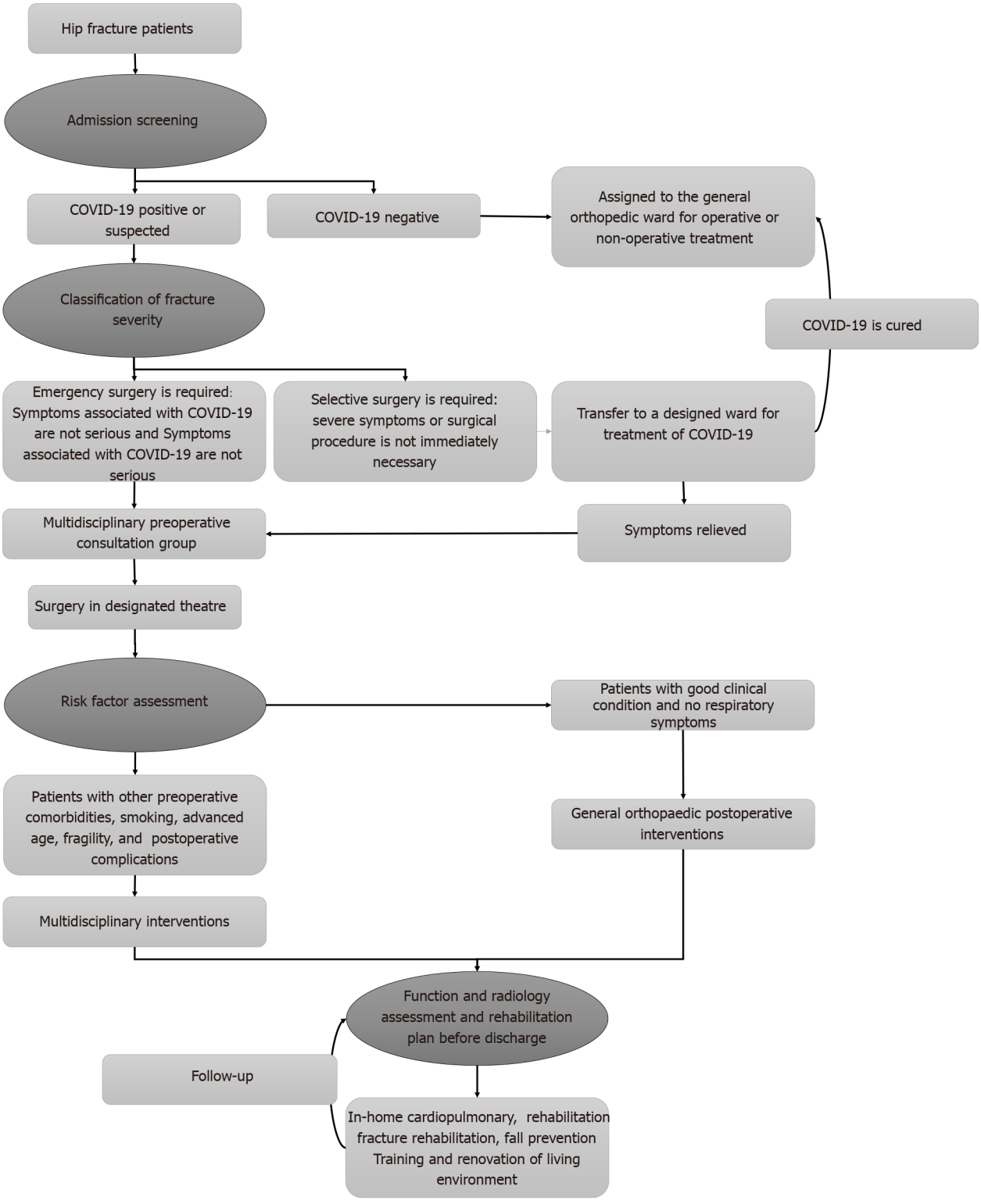
COVID-19 can have significant adverse effects on patients with hip fractures, both directly and indirectly. However, the impact can be effectively reduced by monitoring all aspects of the post-admission process.

In this minireview, we outlined the direct physiological consequences introduced by COVID-19, as well as the practical issues that arise throughout the treatment and diagnosis procedure. By understanding these potential concerns in advance, staff in associated departments will be capable of making rational decisions and acquiring a comprehensive aspect of the progression of the disease. In the following section, we summarized the existing experimental evidence and offer a set of optimized suggestions to improve patient outcomes. The model consists of admission screening, patient triage (determination of treatment), preoperative and intraoperative matters requiring attention, and postoperative care (the clinical flowchart is presented in Figure 2). However, these recommendations are not the solution for all situations. As the prevalence of the epidemic varies across the nations, as does the medical capacity of hospitals, certain studies are required to reach a consensus that could suit more regions and circumstances. Notably, the suggested managements presented above apply not just to COVID-19 now, but also to any future highly contagious respiratory illnesses. Although the epidemic in China is now firmly under control, thanks to the government's attention, we should not be complacent, as the emergence of new and extremely contagious strains of COVID-19, such as Delta and Omicron, could make another outbreak possible. In addition, there are still certain countries in the world where suppression of COVID-19 is not ideal. Thus, research regarding COVID-19 co-morbidity in patients with hip fractures is expected to continue. In the context of COVID-19 ramping wildly, it is imperative to optimize treatment strategies to turn the tables globally.

Fighting the COVID-19 pandemic has become a regular part of our lives, as well as a mountain that healthcare providers must overcome. Elderly people account for a large proportion of COVID-19 deaths [56,57] as they have more comorbidities and are more fragile. Prevention and care in this subgroup are essential, and when combined with a life-threatening trauma, this influences their clinical outcomes. We believe that it is necessary to form a multidisciplinary expert panel, which can not only comprehensively evaluate the timing of surgery for patients, but also provide a reasonable multidisciplinary treatment plan after surgery.

PERSPECTIVE

At present, there is limited information on the perioperative risk of increased mortality in patients who require urgent hip fracture surgery and are infected with COVID-19. Konda *et al*[58] utilized the Score for Trauma Triage in the Geriatric and Middle-Aged, which was originally a tool to predict postoperative in-hospital mortality in trauma patients, to create a research-based strategy for operative vs. nonoperative management of patients with hip fractures who were COVID-19 positive/suspected. For subsequent research, we strongly suggest that more experiments could further refine this risk assessment form into a more comprehensive and adaptable one. The assessment may include the patient's respiratory symptoms and fracture severity rating (which should be given primary weight), presence of complications, inflammatory indicators (such as C-reactive protein, procalcitonin, lactates), clinical scores (*e.g.*, American Society of Anesthesiologists grade, Alvarado score, sequential organ failure assessment score), smoking status, *etc.* Use of this form could provide surgeons, physicians, and other healthcare practitioners with relevant clinical information, helping them make standardized therapeutic decisions by foreseeing potential outcomes. It has been reported that patients with asymptomatic infection or with only mild symptoms show a lower risk of perioperative morbidity and mortality associated with operations. Therefore, the surgical risk assessment for such patients should be reconsidered from that for patients with symptomatic infection[59]. However, there are no cohort studies to prove the effect of asymptomatic infection on surgical or prognostic recovery of hip fracture. Subsequent studies should identify the criteria for assessing surgical risk in these patients and whether asymptomatic infection has an impact on hip fracture outcomes, and if so, what impact.



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Figure 2 Clinical flowchart of the treatment of patients with hip fractures who are coronavirus disease 2019 positive. COVID-19: Coronavirus disease.

In addition, as COVID-19 is a severe acute respiratory infection[60], most articles have placed an emphasis on the short-term clinical impact caused by the disease. However, it is well known that hip fracture patients require regular sustained rehabilitation[61]. Currently, available experimental data does not assist in comprehending the influence of COVID-19 on the long-term recovery of hip fracture. According to the report by McDonald[62], one of the sequelae that can occur in COVID-19 patients, especially in those who develop ARDS during infection, is pulmonary fibrosis. Pulmonary fibrosis results from excessive deposition of extracellular matrix molecules such as collagen, laminin, and fibronectin in the lung parenchyma. Eventually, the efficiency of gas exchange decreases due to

thickened alveolar membrane. Patients will then suffer from decreased lung function and exercise intolerance, fatigue, and dyspnea, which severely delay the restoration process compared to those who possess fully functional lungs. It is critical to make early predictions of the possible long-term sequelae of COVID-19 and to formulate appropriate prevention and intervention strategies. Whether continuous low-intensity physical therapy combined with cardiopulmonary breathing training can better facilitate patients to restore prior functions deserves further investigation.

FOOTNOTES

Author contributions: Qin HC and He Z conducted the original search and wrote the first draft of the paper; Qin HC and Luo ZW screened the selected articles and contributed to subsequent drafts of the manuscript; Zhu YL generated the original idea of this study and provided suggestions; Qin HC and He Z made equal contributions to the work.

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REFERENCES

1 **Veronese N**, Maggi S. Epidemiology and social costs of hip fracture. *Injury* 2018; **49**: 1458-1460 [PMID: 29699731 DOI: 10.1016/j.injury.2018.04.015]
2 **Magaziner J**, Mangione KK, Orwig D, Baumgarten M, Magder L, Terrin M, Fortinsky RH, Gruber-Baldini AL, Beamer BA, Tosteson ANA, Kenny AM, Shardell M, Binder EF, Koval K, Resnick B, Miller R, Forman S, McBride R, Craik RL. Effect of a Multicomponent Home-Based Physical Therapy Intervention on Ambulation After Hip Fracture in Older Adults: The CAP Randomized Clinical Trial. *JAMA* 2019; **322**: 946-956 [PMID: 31503309 DOI: 10.1001/jama.2019.12964]
3 **Yoo JI**, Lee YK, Koo KH, Park YJ, Ha YC. Concerns for Older Adult Patients with Acute Hip Fracture. *Yonsei Med J* 2018; **59**: 1240-1244 [PMID: 30450859 DOI: 10.3349/ymj.2018.59.10.1240]
4 **Ohsfeldt RL**, Choong CK, Mc Collam PL, Abedtash H, Kelton KA, Burge R. Inpatient Hospital Costs for COVID-19 Patients in the United States. *Adv Ther* 2021; **38**: 5557-5595 [PMID: 34609704 DOI: 10.1007/s12325-021-01887-4]
5 **Wiersinga WJ**, Rhodes A, Cheng AC, Peacock SJ, Prescott HC. Pathophysiology, Transmission, Diagnosis, and Treatment of Coronavirus Disease 2019 (COVID-19): A Review. *JAMA* 2020; **324**: 782-793 [PMID: 32648899 DOI: 10.1001/jama.2020.12839]
6 **Koutserimpas C**, Raptis K, Tsakalou D, Papadaki C, Magarakis G, Kourelis K, Samonis G, Alpantaki K. The Effect of Quarantine Due to COVID-19 Pandemic in Surgically Treated Fractures in Greece: a Two-Center Study. *Maedica (Bucur)* 2020; **15**: 332-334 [PMID: 33312248]
7 **Kumar Jain V**, Lal H, Kumar Patralekh M, Vaishya R. Fracture management during COVID-19 pandemic: A systematic review. *J Clin Orthop Trauma* 2020; **11**: S431-S441 [PMID: 32774008 DOI: 10.1016/j.jcot.2020.06.035]
8 **Zhu Y**, Chen W, Xin X, Yin Y, Hu J, Lv H, Li W, Deng X, Zhu C, Zhu J, Zhang J, Ye F, Chen A, Wu Z, Ma Z, Zhang X, Gao F, Li J, Wang C, Zhang Y, Hou Z. Epidemiologic characteristics of traumatic fractures in elderly patients during the outbreak of coronavirus disease 2019 in China. *Int Orthop* 2020; **44**: 1565-1570 [PMID: 32350584 DOI: 10.1007/s00264-020-04575-0]
9 **Damiot A**, Pinto AJ, Turner JE, Gualano B. Immunological Implications of Physical Inactivity among Older Adults during the COVID-19 Pandemic. *Gerontology* 2020; **66**: 431-438 [PMID: 32585674 DOI: 10.1159/000509216]
10 **Kumar A**, Haider Y, Passey J, Khan R, Gaba S, Kumar M. Mortality Predictors in Covid-19 Positive Patients with Fractures: A Systematic Review. *Bull Emerg Trauma* 2021; **9**: 51-59 [PMID: 34150914 DOI: 10.30476/BEAT.2021.87742]
11 **Abrunhosa VM**, Soares CP, Batista Possidonio AC, Alvarenga AV, Costa-Felix RP, Costa ML, Mermelstein C. Induction of skeletal muscle differentiation in vitro by therapeutic ultrasound. *Ultrasound Med Biol* 2014; **40**: 504-512 [PMID: 24412173 DOI: 10.1016/j.ultrasmedbio.2013.10.013]
12 **Wang KC**, Xiao R, Cheung ZB, Barbera JP, Forsh DA. Early mortality after hip fracture surgery in COVID-19 patients: A systematic review and meta-analysis. *J Orthop* 2020; **22**: 584-591 [PMID: 33223732 DOI: 10.1016/j.jor.2020.11.012]
13 **Oputa TJ**, Dupley L, Bourne JT; North West COVID NOF Study Group. One Hundred Twenty-Day Mortality Rates for Hip Fracture Patients with COVID-19 Infection. *Clin Orthop Surg* 2021; **13**: 135-143 [PMID: 34094003 DOI:

10.4055/cios20286]
14 **Kayani B**, Onochie E, Patil V, Begum F, Cuthbert R, Ferguson D, Bhamra JS, Sharma A, Bates P, Haddad FS. The effects of COVID-19 on perioperative morbidity and mortality in patients with hip fractures. *Bone Joint J* 2020; **102-B**: 1136-1145 [PMID: 32634023 DOI: 10.1302/0301-620X.102B9.BJJ-2020-1127.R1]
15 **Turesson E**, Ivarsson K, Thorngren KG, Hommel A. Hip fractures - Treatment and functional outcome. The development over 25 years. *Injury* 2018; **49**: 2209-2215 [PMID: 30366830 DOI: 10.1016/j.injury.2018.10.010]
16 **Wang F**, Kream RM, Stefano GB. Long-Term Respiratory and Neurological Sequelae of COVID-19. *Med Sci Monit* 2020; **26**: e928996 [PMID: 33177481 DOI: 10.12659/MSM.928996]
17 **Biarnés-Suñé A**, Solà-Enríquez B, González Posada MÁ, Teixidor-Serra J, García-Sánchez Y, Manrique Muñóz S. Impact of the COVID-19 pandemic on the mortality of the elderly patient with a hip fracture. *Rev Esp Anestesiol Reanim (Engl Ed)* 2021; **68**: 65-72 [PMID: 33461768 DOI: 10.1016/j.redar.2020.10.003]
18 **Clement ND**, Ng N, Simpson CJ, Patton RFL, Hall AJ, Simpson AHRW, Duckworth AD. The prevalence, mortality, and associated risk factors for developing COVID-19 in hip fracture patients: a systematic review and meta-analysis. *Bone Joint Res* 2020; **9**: 873-883 [PMID: 33350316 DOI: 10.1302/2046-3758.912.BJR-2020-0473.R1]
19 **Al Farii H**, Al Rawahi S, Samaila E, Lavini F, Magnan B, Al Maskari S. Thirty-Day Mortality in COVID-19 Positive Patients With Hip Fractures: A Case-Series and Literature Review. *Geriatr Orthop Surg Rehabil* 2020; **11**: 2151459320972681 [PMID: 33282447 DOI: 10.1177/2151459320972681]
20 **Lim MA**, Pranata R. Coronavirus disease 2019 (COVID-19) markedly increased mortality in patients with hip fracture - A systematic review and meta-analysis. *J Clin Orthop Trauma* 2021; **12**: 187-193 [PMID: 32958988 DOI: 10.1016/j.jcot.2020.09.015]
21 **Egol KA**, Konda SR, Bird ML, Dedhia N, Landes EK, Ranson RA, Solasz SJ, Aggarwal VK, Bosco JA 3rd, Furgiuele DL, Ganta A, Gould J, Lyon TR, McLaurin TM, Tejwani NC, Zuckerman JD, Leucht P; NYU COVID Hip Fracture Research Group. Increased Mortality and Major Complications in Hip Fracture Care During the COVID-19 Pandemic: A New York City Perspective. *J Orthop Trauma* 2020; **34**: 395-402 [PMID: 32482976 DOI: 10.1097/BOT.0000000000001845]
22 **Knisely A**, Zhou ZN, Wu J, Huang Y, Holcomb K, Melamed A, Advincula AP, Lalwani A, Khoury-Collado F, Tergas AI, St Clair CM, Hou JY, Hershman DL, D'Alton ME, Huang YY, Wright JD. Perioperative Morbidity and Mortality of Patients With COVID-19 Who Undergo Urgent and Emergent Surgical Procedures. *Ann Surg* 2021; **273**: 34-40 [PMID: 33074900 DOI: 10.1097/SLA.0000000000004420]
23 **Welch C**, Greig C, Masud T, Wilson D, Jackson TA. COVID-19 and Acute Sarcopenia. *Aging Dis* 2020; **11**: 1345-1351 [PMID: 33269092 DOI: 10.14336/AD.2020.1014]
24 **Perrotta F**, Corbi G, Mazzeo G, Boccia M, Aronne L, D'Agnano V, Komici K, Mazzarella G, Parrella R, Bianco A. COVID-19 and the elderly: insights into pathogenesis and clinical decision-making. *Aging Clin Exp Res* 2020; **32**: 1599-1608 [PMID: 32557332 DOI: 10.1007/s40520-020-01631-y]
25 **Kayani B**, Onochie E, Patil V, Begum F, Cuthbert R, Ferguson D, Bhamra J, Sharma A, Bates P, Haddad FS. Infographic: The effects of COVID-19 on perioperative morbidity and mortality in patients with hip fractures. *Bone Joint J* 2020; **102-B**: 1279-1280 [PMID: 32993335 DOI: 10.1302/0301-620X.102B10.BJJ-2020-1774]
26 **Tsantes AG**, Papadopoulos DV, Trikoupis IG, Goumenos S, Piovani D, Tsante KA, Mavrogenis AF, Vaiopoulos AG, Koulouvaris P, Nikolopoulos GK, Papagelopoulos PJ, Bonovas S, Tsantes AE. The Procoagulant Effect of COVID-19 on the Thrombotic Risk of Patients with Hip Fractures Due to Enhanced Clot Strength and Fibrinolysis Shutdown. *J Clin Med* 2021; **10** [PMID: 34362178 DOI: 10.3390/jcm10153397]
27 **Galivanche AR**, Mercier MR, Schneble CA, Brand J, Pathak N, Varthi AG, Rubin LE, Grauer JN. Clinical Characteristics and Perioperative Complication Profiles of COVID-19-Positive Patients Undergoing Hip Fracture Surgery. *J Am Acad Orthop Surg Glob Res Rev* 2021; **5** [PMID: 34653097 DOI: 10.5435/JAAOSGlobal-D-21-00104]
28 **Hui DS**, Wong KT, Ko FW, Tam LS, Chan DP, Woo J, Sung JJ. The 1-year impact of severe acute respiratory syndrome on pulmonary function, exercise capacity, and quality of life in a cohort of survivors. *Chest* 2005; **128**: 2247-2261 [PMID: 16236881 DOI: 10.1378/chest.128.4.2247]
29 **Ngai JC**, Ko FW, Ng SS, To KW, Tong M, Hui DS. The long-term impact of severe acute respiratory syndrome on pulmonary function, exercise capacity and health status. *Respirology* 2010; **15**: 543-550 [PMID: 20337995 DOI: 10.1111/j.1440-1843.2010.01720.x]
30 **Baker T**, Schell CO, Petersen DB, Sawe H, Khalid K, Mndolo S, Rylance J, McAuley DF, Roy N, Marshall J, Wallis L, Molyneux E. Essential care of critical illness must not be forgotten in the COVID-19 pandemic. *Lancet* 2020; **395**: 1253-1254 [PMID: 32246914 DOI: 10.1016/S0140-6736(20)30793-5]
31 **Yu P**, Wu C, Zhuang C, Ye T, Zhang Y, Liu J, Wang L. The patterns and management of fracture patients under COVID-19 outbreak in China. *Ann Transl Med* 2020; **8**: 932 [PMID: 32953732 DOI: 10.21037/atm-20-4174]
32 **Pass B**, Vajna E, Knauf T, Rascher K, Aigner R, Eschbach D, Lendemans S, Knobe M, Schoeneberg C; Registry for Geriatric Trauma (ATR-DGU). COVID-19 and Proximal Femur Fracture in Older Adults-A Lethal Combination? *J Am Med Dir Assoc* 2022; **23**: 576-580 [PMID: 34678268 DOI: 10.1016/j.jamda.2021.09.027]
33 **Parasher A**. COVID-19: Current understanding of its Pathophysiology, Clinical presentation and Treatment. *Postgrad Med J* 2021; **97**: 312-320 [PMID: 32978337 DOI: 10.1136/postgradmedj-2020-138577]
34 **Hall AJ**, Clement ND, Farrow L, MacLullich AMJ, Dall GF, Scott CEH, Jenkins PJ, White TO, Duckworth AD; IMPACT-Scot Study Group. IMPACT-Scot report on COVID-19 and hip fractures. *Bone Joint J* 2020; **102-B**: 1219-1228 [PMID: 32634029 DOI: 10.1302/0301-620X.102B9.BJJ-2020-1100.R1]
35 **Kristan A**, Omahen S, Tosounidis TH, Cimerman M. When does hip fracture surgery delay affects the length of hospital stay? *Eur J Trauma Emerg Surg* 2022; **48**: 701-708 [PMID: 33388817 DOI: 10.1007/s00068-020-01565-0]
36 **Chen J**, Wang X, Qian H, Ye J, Qian J, Hua J. Correlation between common postoperative complications of prolonged bed rest and quality of life in hospitalized elderly hip fracture patients. *Ann Palliat Med* 2020; **9**: 1125-1133 [PMID: 32498527 DOI: 10.21037/apm-20-891]
37 **De Simone B**, Chouillard E, Di Saverio S, Pagani L, Sartelli M, Biffl WL, Coccolini F, Pieri A, Khan M, Borzellino G, Campanile FC, Ansaloni L, Catena F. Emergency surgery during the COVID-19 pandemic: what you need to know for

practice. *Ann R Coll Surg Engl* 2020; **102**: 323-332 [PMID: 32352836 DOI: 10.1308/rcsann.2020.0097]
38 **Cheung ZB**, Forsh DA. Early outcomes after hip fracture surgery in COVID-19 patients in New York City. *J Orthop* 2020; **21**: 291-296 [PMID: 32549692 DOI: 10.1016/j.jor.2020.06.003]
39 **Ojeda-Thies C**, Cuarental-García J, García-Gómez E, Salazar-Zamorano CH, Alberti-Maroño J, Ramos-Pascua LR. Hip fracture care and mortality among patients treated in dedicated COVID-19 and non-COVID-19 circuits. *Eur Geriatr Med* 2021; **12**: 749-757 [PMID: 33550563 DOI: 10.1007/s41999-021-00455-x]
40 **Neuman MD**, Feng R, Carson JL, Gaskins LJ, Dillane D, Sessler DI, Sieber F, Magaziner J, Marcantonio ER, Mehta S, Menio D, Ayad S, Stone T, Papp S, Schwenk ES, Elkassabany N, Marshall M, Jaffe JD, Luke C, Sharma B, Azim S, Hymes RA, Chin KJ, Sheppard R, Perlman B, Sappenfield J, Hauck E, Hoeft MA, Giska M, Ranganath Y, Tedore T, Choi S, Li J, Kwofie MK, Nader A, Sanders RD, Allen BFS, Vlassakov K, Kates S, Fleisher LA, Dattilo J, Tierney A, Stephens-Shields AJ, Ellenberg SS; REGAIN Investigators. Spinal Anesthesia or General Anesthesia for Hip Surgery in Older Adults. *N Engl J Med* 2021; **385**: 2025-2035 [PMID: 34623788 DOI: 10.1056/NEJMoa2113514]
41 **Thakore RV**, Foxx AM, Lang MF, Sathiyakumar V, Obremskey WT, Boyce RH, Ehrenfeld JM, Sethi MK. Operative intervention for geriatric hip fracture: does type of surgery affect hospital length of stay? *Am J Orthop (Belle Mead NJ)* 2015; **44**: 228-232 [PMID: 25950538]
42 **Macey ARM**, Butler J, Martin SC, Tan TY, Leach WJ, Jamal B. 30-day outcomes in hip fracture patients during the COVID-19 pandemic compared to the preceding year. *Bone Jt Open* 2020; **1**: 415-419 [PMID: 33215132 DOI: 10.1302/2633-1462.17.BJO-2020-0077.R1]
43 **Grelat M**, Pommier B, Portet S, Amelot A, Barrey C, Leroy HA, Madkouri R. Patients with Coronavirus 2019 (COVID-19) and Surgery: Guidelines and Checklist Proposal. *World Neurosurg* 2020; **139**: e769-e773 [PMID: 32344143 DOI: 10.1016/j.wneu.2020.04.155]
44 **Hadfield JN**, Gray AC. The Evolving COVID-19 Effect on Hip Fracture Patients. *Injury* 2020; **51**: 1411-1412 [PMID: 32553412 DOI: 10.1016/j.injury.2020.06.006]
45 **Rasidovic D**, Ahmed I, Thomas C, Kimani PK, Wall P, Mangat K; NOF-COV19 Study Collaborative Group. Impact of COVID-19 on clinical outcomes for patients with fractured hip: a multicentre observational cohort study. *Bone Jt Open* 2020; **1**: 697-705 [PMID: 33263109 DOI: 10.1302/2633-1462.111.BJO-2020-0132.R1]
46 **Raheman FJ**, Rojoa DM, Nayan Parekh J, Berber R, Ashford R. Meta-analysis and metaregression of risk factors associated with mortality in hip fracture patients during the COVID-19 pandemic. *Sci Rep* 2021; **11**: 10157 [PMID: 33980936 DOI: 10.1038/s41598-021-89617-2]
47 **Bwire GM**. Coronavirus: Why Men are More Vulnerable to Covid-19 Than Women? *SN Compr Clin Med* 2020; **2**: 874-876 [PMID: 32838138 DOI: 10.1007/s42399-020-00341-w]
48 **Ali MAM**, Spinler SA. COVID-19 and thrombosis: From bench to bedside. *Trends Cardiovasc Med* 2021; **31**: 143-160 [PMID: 33338635 DOI: 10.1016/j.tcm.2020.12.004]
49 **Dobesh PP**, Trujillo TC. Coagulopathy, Venous Thromboembolism, and Anticoagulation in Patients with COVID-19. *Pharmacotherapy* 2020; **40**: 1130-1151 [PMID: 33006163 DOI: 10.1002/phar.2465]
50 **Sprague E**, Reynolds S, Brindley P. Patient Isolation Precautions: Are They Worth It? *Can Respir J* 2016; **2016**: 5352625 [PMID: 27445547 DOI: 10.1155/2016/5352625]
51 **Upadhyaya GK**, Iyengar K, Jain VK, Vaishya R. Challenges and strategies in management of osteoporosis and fragility fracture care during COVID-19 pandemic. *J Orthop* 2020; **21**: 287-290 [PMID: 32523258 DOI: 10.1016/j.jor.2020.06.001]
52 **Iolascon G**, Moretti A, Giamattei MT, Migliaccio S, Gimigliano F. Prevalent fragility fractures as risk factor for skeletal muscle function deficit and dysmobility syndrome in post-menopausal women. *Aging Clin Exp Res* 2015; **27** Suppl 1: S11-S16 [PMID: 26204997 DOI: 10.1007/s40520-015-0417-1]
53 **Cuffaro L**, Di Lorenzo F, Bonavita S, Tedeschi G, Leocani L, Lavorgna L. Dementia care and COVID-19 pandemic: a necessary digital revolution. *Neurol Sci* 2020; **41**: 1977-1979 [PMID: 32556746 DOI: 10.1007/s10072-020-04512-4]
54 **Alsaffar WA**, Alwesaibi AA, Alhaddad MJ, Alsenan ZK, Alsheef HJ, Alramadan SH, Aljassas HA, Alsaghirat MA, Alzahrani HJ. The Effectiveness of COVID-19 Vaccines in Improving the Outcomes of Hospitalized COVID-19 Patients. *Cureus* 2022; **14**: e21485 [PMID: 35103227 DOI: 10.7759/cureus.21485]
55 **Lv G**, Yuan J, Xiong X, Li M. Mortality Rate and Characteristics of Deaths Following COVID-19 Vaccination. *Front Med (Lausanne)* 2021; **8**: 670370 [PMID: 34055843 DOI: 10.3389/fmed.2021.670370]
56 **Mi B**, Chen L, Xiong Y, Xue H, Zhou W, Liu G. Characteristics and Early Prognosis of COVID-19 Infection in Fracture Patients. *J Bone Joint Surg Am* 2020; **102**: 750-758 [PMID: 32379114 DOI: 10.2106/JBJS.20.00390]
57 **Grasselli G**, Greco M, Zanella A, Albano G, Antonelli M, Bellani G, Bonanomi E, Cabrini L, Carlesso E, Castelli G, Cattaneo S, Cereda D, Colombo S, Coluccello A, Crescini G, Forastieri Molinari A, Foti G, Fumagalli R, Iotti GA, Langer T, Latronico N, Lorini FL, Mojoli F, Natalini G, Pessina CM, Ranieri VM, Rech R, Scudeller L, Rosano A, Storti E, Thompson BT, Tirani M, Villani PG, Pesenti A, Cecconi M; COVID-19 Lombardy ICU Network. Risk Factors Associated With Mortality Among Patients With COVID-19 in Intensive Care Units in Lombardy, Italy. *JAMA Intern Med* 2020; **180**: 1345-1355 [PMID: 32667669 DOI: 10.1001/jamainternmed.2020.3539]
58 **Konda SR**, Ranson RA, Solasz SJ, Dedhia N, Lott A, Bird ML, Landes EK, Aggarwal VK, Bosco JA 3rd, Furgiuele DL, Gould J, Lyon TR, McLaurin TM, Tejwani NC, Zuckerman JD, Leucht P, Ganta A, Egol KA; NYU COVID Hip Fracture Research Group. Modification of a Validated Risk Stratification Tool to Characterize Geriatric Hip Fracture Outcomes and Optimize Care in a Post-COVID-19 World. *J Orthop Trauma* 2020; **34**: e317-e324 [PMID: 32815845 DOI: 10.1097/BOT.0000000000001895]
59 **Weitzner ZN**, Schumm MA, Hu T, Wu JX. Short-term perioperative outcomes among patients with concurrent asymptomatic and mild SARS-CoV-2 infection: A retrospective, multicenter study. *Surgery* 2021 [PMID: 35109982 DOI: 10.1016/j.surg.2021.12.024]
60 **Carpenter CR**, Mudd PA, West CP, Wilber E, Wilber ST. Diagnosing COVID-19 in the Emergency Department: A Scoping Review of Clinical Examinations, Laboratory Tests, Imaging Accuracy, and Biases. *Acad Emerg Med* 2020; **27**: 653-670 [PMID: 32542934 DOI: 10.1111/acem.14048]
61 **Lee SY**, Yoon BH, Beom J, Ha YC, Lim JY. Effect of Lower-Limb Progressive Resistance Exercise After Hip Fracture

Surgery: A Systematic Review and Meta-Analysis of Randomized Controlled Studies. *J Am Med Dir Assoc* 2017; **18**: 1096.e19-1096.e26 [PMID: 29033325 DOI: 10.1016/j.jamda.2017.08.021]

62 **McDonald LT**. Healing after COVID-19: are survivors at risk for pulmonary fibrosis? *Am J Physiol Lung Cell Mol Physiol* 2021; **320**: L257-L265 [PMID: 33355522 DOI: 10.1152/ajplung.00238.2020]

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MINIREVIEWS

Topical use of tranexamic acid: Are there concerns for cytotoxicity?

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Abstract

Tranexamic acid (TXA) has revolutionized modern blood management in orthopaedic surgery, especially in total joint arthroplasty, by significantly reducing blood loss and transfusion rates. It is an antifibrinolytic agent and a synthetic derivative of the amino acid lysine, which can inhibit the activation of plasminogen and the fibrin breakdown process. The administration of TXA can be intravenous (IV), topical, and oral. In patients where the IV administration is contraindicated, topical use is preferred. Topical administration of the drug theoretically increases concentration at the operative site with reduced systemic exposure, reduces cost, and gives the surgeon the control of the administration. According to recent studies, topical administration of TXA is not inferior compared to IV administration, in terms of safety and efficacy. However, there are concerns regarding the possible toxicity in the cartilage tissue with the topical use of TXA mainly in hemiarthroplasty operations of the hip, unilateral knee arthroplasties, total knee arthroplasties where the patella is not resurfaced, and other intraarticular procedures, like anterior cruciate ligament reconstruction. The purpose of the present review is to present all the recent updates on the use of TXA focusing on the toxicity on chondrocytes and the articular cartilage that may or may not be provoked by the topical use of TXA.

Key Words: Tranexamic acid; Topical use; Cytotoxicity; Orthopaedic surgery

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Core Tip: Tranexamic acid (TXA) is an antifibrinolytic agent and is associated with decreased blood loss in surgical procedures. It is widely used in major orthopaedic procedures in order to decrease blood transfusion needs. TXA can be administered intravenously; however, topical administration of the drug increases concentration at the operative site. There are concerns that this increased concentration may cause toxicity in the cartilage tissue. In this review, we present the recent literature regarding the cytotoxic effects of the topical administration of TXA.

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INTRODUCTION

Tranexamic acid (TXA) is an antifibrinolytic agent and a synthetic derivative of the amino acid lysine, which can inhibit the activation of plasminogen and the fibrin breakdown process[1]. Plasminogen is a glycoprotein pro-enzyme which is produced in the liver. Plasminogen molecules are folded into loops and lysine binding sites are located at the end of these loops. These lysine binding sites on plasminogen are connected with lysine residues on fibrin. Tissue plasminogen activator is also released by endothelial cells and binds to fibrin, causing the conversion of plasminogen to plasmin. Plasmin cleaves fibrin into small fragments like D-dimers. This abruption causes the exposure of more lysine residues to plasminogen, therefore accelerating fibrinolysis[2]. The fact that TXA is a synthetic derivative of the amino acid lysine causes the attachment of the lysine residues to the lysine binding sites on plasminogen, thus preventing the binding of plasminogen to fibrin and blocking its activation to plasmin[2,3]. At higher concentrations, TXA is also a noncompetitive inhibitor of plasmin, therefore it stabilizes the clot formation[4]. Numerous studies conducted in animal tissue samples showed that TXA increases thrombus formation in a dose-dependent manner[5]. Plasminogen receptors are also located on endothelial cells, monocytes, lymphocytes, and platelets, which indicates the role of plasminogen in inflammation. Thus, TXA may have another role, by inhibiting this procedure, too[6].

TXA is associated with decreased blood loss in surgical procedures and inhibits the activation of plasminogen to a greater extent in comparison with another major antifibrinolytic agent, epsilon-aminocaproic acid (EACA)[6,7]. TXA does not seem to be associated with a major difference in transfusion rates when compared with EACA[6].

After administration of a mean TXA intravenous dose of 10 mg/kg on healthy individuals, peak concentration of the drug is observed at 1 h after administration and its half-life is approximately 2 h, with 90% excreted at 24 h. TXA remains in serum for approximately 8 h and in tissues for 17 h. Nevertheless, these pharmacokinetic factors may be different in patients that have been through major trauma and the efficacious TXA levels in these patients may differ with those in healthy individuals[7].

Nevertheless, there are concerns that topical use of TXA may be toxic for chondrocytes and surrounding soft tissue, as stated in numerous studies[3,4,8-11]. The current manuscript is a narrative review and its purpose is to present the recent literature regarding the effect of the topical use of TXA, whether it can cause toxicity on chondrocytes and articular cartilage, and if there is a standard safe level of the drug at which it can be harmless and efficacious.

USE OF TRANEXAMIC ACID (TXA) IN ORTHOPEDIC SURGERY

TXA can be effective to reduce blood loss in major surgical procedures and severe traumatic conditions. Thus, TXA can decrease the blood transfusion needs without increasing the risk of thromboembolic events. Many studies have supported its use in major orthopedic procedures[8,9,12-17]. Fillingham *et al*[9] showed that TXA administration can reduce blood loss during total knee arthroplasty by approximately 100 mL, compared to placebo. Yi *et al*[8] have also shown that a group of patients that received TXA after total hip arthroplasty had a lower blood transfusion rate in comparison with the placebo group. These patients also had a lower mean total blood loss varying form approximately 200 mL to 350 mL in comparison with the placebo group[8]. Also, Li *et al*[12] proved that a group of patients treated with TXA after spinal surgery had significantly lower blood loss and the number of patients that required blood transfusion was notably reduced, irrespective of using TXA at high or low dosage[10]. Generally, TXA has demonstrated efficacy in hip[8], knee[9], and shoulder[14] arthroplasties as well as in spinal surgery[12] and anterior cruciate ligament reconstruction[13]. Farrow *et al*[15] found moderate quality evidence that TXA administration can reduce blood transfusion rate in patients undergoing hip fracture surgery, so the effectiveness of TXA in this surgical procedure is under investigation.

Numerous studies have also proved its efficacy during trauma operations based on data from the CRASH-2 trial and showed that TXA can reduce the mortality rates in trauma patients due to bleeding [16,17]. Few studies suggested the lack of potential benefit from the use of TXA in major orthopaedic procedures. For example, Lack *et al*[18] concluded that there are no significant differences in blood loss and transfusion rates between TXA and placebo. However, the number of the studies supporting this conclusion is very limited and this heterogeneity can potentially be attributed to the variety of methods used for calculating the blood loss.

CONTRAINDICATIONS

Despite its wide use in major orthopaedic operations, TXA cannot be used in certain cases. More specifically, there are absolute and relative contraindications for TXA administration. Hypersensitivity and allergy to TXA as well as active thromboembolic disease and fibrinolytic conditions with consumption coagulopathy are the absolute contraindications for TXA[19].

The relative contraindications must consider the association between risk and benefit of TXA[19]. Relative contraindications include renal dysfunction, thrombosis disorders, and preexisting coagulopathy or oral anticoagulants[19]. TXA is also contraindicated in patients with a high risk of seizures[19,20]. Pregnancy is another contraindication, but TXA can be administered when it is vitally indicated[20].

TXA ADMINISTRATION AND SAFE LEVELS

TXA can be administrated through the intravenous (IV) and oral route as well as topical. However, IV and oral TXA administration is associated with an increased risk of systematic complications, such as thromboembolic events[21]. Ker *et al*[22] showed that although IV TXA can minimize blood loss during surgeries, it is arguable whether it can cause major thromboembolic events in the future. In addition, since TXA is a derivative of the amino acid lysine and goes through ionization in physiologic environment, it is expected that its absorption through membranes may be inadequate. Therefore, its bioavailability will be moderate and higher doses of the drug may be required in order to reach the desirable levels of TXA in articular cartilage, thus causing major systematic complications[23]. On the other hand, topical administration of the drug may have many benefits like increased concentration at the operative site with reduced systemic exposure, cost reduction, and surgeon control[24]. It has been also shown that topical administration is not inferior to IV administration, in terms of safety and efficacy [25,26]. Abdel *et al*[26] and Xu *et al*[27] showed that IV administration of TXA has no advantage over topical administration of the drug as they both caused lower rates of blood transfusion and these two groups had no clinically significant differences. However, many authors investigated the combined route of administration of TXA, suggesting that combining both topical and IV administration of the drug could potentially have a beneficial effect in reducing blood loss during major orthopaedic procedures[28]. It is not clear yet whether this combined route can lead to a better result, concerning the blood loss and the blood transfusion rates[29]. Dong *et al*[28] suggested that combined topical and intravenous administration can further reduce blood loss while Li *et al*[29] did not support this conclusion and suggested that this technique has no additional benefits.

TXA can be administered topically using various techniques[30]. Intra-articular or peri-articular application is the most common technique of TXA administration[30]. Some surgeons perform a peri-operative wash of the drug in order to avoid its topical side effects[30]. Clamping drainage is another proposed technique which creates an intra-articular tamponade, thus producing temporary haemostasis and increasing the tissue contact time with the drug[31].

TXA was supported as a safe drug for topical use in a few studies (Table 1). In the study of Degirmenci *et al*[1], an *in vivo* study on experimental animals, TXA seemed to have a significant contribution to the healing of osteochondral defects. This was observed not only macroscopically but also histopathologically, where samples treated with TXA had clearly better recovery than the control groups. More specifically, the macroscopic examination of the animal samples was performed by observing any abnormality of the location, color, shape, and size of the tissue *in situ*, 4 and 8 wk after TXA administration. The group that received TXA seemed to have better recovery, after both 4 and 8 wk, in comparison with the control group. Histopathologically, the group that received TXA had higher regeneration rate of subchondral tissue and cartilage tissue repair rate than the control group. No problems were mentioned in terms of safety of the drug. Ambra *et al*[3], in a study carried out on experimental animal samples, also supported the efficacy and safety of the drug. Images of full-thickness cartilage sections showed a similar number of live cells, as well as a minimal presence of dead cells, no matter the duration of incubation and the concentrations of TXA administered. Moreover, this study suggested that TXA doses up to 4 mg/mL for up to 6 h did not seem to have any detrimental effect on cell viability. This study was carried out on experimental animal tissue; however, samples of the animals that were chosen are the closest to the human samples. Also, TXA doses were adapted

Table 1 Characteristics and outcomes of studies that considered tranexamic acid as a safe drug

Ref.	Tissue	Doses	Time of exposure	Outcome
Ambra *et al*[3], 2017	Animal samples (Yucatan minipigs)	1, 2, and 4 mg/mL	1, 3, and 6 h	No effect on cell viability
Marmotti *et al* [4], 2016	Human samples (cartilage and synovial tissues)	7 mg/mL in both cartilage and synovial tissues	2 wk for cartilage tissue and 48 h for synovial tissue	No effect on synoviocyte morphology
Degirmenci *et al* [1], 2019	Animal samples (rabbits)	Not mentioned	Not mentioned	Healing rate was improved after TXA administration and no detrimental effects were observed
Bolam *et al*[29], 2020	Human and animal samples	1, 2, 4, 20, 25, 50, and 100 mg/mL	10 min, 1 h, 2 h, 4 h, 24 h, and 48 h	No effect on cell viability and morphology when treated at doses lower than 20 mg/mL
Wang *et al*[33], 2021	Human samples (fibroblast cells)	12, 5, 25, 50, and 100 mg/mL	10 min, 6 h, 12 h, 24 h, and 48 h	No effect on fibroblast cells in a time- and dose-dependent way

TXA: Tranexamic acid.

depending on the thickness of each tissue sample.

Marmotti *et al*[4] conducted another study, in which human tissue samples were harvested. This study also supported the hypothesis that TXA is a safe drug. Low doses of TXA (7 mg/mL) were administered for 48 h and the samples were assessed after short (immediately after exposure) and long time of exposure (1, 2, and 6 wk). The drug was completely safe and did not have any effect on cells' ability to migrate. Also, cells treated with TXA did not seem to have any effects in terms of morphology, no matter the time of exposure, in comparison with the control group. In this study, a cell phenotype analysis was also conducted between the group that received TXA and the control group. Results showed that TXA exposure had no significant effects on cell phenotype after both long term and brief time of exposure. A further biochemical analysis investigated any possible alteration in glycosaminoglycan (GAG) concentration but no significant difference was noted between the TXA-treated group and the control group. Bolam *et al*[30] supported in their scoping review that TXA is a safe drug, when administered topically. More specifically, they included 15 studies that were considered eligible for their review. Some of these studies used human tissue samples while others used animal tissue samples. The authors concluded that there is a dose-dependent effect of TXA on chondrocytes, tenocytes, synoviocytes, and periosteum-derived cells. Both human and animal tissue samples were exposed to varying doses of the drug (1, 2, 4, 20, 25, 50, and 100 mg/mL) for different times of exposure (from 10 min to 48 h). The cultures that were exposed to TXA doses higher than 20 mg/mL had reduced cell viability and altered cell morphology. Thus, treatment with doses lower than 20 mg/mL had no significant detrimental effects. This conclusion supports the safety of the drug in a dose-dependent way.

Wang *et al*[32] studied the effects of topical administration of TXA on human fibroblast cells. These cells where cultured for a brief (10 min) and long time (6, 12, 24, and 48 h) after exposure to different drug concentrations (12.5, 25, 50, and 100 mg/mL). The authors suggested that there is a time and dose-dependent way in which TXA affects the fibroblast cells. More specifically, the samples had no detrimental effects when exposed to a high concentration of TXA (100 mg/mL) but for a brief time (10 min) or when exposed to a lower concentration of TXA (12.5 mg/mL) for a long time (from 6 to 48 h). However, high concentrations of the drug for a long period of time had clear effects concerning cell viability.

HOW TXA AFFECTS CELL CYCLE

In eukaryotic cells, the cell cycle has five different phases, G0, G1, S, G2, and M in order. In G0 phase, there is a cell cycle arrest, while in G1 phase, cells are gaining mass and activating growth signals. G2 is also a phase where cells are growing and organizing their genome. In S phase, the duplication of the chromosomes occurs, and in M-phase, the duplicated chromosomes and the cell are divided[33]. In order to investigate the way in which TXA affects the biological functions of cells, Goderecci *et al*[34] assessed the effects of the drug on the cell cycle. Cells incubated with TXA for only 10 min did not seem to have any significant alterations in terms of cell cycle profile. However, when cells were treated with TXA for 24 h or 48 h, there were significant changes. The number of cells in the G0/G1 phase was decreased, while there was an increase of cells in the G2/M phase and a significant increase of cells in the S phase, when compared to the control group and the group incubated for 10 min. As for the cells treated with TXA for 10 min and incubated with fresh medium for 24 h, there was an increased number of cells in the G0/G1 phase and a considerable decrease of cells in the G2/M phase, approaching the cell cycle profile of cells in the control group. Another study that investigated the potential mechanism by

which TXA could cause cytotoxicity, suggests that a caspase-3-dependent apoptotic mechanism could be responsible for the detrimental effects of TXA in human cells[10].

TXA CYTOTOXICITY

However, intraarticular TXA administration leads to exposure of intact articular cartilage to the drug. Consequently, there have been many concerns that TXA may cause detrimental effects on articular cartilage and have cytotoxic effects on chondrocytes, especially since chondrocyte death is related with the development of further cartilage degeneration and osteoarthritis[3].

TXA can cause massive cytotoxicity (Table 2). McLean *et al*[10] conducted a study where human tendon tissue, synovial tissue, and cartilage tissue were obtained during major orthopaedic surgeries and TXA seemed to have significant effects on each kind of tissue[26]. All samples were exposed to a wide range of TXA concentrations (1, 50, and 100 mg/mL) for 4 h, 16 h, or 24 h[10]. A significant reduction in cell viability as well as high rates of apoptosis were observed in all types of tissue in a time- and dose-dependent way. McLean *et al*[10] tried to identify potential mechanisms that may cause these high rates of apoptosis and they came to the conclusion that increased amount of apoptotic proteins occurred in tenocytes and chondrocytes, in comparison with the control group, thus suggesting that TXA-mediated cell death may be caused by apoptotic proteins like caspase-3. Lower doses had a lower impact on cells but still influenced cell function. Moreover, the authors reported that a high percentage of cell death occurred in the control group, most likely due to tissue drying between surgical harvesting and completion of graft preparation and also due to age-related changes, as most of the samples were harvested from elderly patients. However, they did not seem to have any major impact on the study outcome as these factors affected every sample group.

Parker *et al*[11] also proved the drug's cytotoxic effects by exposing human chondrocytes on 2D and 3D cultures to TXA (10, 20, and 40 mg/mL for 3 h and 6 h). On 2D cultures, chondrocytes were seeded onto numerous tissue culture plastic trays while on 3D cultures the authors tried to simulate the 3D nature of articular cartilage by using chondrocyte-laden gelatine-methacryloyl (GelMA) hydrogels. However, this study also suggests that there may be a safe dose for the drug. More specifically, on the 2D cell-culture model, the drug had significant effects on cell viability at doses between 20 mg/mL and 40 mg/mL. On the contrary, cells treated with doses lower than 20 mg/mL did not seem to be affected by the drug. In 3D cultures, cell viability was decreased in a time- and dose-dependent way. Furthermore, Parker *et al*[11] inspected the effect of TXA on glycosaminoglycan GAG concentration and found no significant differences between the control group and the groups exposed to the drug, thus suggesting that high doses of TXA can cause cell death but they do not affect the quality of the cartilage tissue. Another study, carried out by Tuttle *et al*[24] on murine and bovine chondrocytes, also reached the conclusion that TXA can be cytotoxic. Treatment with high doses of TXA (50 and 100 mg/mL) had clear detrimental effects on chondrocyte viability in a time-dependent way. However, cells treated with 25 mg/mL had no considerable decrease in cell viability. Moreover, in this study it was observed that there was a small but significant loss of GAG in groups that were treated with TXA in comparison with the control groups, in contrary to the conclusion of Parker *et al*[11] suggesting that TXA does not affect GAG concentrations. These studies did not take into consideration all the pharmacological factors that normally take place inside the human joint. The time of cell exposure to TXA in an *in vitro* study is longer than the time of exposure that theoretically occurs *in vivo* where other kinds of cells (inflammatory cells and platelets) could have a potential role in the drug's clearance. As a result, McLean *et al*[10] suggested that the *in vitro* nature of these studies might have an influence on the results.

Another interesting finding is that washing the drug out of the cultures after a few minutes of exposure seems to decrease TXA's cytotoxicity[34]. According to Goderecci *et al*[34], when the drug was washed out of the cultures, only the highest dose of TXA (100 mg/mL) affected cell cycle profile and cell viability. However, 20, 50, and 70 mg/mL of TXA did not have any detrimental effect on cell function when the drug was washed out after 10 min of incubation. These samples were compared with other samples that were exposed to same TXA concentrations for 24 h and 48 h without washing the drug out, in which TXA had significant effects at doses higher than 50 mg/mL. Tuttle *et al*[24] observed the same outcome when animal tissue samples were incubated with TXA for different amounts of time. Samples were incubated with various TXA concentrations for three different time points, 8 h, 24 h, and 48 h. Samples incubated with high TXA levels presented complete cell death, no matter the time of exposure. However, at low levels of TXA, cell viability was notably lower in samples incubated for 24 h when compared with samples incubated for 8 h. Complete cell death was observed in the 48 h sample, thus supporting the conclusion that the amount of time that cells are exposed to TXA is a major factor concerning the cytotoxicity of the drug.

A few studies observed the effects of TXA in different kind of tissue samples. Marmotti *et al*[4] carried out a study, in which human cartilage and synovial biopsies were obtained from patients during major orthopedic procedures. Each kind of tissue was incubated with the same concentration of TXA for the same amount of time. TXA had the same effects on those groups, and it showed no cytotoxicity on both samples and was completely safe for all types of cells. Other investigators harvested synovial and

Table 2 Characteristics and outcomes of studies that proved cytotoxic effects of tranexamic acid

Ref.	Tissue	Doses	Time of exposure	Outcome
Tuttle *et al* [22], 2015	Animal samples (bovine and murine)	25, 50, and 100 mg/mL in murine chondrocytes and 100 mg/mL in bovine chondrocytes	8, 24, and 48 h for both bovine and murine explants	Cell viability was notably decreased as TXA dose and incubation time were increased
Parker *et al* [28], 2018	Human samples (chondrocytes on 2D and 3D models)	5, 10, 20, and 40 mg/mL in 2D cultures and 10, 20, and 40 mg/mL in 3D cultures	3, 6 and 12 h for the 2D models and 3 h for the 3D models	Cell viability, cellular metabolic activity, and number of attached cells were considerably decreased in a dose-dependent way
Goderecci *et al*[26], 2019	Human samples (chondrocytes)	20, 50, 70, and 100 mg/mL	10 min, 24 h, and 48 h	Chondrocyte viability and cell cycle profile were affected in a dose- and time-dependent way
McLean *et al* [27], 2019	Human samples (tendon, synovial, and cartilage tissues)	0, 1, 50, and 100 mg/mL	1, 4, and 24 h	Cell viability and apoptosis rate were affected at higher doses

TXA: Tranexamic acid.

cartilage samples from patients who were also treated with the same TXA doses for the same amount of time[10]. Apoptosis rate was approximately the same for all three types of tissue. Viability was decreased in all types of cells at different time points for each dose level; however, the detrimental result was the same in all tissue samples. Thus, TXA seems to interact, in the same way, with all types of tissue and it has the same effects in all types of cells.

EFFECTS OF TXA ON GLYCOSAMINOGLYCAN CONCENTRATION

Marmotti *et al*[4] proved in their study that TXA did not cause any significant change in GAG concentration by conducting a biochemical analysis. Moreover, Parker *et al*[11] supported this conclusion as they noted no significant difference in GAG concentration between the TXA-treated cells and the placebo-treated cells and thus suggested that TXA had no effect on the quality of cartilage tissue irrespective of the drug's toxicity to chondrocytes[27]. However, Tuttle *et al*[24] observed in their study that TXA had a small but significant effect on GAG concentration, in contrary to the conclusions of Marmotti *et al*[4] and Parker *et al*[11]. This differentiation may be due to the nonidentical period for which cells were exposed to TXA, thus causing a different effect on GAG concentration in each study. Parker *et al*[11] used a shorter and more clinically appropriate length of exposure to the drug to come to a more accurate conclusion[27].

EFFECTS OF TXA DEPENDING ON PATIENT AGE

TXA may have different effects on chondrocytes depending on the age of patients. Marmotti *et al*[4] obtained human biopsies from young donors (patients between 14 and 40 years old) in order to inspect the short- and long-term effects of TXA (7 mg/mL) on these samples. Biopsies from young donors did not seem to develop any kind of damage in terms of morphologic and immunophenotypic characteristics no matter the time of exposure. However, McLean *et al*[10] harvested tissue samples from older patients (specific age not provided) undergoing total knee and hip arthroplasties. In this study, just like previously, biopsies were checked for any effect of TXA after a short and a long period of incubation. Cell viability was significantly reduced after 24 h of exposure to TXA, regardless of the TXA dose. This suggests that TXA may be safer for younger patients and cause more serious detrimental effects in older patients.

FUTURE PERSPECTIVES

While many studies have been carried out on tissue samples, it is important to carry out *in vivo* studies in order to support the data that were obtained from *in vitro* studies, considering all the pharmacological interactions inside the human joint such as drug clearance and tissue distribution, and observe the development of any side effects. Additionally, more studies are needed to confirm the possibility that there is a safe TXA dose for topical use.

Safety of the drug is quite important as well as effectiveness of the drug. Studies should not only suggest the safe doses of TXA but also inspect the healing process at each dose level and if TXA

contributes in the recovery process. Moreover, more data is needed to clarify the molecular mechanism of TXA cytotoxicity. This could help us understand the process through which TXA causes detrimental effects in human cells and make clear its molecular correlation with cell apoptosis.

Effects of TXA on GAG concentration are only discussed in a limited number of studies. This is an interesting topic that should be furtherly discussed. Many studies suggest that TXA is cytotoxic, but we should also clarify whether TXA causes any significant differences in GAG concentration. This will help us to conclude whether the drug affects the quality of cartilage tissue, irrespective of any cytotoxic effects that the drug may have.

A topic that is not greatly discussed and should be furtherly investigated is the cost *vs* benefit of a potential therapeutic intervention with topical TXA. Clinical studies should be carried out to investigate whether the efficacy of topical use of TXA is as great as the cost of the drug and if there is a point to use the drug topically instead of IV.

CONCLUSION

Given the low evidence of the available literature and the lack of clinical data, there seems to be no clear outcome considering the effects of the drug on chondrocytes, as some studies suggest that TXA is clearly cytotoxic[10,11,24,34] while others support the safety of the drug[1,3,4]. Most of these studies came to the conclusion that TXA can have effects on chondrocytes in a time- and dose-dependent way [10,11,24,34]. Higher doses can cause detrimental effects on cells especially when they are exposed to the drug for a long period of time[24,34]. Other studies suggest that TXA seems to have the same effects on every type of tissue inside the human joint and each type of cell interacts in the same way with the drug [4,10]. Nevertheless, some studies proved that there seems to be a safe TXA level at which the healing process can continue without any effects on the joint function[1,3,4,11,24]. There are indications that high doses of TXA can affect the cell cycle profile, but this suggestion needs further investigation[34]. The suggestion that the effects of TXA depend on the age group of the patients also needs further investigation[4,10].

FOOTNOTES

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REFERENCES

1 **Degirmenci E**, Ozturan KE, Sahin AA, Yilmaz F, Kaya YE. Effects of tranexamic acid on the recovery of osteochondral defects treated by microfracture and acellular matrix scaffold: an experimental study. *J Orthop Surg Res* 2019; **14**: 105 [PMID: 30992060 DOI: 10.1186/s13018-019-1144-7]

2 **Cesarman-Maus G**, Hajjar KA. Molecular mechanisms of fibrinolysis. *Br J Haematol* 2005; **129**: 307-321 [PMID: 15842654 DOI: 10.1111/j.1365-2141.2005.05444.x]

3 **Ambra LF**, de Girolamo L, Niu W, Phan A, Spector M, Gomoll AH. No effect of topical application of tranexamic acid on articular cartilage. *Knee Surg Sports Traumatol Arthrosc* 2019; **27**: 931-935 [PMID: 29119286 DOI: 10.1007/s00167-017-4746-9]

4 **Marmotti A**, Mattia S, Mangiavini L, Bonasia DE, Bruzzone M, Dettoni F, Rosso F, Blonna D, Rossi R, Castoldi F, Peretti GM. Tranexamic acid effects on cartilage and synovial tissue: an *in vitro* study for a possible safe intra-articular use. *J Biol Regul Homeost Agents* 2016; **30**: 33-40 [PMID: 28002898]

5 **Ng W**, Jerath A, Wąsowicz M. Tranexamic acid: a clinical review. *Anaesthesiol Intensive Ther* 2015; **47**: 339-350 [PMID: 25797505 DOI: 10.5603/AIT.a2015.0011]

6 **Bradley KE**, Ryan SP, Penrose CT, Grant SA, Wellman SS, Attarian DE, Green CL, Risoli T Jr, Bolognesi MP. Tranexamic acid or epsilon-aminocaproic acid in total joint arthroplasty? *Bone Joint J* 2019; **101-B**: 1093-1099 [PMID: 31474134 DOI: 10.1302/0301-620X.101B9.BJJ-2018-1096.R1]

7 **Ramirez RJ**, Spinella PC, Bochicchio GV. Tranexamic Acid Update in Trauma. *Crit Care Clin* 2017; **33**: 85-99 [PMID: 27894501 DOI: 10.1016/j.ccc.2016.08.004]

8 **Yi Z**, Bin S, Jing Y, Zongke Z, Pengde K, Fuxing P. Tranexamic Acid Administration in Primary Total Hip Arthroplasty: A Randomized Controlled Trial of Intravenous Combined with Topical Versus Single-Dose Intravenous Administration. *J Bone Joint Surg Am* 2016; **98**: 983-991 [PMID: 27307358 DOI: 10.2106/JBJS.15.00638]

9 **Fillingham YA**, Ramkumar DB, Jevsevar DS, Yates AJ, Shores P, Mullen K, Bini SA, Clarke HD, Schemitsch E, Johnson RL, Memtsoudis SG, Sayeed SA, Sah AP, Della Valle CJ. The Efficacy of Tranexamic Acid in Total Knee Arthroplasty: A Network Meta-Analysis. *J Arthroplasty* 2018; **33**: 3090-3098.e1 [PMID: 29805106 DOI: 10.1016/j.arth.2018.04.043]

10 **McLean M**, McCall K, Smith IDM, Blyth M, Kitson SM, Crowe LAN, Leach WJ, Rooney BP, Spencer SJ, Mullen M, Campton JL, McInnes IB, Akbar M, Millar NL. Tranexamic acid toxicity in human periarticular tissues. *Bone Joint Res* 2019; **8**: 11-18 [PMID: 30800295 DOI: 10.1302/2046-3758.81.BJR-2018-0181.R1]

11 **Parker JD**, Lim KS, Kieser DC, Woodfield TBF, Hooper GJ. Is tranexamic acid toxic to articular cartilage when administered topically? *Bone Joint J* 2018; **100-B**: 404-412 [PMID: 29589496 DOI: 10.1302/0301-620X.100B3.BJJ-2017-1135.R1]

12 **Li ZJ**, Fu X, Xing D, Zhang HF, Zang JC, Ma XL. Is tranexamic acid effective and safe in spinal surgery? *Eur Spine J* 2013; **22**: 1950-1957 [PMID: 23657623 DOI: 10.1007/s00586-013-2774-9]

13 **Karaaslan F**, Karaoğlu S, Yurdakul E. Reducing Intra-articular Hemarthrosis After Arthroscopic Anterior Cruciate Ligament Reconstruction by the Administration of Intravenous Tranexamic Acid: A Prospective, Randomized Controlled Trial. *Am J Sports Med* 2015; **43**: 2720-2726 [PMID: 26337246 DOI: 10.1177/0363546515599629]

14 **Gillespie R**, Shishani Y, Joseph S, Streit JJ, Gobezie R. Neer Award 2015: A randomized, prospective evaluation on the effectiveness of tranexamic acid in reducing blood loss after total shoulder arthroplasty. *J Shoulder Elbow Surg* 2015; **24**: 1679-1684 [PMID: 26480877 DOI: 10.1016/j.jse.2015.07.029]

15 **Farrow LS**, Smith TO, Ashcroft GP, Myint PK. A systematic review of tranexamic acid in hip fracture surgery. *Br J Clin Pharmacol* 2016; **82**: 1458-1470 [PMID: 27492116 DOI: 10.1111/bcp.13079]

16 **CRASH-2 trial collaborators**, Shakur H, Roberts I, Bautista R, Caballero J, Coats T, Dewan Y, El-Sayed H, Gogichaishvili T, Gupta S, Herrera J, Hunt B, Iribhogbe P, Izurieta M, Khamis H, Komolafe E, Marrero MA, Mejía-Mantilla J, Miranda J, Morales C, Olaomi O, Olldashi F, Perel P, Peto R, Ramana PV, Ravi RR, Yutthakasemsunt S. Effects of tranexamic acid on death, vascular occlusive events, and blood transfusion in trauma patients with significant haemorrhage (CRASH-2): a randomised, placebo-controlled trial. *Lancet* 2010; **376**: 23-32 [PMID: 20554319 DOI: 10.1016/S0140-6736(10)60835-5]

17 **Roberts I**, Perel P, Prieto-Merino D, Shakur H, Coats T, Hunt BJ, Lecky F, Brohi K, Willett K; CRASH-2 Collaborators. Effect of tranexamic acid on mortality in patients with traumatic bleeding: prespecified analysis of data from randomised controlled trial. *BMJ* 2012; **345**: e5839 [PMID: 22968527 DOI: 10.1136/bmj.e5839]

18 **Lack WD**, Crist BD, Seymour RB, Harvin W, Karunakar MA; TXA Study Group‖. Effect of Tranexamic Acid on Transfusion: A Randomized Clinical Trial in Acetabular Fracture Surgery. *J Orthop Trauma* 2017; **31**: 526-530 [PMID: 28938283 DOI: 10.1097/BOT.0000000000000968]

19 **Goobie SM**, Faraoni D. Tranexamic acid and perioperative bleeding in children: what do we still need to know? *Curr Opin Anaesthesiol* 2019; **32**: 343-352 [PMID: 30893114 DOI: 10.1097/ACO.0000000000000728]

20 **Pabinger I**, Fries D, Schöchl H, Streif W, Toller W. Tranexamic acid for treatment and prophylaxis of bleeding and hyperfibrinolysis. *Wien Klin Wochenschr* 2017; **129**: 303-316 [PMID: 28432428 DOI: 10.1007/s00508-017-1194-y]

21 **Kim C**, Park SS, Davey JR. Tranexamic acid for the prevention and management of orthopedic surgical hemorrhage: current evidence. *J Blood Med* 2015; **6**: 239-244 [PMID: 26345147 DOI: 10.2147/JBM.S61915]

22 **Ker K**, Edwards P, Perel P, Shakur H, Roberts I. Effect of tranexamic acid on surgical bleeding: systematic review and cumulative meta-analysis. *BMJ* 2012; **344**: e3054 [PMID: 22611164 DOI: 10.1136/bmj.e3054]

23 **Karaman R**, Ghareeb H, Dajani KK, Scrano L, Hallak H, Abu-Lafi S, Mecca G, Bufo SA. Design, synthesis and *in vitro* kinetic study of tranexamic acid prodrugs for the treatment of bleeding conditions. *J Comput Aided Mol Des* 2013; **27**: 615-635 [PMID: 23881217 DOI: 10.1007/s10822-013-9666-2]

24 **Tuttle JR**, Feltman PR, Ritterman SA, Ehrlich MG. Effects of Tranexamic Acid Cytotoxicity on In Vitro Chondrocytes. *Am J Orthop (Belle Mead NJ)* 2015; **44**: E497-E502 [PMID: 26665251]

25 **Gomez-Barrena E**, Ortega-Andreu M, Padilla-Eguiluz NG, Pérez-Chrzanowska H, Figueredo-Zalve R. Topical intra-articular compared with intravenous tranexamic acid to reduce blood loss in primary total knee replacement: a double-blind, randomized, controlled, noninferiority clinical trial. *J Bone Joint Surg Am* 2014; **96**: 1937-1944 [PMID: 25471907 DOI: 10.2106/JBJS.N.00060]

26 **Abdel MP**, Chalmers BP, Taunton MJ, Pagnano MW, Trousdale RT, Sierra RJ, Lee YY, Boettner F, Su EP, Haas SB, Figgie MP, Mayman DJ. Intravenous Versus Topical Tranexamic Acid in Total Knee Arthroplasty: Both Effective in a Randomized Clinical Trial of 640 Patients. *J Bone Joint Surg Am* 2018; **100**: 1023-1029 [PMID: 29916929 DOI: 10.2106/JBJS.17.00908]

27 **Xu JW**, Qiang H, Li TL, Wang Y, Wei XX, Li F. Efficacy of topical *vs* intravenous tranexamic acid in reducing blood loss and promoting wound healing in bone surgery: A systematic review and meta-analysis. *World J Clin Cases* 2021; **9**: 4210-4220 [PMID: 34141783 DOI: 10.12998/wjcc.v9.i17.4210]

28 **Dong Y**, Liang J, Tong B, Shen J, Zhao H, Li Q. Combined topical and intravenous administration of tranexamic acid further reduces postoperative blood loss in adolescent idiopathic scoliosis patients undergoing spinal fusion surgery: a randomized controlled trial. *BMC Musculoskelet Disord* 2021; **22**: 663 [PMID: 34372818 DOI: 10.1186/s12891-021-04562-5]

29 **Li S**, Lu Q, Guo X, Zhang M, Miao Z, Luo D, Liu P. Intravenous Combined with Topical Tranexamic Acid Administration Has No Additional Benefits Compared with Intravenous Administration Alone in High Tibial Osteotomy: A Retrospective Case-Control Study. *Orthop Surg* 2020; **12**: 515-523 [PMID: 32162488 DOI: 10.1111/os.12652]

30 **Bolam SM**, O'Regan-Brown A, Paul Monk A, Musson DS, Cornish J, Munro JT. Toxicity of tranexamic acid (TXA) to intra-articular tissue in orthopaedic surgery: a scoping review. *Knee Surg Sports Traumatol Arthrosc* 2021; **29**: 1862-1871 [PMID: 32860523 DOI: 10.1007/s00167-020-06219-7]

31 **Stucinskas J**, Tarasevicius S, Cebatorius A, Robertsson O, Smailys A, Wingstrand H. Conventional drainage *vs* four hour clamping drainage after total knee arthroplasty in severe osteoarthritis: a prospective, randomised trial. *Int Orthop* 2009; **33**: 1275-1278 [PMID: 18925394 DOI: 10.1007/s00264-008-0662-4]

32 **Wang F**, Wang SG, Yang Q, Nan LP, Cai TC, Wu DS, Zhang L. Cytotoxicity and Effect of Topical Application of Tranexamic Acid on Human Fibroblast in Spine Surgery. *World Neurosurg* 2021; **153**: e380-e391 [PMID: 34224885 DOI: 10.1016/j.wneu.2021.06.125]

33 **Barnum KJ**, O'Connell MJ. Cell cycle regulation by checkpoints. *Methods Mol Biol* 2014; **1170**: 29-40 [PMID: 24906307 DOI: 10.1007/978-1-4939-0888-2_2]

34 **Goderecci R**, Giusti I, Necozione S, Cinque B, D'Ascenzo S, Dolo V, Calvisi V. Short exposure to tranexamic acid does not affect, in vitro, the viability of human chondrocytes. *Eur J Med Res* 2019; **24**: 15 [PMID: 30795796 DOI: 10.1186/s40001-019-0373-x]

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MINIREVIEWS

Managements of osteoporotic vertebral compression fractures: A narrative review

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Abstract

Osteoporotic vertebral compression fractures (OVCFs) are the most common fragility fracture and significantly influence the quality of life in the elderly. Currently, the literature lacks a comprehensive narrative review of the management of OVCFs. The purpose of this study is to review background information, diagnosis, and surgical and non-surgical management of the OVCFs. A comprehensive search of PubMed and Google Scholar for articles in the English language between 1980 and 2021 was performed. Combinations of the following terms were used: compression fractures, vertebral compression fractures, osteoporosis, osteoporotic compression fractures, vertebroplasty, kyphoplasty, bisphosphonates, calcitonin, and osteoporosis treatments. Additional articles were also included by examining the reference list of articles found in the search. OVCFs, especially those that occur over long periods, can be asymptomatic. Symptoms of acute OVCFs include pain localized to the mid-line spine, a loss in height, and decreased mobility. The primary treatment regimens are pain control, medication management, vertebral augmentation, and anterior or posterior decompression and reconstructions. Pain control can be achieved with acetaminophen or nonsteroidal anti-inflammatory drugs for mild pain or opioids and/or calcitonin for moderate to severe pain. Bisphosphonates and denosumab are the first-line treatments for osteoporosis. Vertebroplasty and kyphoplasty are reserved for patients who have not found symptomatic relief through conservative methods and are effective in achieving pain relief. Vertebroplasty is less technical and cheaper than kyphoplasty but could have more complications. Calcium and vitamin D supplementation can have a protective and therapeutic effect. Management of OVCFs must be combined with multiple approaches. Appropriate exercises and activity modification are important in fracture prevention. Medication with different mechanisms of action is a critical long-term causal treatment strategy. The minimally invasive surgical interventions such as

vertebroplasty and kyphoplasty are reserved for patients not responsive to conservative therapy and are recognized as efficient stopgap treatment methods. Posterior decompression and fixation or Anterior decompression and reconstruction may be required if neurological deficits are present. The detailed pathogenesis and related targeted treatment options still need to be developed for better clinical outcomes.

Key Words: Vertebral body; Osteoporosis; Fragility fractures; Osteoporotic vertebral compression fractures; Kyphoplasty; Vertebroplasty

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Core Tip: Management of osteoporotic vertebral compression fractures must be combined with multiple approaches. Appropriate exercises and activity modification are important in fracture prevention. Medication with different mechanisms of action is a critical long-term causal treatment strategy. The minimally invasive surgical interventions such as vertebroplasty and kyphoplasty are reserved for patients not responsive to conservative therapy and are recognized as efficient stopgap treatment methods. Posterior decompression and fixation or Anterior decompression and reconstruction may be required if neurological deficits are present.

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INTRODUCTION

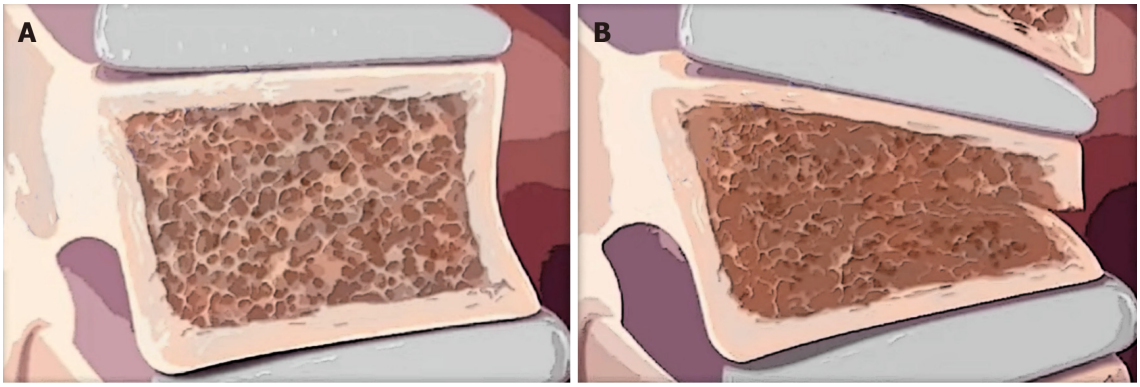
Osteoporotic vertebral compression fractures (OVCFs) are the most common fragility fracture and are a marker of osteoporosis[1]. In the United States, approximately 700,000 OVCFs occur annually[2]. OVCFs and hip fractures are estimated to cost between $10 and $15 billion annually, indicating the immense burden of these conditions[3]. Along with the financial burden, osteoporotic fractures are associated with a decrease in health-related quality of life and quality-adjusted life years[4-6]. Therefore, it is imperative to better understand this prevalent condition and how to prevent and treat it.

Despite how common VCFs are, there has not been a definitive treatment course for patients suffering from these conditions. Overall, managing an acute OVCF includes pain control, activity modification, education, and treatment of the underlying osteoporosis. Patients can be treated conservatively with rest and/or medications or surgical management, such as vertebroplasty and kyphoplasty. However, there are no treatment algorithms to decide the best course of action. The American Academy of Orthopedic Surgeons (AAOS) developed a clinical practice guideline with 11 recommendations for treating osteoporotic VCFs, but only 1 has a strong recommendation and 1 has a moderate recommendation; the other 9 are weak or inconclusive[7]. This lack of robust evidence for specific treatment methods over others provides clinicians with leniency to make decisions based primarily on personal experience.

This review aims to provide a comprehensive overview of the presentation and treatment of osteoporotic vertebral compression fractures.

DIAGNOSIS AND MANIFESTATION

Even though OVCFs are very common, they are often undiagnosed because patients can be asymptomatic, especially those that occur slowly over time[1]. Further contributing to the lack of diagnosis is the fact that neurological complications are rare and acute symptoms can be overlooked[8, 9]. Some signs that can be indicative of OVCFs are a decrease in height, change in kyphosis (when adjusted for age, Figure 1), acute-onset back pain that increases when changing posture and decreases when lying supine, and limited mobility[1,9]. These acute fractures typically occur in the lower thoracic vertebra and can be due to a fall in people with moderate osteoporosis or minor activities such as coughing in people with severe osteoporosis[1]. The pain is usually well localized to the midline spine but often refers to a unilateral or bilateral pattern into the flank, anterior abdomen, or the posterior superior iliac spine[10]. Diagnosis can be determined based on history and physical exam (*e.g.*, tenderness over vertebrae; neurological assessment) and imaging. Magnetic resonance imaging (MRIs) and computed tomography (CT) scans are used to determine the timing and extent of the fracture along



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Figure 1 Osteoporotic vertebra. A: Osteoporotic vertebra before a compression fracture; B: Osteoporotic vertebra after a compression fracture. Note the wedge shape of the vertebral body, which can cause kyphotic deformity.

with soft-tissue or spinal cord involvement[11].

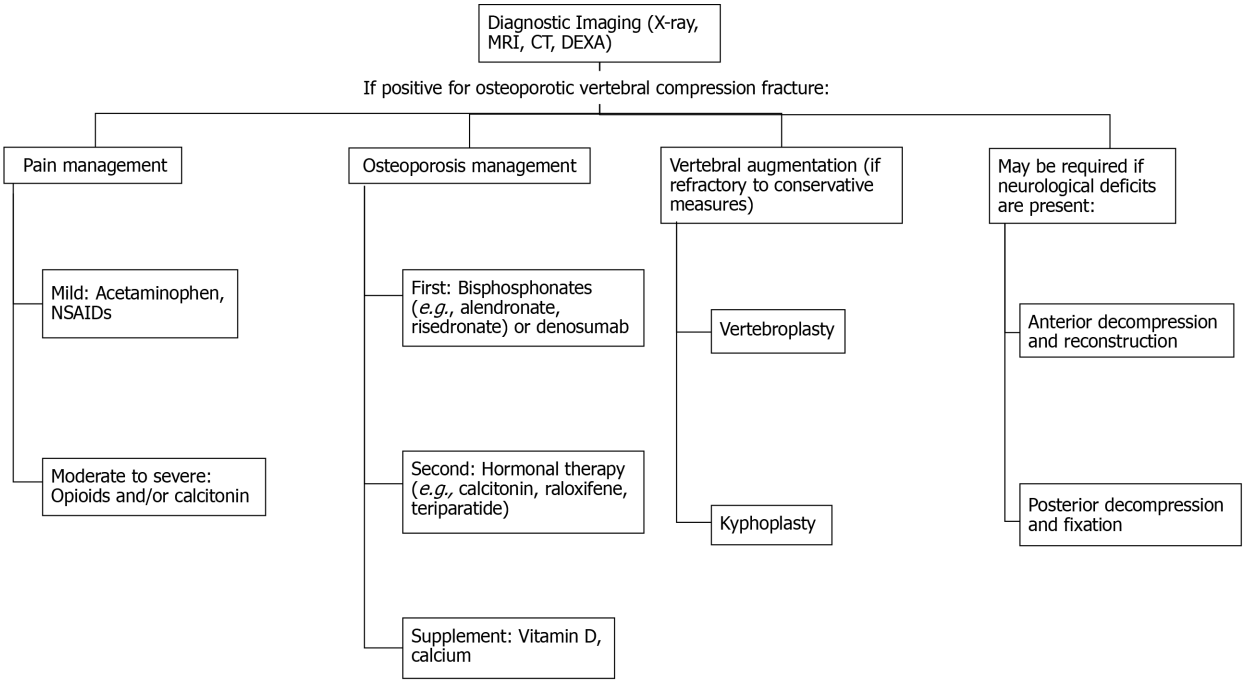
Evaluation for osteoporosis should be done as soon as possible after the VCF if not already diagnosed. Dual-energy X-ray absorptiometry (DEXA) is used to measure bone mineral density (BMD) and confirm the diagnosis of osteoporosis[12]. Osteoporosis is the most prevalent bone disorder worldwide and is defined as a T-score of -2.5 SD below the BMD of a healthy younger person of the same sex[13-15]. Low bone density, or osteopenia, is defined as a T-score between -1 and -2.5. The decrease in BMD is primarily due to loss of gonadal function and aging, but by two different mechanisms[16]. The loss of gonadal function, specifically a decrease in estrogens especially seen in postmenopausal women, results in excessive osteoclast activity, whereas in aging, the demand for osteoblasts outweighs the supplies[16,17]. These two different causes of osteoporosis also differ in the location they affect: postmenopausal bone loss is mainly in trabecular bone whereas aging-associated bone loss occurs mainly in cortical bone[16]. The excessive increase in reabsorption or decreased formation leads to compromised bone volume and integrity, thus increasing the risk of fracture. Other risk factors for osteoporosis include inadequate calcium and vitamin D levels. Vitamin D improves the absorption of calcium from the gut and helps ensure there are adequate calcium levels for normal bone mineralization[18]. The evaluation of an OVCF also includes assessment for neurologic findings, which may necessitate further imaging and consultation with a spine surgeon depending on the results; laboratory evaluation to assess for malignancy, such as multiple myeloma, and secondary causes of osteoporosis, including adverse effects of drug therapy, immobilization, and endocrine disorders, may be indicated[19].

Treatments of OVCF remain challenging. They usually include pain management, Anti-osteoporosis medications, vertebral augmentation, and surgical decompression and reconstruction (Figure 2).

PAIN MANAGEMENT

Nonsteroidal anti-inflammatory drugs (NSAIDs) and opioid analgesics are the most commonly used medications for pain control[20]. The choice of the initial agent depends upon the severity of pain[21]. Acetaminophen or NSAIDs, such as ibuprofen and naproxen, are the first-line options for patients with mild pain. These medications are easily accessible over the counter and used due to their perceived safety and relatively low cost[22]. Even though NSAIDs are used first is partially due to the incidence of more serious risks associated with other medications such as opioids and tricyclic depressants, they are not without their own adverse effects[22]. Some significant complications from the use of NSAIDs include gastrointestinal toxicity, cardiovascular thrombotic events, stroke, and renal toxicity; there is an increased risk of these complications in older patients and those with preexisting conditions (*e.g.*, cardiovascular disease, heart failure, impaired renal function), which are more prevalent in older populations[22-24]. Clinicians should be aware of potential contraindications for NSAID treatment in their patients and consider gastrointestinal protective therapy for those prescribed NSAIDs.

If the pain is not managed with initial medications or is moderate to severe, opioids and calcitonin are options. Calcitonin is unique because it has a positive impact on bone health, as discussed later in this review, and can provide pain relief possibly through modulating nociception in the central nervous system[25]. Opioids are typically required at the outset for patients with severe pain with an acute (0 to 4 wk) VCF. It has been suggested that initial treatment with an opioid is combined with low-dose acetaminophen. There is sufficient evidence of the short-term efficacy of opioids, but the long-term effectiveness is diminished because of serious adverse reactions[26]. These adverse events include constipation, nausea and vomiting, dizziness, drowsiness, dependence, and abuse[27]. Because the risks



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Figure 2 Treatment steps for osteoporotic vertebral compression fractures. NSAIDs: Nonsteroidal anti-inflammatory drugs; MRI: Magnetic resonance imaging; CT: Computed tomography; DEXA: Dual-energy X-ray absorptiometry.

of opioid use for chronic back pain outweighs the benefits, the American Academy of Neurology recommends against using opioid pain medications in this patient demographic[26]. Similarly, the AAOS are unable to recommend for or against opioids/analgesics for neurologically intact and symptomatic VCF patients[7]. Muscle relaxants can be used initially, but their long-term use is not recommended for similar reasons as long-term opioid use[28].

A brace can also be used for pain relief because it stabilizes the spine. Bracing can be used initially in the acute and subacute phases but should not be used long-term because atrophy of the core musculature can occur with prolonged use[28]. Additionally, the efficacy of bracing in preventing future vertebral body collapse has not been established and it is often poorly tolerated in older patients[29]. The AAOS is also inconclusive in its stance on bracing and other forms of therapy such as exercise[7]. If patients choose to exercise, programs should be implemented to improve flexibility, muscle strength, and core and gait stability[30]. It is important to note that exercise regimens should be tapered as pain improves[11]. Another potential treatment method for fracture repair is low-level laser therapy (LLLT). Although the exact mechanisms of LLLT are unknown, it is hypothesized to increase angiogenesis and bone formation while decreasing inflammation, as tested in animal studies[31,32]. LLLT could accelerate fracture healing and thus improve patient outcomes by enhancing callus formation, but there is limited evidence for its use in patients with bone fractures[33]. Further research into the mechanisms of LLLT and the appropriate parameters for therapeutic use and minimal side effects need to be studied before clinical application.

SURGICAL TREATMENT AND OUTCOMES

Patient selection is a critical factor for both the decision to perform vertebral augmentation and the selection of the type of procedure. Surgical interventions are typically reserved for those who have not experienced relief from medical management. For patients with incapacitating pain from acute and subacute vertebral compression fractures who are unable to taper parenteral or transition to oral opioids within seven d of admission or have intolerable sedation, constipation, or delirium from this therapy, it has been suggested that vertebral augmentation be performed rather than continue medical management. This is typically performed during the initial hospitalization. A vertebral augmentation is also an option for those without improvement in pain despite four to six weeks of conservative management with oral opioids and calcitonin, or for those who are intolerant of oral opioids.

The two main surgical treatment options are vertebroplasty and kyphoplasty. Vertebroplasty involves injecting cement, such as polymethylmethacrylate, directly into the fractured vertebrae for pain relief and fracture stabilization[34]. Success rates for pain relief and functional improvement after vertebroplasty range between 78% and 90%[35-39]. Some complications include cement extravasation

(the most common), rib fracture, radiculopathy, spinal cord compression, and cement pulmonary embolism[40-43]. However, studies have demonstrated no significant difference in pain improvement or pain-related disability when comparing patients who underwent vertebroplasty and a control group[44-46].

Kyphoplasty involves inflating a balloon in the bone and then injecting cement into the cavity[34]. This method has similar success to vertebroplasty in pain relief and functional improvement but is more successful at restoring the kyphotic angle[47]. However, there have been fewer complications associated with kyphoplasty compared to vertebroplasty, partly due to decreasing the risk of cement leakage (Figure 3)[34,48-51].

The characteristics of the VCF can influence which surgical procedure is performed. The AAOS strongly recommends against vertebroplasty in patients with an osteoporotic VCF on imaging with correlating signs and symptoms and are neurologically intact[7]. Kyphoplasty is weakly recommended in this patient demographic[7]. The AAOS cannot recommend or be against any treatment for patients who are not neurologically intact[7]. Based on the recommendations of the AAOS and relatively fewer complications, kyphoplasty is most likely to be the preferred surgical method in treating symptomatic VCFs. However, kyphoplasty is more technically challenging than vertebroplasty as it involves bilateral placement in nearly all cases and relies on the use of a balloon tamponade system that can have its own technical difficulties. Additionally, vertebroplasty does not commit to a bipedicular approach, does not rely on the performance of a balloon system, and is less expensive by approximately $5000[52]. The difference between these two procedures should be discussed with the patient, so they can be involved in the decision-making process.

Other surgical interventions include decompression then screw implantation and vertebral fixation. Decompression is indicated if the patient has neurological deficits due to neural compression. Additionally, screw augmentation can be used to increase the pull-out strength and may be combined with cement injection if fenestrated screws are used[53]. Vertebral fixation, specifically posterior vertebral fixation, has limited indications, including burst fractures, multiple VCFs causing kyphotic deformity, and malunion[53]. Both of these interventions can be combined with cement injection, so they can result in similar complications as vertebroplasty and kyphoplasty, such as cement extravasation.

PHARMACEUTICAL TREATMENT AND PREVENTION

Pharmaceutical therapy can also be initiated for treatment or prevention and is the recommended therapy for long-term treatment of OVCFs. The first-line drug treatment for osteoporosis is bisphosphonates. The FDA has approved this drug class for the prevention and treatment of osteoporosis. Bisphosphonates work by inhibiting osteoclast activation and decreasing bone resorption, leading to a decrease in bone loss[54-56]. Alendronate, an aminobisphosphonate, is often the specific first-line treatment because its efficacy in reducing fracture risk and favorable safety profile[57]. Alendronate significantly decreases the risk of fractures, specifically by 44% for radiographic vertebral fractures and 57% for osteoporotic women or those with an existing vertebral fracture[59,59]. Another aminobisphosphonate considered first-line, risedronate, has been shown to have a relative risk reduction in vertebral fractures of 39%[60]. Over three years, risedronate decreased the vertebral fracture risk by 41%[61]. The main adverse effects of bisphosphonates are gastrointestinal complications, such as reflux, esophagitis, and gastric ulcers[20]. Bisphosphonates, especially oral bisphosphonates, are contraindicated for patients who cannot tolerate the gastrointestinal side effects or have esophageal dysmotility.

Denosumab is another popular medication used for treating osteoporosis that can increase BMD[62,63]. It is a human monoclonal antibody that inhibits RANKL and thus prevents the formation and activation of osteoclasts. Unlike other osteoporosis medications, denosumab is administered subcutaneously every six mo, which can be more convenient for the patient and increase compliance, given that compliance with anti-osteoporotic therapy is lacking[64]. When administered for three years, denosumab has been shown to decrease the risk of vertebral, nonvertebral, and hip fractures in postmenopausal women[65]. Importantly, there were no differences in the incidence of adverse events (*e.g.*, infection, hypocalcemia, cancer, cardiovascular events) between patients who received denosumab and those who received a control[66]. Because of the infrequent administration of denosumab, its effectiveness, and its lack of adverse effects, denosumab is a promising treatment option.

Calcitonin is a thyroid hormone (TH) that can also be used for the prevention and treatment of postmenopausal osteoporosis[66]. Calcitonin decreases the resorption of bone by osteoclasts and can increase bone density in postmenopausal women while potentially reducing the risk of VCFs[67,68]. The AAOS moderately recommends a four-week regiment of calcitonin for patients with an acute (0-5 d after identifiable event or onset of symptoms) symptomatic osteoporotic VCF (confirmed with imaging) and who are neurologically intact[7]. There are other hormone therapies available, such as selective estrogen receptor modulators like raloxifene or parathyroid hormone analogs like teriparatide that have a positive impact on reducing fracture risk, but the use of hormone therapy for osteoporosis has declined[69,70]. The increase in the risk of cardiovascular complications (*e.g.*, stroke, coronary heart disease) and breast cancer have led to a decrease in the use of hormone therapy[71,74].

Table 1 Pharmaceutical management of osteoporosis and efficacy

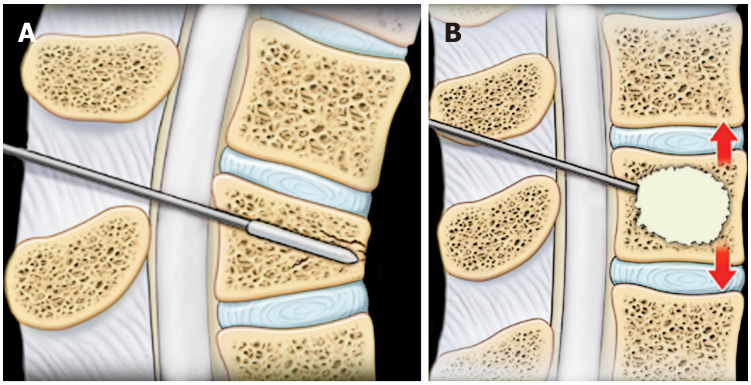
Drug	Dosing	Efficacy	Adverse effects
Bisphosphonates			
Alendronate	10 mg daily, PO; 70 mg weekly, PO	RR of 0.55 in postmenopausal women compared to placebo	Esophageal irritation; Dyspepsia; Acute phase reaction; Atrial fibrillation; Musculoskeletal pain; Renal toxicity; Atypical fracture; Osteonecrosis of the jaw
Ibandronate	2.5 mg daily, PO; 150 mg monthly, PO; 3 mg every 3 mo, IV	RR between 0.50 and 0.62 in postmenopausal women compared to placebo	
Risedronate	5 mg daily, PO; 35 mg weekly, PO; 150 mg monthly, PO	RR of 0.64 in postmenopausal women compared to placebo	
Zoledronate	5 mg annually, IV	7% increase in spine BMD; RR of 0.23 in postmenopausal women compared to placebo	
Rankl inhibitors			
Denosumab	60 mg every 6 mo, SQ	68% decrease in incidence of radiographic vertebral fractures; 9.2% increase in lumbar spine BMD	Fatigue; Weakness; Diarrhea; Hypophosphatemia
Hormones			
Raloxifene (SERM)	60 mg daily, PO; 120 mg daily, PO	RR of 0.65 in postmenopausal women compared to placebo (60 mg); RR of 0.54 in postmenopausal women compared to placebo (120 mg); 2.6% increase in lumbar spine BMD (60 mg); 2.5% in lumbar spine BMD (120 mg)	Flu syndrome; Vasodilation; Endometrial cavity fluid; Peripheral edema
Teriparatide (PTH)	20 microg daily, SQ; 40 microg daily, SQ	65% decrease in fracture risk (20 microg); 69% decrease in fracture risk (40 microg); 9% increase in lumbar spine BMD (20 microg); 13% increase in lumbar spine BMD (40 microg)	Nausea; Headache; Dizziness; Leg cramps
Calcitonin (TH)	200 mg daily, IN	33% decrease in fracture risk; 1%-1.5% increase in lumbar spine BMD	Epistaxis; Rhinitis; Ulceration of nasal mucosa; Hypocalcemia
Supplementations			
Vitamin D	400 IU daily, PO	15% decrease in fracture risk	-
Calcium	1500 mg daily, PO		

PO: Orally; RR: Relative risk; IV: Intravenous; BMD: ; SQ: Subcutaneous; IN: Intranasal; SERM: Selective estrogen receptor modulators; PTH: Parathyroid hormone; TH: Thyroid hormone; IU: International unit.

Supplementation can also have a positive impact on bone health. Postmenopausal osteoporotic women should receive 1500 mg of calcium and 400 IU of vitamin D daily[29]. Calcium plus vitamin D supplementation has been shown to significantly reduce the risk of fractures by 15%[18]. Exercise and physical therapy can also strengthen bones to prevent fractures. Strengthening the spinal extensor muscles can increase bone density and decrease the risk of VCFs[75]. Additional lifestyle modifications can also be implemented to reduce the risk of vertebral fractures. For example, patients should be advised to quit smoking and consume less alcohol (< 3 drinks/d) to decrease their risk for osteoporotic vertebral fractures[28]. Table 1 summarizes the different pharmaceutical managements of osteoporosis and their efficacy; different medications have different routes of administration (PO = orally, IV = intravenous, SQ = subcutaneous, IN = intranasal) and different effects on the relative risk of fracture (RR). It is important to note that certain side effects, such as renal toxicity and atypical fracture are extremely rare, as depicted by the asterisk.

CONCLUSION

Osteoporosis is a chronic disease with a great clinical impact on the increasing geriatric population and OVCFs are seen most frequently. Therefore, it is essential to understand the manifestation and treatment of these conditions. Steps for diagnosis and treatment of OVCFs can follow these recommendations: (1) Obtain diagnostic imaging (X-ray, MRI, or CT) and DEXA scan; (2) Pain management: (a) Mild: Acetaminophen or NSAIDs; and (b) Moderate to severe: Opioids and/or calcitonin; (3) Osteoporosis management: (a) First-line: bisphosphonates (*e.g.*, alendronate, risedronate, *etc.*) or denosumab; (b) Second-line: hormonal therapy (*e.g.*, calcitonin, raloxifene, teriparatide, *etc.*); and (c) Supplements: Vitamin D and calcium; (4) Vertebral augmentation (if refractory to above): Vertebroplasty, or Kyphoplasty; and (5) Posterior decompression and fixation or Anterior decompression and



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Figure 3 Kyphoplasty. A: Kyphoplasty involves inserting a balloon into the vertebral body with compression fractures; B: Kyphoplasty involves inflating a balloon to reduce the fractures and injecting cement into the cavity to fix the fractures.

reconstruction may be required if neurological deficits are present.

This narrative review summarized the current literature surrounding OVCFs and serves as a guideline for managing these fractures. The detailed pathogenesis and related targeted treatment options still need to be developed for better clinical outcomes.

FOOTNOTES

Author contributions: Liu J and Ebraheim NA designed the research study; Patel D performed the data collection; Patel D, Liu J, and Ebraheim NA analyzed the data and wrote the manuscript; all authors have read and approved the final manuscript.

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REFERENCES

1 **Kutsal FY**, Ergin Ergani GO. Vertebral compression fractures: Still an unpredictable aspect of osteoporosis. *Turk J Med Sci* 2021; **51**: 393-399 [PMID: 32967415 DOI: 10.3906/sag-2005-315]
2 **Riggs BL**, Melton LJ 3rd. The worldwide problem of osteoporosis: insights afforded by epidemiology. *Bone* 1995; **17**: 505S-511S [PMID: 8573428 DOI: 10.1016/8756-3282(95)00258-4]
3 **Marwick C**. Consensus Panel Considers Osteoporosis. *JAMA* 2000; **283**: 2093-2095 [DOI: 10.1001/jama.283.16.2093-JMN0426-3-1]
4 **Oleksik A**, Lips P, Dawson A, Minshall ME, Shen W, Cooper C, Kanis J. Health-related quality of life in postmenopausal women with low BMD with or without prevalent vertebral fractures. *J Bone Miner Res* 2000; **15**: 1384-1392 [PMID: 10893688 DOI: 10.1359/jbmr.2000.15.7.1384]
5 **Oleksik AM**, Ewing S, Shen W, van Schoor NM, Lips P. Impact of incident vertebral fractures on health related quality of life (HRQOL) in postmenopausal women with prevalent vertebral fractures. *Osteoporos Int* 2005; **16**: 861-870 [PMID: 15558238 DOI: 10.1007/s00198-004-1774-3]
6 **Tosteson AN**, Gabriel SE, Grove MR, Moncur MM, Kneeland TS, Melton LJ 3rd. Impact of hip and vertebral fractures on quality-adjusted life years. *Osteoporos Int* 2001; **12**: 1042-1049 [PMID: 11846331 DOI: 10.1007/s001980170015]

7 **Esses SI**, McGuire R, Jenkins J, Finkelstein J, Woodard E, Watters WCI. The Treatment of Symptomatic Osteoporotic Spinal Compression Fractures. *J Am Acad Orthop Surg* 2011; **19**: 176-182 [DOI: 10.5435/00124635-201103000-00007]

8 **Picazo DR**, Villaescusa JR, Martínez EP, Pérez FD. Late collapse osteoporotic vertebral fracture in an elderly patient with neurological compromise. *Eur Spine J* 2014; **23**: 2696-2702 [PMID: 23778750 DOI: 10.1007/s00586-013-2751-3]

9 **Varacallo MA**, Fox EJ. Osteoporosis and its complications. *Med Clin North Am* 2014; **98**: 817-831, xii [PMID: 24994054 DOI: 10.1016/j.mcna.2014.03.007]

10 **Rosen HN**, Walega DR. Osteoporotic thoracolumbar vertebral compression fractures: Clinical manifestations and treatment. In: Rosen CJ, Mulder JE, editors. UpToDate, 2020. [cited 20 January 2022]. Available from: https://www.uptodate.com/contents/osteoporotic-thoracolumbar-vertebral-compression-fractures-clinical-manifestations-and-treatment#!

11 **McCarthy J**, Davis A. Diagnosis and Management of Vertebral Compression Fractures. *Am Fam Physician* 2016; **94**: 44-50 [PMID: 27386723]

12 **Cosman F**, de Beur SJ, LeBoff MS, Lewiecki EM, Tanner B, Randall S, Lindsay R; National Osteoporosis Foundation. Clinician's Guide to Prevention and Treatment of Osteoporosis. *Osteoporos Int* 2014; **25**: 2359-2381 [PMID: 25182228 DOI: 10.1007/s00198-014-2794-2]

13 Assessment of fracture risk and its application to screening for postmenopausal osteoporosis. Report of a WHO Study Group. *World Health Organ Tech Rep Ser* 1994; **843**: 1-129 [PMID: 7941614]

14 **Coughlan T**, Dockery F. Osteoporosis and fracture risk in older people. *Clin Med (Lond)* 2014; **14**: 187-191 [PMID: 24715132 DOI: 10.7861/clinmedicine.14-2-187]

15 **Kanis JA**. Diagnosis of osteoporosis and assessment of fracture risk. *The Lancet* 2002; **359**: 1929-1936 [DOI: 10.1016/S0140-6736(02)08761-5]

16 **Manolagas SC**, Jilka RL. Bone marrow, cytokines, and bone remodeling. Emerging insights into the pathophysiology of osteoporosis. *N Engl J Med* 1995; **332**: 305-311 [PMID: 7816067 DOI: 10.1056/NEJM199502023320506]

17 **Parfitt A**. Bone-forming cells in clinical condictions. *The osteoblast and osteocyte* 1990

18 **Weaver CM**, Alexander DD, Boushey CJ, Dawson-Hughes B, Lappe JM, LeBoff MS, Liu S, Looker AC, Wallace TC, Wang DD. Calcium plus vitamin D supplementation and risk of fractures: an updated meta-analysis from the National Osteoporosis Foundation. *Osteoporos Int* 2016; **27**: 367-376 [PMID: 26510847 DOI: 10.1007/s00198-015-3386-5]

19 **Fitzpatrick LA**. Secondary causes of osteoporosis. *Mayo Clin Proc* 2002; **77**: 453-468 [PMID: 12004995 DOI: 10.4065/77.5.453]

20 **Genev IK**, Tobin MK, Zaidi SP, Khan SR, Amirouche FML, Mehta AI. Spinal Compression Fracture Management: A Review of Current Treatment Strategies and Possible Future Avenues. *Global Spine J* 2017; **7**: 71-82 [PMID: 28451512 DOI: 10.1055/s-0036-1583288]

21 **Toyoda H**, Takahashi S, Hoshino M, Takayama K, Iseki K, Sasaoka R, Tsujio T, Yasuda H, Sasaki T, Kanematsu F, Kono H, Nakamura H. Characterizing the course of back pain after osteoporotic vertebral fracture: a hierarchical cluster analysis of a prospective cohort study. *Arch Osteoporos* 2017; **12**: 82 [PMID: 28942501 DOI: 10.1007/s11657-017-0377-5]

22 **McCarberg BH**. NSAIDs in the older patient: balancing benefits and harms. *Pain Med* 2013; **14** Suppl 1: S43-S44 [PMID: 24373111 DOI: 10.1111/pme.12253]

23 **Singh G**. Recent considerations in nonsteroidal anti-inflammatory drug gastropathy. *Am J Med* 1998; **105**: 31S-38S [PMID: 9715832 DOI: 10.1016/s0002-9343(98)00072-2]

24 Recommendations for the medical management of osteoarthritis of the hip and knee: 2000 update. American College of Rheumatology Subcommittee on Osteoarthritis Guidelines. *Arthritis Rheum* 2000; **43**: 1905-1915 [PMID: 11014340 DOI: 10.1002/1529-0131(200009)43:9<1905::AID-ANR1>3.0.CO;2-P]

25 **Gennari C**. Analgesic effect of calcitonin in osteoporosis. *Bone* 2002; **30**: 67-70 [DOI: 10.1016/S8756-3282(02)00713-5]

26 **Franklin GM**; American Academy of Neurology. Opioids for chronic noncancer pain: a position paper of the American Academy of Neurology. *Neurology* 2014; **83**: 1277-1284 [PMID: 25267983 DOI: 10.1212/WNL.0000000000000839]

27 **Busse JW**, Wang L, Kamaleldin M, Craigie S, Riva JJ, Montoya L, Mulla SM, Lopes LC, Vogel N, Chen E, Kirmayr K, De Oliveira K, Olivieri L, Kaushal A, Chaparro LE, Oyberman I, Agarwal A, Couban R, Tsoi L, Lam T, Vandvik PO, Hsu S, Bala MM, Schandelmaier S, Scheidecker A, Ebrahim S, Ashoorion V, Rehman Y, Hong PJ, Ross S, Johnston BC, Kunz R, Sun X, Buckley N, Sessler DI, Guyatt GH. Opioids for Chronic Noncancer Pain: A Systematic Review and Meta-analysis. *JAMA* 2018; **320**: 2448-2460 [PMID: 30561481 DOI: 10.1001/jama.2018.18472]

28 **Garg B**, Dixit V, Batra S, Malhotra R, Sharan A. Non-surgical management of acute osteoporotic vertebral compression fracture: A review. *J Clin Orthop Trauma* 2017; **8**: 131-138 [PMID: 28720988 DOI: 10.1016/j.jcot.2017.02.001]

29 **Kim DH**, Vaccaro AR. Osteoporotic compression fractures of the spine; current options and considerations for treatment. *Spine J* 2006; **6**: 479-487 [PMID: 16934715 DOI: 10.1016/j.spinee.2006.04.013]

30 **Sinaki M**. Exercise for Patients With Osteoporosis: Management of Vertebral Compression Fractures and Trunk Strengthening for Fall Prevention. *PM R* 2012; **4**: 882-888 [DOI: 10.1016/j.pmrj.2012.10.008]

31 **Kazem Shakouri S**, Soleimanpour J, Salekzamani Y, Oskuie MR. Effect of low-level laser therapy on the fracture healing process. *Lasers Med Sci* 2010; **25**: 73-77 [PMID: 19399356 DOI: 10.1007/s10103-009-0670-7]

32 **Medalha CC**, Santos AL, Veronez Sde O, Fernandes KR, Magri AM, Renno AC. Low level laser therapy accelerates bone healing in spinal cord injured rats. *J Photochem Photobiol B* 2016; **159**: 179-185 [PMID: 27077555 DOI: 10.1016/j.jphotobiol.2016.03.041]

33 **Arjmand B**, Khodadost M, Jahani Sherafat S, Rezaei Tavirani M, Ahmadi N, Hamzeloo Moghadam M, Okhovatian F, Rezaei Tavirani S, Rostami-Nejad M. Low-Level Laser Therapy: Potential and Complications. *J Lasers Med Sci* 2021; **12**: e42 [PMID: 34733765 DOI: 10.34172/jlms.2021.42]

34 **Teyssédou S**, Saget M, Pries P. Kyphopasty and vertebroplasty. *Orthop Traumatol Surg Res* 2014; **100**: S169-S179 [PMID: 24406028 DOI: 10.1016/j.otsr.2013.11.005]

35 **Deramond H**, Depriester C, Galibert P, Le Gars D. Percutaneous vertebroplasty with polymethylmethacrylate. Technique, indications, and results. *Radiol Clin North Am* 1998; **36**: 533-546 [PMID: 9597071 DOI: 10.1016/s0033-8389(05)70042-7]

36 **Gangi A**, Guth S, Imbert JP, Marin H, Dietemann J-L. Percutaneous Vertebroplasty: Indications, Technique, and Results. *RadioGraphics* 2003; **23**: e10-e [DOI: 10.1148/rg.e10]

37 **Hulme PA**, Krebs J, Ferguson SJ, Berlemann U. Vertebroplasty and kyphoplasty: a systematic review of 69 clinical studies. *Spine (Phila Pa 1976)* 2006; **31**: 1983-2001 [PMID: 16924218 DOI: 10.1097/01.brs.0000229254.89952.6b]

38 **Peters KR**, Guiot BH, Martin PA, Fessler RG. Vertebroplasty for osteoporotic compression fractures: current practice and evolving techniques. *Neurosurgery* 2002; **51**: S96-103 [PMID: 12234436]

39 **Predey TA**, Sewall LE, Smith SJ. Percutaneous vertebroplasty: new treatment for vertebral compression fractures. *Am Fam Physician* 2002; **66**: 611-615 [PMID: 12201552]

40 **Mathis JM**, Barr JD, Belkoff SM, Barr MS, Jensen ME, Deramond H. Percutaneous vertebroplasty: a developing standard of care for vertebral compression fractures. *AJNR Am J Neuroradiol* 2001; **22**: 373-381 [PMID: 11156786]

41 **Cotten A**, Dewatre F, Cortet B, Assaker R, Leblond D, Duquesnoy B. Percutaneous vertebroplasty for osteolytic metastases and myeloma: effects of the percentage of lesion filling and the leakage of methyl methacrylate at clinical follow-up. *Radiology* 1996; **200**: 525-530 [DOI: 10.1148/radiology.200.2.8685351]

42 **Deramond H**, Depriester C, Toussaint P, Galibert P. Percutaneous Vertebroplasty. *Semin Musculoskelet Radiol* 1997; **1**: 285-296 [PMID: 11387078 DOI: 10.1055/s-2008-1080150]

43 **Padovani B**, Kasriel O, Brunner P, Peretti-Viton P. Pulmonary embolism caused by acrylic cement: a rare complication of percutaneous vertebroplasty. *AJNR Am J Neuroradiol* 1999; **20**: 375-377 [PMID: 10219399]

44 **Buchbinder R**, Osborne RH, Ebeling PR, Wark JD, Mitchell P, Wriedt C, Graves S, Staples MP, Murphy B. A randomized trial of vertebroplasty for painful osteoporotic vertebral fractures. *N Engl J Med* 2009; **361**: 557-568 [PMID: 19657121 DOI: 10.1056/NEJMoa0900429]

45 **Kallmes DF**, Comstock BA, Heagerty PJ, Turner JA, Wilson DJ, Diamond TH. A randomized trial of vertebroplasty for osteoporotic spinal fractures. *N Engl J Med* 2009; **361**: 569-579 [DOI: 10.1056/NEJMoa0900563]

46 **McCullough BJ**, Comstock BA, Deyo RA, Kreuter W, Jarvik JG. Major medical outcomes with spinal augmentation *vs* conservative therapy. *JAMA Intern Med* 2013; **173**: 1514-1521 [PMID: 23836009 DOI: 10.1001/jamainternmed.2013.8725]

47 **Kurra S**, Metkar U, Lieberman IH, Lavelle WF. The Effect of Kyphoplasty on Mortality in Symptomatic Vertebral Compression Fractures: A Review. *Int J Spine Surg* 2018; **12**: 543-548 [PMID: 30364815 DOI: 10.14444/5066]

48 **Lee MJ**, Dumonski M, Cahill P, Stanley T, Park D, Singh K. Percutaneous treatment of vertebral compression fractures: a meta-analysis of complications. *Spine (Phila Pa 1976)* 2009; **34**: 1228-1232 [PMID: 19444071 DOI: 10.1097/BRS.0b013e3181a3c742]

49 **Zhang JD**, Poffyn B, Sys G, Uyttendaele D. Comparison of vertebroplasty and kyphoplasty for complications. *Orthop Surg* 2011; **3**: 158-160 [PMID: 22009645 DOI: 10.1111/j.1757-7861.2011.00141.x]

50 **Garnier L**, Tonetti J, Bodin A, Vouaillat H, Merloz P, Assaker R, Court C; French Society for Spine Surgery. Kyphoplasty *vs* vertebroplasty in osteoporotic thoracolumbar spine fractures. Short-term retrospective review of a multicentre cohort of 127 consecutive patients. *Orthop Traumatol Surg Res* 2012; **98**: S112-S119 [PMID: 22939104 DOI: 10.1016/j.otsr.2012.03.018]

51 **Li X**, Yang H, Tang T, Qian Z, Chen L, Zhang Z. Comparison of kyphoplasty and vertebroplasty for treatment of painful osteoporotic vertebral compression fractures: twelve-month follow-up in a prospective nonrandomized comparative study. *J Spinal Disord Tech* 2012; **25**: 142-149 [PMID: 21423053 DOI: 10.1097/BSD.0b013e318213c113]

52 **Mehio AK**, Lerner JH, Engelhart LM, Kozma CM, Slaton TL, Edwards NC, Lawler GJ. Comparative hospital economics and patient presentation: vertebroplasty and kyphoplasty for the treatment of vertebral compression fracture. *AJNR Am J Neuroradiol* 2011; **32**: 1290-1294 [PMID: 21546460 DOI: 10.3174/ajnr.A2502]

53 **Prost S**, Pesenti S, Fuentes S, Tropiano P, Blondel B. Treatment of osteoporotic vertebral fractures. *Orthop Traumatol Surg Res* 2021; **107**: 102779 [PMID: 33321233 DOI: 10.1016/j.otsr.2020.102779]

54 **Drake MT**, Clarke BL, Khosla S. Bisphosphonates: mechanism of action and role in clinical practice. *Mayo Clin Proc* 2008; **83**: 1032-1045 [PMID: 18775204 DOI: 10.4065/83.9.1032]

55 **Rodan GA**, Fleisch HA. Bisphosphonates: mechanisms of action. *J Clin Invest* 1996; **97**: 2692-2696 [PMID: 8675678 DOI: 10.1172/JCI118722]

56 **Russell LA**. Osteoporosis and Orthopedic Surgery: Effect of Bone Health on Total Joint Arthroplasty Outcome. *Current Rheumatology Reports* 2013; **15** [DOI: 10.1007/s11926-013-0371-x]

57 **Ensrud KE**, Schousboe JT. Clinical practice. Vertebral fractures. *N Engl J Med* 2011; **364**: 1634-1642 [PMID: 21524214 DOI: 10.1056/NEJMcp1009697]

58 **Cummings SR**, Black DM, Thompson DE, Applegate WB, Barrett-Connor E, Musliner TA, Palermo L, Prineas R, Rubin SM, Scott JC, Vogt T, Wallace R, Yates AJ, LaCroix AZ. Effect of alendronate on risk of fracture in women with low bone density but without vertebral fractures: results from the Fracture Intervention Trial. *JAMA* 1998; **280**: 2077-2082 [PMID: 9875874 DOI: 10.1001/jama.280.24.2077]

59 **Black DM**, Thompson DE, Bauer DC, Ensrud K, Musliner T, Hochberg MC, Nevitt MC, Suryawanshi S, Cummings SR; Fracture Intervention Trial. Fracture risk reduction with alendronate in women with osteoporosis: the Fracture Intervention Trial. FIT Research Group. *J Clin Endocrinol Metab* 2000; **85**: 4118-4124 [PMID: 11095442 DOI: 10.1210/jcem.85.11.6953]

60 **Wells G**, Cranney A, Peterson J, Boucher M, Shea B, Robinson V, Coyle D, Tugwell P. Risedronate for the primary and secondary prevention of osteoporotic fractures in postmenopausal women. *Cochrane Database Syst Rev* 2008; CD004523 [PMID: 18254053 DOI: 10.1002/14651858.CD004523.pub3]

61 **Harris ST**, Watts NB, Genant HK, McKeever CD, Hangartner T, Keller M, Chesnut CH 3rd, Brown J, Eriksen EF, Hoseyni MS, Axelrod DW, Miller PD. Effects of risedronate treatment on vertebral and nonvertebral fractures in women with postmenopausal osteoporosis: a randomized controlled trial. Vertebral Efficacy With Risedronate Therapy (VERT) Study Group. *JAMA* 1999; **282**: 1344-1352 [PMID: 10527181 DOI: 10.1001/jama.282.14.1344]

62 **Gu HF**, Gu LJ, Wu Y, Zhao XH, Zhang Q, Xu ZR, Yang YM. Efficacy and Safety of Denosumab in Postmenopausal Women With Osteoporosis: A Meta-Analysis. *Medicine (Baltimore)* 2015; **94**: e1674 [PMID: 26554766 DOI: 10.1097/MD.0000000000001674]

63 **Hildebrand GK**, Kasi A. Denosumab. 2021 Dec 7. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing, 2022 [PMID: 30571009]

64 **Rabenda V**, Vanoverloop J, Fabri V, Mertens R, Sumkay F, Vannecke C, Deswaef A, Verpooten GA, Reginster JY. Low incidence of anti-osteoporosis treatment after hip fracture. *J Bone Joint Surg Am* 2008; **90**: 2142-2148 [PMID: 18829912 DOI: 10.2106/JBJS.G.00864]

65 **Cummings SR**, San Martin J, McClung MR, Siris ES, Eastell R, Reid IR, Delmas P, Zoog HB, Austin M, Wang A, Kutilek S, Adami S, Zanchetta J, Libanati C, Siddhanti S, Christiansen C; FREEDOM Trial. Denosumab for prevention of fractures in postmenopausal women with osteoporosis. *N Engl J Med* 2009; **361**: 756-765 [PMID: 19671655 DOI: 10.1056/NEJMoa0809493]

66 **Watts NB**, Diab DL. Long-term use of bisphosphonates in osteoporosis. *J Clin Endocrinol Metab* 2010; **95**: 1555-1565 [PMID: 20173017 DOI: 10.1210/jc.2009-1947]

67 **Kallio DM**, Garant PR, Minkin C. Ultrastructural effects of calcitonin on osteoclasts in tissue culture. *J Ultrastruct Res* 1972; **39**: 205-216 [PMID: 4337397 DOI: 10.1016/s0022-5320(72)90017-2]

68 **Cranney A**, Tugwell P, Zytaruk N, Robinson V, Weaver B, Shea B, Wells G, Adachi J, Waldegger L, Guyatt G; Osteoporosis Methodology Group and The Osteoporosis Research Advisory Group. Meta-analyses of therapies for postmenopausal osteoporosis. VI. Meta-analysis of calcitonin for the treatment of postmenopausal osteoporosis. *Endocr Rev* 2002; **23**: 540-551 [PMID: 12202469 DOI: 10.1210/er.2001-6002]

69 **Delmas PD**, Ensrud KE, Adachi JD, Harper KD, Sarkar S, Gennari C, Reginster JY, Pols HA, Recker RR, Harris ST, Wu W, Genant HK, Black DM, Eastell R; Mulitple Outcomes of Raloxifene Evaluation Investigators. Efficacy of raloxifene on vertebral fracture risk reduction in postmenopausal women with osteoporosis: four-year results from a randomized clinical trial. *J Clin Endocrinol Metab* 2002; **87**: 3609-3617 [PMID: 12161484 DOI: 10.1210/jcem.87.8.8750]

70 **Neer RM**, Arnaud CD, Zanchetta JR, Prince R, Gaich GA, Reginster JY, Hodsman AB, Eriksen EF, Ish-Shalom S, Genant HK, Wang O, Mitlak BH. Effect of parathyroid hormone (1-34) on fractures and bone mineral density in postmenopausal women with osteoporosis. *N Engl J Med* 2001; **344**: 1434-1441 [PMID: 11346808 DOI: 10.1056/NEJM200105103441904]

71 **Ralston S**. Bisphosphonates for Osteoporosis. In: Harrison-Woolrych M, editor. Medicines For Women. Cham: Springer International Publishing, 2015: 345-371 [DOI: 10.1007/978-3-319-12406-3_12]

72 **Jeremiah MP**, Unwin BK, Greenawald MH, Casiano VE. Diagnosis and Management of Osteoporosis. *Am Fam Physician* 2015; **92**: 261-268 [PMID: 26280231]

73 **Cauley JA**, Robbins J, Chen Z, Cummings SR, Jackson RD, LaCroix AZ, LeBoff M, Lewis CE, McGowan J, Neuner J, Pettinger M, Stefanick ML, Wactawski-Wende J, Watts NB; Women's Health Initiative Investigators. Effects of estrogen plus progestin on risk of fracture and bone mineral density: the Women's Health Initiative randomized trial. *JAMA* 2003; **290**: 1729-1738 [PMID: 14519707 DOI: 10.1001/jama.290.13.1729]

74 **Rossouw JE**, Anderson GL, Prentice RL, LaCroix AZ, Kooperberg C, Stefanick ML, Jackson RD, Beresford SA, Howard BV, Johnson KC, Kotchen JM, Ockene J; Writing Group for the Women's Health Initiative Investigators. Risks and benefits of estrogen plus progestin in healthy postmenopausal women: principal results From the Women's Health Initiative randomized controlled trial. *JAMA* 2002; **288**: 321-333 [PMID: 12117397 DOI: 10.1001/jama.288.3.321]

75 **Sinaki M**, Itoi E, Wahner HW, Wollan P, Gelzcer R, Mullan BP, Collins DA, Hodgson SF. Stronger back muscles reduce the incidence of vertebral fractures: a prospective 10 year follow-up of postmenopausal women. *Bone* 2002; **30**: 836-841 [PMID: 12052450 DOI: 10.1016/s8756-3282(02)00739-1]

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MINIREVIEWS

Hip prosthetic loosening and periprosthetic osteolysis: A commentary

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Abstract

Prosthetic loosening and periprosthetic osteolysis have been debated for decades, both in terms of the timing and nature of the triggering events. The hypothesis of wear-particle-induced loosening states that wear particles cause a foreign-body response leading to periprosthetic osteolysis and ultimately to late prosthetic loosening, *i.e.*, that the osteolysis precedes the loosening. The theory of early loosening, on the other hand, postulates that the loosening is already initiated during or shortly after surgery, *i.e.*, that the osteolysis is secondary to the loosening. This commentary focuses on the causal relationship between prosthetic loosening and periprosthetic osteolysis.

Key Words: Hip prosthesis; Radiostereometric analysis; Prosthesis failure; Osteoclasts; Bone resorption; Alarmins

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Core Tip: Prosthetic loosening and periprosthetic osteolysis have been debated for decades. Some authors claim that the osteolysis precedes the loosening, others that the osteolysis is secondary to the loosening. This commentary focuses on their causal relationship.

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INTRODUCTION

Hip arthroplasty is one of the most successful of all orthopedic operations, but the

results do deteriorate with time due to loosening. In the 1970s, the hypothesis of wear-particle-induced loosening, later called particle disease, was proposed: It was assumed that wear particles cause a foreign-body response leading to periprosthetic osteolysis and ultimately to late prosthetic loosening. Wear particles are still widely considered to be the main cause of loosening[1-4]. However, there is much evidence that loosening is already initiated during or shortly after surgery (due to insufficient initial fixation or resorption of a necrotic bone bed) and that the prosthetic micromovements then cause devitalizing periprosthetic fluid pressure fluctuations leading to periprosthetic osteolysis[5-9]. This commentary focuses on the causal relationship between prosthetic loosening and periprosthetic osteolysis.

WEAR PARTICLES *PER SE* DO NOT INDUCE OSTEOLYSIS

The hypothesis of wear-particle-induced loosening presupposes that wear particles are somehow transported into the interface between bone and prosthesis and once there, trigger a foreign-body response leading to periprosthetic osteolysis (and ultimately to prosthetic loosening). However, histological studies indicate that a stable implant has a biological barrier that prevents wear particles from entering into the bone-prosthetic interface[10,11]. Even if the biological barrier were defective, experiments have shown that *uncontaminated* particles (if very gently deposited between the bone surface and a stable implant) do not induce osteolysis[12,13]. Thus, wear particles *per se* appear not to induce osteolysis.

ENDOTOXINS AND DAMPS CAN INDUCE OSTEOLYSIS

Wear particles contaminated by endotoxins can induce transient osteolysis[14,15], but it has been experimentally shown that endotoxins are rapidly eliminated or inactivated[13]. By contrast, prosthetic micromovements of *loosened* prosthetic components can cause sustained, devitalizing spikes of high fluid pressure in the bone-implant interface, which can lead to progressive periprosthetic osteolysis[5-9]. The molecular mechanism appears to be that necrotic osteocytes release DAMPs (damage-associated molecular patterns, danger signals, or alarmins)[16], which, *via* a unique pattern recognition receptor, reinforce osteoclastogenesis[17]. DAMPs, released due to prosthetic loosening, may, therefore, (unlike endotoxins) induce sustained excessive osteoclast activity and thus cause progressive periprosthetic osteolysis.

DAMPS-COATED PARTICLES CAN INHIBIT BONE INGROWTH

A series of animal experiments with polyethylene particles inserted into the interface between the bone and a movable part of a previously installed implant have shown inhibition of bone ingrowth only when combined with movements at the interface, *i.e.* no inhibition occurred at a stable interface. Remarkably, after the movements ceased, the inhibition of bone ingrowth persisted if particles were present, while no inhibition occurred in the control group without particles[12].

A plausible explanation of the persistent inhibition of bone ingrowth after the movements ceased is that the movements caused the release of DAMPs, that adhered to the polyethylene particles at the interface, thus forming DAMPs-coated bone-formation-inhibiting polyethylene particles. Varying degrees of DAMPs-coating may actually explain why different authors have come to very different conclusions about the importance of the material and size of the wear particles in loosening (a significant foreign-body response to particles of cement, metal, and polyethylene have been reported, but also no or almost no response)[18]. A similar mechanism (DAMPs-coated particles) for osteolysis may also apply to experimental models exposed to both surgical trauma and wear particles.

UNCEMENTED PROSTHETIC COMPONENTS DO NOT FORM DAMPS-COATED CEMENT PARTICLES

Radiostereometric analysis (RSA) enables highly accurate *in vivo* measurements of the prosthetic component migration after surgery. Many RSA studies of hip prostheses have shown that early migration poses a risk of future failure—the larger the early migration, the greater the risk of future failure[19-24]. However, some RSA studies indicate that certain uncemented femoral components appear to achieve stability and possibly even osseointegration during the healing period despite significant early migration[25-27].

If, as suggested in these studies, these uncemented femoral components (unlike cemented femoral components with similar significant early migration) really become osseointegrated during the healing period, a probable explanation is that no DAMPs-coated cement particles, which could inhibit bone ingrowth and thereby prevent osseointegration, have been formed.

CONCLUSION

The recent clarification of the molecular mechanism behind osteoclastogenesis (the pattern recognition receptor to osteocyte-derived DAMPs)[17] allows us to better understand the causal relationship between prosthetic loosening and periprosthetic osteolysis: Loosening is initiated during or shortly after surgery (due to insufficient initial fixation or resorption of a necrotic bone bed). The micromovements of thus loosened prosthetic components may, *via* periprosthetic fluid pressure fluctuations, cause necrotic osteocytes, which release DAMPs that reinforce the osteoclast activity and lead to periprosthetic osteolysis. Later and *secondary to loosening*, DAMPs-coated wear particles may be formed, which, by inhibiting bone ingrowth, may affect the progression of loosening.

FOOTNOTES

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REFERENCES

1 **Goodman SB**, Gibon E, Pajarinen J, Lin TH, Keeney M, Ren PG, Nich C, Yao Z, Egashira K, Yang F, Konttinen YT. Novel biological strategies for treatment of wear particle-induced periprosthetic osteolysis of orthopaedic implants for joint replacement. *J R Soc Interface* 2014; **11**: 20130962 [PMID: 24478281 DOI: 10.1098/rsif.2013.0962]
2 **Sukur E**, Akman YE, Ozturkmen Y, Kucukdurmaz F. Particle disease: A current review of the biological mechanisms in periprosthetic osteolysis after hip arthroplasty. *Open Orthop J* 2016; **10**: 241-251 [PMID: 27499822 DOI: 10.2174/1874325001610010241]
3 **Kandahari AM**, Yang X, Laroche KA, Dighe AS, Pan D, Cui Q. A review of UHMWPE wear-induced osteolysis: the role for early detection of the immune response. *Bone Res* 2016; **4**: 16014 [PMID: 27468360 DOI: 10.1038/boneres.2016.14]
4 **Goodman SB**, Gallo J. Periprosthetic osteolysis: mechanisms, prevention and treatment. *J Clin Med* 2019; **8**: 2091 [PMID: 31805704 DOI: 10.3390/jcm8122091]
5 **Aspenberg P**, van der Vis H. Fluid pressure may cause periprosthetic osteolysis. Particles are not the only thing. *Acta Orthop Scand* 1998; **69**: 1-4 [PMID: 9524506 DOI: 10.3109/17453679809002344]
6 **Skoglund B**, Aspenberg P. PMMA particles and pressure--a study of the osteolytic properties of two agents proposed to cause prosthetic loosening. *J Orthop Res* 2003; **21**: 196-201 [PMID: 12568949 DOI: 10.1016/S0736-0266(02)00150-X]
7 **Fahlgren A**, Bostrom MP, Yang X, Johansson L, Edlund U, Agholme F, Aspenberg P. Fluid pressure and flow as a cause of bone resorption. *Acta Orthop* 2010; **81**: 508-516 [PMID: 20718695 DOI: 10.3109/17453674.2010.504610]
8 **Mjöberg B**. Is early migration enough to explain late clinical loosening of hip prostheses? *EFORT Open Rev* 2020; **5**: 113-117 [PMID: 32175098 DOI: 10.1302/2058-5241.5.190014]
9 **Mjöberg B**. Hip prosthetic loosening: A very personal review. *World J Orthop* 2021; **12**: 629-639 [PMID: 34631447 DOI: 10.5312/wjo.v12.i9.629]
10 **Linder L**, Carlsson ÅS. The bone-cement interface in hip arthroplasty. A histologic and enzyme study of stable

components. *Acta Orthop Scand* 1986; **57**: 495-500 [PMID: 3577714 DOI: 10.3109/17453678609014777]
11 **Sundfeldt M**, Widmark M, Johansson CB, Campbell P, Carlsson LV. Effect of submicron polyethylene particles on an osseointegrated implant: an experimental study with a rabbit patello-femoral prosthesis. *Acta Orthop Scand* 2002; **73**: 416-424 [PMID: 12358115 DOI: 10.1080/00016470216314]
12 **Aspenberg P**, Herbertsson P. Periprosthetic bone resorption. Particles *vs* movement. *J Bone Joint Surg Br* 1996; **78**: 641-646 [PMID: 8682835]
13 **Skoglund B**, Larsson L, Aspenberg PA. Bone-resorptive effects of endotoxin-contaminated high-density polyethylene particles spontaneously eliminated in vivo. *J Bone Joint Surg Br* 2002; **84**: 767-773 [PMID: 12188502 DOI: 10.1302/0301-620x.84b5.11775]
14 **Bi Y**, Seabold JM, Kaar SG, Ragab AA, Goldberg VM, Anderson JM, Greenfield EM. Adherent endotoxin on orthopedic wear particles stimulates cytokine production and osteoclast differentiation. *J Bone Miner Res* 2001; **16**: 2082-2091 [PMID: 11697805 DOI: 10.1359/jbmr.2001.16.11.2082]
15 **Greenfield EM**, Bi Y, Ragab AA, Goldberg VM, Nalepka JL, Seabold JM. Does endotoxin contribute to aseptic loosening of orthopedic implants? *J Biomed Mater Res B Appl Biomater* 2005; **72**: 179-185 [PMID: 15449253 DOI: 10.1002/jbm.b.30150]
16 **Rock KL**, Kono H. The inflammatory response to cell death. *Annu Rev Pathol* 2008; **3**: 99-126 [PMID: 18039143 DOI: 10.1146/annurev.pathmechdis.3.121806.151456]
17 **Andreev D**, Liu M, Weidner D, Kachler K, Faas M, Grüneboom A, Schlötzer-Schrehardt U, Muñoz LE, Steffen U, Grötsch B, Killy B, Krönke G, Luebke AM, Niemeier A, Wehrhan F, Lang R, Schett G, Bozec A. Osteocyte necrosis triggers osteoclast-mediated bone loss through macrophage-inducible C-type lectin. *J Clin Invest* 2020; **130**: 4811-4830 [PMID: 32773408 DOI: 10.1172/JCI134214]
18 **Mjöberg B**. Theories of wear and loosening in hip prostheses. Wear-induced loosening *vs* loosening-induced wear--a review. *Acta Orthop Scand* 1994; **65**: 361-371 [PMID: 8042497 DOI: 10.3109/17453679408995473]
19 **Kärrholm J**, Borssén B, Löwenhielm G, Snorrason F. Does early micromotion of femoral stem prostheses matter? *J Bone Joint Surg Br* 1994; **76**: 912-917 [PMID: 7983118]
20 **Nieuwenhuijse MJ**, Valstar ER, Kaptein BL, Nelissen RG. Good diagnostic performance of early migration as a predictor of late aseptic loosening of acetabular cups: results from ten years of follow-up with Roentgen stereophotogrammetric analysis (RSA). *J Bone Joint Surg Am* 2012; **94**: 874-880 [PMID: 22617914 DOI: 10.2106/JBJS.K.00305]
21 **Pijls BG**, Nieuwenhuijse MJ, Fiocco M, Plevier JW, Middeldorp S, Nelissen RG, Valstar ER. Early proximal migration of cups is associated with late revision in THA: a systematic review and meta-analysis of 26 RSA studies and 49 survival studies. *Acta Orthop* 2012; **83**: 583-591 [PMID: 23126575 DOI: 10.3109/17453674.2012.745353]
22 **Klerken T**, Mohaddes M, Nemes S, Kärrholm J. High early migration of the revised acetabular component is a predictor of late cup loosening: 312 cup revisions followed with radiostereometric analysis for 2-20 years. *Hip Int* 2015; **25**: 471-476 [PMID: 25952912 DOI: 10.5301/hipint.5000246]
23 **van der Voort P**, Pijls BG, Nieuwenhuijse MJ, Jasper J, Fiocco M, Plevier JW, Middeldorp S, Valstar ER, Nelissen RG. Early subsidence of shape-closed hip arthroplasty stems is associated with late revision. A systematic review and meta-analysis of 24 RSA studies and 56 survival studies. *Acta Orthop* 2015; **86**: 575-585 [PMID: 25909455 DOI: 10.3109/17453674.2015.1043832]
24 **Johanson PE**, Antonsson M, Shareghi B, Kärrholm J. Early subsidence predicts failure of a cemented femoral stem with minor design changes. *Clin Orthop Relat Res* 2016; **474**: 2221-2229 [PMID: 27188836 DOI: 10.1007/s11999-016-4884-2]
25 **Weber E**, Sundberg M, Flivik G. Design modifications of the uncemented Furlong hip stem result in minor early subsidence but do not affect further stability: a randomized controlled RSA study with 5-year follow-up. *Acta Orthop* 2014; **85**: 556-561 [PMID: 25175668 DOI: 10.3109/17453674.2014.958810]
26 **Aro E**, Alm JJ, Moritz N, Mattila K, Aro HT. Good stability of a cementless, anatomically designed femoral stem in aging women: a 9-year RSA study of 32 patients. *Acta Orthop* 2018; **89**: 490-495 [PMID: 29987941 DOI: 10.1080/17453674.2018.1490985]
27 **Floerkemeier T**, Budde S, Lewinski GV, Windhagen H, Hurschler C, Schwarze M. Greater early migration of a short-stem total hip arthroplasty is not associated with an increased risk of osseointegration failure: 5th-year results from a prospective RSA study with 39 patients, a follow-up study. *Acta Orthop* 2020; **91**: 266-271 [PMID: 32106733 DOI: 10.1080/17453674.2020.1732749]

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ORIGINAL ARTICLE

Basic Study

Reducing bacterial adhesion to titanium surfaces using low intensity alternating electrical pulses

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Abstract

BACKGROUND

Orthopedic implant-related infection remains one of the most serious complications after orthopedic surgery. In recent years, there has been an increased scientific interest to improve prevention and treatment strategies. However, many of these strategies have focused on chemical measures.

AIM

To analyze the effect of alternating current electrical fields on bacterial adherence to titanium surfaces.

METHODS

Staphylococcus aureus (*S. aureus*) and *Escherichia coli* (*E. coli*) were exposed to 6.5 V electrical currents at different frequencies: 0.5 Hz, 0.1 Hz, and 0.05 Hz. After exposure, a bacterial count was then performed and compared to the control model. Other variables registered included the presence of electrocoagulation of the medium, electrode oxidation and/or corrosion, and changes in pH of the medium.

RESULTS
The most effective electrical model for reducing *S. aureus* adhesion was 6.5 V alternating current at 0.05 Hz achieving a 90% adhesion reduction rate. For *E. coli*, the 0.05 Hz frequency model also showed the most effective results with a 53% adhesion reduction rate, although these were significantly lower than *S. aureus*. Notable adhesion reduction rates were observed for *S. aureus* and *E.coli* in the studied conditions. However, the presence of electrode oxidation makes us presume these conditions are not optimal for *in vivo* use.

CONCLUSION
Although our findings suggest electrical currents may be useful in preventing bacterial adhesion to metal surfaces, further research using other electrical conditions must be examined to consider their use for *in vivo* trials.

Key Words: Electrical fields; Bacterial adhesion; Orthopedic infection; Titanium; Metal surfaces

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Core Tip: Current strategies to prevent orthopedic implant infections have focused on chemical measures. Our data suggest electrical currents may be useful in preventing *Staphylococcus aureus* and *Escherichia coli* adhesion to titanium surfaces. Reduction in adhesion rates of up to 90% were observed when applying low intensity alternating currents on titanium surfaces. Further research is needed to consider the use of electrical currents for infection prevention in an *in vivo* scenario.

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INTRODUCTION

Orthopedic implant-related infection remains one of the most serious complications after orthopedic surgery. The incidence of infection after fracture surgery varies depending on the mechanism of injury from 1% in low energy closed fractures and up to 30% in high energy open fractures[1]. The incidence of infection after primary hip and knee arthroplasty is 1%-3% and increases to up to 15% in revision surgery[2]. The management of orthopedic implant-related infection usually requires a combination of surgical and prolonged courses of antibiotic treatment. In recent years, there has been an increased scientific interest to improve prevention and treatment strategies. Many of these strategies have focused on chemical measures to reduce and treat infections.

Although the exact physiopathology of implant-related infections is unknown, infections are preceded by contamination of the surgical site (during surgery, postoperatively, or by hematogenous seeding) followed by bacterial adhesion and biofilm formation on the metal surface. Depending on several variables such as bacterial load, host immunity, and microorganism virulence, early or delayed implant infections can occur.

The antibacterial properties of electric currents have been used since the past century. In 1919, Anderson *et al*[3] published a method to sterilize milk using low frequency alternating current (AC). In non-medical related fields such as industrial water or food processing, high voltage electrical currents are commonly used to eliminate microorganisms and debris.

Focusing on the medical field, Costerton *et al*[4] were the first to postulate the potential uses of electrical currents for the treatment of artificial implant infections. From that point on, an increasing number of *in vitro* studies have demonstrated the capacity of low-intensity electrical currents to inhibit bacterial growth of different *Staphylococcus aureus* (*S. aureus*), *Pseudomonas aeruginosa,* and *Staphylococcus epidermidis* strains. Moreover, they described the "bioelectric" effect caused by the antibacterial synergies between antibiotics and electric fields against biofilm bacteria[5].

However, many of these studies are focused on the use of direct current (DC). It is important to note that DC has potential drawbacks for its *in vivo* use. DC generates water electrolysis and can cause changes in pH and free radicals that could be cytotoxic. Furthermore, DC generates higher amounts of energy that can cause electrocorrosion and/or oxidation of the metal electrodes making its applicability limited in clinical scenarios with metallic implants.

Orthopedic surgical procedures commonly involve the use of biocompatible metals such as titanium. The reduction of bacterial adherence to metal surfaces using electrical fields has been described for stainless steel[6]. To the best of our knowledge, there is no evidence of the effect of electrical currents on reducing bacterial adherence to titanium surfaces.

The objective of our study was to analyze the effect of AC electrical fields on bacterial adherence to a titanium surface for gram-positive and gram-negative bacteria. The secondary objective was to analyze the effect of electrical fields to titanium and the medium.

MATERIALS AND METHODS

Titanium plate manufacturing

The medical titanium (Ti-6Al-4V) components used in our study were manufactured and supplied by AMES S.A. (Sant Feliu de Llobregat, Barcelona, Spain) Circular disks were obtained from cutting titanium bars. Each disk was mechanically polished to remove irregularities and to promote identical physical conditions at the surface for all disks.

Design and manufacturing of culture plates

The design of a culture plate that would allow a simultaneous number of tests with different electrical conditions was important to standardize the study process and optimize resources. A self-designed 12-well culture plate was designed and manufactured by Innovative Minds S.L. to achieve this goal. Using a standard plastic 12-well culture plate with 3 rows and 4 columns (Nunclon-Thermo Scientific), holes were drilled at the bottom of each of the wells to fit titanium electrodes at the base. The top or lid of the wells was also drilled to place a disk at the top to serve as an electrode. This setup allowed the 12 wells to have cylindrical titanium electrodes at the top and bottom of each well. All electrodes were connected to a generator and an amplifier as seen in Figure 1A. The function generator had four separate connections to allow four different trials to be performed simultaneously and in a triplicated manner. To generate the desired waveforms, an AFG1022 Dual Channel Arbitrary Function Generator (Tektronix Inc., Beaverton, OR, United States) was used. The signal was amplified by an OPA548EVM Power Operational Amplifier (Texas Instruments Incorporated, Dallas, TX, United States). One amplifier per channel was used. The power op-amps were powered by an off-the-shelf 15 V symmetric power supply. (Figure 1A and B).

Effects of the electrical field on titanium and medium without bacteria

Before conducting the study with bacteria, we performed a series of analyses to evaluate possible interactions between electrical fields and the titanium plates and brain heart infusion (BHI) medium.

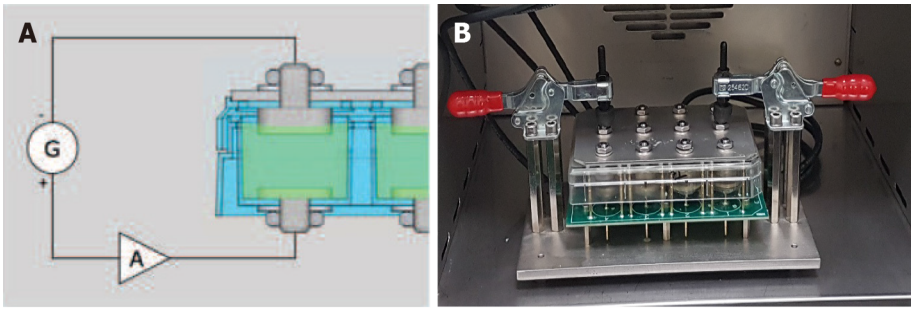
The main objectives of this test were: (1) To obtain the threshold voltage at which electrocoagulation and electrolysis were seen in the culture medium; and (2) To evaluate if at this point of voltage there was macroscopic signs of oxidation of titanium plates. For these reasons, two 15 mm diameter and 2 mm thick titanium disks were suspended at the base of a well in a 6-well culture plate (Nuclon Delta Surface, Thermo Fisher Scientific, Waltham, MA, United States) petri dish covered in 4 mm of BHI. The two disks were separated by a 5 mm distance as shown in Figure 2A. The left electrode was connected to the negative (catode) pole of a DC power supply, while the right electrode was connected to the positive (anode) electrode of the same supply. A USB microscope [913-2478, Electrocomponents PLC (RS Pro), London, United Kingdom] was set up and shown in Figure 2B to visualize and count bubble formation. A constant potential difference was applied between the two electrodes during a 10-min period. We then evaluated: (1) The presence of titanium oxidation by controlling the change of color of the surface; (2) The presence of bubbles and the quantity during one minute to estimate the number of bubbles formed during exposure; and (3) The formation of lumps as a consequence of medium electrocoagulation.

The presence of lumps was evaluated using a Zeiss Neon scanning electron microscope operated at 15 keV, equipped with energy dispersive X-ray spectroscopy to examine their composition. Energy dispersive X-ray spectroscopy line profile and energy dispersive X-ray spectroscopy mapping analyses were performed to detect the presence of calcium, phosphate, sodium, and potassium.

Bacterial adhesion experiments

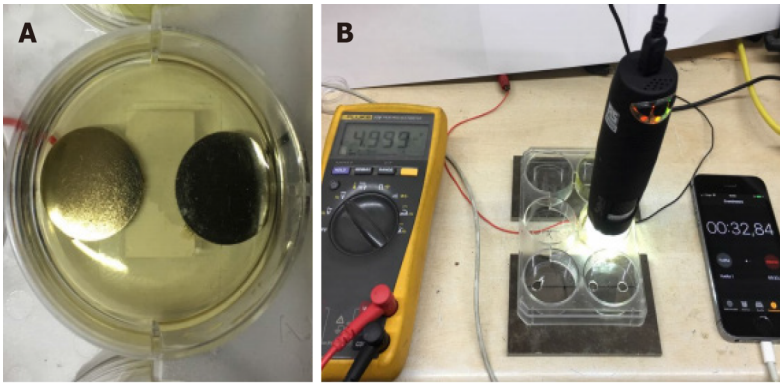
Using the self-designed 12-well culture plate mentioned above, we analyzed the potential effect of electrical currents in reducing bacterial adhesion to a titanium metal surface. Our self-designed culture plate allowed four different conditions to be tested by triplicate at the same time.

The experiments were performed using a gram-positive strain, *S. aureus* (CCUG 15915), and a gram-negative strain, *Escherichia coli* (*E. coli*) (CECT 101). Both bacteria were individually streaked in BHI (Scharlab SL, Spain) agar plates. Colonies were grown in BHI broth overnight at 37 ºC and diluted to an OD600 of 0.2. Three milliliters of this medium were then inoculated to the self-designed plates containing titanium discs. Bacteria were incubated at 37 ºC for 2 h, applying 6.5 V pulsed electrical



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Figure 1 Design of the 12-well culture plate. A: The connection to the generator, the amplifier, and both electrodes in one of the wells of the plate. The lower electrode acted as a cathode, and the upper electrode acted as an anode; B: Photograph of the function generator with four separate connections to allow four different trials to be performed simultaneously. There are three rows of wells on the culture plate allowing tests to be triplicated.



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Figure 2 Electrical field application without bacteria. A: Initial setup of the titanium disks; B: Microscope used to visualize titanium oxidation and bubble formation.

currents at different frequencies, *i.e.* 0.5 Hz, 0.1 Hz, and 0.05 Hz, to prevent attachment. A control without exposure to electrical fields was used as maximum bacterial adhesion. Each condition was tested with titanium electrodes provided at each end of the wells.

After exposure, non-adhered bacteria were removed by aspiration of the medium followed by three rinses with PBS. Then, 1 mL PBS was added, and the plate was sonicated in a Xuba1 Ultrasonic bath (Grant Instruments, United Kingdom) to detach the bacteria adhered to the bottom titanium electrode. Subsequently, serial dilutions of detached bacteria were streaked onto BHI agar plates and incubated overnight at 37 ºC. Colony-forming units per milliliter were counted. All tests were repeated three times, and mean values were reported.

Presence of bacteria at the titanium disc surface was evaluated by scanning electron microscope. After incubating the bacteria with different electrical currents as described above, discs were rinsed thrice with PBS, and bacteria were fixed with a 2.5% glutaraldehyde solution. Discs were then washed and dehydrated in a series of increasing ethanol solutions for 20 min each. Complete dehydration was performed after incubation in hexamethyldisilazane. Dried samples were covered with a thin carbon layer and mounted on aluminum stubs. Samples were observed using a Zeiss Neon at an operating voltage of 5 kV.

Other variables registered included presence of electrocoagulation of the medium (lumps), electrode oxidation, and changes in pH of the medium. The pH was measured in the collected supernatants using a selective MultiMeter MM41 (Crison Instruments) electrode.

The results shown in this manuscript are part of a thesis project titled "Utility of electrical currents for the prevention and treatment of orthopedic implant-related infections" (Universitat de Barcelona).

RESULTS

Effects of the electrical field on culture medium

During our preliminary tests, we had observed the formation of hydrogen microbubbles from the negative electrode and a fewer amount of oxygen bubbles from the positive electrode when high

voltages were used. This phenomenon was attributed to electrolysis. We therefore had to establish the threshold potential at which electrolysis did not occur for our setup. Our results showed the decomposition potential for our setup started at 5 V. An exponential increase in bubble formation was reported at 6.5 V (Figure 3).

We also noted the formation of lumps in the culture medium due to electrocoagulation. For this reason, we tested two different voltages, 7.5 V and 6.5 V, to evaluate the effect of electrocoagulation in our medium. We applied these potential differences and observed there was an increased agglomeration when using 7.5 V. We did not observe agglomeration using 6.5 V. Taking into consideration these results, we decided to establish 6.5 V as a safe potential difference in our setup to minimize the effect of electrolysis and electrocoagulation on our results.

Bacterial adhesion experiments

After establishing a reference voltage at which electrocoagulation and electrolysis were minimized, we proceeded to carry out the experiments on bacteria following the previously described methodology.

The most effective electrical model for reducing *S. aureus* adhesion was 6.5 V AC at 0.05 Hz achieving a 90% adhesion reduction rate. Bacterial counts in the control were 4.22e6 colony-forming units (Figure 4A).

For *E. coli*, the 0.05 Hz frequency model also showed the most effective results with a 53% adhesion reduction rate, although these were lower than *S. aureus*. Bacterial counts in the control were 6.53e6 colony-forming units (Figure 4B).

Although we performed tests to establish a high threshold voltage to minimize the effects of electrocoagulation and electrolysis of the culture medium, these phenomena were observed in all tests when bacteria were present in the medium. The lumps were analyzed using energy dispersion X-ray spectroscopy to determine their composition. We concluded these were formed by titanium ions, due to oxidation of the electrode, and other ions (P, K, Na) from the salts in the medium. Furthermore, when the lumps were visualized under an electron microscope, bacteria were seen in the surface and inside the lumps as shown in Figure 5.

No changes in pH were found in any of the tests performed. In all studied conditions, anodizing at the titanium electrodes was observed creating an ochre and purple coloring (Figure 6).

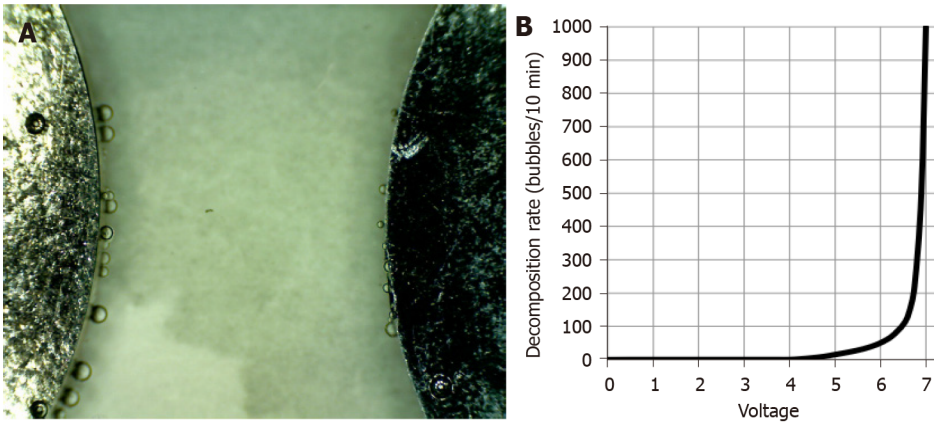
DISCUSSION

The results of our study suggest it is possible to achieve a reduction in the adhesion of *S. aureus* and *E. coli* to titanium surfaces using low intensity alternating pulsed electrical currents. Most current research regarding electrical currents and bacterial adhesion to metal surfaces have been performed in a variety of custom-designed electrical devices to serve the purpose. Previous results using parallel plate flow chambers as described by Poortinga *et al*[7] and performed by van der Borden *et al*[8,9] showed that a variety of staphylococcal strains could be detached from surgical stainless steel by the application of a direct electrical current. The authors of this study attributed this detachment mechanism to an ionic-strength dependent transfer of electrons. This explained the increased detachment rate with higher currents. They also described the detachment force to be proportional to the voltage applied and that this force needs to overcome the attractive Lifshitz-Van der Waals and the acid-base forces between the adhering bacteria and the surface.

To reduce the number of bacteria adhered to a metal surface; these forces also need to be neutralized. The mechanism of bacterial adhesion to metal surfaces is complicated. Bacterial adhesion to a metal surface can be described as a two-phase process including an initial and reversible phase (phase one) and a time-dependent irreversible phase (phase two), which was first proposed by Marshall *et al*[10,11]. Planktonic bacteria interact with metal surfaces following a series of physical forces such as gravity, electrostatic charges, hydrophobic interactions, Brownian motion, and van der Waals attraction forces. In phase one, when the cell and the surface come into close contact (< 3 nm), short-range interactions such as hydrogen bonding and ionic and dipole interactions become effective for bacterial adhesion. At this point the electrical currents play an important role for preventing bacterial adhesion to metal surfaces by interacting with these forces. In the second phase of adhesion, molecular reactions between bacterial surface structures become predominant[12]. Other factors affecting bacterial adhesion include characteristics of bacteria themselves, the target material surface, and environmental factors such as the presence of serum proteins or bactericidal substances[12].

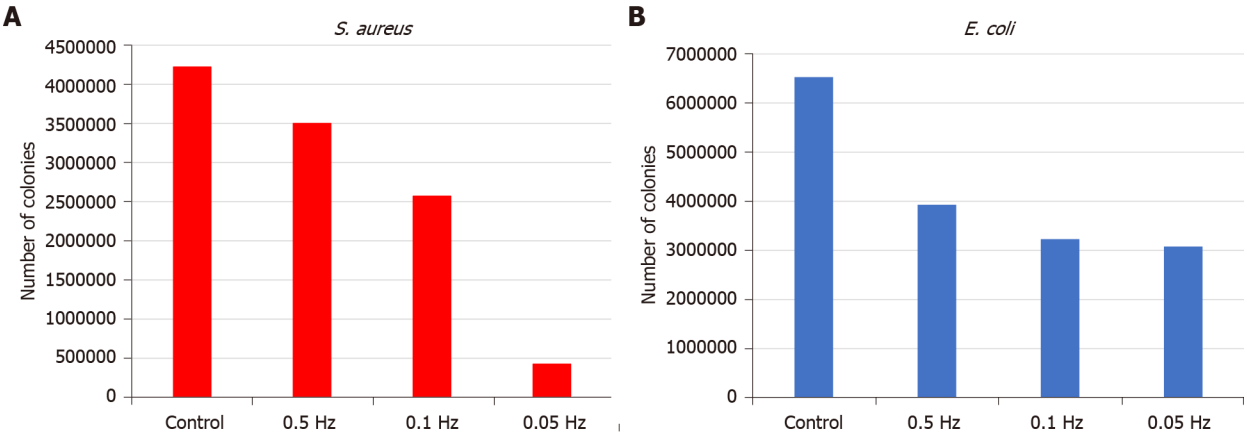
Regarding the electrical model, the most successful studies have used DC currents. Theoretically, under the influence of ACs, fewer electrons and therefore less energy is applied to the system. This could explain the lower rate of adhesion reduction achieved by ACs compared to DCs described by van der Borden *et al*[8]. However, the use of AC could prove to be feasible for the treatment in clinical *in vivo* scenarios.

Our study results show adhesion reduction rates of up to 90% for *S. aureus* using AC low intensity alternating pulses. However, we only achieved 53% adhesion reduction rates for *E. coli*. As previously pointed out, many factors influence bacterial adhesion. We believe this difference could be explained by



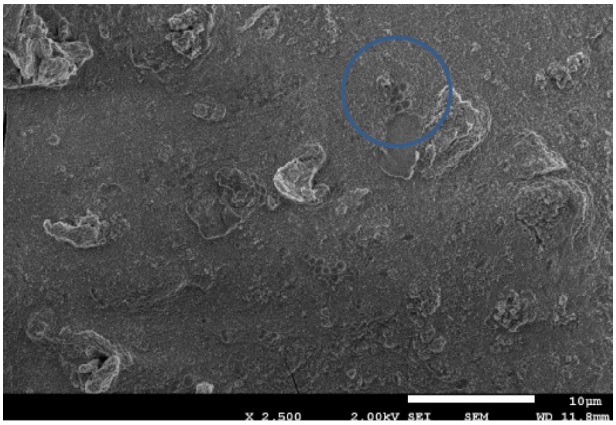
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Figure 3 Microbubble formation test and results. A: Microbubble formation at the cathode using a 7 V current; B: Bubble rate formation on the X-axis compared to voltage. Exponential formation of bubbles after 5V.



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Figure 4 Results for colony-forming units. A: Results for colony-forming units of *Staphylococcus aureus* for the studied conditions; B: Results for colony-forming units of *Escherichia coli* for the studied conditions. *S. aureus*: *Staphylococcus aureus; E. coli*: *Escherichia coli*.



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Figure 5 Bacteria inside the lumps formed by electrocoagulation of the medium.

the different cell structure of the studied bacteria. Most prokaryotic cells are known to have a rigid cell wall. This cell wall is essential for viability, protection, and structure. There are significant differences in the composition of *S. aureus* and *E. coli* cell walls. The Gram stain test is a quick way to classify bacteria into two broad categories (gram-positive or gram-negative) according to their cell wall characteristics. The most significant difference between these two groups of bacteria is that gram-positive bacteria are



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Figure 6 Anodizing of the titanium surfaces.

marked by the absence of an outer lipid cell membrane. In general, gram-positive bacteria are considered monoderms and have a single lipid layer as opposed to gram negative bacteria that are diderms and have two lipid layers. We have hypothesized that our results improve when increasing the amount of energy applied to *S. aureus* but remain constant with *E. coli* due to these structural differences, making gram negative bacteria more resistant to forces caused by electrical currents.

Changes in pH have also been described to influence bacterial growth. This principle is commonly used in detergents and disinfectants to kill bacteria[13]. Large variations in external pH have biocidal effects on bacteria[14]. In our study, we did not observe changes in pH. For this reason, we can establish that the effect on bacterial adhesion is directly related to the electrical current and not caused by a change of pH in the medium.

Additionally, the effects of electrolysis and electrocoagulation in the presence of bacteria and BHI have shown several a priori unexpected reactions. The formation of lumps formed due to electrocoagulation of the medium showed the presence of bacteria when examined under an electron microscope. Additionally, we cultured these lumps to establish if there was living bacteria. Although we cannot be sure if the samples were contaminated by the suspended bacteria in the culture medium, we can almost be sure electrical fields, at the voltages used, do not directly kill bacteria, and prevent them from adhering to the metal surface. To the best of our knowledge there are no current studies in the literature that evaluated this phenomenon. Therefore, we have not found any references regarding this topic.

CONCLUSION

Notable adhesion reduction rates were observed for *S. aureus* and *E. coli* in the studied conditions. However, the presence of electrolysis and electrode oxidation lead us to presume these conditions are not optimal for *in vivo* use. Although our findings suggest alternating electrical currents may be useful in preventing bacterial adhesion to titanium, further research using other electrical conditions must be examined to consider their use for *in vivo* trials.

ARTICLE HIGHLIGHTS

Research background

Orthopedic implant-related infection remains one of the most serious complications after orthopedic surgery. In recent years, there has been an increased scientific interest to improve prevention and treatment strategies. Many of these strategies have focused on chemical measures to reduce and treat infections.

Research motivation

Our study group has been developing novel strategies for the treatment and prevention of orthopedic implant-related infections. These have been focused on the application of electrical currents to surface metals in the presence of bacteria to prevent adhesion and disrupt biofilm formation.

Research objectives

The objective of our study was to analyze the effect of alternating current electrical fields on bacterial adherence to a titanium surface for gram-positive and gram-negative bacteria.

Research methods

Using a self-designed 12-well culture plate, we analyzed the potential effect of electrical currents in reducing bacterial adhesion to a titanium metal surface. Gram-positive bacteria, represented by *Staphylococcus aureus* (*S. aureus*), and gram-negative bacteria, represented by *Escherichia coli* (*E. coli*), were exposed to 6.5 V electrical currents at different frequencies: 0.5 Hz, 0.1 Hz, and 0.05 Hz. After exposure, colony-forming units per milliliter were counted and compared to a control without exposure to electrical currents.

Research results

The most effective electrical model for reducing *S. aureus* adhesion was 6.5 V alternating current at 0.05 Hz achieving a 90% adhesion reduction rate. For *E. coli*, the 0.05 Hz frequency model also showed the most effective results with a 53% adhesion reduction rate, although these were significantly lower than *S. aureus*.

Research conclusions

Our results demonstrate electrical fields may have promising applications in preventing bacterial adhesion to titanium metal surfaces. However, the presence of electrolysis and electrode oxidation lead us to presume these conditions may not be optimal for *in vivo* use.

Research perspectives

Further research using other electrical conditions must be examined to consider their use for *in vivo* trials.

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FOOTNOTES

Author contributions: Bernaus M, Guillem-Martí J, and Font-Vizcarra L have made substantial contributions to research design, acquisition, analysis, interpretation of data, and drafting the manuscript; Bermúdez A, Calero JA, Torres D, and Veloso M have made substantial contributions to interpretation of data and critically revising the manuscript; All authors have read and approved the final submitted manuscript.

Conflict-of-interest statement: Each author certifies that he or she has no commercial associations (*e.g.*, consultancies, stock ownership, equity interest, patent/Licensing arrangements, *etc.*) that might pose a conflict of interest in connection with the submitted article.

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REFERENCES

1 **Papakostidis C**, Kanakaris NK, Pretel J, Faour O, Morell DJ, Giannoudis PV. Prevalence of complications of open tibial shaft fractures stratified as per the Gustilo-Anderson classification. *Injury* 2011; **42**: 1408-1415 [PMID: 22019355 DOI:

10.1016/j.injury.2011.10.015]
2 **Kurtz SM**, Ong KL, Lau E, Bozic KJ, Berry D, Parvizi J. Prosthetic joint infection risk after TKA in the Medicare population. *Clin Orthop Relat Res* 2010; **468**: 52-56 [PMID: 19669386 DOI: 10.1007/s11999-009-1013-5]
3 **Anderson AK**, Finkelstein R. A Study of the Electro-Pure Process of Treating Milk. *J Dairy Sci* 1919; **2**: 374-406 [DOI: 10.3168/jds.s0022-0302(19)94338-4]
4 **Costerton JW**, Ellis B, Lam K, Johnson F, Khoury AE. Mechanism of electrical enhancement of efficacy of antibiotics in killing biofilm bacteria. *Antimicrob Agents Chemother* 1994; **38**: 2803-2809 [PMID: 7695266 DOI: 10.1128/AAC.38.12.2803]
5 **Blenkinsopp SA**, Khoury AE, Costerton JW. Electrical enhancement of biocide efficacy against Pseudomonas aeruginosa biofilms. *Appl Environ Microbiol* 1992; **58**: 3770-3773 [PMID: 1482196 DOI: 10.1128/aem.58.11.3770-3773.1992]
6 **Muñoz-Mahamud E**, González-Cuevas A, Sierra JM, Diaz-Brito V, Bermúdes A, Soriano A, Castellanos J, Font-Vizcarra L. Pulsed electric fields reduce bacterial attachment to stainless steel plates. *Acta Orthop Belg* 2018; **84**: 11-16 [PMID: 30457494]
7 **Poortinga AT**, Bos R, Busscher HJ. Controlled electrophoretic deposition of bacteria to surfaces for the design of biofilms. *Biotechnol Bioeng* 2000; **67**: 117-120 [PMID: 10581443 DOI: 10.1002/(sici)1097-0290(20000105)67:1<117::aid-bit14>3.0.co;2-6]
8 **van der Borden AJ**, van der Mei HC, Busscher HJ. Electric-current-induced detachment of Staphylococcus epidermidis strains from surgical stainless steel. *J Biomed Mater Res B Appl Biomater* 2004; **68**: 160-164 [PMID: 14737763 DOI: 10.1002/jbm.b.20015]
9 **van der Borden AJ**, van der Mei HC, Busscher HJ. Electric block current induced detachment from surgical stainless steel and decreased viability of Staphylococcus epidermidis. *Biomaterials* 2005; **26**: 6731-6735 [PMID: 15979141 DOI: 10.1016/j.biomaterials.2004.04.052]
10 **Marshall KC**. Mechanisms of Bacterial Adhesion at Solid-Water Interfaces. In: Savage DC, Fletcher M. Bacterial Adhesion. New York: Plenum Press, 1985: 133-161
11 **Marshall KC**, Stout R, Mitchell R. Mechanism of the Initial Events in the Sorption of Marine Bacteria to Surfaces. *J Gen Microbiol* 1971; **68**: 337-348 [DOI: 10.1099/00221287-68-3-337]
12 **Katsikogianni M**, Missirlis YF. Concise review of mechanisms of bacterial adhesion to biomaterials and of techniques used in estimating bacteria-material interactions. *Eur Cell Mater* 2004; **8**: 37-57 [PMID: 15593018 DOI: 10.22203/ecm.v008a05]
13 **Garrett TR**, Bhakoo M, Zhang Z. Bacterial adhesion and biofilms on surfaces. *Prog Nat Sci* 2008; **18**: 1049-1056 [DOI: 10.1016/j.pnsc.2008.04.001]
14 **Booth IR**. Regulation of cytoplasmic pH in bacteria. *Microbiol Rev* 1985; **49**: 359-378 [PMID: 3912654 DOI: 10.1128/mr.49.4.359-378.1985]

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ORIGINAL ARTICLE

Basic Study

Content of blood cell components, inflammatory cytokines and growth factors in autologous platelet-rich plasma obtained by various methods

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Abstract

BACKGROUND

The evaluation of the efficacy of platelet-rich plasma (PRP) in clinical practice yields conflicting results and raises numerous controversies. This may be due to different concentrations of biologically active components in PRP obtained with the use of different methods of gravity separation.

AIM

To compare the content, repeatability and correlations between biologically active components in PRP obtained with four different commercial systems.

METHODS

From a whole blood sample of each of 12 healthy male volunteers, 4 PRP samples were prepared using 4 different commercial kits [Arthrex Autologous Conditioned Plasma (ACP), Mini GPS III, Xerthra, Dr. PRP] in accordance with the instructions provided by the manufacturers. A comparative analysis of blood cell

components - 13 selected inflammatory cytokines and 7 growth factors - in the obtained PRP samples was performed using the Kruskal-Wallis test by ranks. The repeatability of results in each method was evaluated by the estimation of the coefficient of variation. The Spearman correlation was used to estimate the relationship between blood cell content and cytokines.

RESULTS

Significantly higher concentrations of platelets (PLT), white blood cells (WBC) and red blood cells (RBC) were found in PRP obtained with the use of Mini GPS III than in PRP obtained using other systems. Significant differences in the content of growth factors and cytokines in PRP were found. A positive correlation of the amount of PLT, RBC and WBC with the concentration of most of the growth factors was found but in only three inflammatory cytokines. The obtained correlations between blood cell components and cytokines differed between the systems in terms of statistical significance, which may be due to insufficient sample size. The repeatability of the obtained PLT concentration also varied between protocols with the lowest in Xerthra and the highest in Arthrex ACP.

CONCLUSION

Significant differences in the content of biologically active components and their repeatability were found in PRP obtained by various methods, providing new data for further research.

Key Words: Platelet-rich plasma; Cytokines; Chemokines; Growth factors

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Core Tip: The presented study showed important differences between blood cell components and levels of selected growth factors and inflammatory cytokines in platelet-rich plasma obtained with four different commercial preparation systems in a single-donor model. The range of cytokines analyzed far exceeded the ranges investigated in earlier publications. This was also the first study to pay attention to the repeatability of the quality of the obtained platelet-rich plasma (PRP). New positive correlations were found between platelet content in PRP and several cytokines (Hepatocyte growth factor, Interleukin-1β, Monocyte chemoattractant protein-1, Interleukin-8, Interleukin-18). The demonstrated positive correlation between red blood cell content in PRP and cytokines has never been described before.

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INTRODUCTION

Autologous platelet-rich plasma (PRP) therapy is a method known for many years used in the treatment of various diseases. Nowadays, despite numerous controversies, it is widely used, especially in aesthetic medicine, orthopedics and sports medicine[1-6]. The method involves preparation from the patient's blood sample of plasma with a concentration of platelets higher than physiological and then its injection into pathological tissues[2,6-8].

In the human body, platelets are involved in the repairing processes, inter alia, by releasing different cytokines including growth factors from their α granules[2,6,9-11]. Inflammatory cytokines have also an important role in the initiation of the healing process, chemotaxis and keratinocyte proliferation but their excess can impair regeneration[12].

The essence of treatment with PRP is to accelerate the repairing processes by delivering a high concentration of platelet-derived growth factors and other cytokines directly to the affected area[6,13]. Attempts have been made to use PRP for treating diseases in which the repairing processes are impaired or when PRP was expected to accelerate healing as much as possible. This applies especially to chronic overuse injuries such as enthesopathies or tendinopathies, to the acceleration of the healing process of many different sports injuries of ligaments, tendons and muscles but also to bone union disorders and hard-healing wounds[6,13-16]. Intraarticular PRP injections used in osteoarthritis may be beneficial in the alleviation of chronic pain helping to increase the physical activity of patients[4,17-19].

The production of autologous platelet-rich plasma using commercial kits is a fast, convenient, affordable and safe way to obtain high concentrations of the desired growth factors[13,20]. By now it is known that too low platelet concentration is insufficient to induce a tissue response but too high a concentration can even have some negative impact on tissue healing[21,22].

There is an increasing number of manufacturers providing commercial kits that enable the quick, easy and safe preparation of PRP in an outpatient setting. Such kits differ from one another by some parameters such as the amount of material collected from the patient, the type of anticoagulant, the structure of the separator, the time and speed of centrifugation, the method of extraction and activation of the obtained plasma. They also differ in the assumed concentration that they allow to obtain and the presence of leukocytes in the final product[2,20,23-25]. Such a multitude of variables makes it impossible to reliably assess the effectiveness of therapies with different autologous platelet-rich plasma preparations without providing detailed information[21]. Furthermore, only a small number of studies on relatively small populations have shown significant differences in the desired cytokine content by testing only a few from many commercially available PRP systems. Despite many years of clinical use of PRP, there is still a remarkable scarcity of relevant and reliable information about its biologically active compounds. This lack of information was the main reason for the previous preliminary study conducted by the present authors[26]. Its results encouraged the authors to expand the study with a larger population and a greater amount of analyzed cytokines.

MATERIALS AND METHODS

Study aim, design and setting of the study

The goal of this study was to compare the content of blood cell components, selected inflammatory cytokines and selected growth factors in PRP samples obtained with the use of various commercial kits, to find any correlations between those biologically active components and to establish their repeatability within each method.

The study was designed as a single-center prospective non-randomized case-series descriptive laboratory study and was conducted in a medical university laboratory in the autumn of 2020 by clinicians from the Department of Trauma and Hand Surgery and the Department of Sports Medicine in cooperation with laboratory researchers from the Faculty of Pharmacy.

It was conducted in accordance with the standards of Good Clinical Practice. The study was approved by the institutional bioethics committee. All participants signed informed consent to participate in the study. The study followed the Minimum Information for Studies Evaluating Biologics in Orthopedics (MIBO) guidelines[27].

Characteristics of participants

The study involved 12 healthy male volunteers, aged 24-35 years (mean ± SD, 28.92 ± 3.15 y.o.). The mean height, body weight and body mass index were 182.42 ± 5.14 cm, 86.92 ± 8.73 kg and 26.16 ± 2.83 kg/m^2, respectively. The inclusion criteria were: the age of 20-35 years, the absence of serious diseases and conditions that could affect the amount and function of blood cell components (in particular diabetes, blood dyscrasia, inflammatory conditions, cancer, pre-existing joint pathologies). Volunteers who, in the two weeks preceding the study, were taking drugs that may interfere with the function of platelets or may affect the quantity or quality of blood cell components (in particular antiplatelet or anti-inflammatory drugs) were excluded from the study.

Each volunteer, after signing the informed consent, was asked to complete a questionnaire with personal information about age, height, weight, diseases, medications, sports activities and nicotine addiction. A vast majority of the respondents (91.67%) declared practicing sports at least once a week, and none of them regularly smoked cigarettes.

PRP preparation

Four commercially available systems for the preparation of PRP intended for use in orthopedics and sports medicine were selected: the Arthrex Autologous Conditioned Plasma (ACP) Double Syringe System (Arthrex Inc., United States), the Mini GPS III Platelet Concentration System (Biomet Inc., United States), the Xerthra PRP kit (Biovico Sp. z o.o., Poland), Dr. PRP (Rmedica, Republic of Korea).

Following the principles of asepsis, 74 mL of whole blood was collected and divided immediately into:

- 2 mL to a probe with ethylenediaminetetraacetic acid (EDTA).
- 13.5 mL to a double-syringe with 1.5 mL of anticoagulant citrate dextrose solution A (ACD-A) from Arthrex ACP.
- 27 mL to a syringe with 3 mL of ACD-A for the Mini GPS III kit.
- 13.5 mL to a syringe with 1.5 mL of 3.13% sodium citrate for the Xerthra kit.
- 18 mL to a syringe with 2 mL of 3.13% sodium citrate for the Dr. PRP kit.

The four samples of liquid-form PRP were prepared simultaneously from blood obtained from each volunteer using 4 different commercial kits according to the manuals provided by the manufacturers. The main characteristics of the PRP protocols are listed in Table 1 and illustrated in Figure 1.

Analysis of blood cell composition

First, the whole blood samples collected for EDTA were analyzed. The time between blood draw, PRP processing, extraction and activation did not exceed 1 h. All preparations were conducted in daylight and at room temperature. The whole blood count and blood cell composition of PRP samples were analyzed using an automatic laboratory analyzer Mindray BC-5150 (Shenzhen Mindray Bio-Medical Electronics Co., PRC) which needs 20 μL for each analysis. Immediately after PRP preparation, each sample was transferred into Eppendorf polypropylene tubes and then shaken gently for 30 s directly before analysis. Platelet capture efficiency (PCE) was calculated with the formula below, described previously by J. Magalon[23].

PCE (%) = [Volume of PRP obtained (mL) × platelet concentration in PRP (G/L)]/[Net volume of whole blood collected (mL) × platelet concentration in whole blood (G/L)].

Platelet activation and sample storage

The remaining PRP (1 ml) was dispensed into Eppendorf polypropylene tubes and then activated through a double freeze-thaw process (30 min for each step) according to the procedure described by R. Zimmermann[25]. The activated samples were frozen to the temperature of -80 °C and stored for further analysis.

Analysis of the content of inflammatory cytokines and growth factors

The samples were thawed to room temperature and centrifuged for 5 min at 2500 revolutions per minute in a Micro Star 17 microcentrifuge (VWR International Company, Thermo Electron LED, Germany) immediately before performing the composition analysis of selected cytokines using flow cytometry.

A LEGENDplex™ Custom Human 7-plex Panel (BioLegend, United States) was used to quantify the following platelet growth factors:

- Transforming Growth Factor-β1 (TGF-β1, free active).
- Epidermal growth factor (EGF).
- Fibroblast Growth Factor- basic (FGF-basic).
- Vascular endothelial growth factor (VEGF).
- Hepatocyte growth factor (HGF).
- Platelet-Derived Growth Factor-AA (PDGF-AA).
- Platelet-Derived Growth Factor-BB (PDGF-BB).

LEGENDplex™ Human Inflammation Panel 1 (BioLegend, United States) was used to quantitatively measure 13 human inflammatory cytokines:

- Interleukin-1β (IL-1β).
- Interferon-α2 (IFN-α2).
- Interferon-γ (IFN-γ).
- Tumor Necrosis Factor α (TNF-α).
- Monocyte Chemoattractant Protein-1 (MCP-1; CCL2).
- Interleukin-6 (IL-6).
- Interleukin-8 (CXCL8).
- Interleukin-10 (IL-10).
- Interleukin-12p70 (IL-12p70).
- Interleukin-17A (IL-17A).
- Interleukin-18 (IL-18).
- Interleukin-23 (IL-23).
- Interleukin-33 (IL-33).

BioLegend's LEGENDplex™ assays are bead-based multiplex immunoassays that use fluorescence-encoded beads and flow cytometer measurements. The concentrations of particular cytokines were determined by means of a standard curve generated during the performance of the test. The analyses were conducted according to the manufacturer's procedure. The samples were acquired on CyFlow SPACE and CyFlow CUBE flow cytometer (Sysmex-Partec, Germany) using a 488 nm laser with a 536/40 (BP) filter for the PE fluorochrome, and a 638 nm laser with 675/20 (BP) for the APC fluorochrome. The results were analyzed with LEGENDplex™ Data Analysis Software V.8.0 (Vigene Tech Inc., United States).

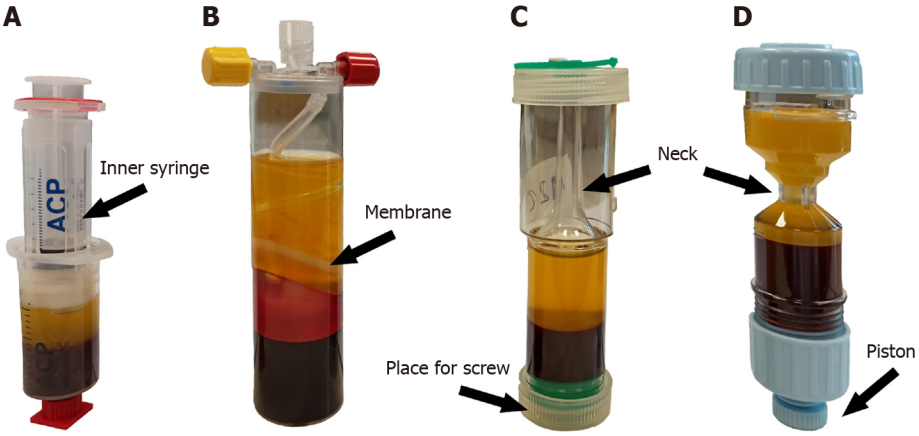
Statistical analysis

The results were statistically analyzed using Statistica 13.3 software (TIBCO Software Inc, United States). Arithmetic means ± SD were calculated. The Shapiro-Wilk test was used to analyze the compliance of the distribution of the analyzed variables with normal distribution. The Kruskal-Wallis test by ranks (one-way analysis of variance on ranks) with Dunn's post-hoc test was used to compare

Table 1 The main characteristics of the platelet-rich plasma protocols used in the study

	Arthrex ACP	Mini GPS III	Xerthra	Dr. PRP
Amount of blood collected	13.5 mL	27 mL	13.5 mL	18 mL
Final amount of PRP	4 mL	3 mL	1.5 mL	3 mL
Drawn blood/obtained PRP	3.38:1	9:1	9:1	6:1
Anticoagulant type	ACD-A	ACD-A	3.13% SOD CITR	3.13% SOD CITR
Anticoagulant amount	1.5 mL	3 mL	1.5 mL	2 mL
Number of spins	1	1	1	1
RPM	1500	3200	3500	3100
Centrifugation time	5′	15′	5′	4′
Removal of PPP	no	yes	yes	yes
Expected WBC content	low	high, 5x	low	low
Expected PLT concentration	2-3 x	9.3 x	2-13 x	4-5 x
Dedicated centrifuge	Yes	Yes	Yes	Yes
Activation method	*In vivo*	*In vivo*	*In vivo*	*In vivo*
Type of PRP	Conditioned Plasma	LR-PRP	LP-PRP	LP-PRP

ACD-A: Anticoagulant citrate dextrose solution A; LR-PRP: Leukocyte-rich platelet-rich plasma; LP-PRP: Leukocyte-poor platelet-rich plasma; PPP: Platelet-poor plasma; RPM: Revolutions per minute; SOD CITR: Sodium citrate.



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Figure 1 Different platelet-rich plasma kits after centrifugation. Highlight specific items in each kit used for platelet-rich plasma (PRP) extraction. A: Arthrex autologous conditioned plasma, the prepared plasma is transferred by pulling it into the inner syringe in a double-syringe system; B: Mini GPS III, PRP is automatically separated during centrifugation by a special membrane in the separator; C: Xerthra, the controller screw placed at the bottom is used to move the PRP to the neck of the tube; D: Dr. PRP, the piston is used to push PRP to the tube's neck.

the concentrations of platelets (PLT), white blood cells (WBC), red blood cells (RBC) and cytokines between each protocol. Spearman's rank correlation coefficient was used to find any relationship between blood cell components and cytokines. The strength of the correlation was determined for ρ-value: negligible for $\rho \leq 0.2$, week for $\rho \leq 0.4$, moderate for $\rho \leq 0.6$, strong for $\rho \leq 0.8$ and very strong for $\rho > 0.8$. The repeatability of the results obtained for each of the methods was estimated as the coefficient of variation (CV) which is the ratio of the standard deviation to the mean, multiplied by 100%. High repeatability was established as a CV < 25%, moderate as a CV = 25%-44%, weak as a CV = 45%-99% and very weak as a CV > 100%. Statistical significance was established at the level of $P \leq 0.05$.

Power analysis for PRP comparison was performed using automatic software calculation for several means one-way ANOVA with the use of Root Mean Square Standardized Effect. The statistical power of the tests was set at 0.8. Based on the magnitude of the effect calculated according to the preliminary study, it was estimated that in order to show significant blood cell component differences between the PRP groups with a test power of 0.8, each group should have a minimum of 6 subjects. Similarly, the

population needed to show differences in GF levels differs depending on the factor tested (from 8 to 61 subjects). Group size could not be estimated for differences in inflammatory cytokine levels as there were no previous studies to provide the necessary data. The authors calculated that 48 PRP samples divided into four groups should be sufficient to achieve the assumed goal of the study.

RESULTS

Whole blood count

The blood counts of all participants are shown in the Table 2.

Blood cell components of PRP samples

The highest concentrations of PLT, WBC and RBC in PRP were obtained with Mini GPS III. Platelet concentration in PRP obtained with Mini GPS III was significantly higher than that obtained with Artherx ACP ($P < 0.001$), Xerthra ($P < 0.001$) and Dr. PRP ($P < 0.008$). The differences between the remaining systems were not significant ($P > 0.05$). The situation was similar with the ability to concentrate PLT above the baseline with 5.05 × for Mini GPS III which was significantly higher than for other systems, for which it ranged from 1.47 to 2.14 ($P < 0.05$). Four PRP samples prepared on Xerthra did not exceed the whole blood baseline level of PLT concentration and the other four exceeded it by more than 2 times. Only one sample prepared with Dr. PRP and none of the samples prepared with Mini GPS III and Arthrex failed to exceed the baseline level.

WBC concentration and neutrophil count also significantly differ only when comparing Mini GPS III with other systems ($P < 0.005$) but they do not differ significantly between those other systems ($P > 0.05$). Lymphocytes, monocytes, eosinophils and basophils were on a detectable level only in Mini GPS III PRPs.

The highest RBC contamination in the samples was observed for Mini GPS III and it was significantly higher compared to other systems ($P < 0.001$). RBC concentrations in Arthrex ACP, Xerthra and Dr. PRP were all barely detectable and amounted to 0.05, 0.02 and 0.01 × 10^{12}/L, respectively.

Several means one-way ANOVA power analysis of these multiple comparisons reached levels above 0.99. All blood cell components are shown in Table 3.

Platelet capture efficiency

PCE values, in descending order, were obtained for Mini GPS III at 56.15% ± 7.44%, Arthrex ACP at 43.68% ± 5.32%, Dr. PRP at 35.61% ± 12.13% and for Xerthra at 21.79% ± 18.98% (Figure 2). Statistical analysis showed significant differences only between Mini GPS III and Xerthra ($P < 0.001$) and Dr. PRP ($P = 0.001$).

Repeatability of the obtained concentrations in PRP samples

The coefficient of variation (CV) showed the highest repeatability of PLT concentrations for Arthrex ACP (12.18%) and the Biomet GPS III system (13.25%). The least predictable PLT concentrations were provided by the Xerthra PRP kit (95.95%). The results of CV for WBC and RBC concentrations seem noteworthy only for LR-PRP obtained for Mini GPS III. The repeatability was moderate for WBC (CV = 26.79%) and weak for RBC (CV = 56%). All CV results are shown in Table 4.

The concentrations of growth factors and inflammatory cytokines in PRP samples

The highest concentrations of EGF, VEGF, HGF, PDGF-AA and PDGF-BB were found in PRP samples obtained with Mini GPS III and the lowest in samples obtained with Arthrex ACP, and the differences for the first four were statistically significant with P values = 0.005, 0.02, 0.01 and 0.006, respectively. A statistically significant difference was also found between Mini GPS III and Xerthra in the concentration of EGF ($P = 0.04$) and PDGF-AA ($P = 0.04$). Several means one-way ANOVA power analysis of these multiple comparisons showed insufficient levels (< 0.8) for TGF-β1, FGF-basic, VEGF, HGF and PDGF-BB suggesting the insufficient sample size in this regard. Mean results with standard deviations of all tested growth factors are included in Supplementary Table 1 and highlighted in Figure 3.

Among all tested inflammatory cytokines, statistically significant differences between systems were found only in the levels of IL-8 and IL-18. IL-8 concentration in PRP obtained with Mini GPS III (734.85 pg/mL) was higher than in that obtained with Arthrex ACP (139.53 pg/mL, $P = 0.02$) and the Xerthra PRP kit (122.98 pg/mL, $P = 0.004$). IL18 concentration was the highest in PRP from MiniGPS III (1377 pg/mL) with a significant difference compared to Arthrex ACP (509.41 pg/mL, $P = 0.04$), the Xerthra PRP kit (283.01 pg/mL, $P < 0.001$) and Dr. PRP (414.02 pg/mL, $P = 0.007$). Unfortunately, several means one-way ANOVA power analysis of these multiple comparisons showed levels above 0.8 only for IL-18, which makes correct interpretation of the obtained results much more difficult. Mean results with standard deviations of all the tested cytokines are included in Supplementary Table 1 and highlighted in Figure 4.

Table 2 Whole blood count with differential leukocyte of all participants

Differential leukocyte	Blood count
RBC (10^{12}/L)	4.97 ± 0.43
PLT (10^9/L)	240.67 ± 49.85
WBC (10^9/L)	6.49 ± 1.49
Neutrophils (10^9/L)	3.79 ± 1.29
Lymphocytes (10^9/L)	2.08 ± 0.45
Monocytes (10^9/L)	0.45 ± 0.13
Eosinophils (10^9/L)	0.14 ± 0.08
Basophils (10^9/L)	0.04 ± 0.01

RBC: Red blood cells; PLT: Platelets; WBC: White blood cells.

Table 3 Concentrations of blood cell components in platelet-rich plasma samples

	Arthrex ACP	Mini GPS III	Xerthra	Dr. PRP
PLT (10^9/L)	357.33 ± 99.01	1212.67 ± 268.63	455.27 ± 362.92	499.75 ± 153.46
WBC (10^9/L)	0.87 ± 1.01	34.19 ± 11.18	1.80 ± 2.55	0.60 ± 0.87
Neutrophils (10^9/L)	0.87 ± 1.01	16.71 ± 9.89	1.80 ± 2.55	0.60 ± 0.87
RBC (10^{12}/L)	0.05 ± 0.08	1.49 ± 0.86	0.02 ± 0.02	0.01 ± 0.01
xPLT	1.47 ± 0.18	5.05 ± 0.67	1.96 ± 1.71	2.14 ± 0.73
xWBC	0.14 ± 0.17	5.27 ± 1.41	0.29 ± 0.4	0.10 ± 0.16
xRBC	0.01 ± 0.02	0.30 ± 0.17	0.00	0.00

PLT: Platelets; WBC: White blood cells; RBC: Red blood cells; ACP: Autologous Conditioned Plasma; PRP: Platelet-rich plasma.

Table 4 The coefficient of variation in the concentration of blood cell components for different platelet-rich plasma preparation systems

	WBC	RBC	PLT
Arthrex ACP [%]	114.80	175.69	12.18
Mini GPS III [%]	26.79	56.83	13.25
Xerthra [%]	149.38	133.98	95.95
Dr. PRP [%]	151.45	95.10	34.05

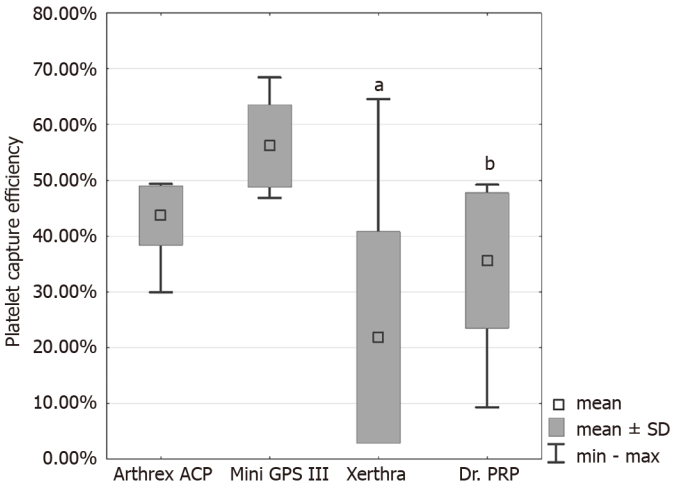
ACP: Autologous Conditioned Plasma; WBC: White blood cells; RBC: Red blood cells; PLT: Platelets; PRP: Platelet-rich plasma.

Correlation between blood cell components and cytokines

Significant positive correlations of PLT, WBC and RBC concentrations with the following growth factors: EGF, VEGF, HGF, PDGF-AA, PDGF-BB were found. Most of them were weak or moderate. A strong Spearman correlation was found between PLT and EGF ($\rho = 0.602$, $P < 0.001$), PLT and PDGF-AA ($\rho = 0.637$, $P < 0.001$). All correlations are presented in Supplementary Figure 1.

Positive significant correlations of PLT, WBC and RBC concentrations with the following inflammatory cytokines: IL-1β, MCP-1, IL-8, IL-18 were found. A strong Spearman correlation was found only between PLT and IL-18 ($\rho = 0.627$, $P < 0.001$). All correlations are presented in Supplementary Figure 1.

The correlations between blood cell components and growth factors or cytokines in PRP samples vary widely between different systems. In PRP samples obtained with Arthrex ACP, a significant Spearman correlation was found between PLT and PDGF-AA, INF- γ, IL-8. In PRP samples prepared with Mini GPS III System, a significant positive correlation was found between RBC and IL-1β, IL-18. In PRP prepared with Xerthra, a significant positive correlation was found between PLT and EGF, VEGF, PDGF-AA, IL-18; between WBC and TGF-β1, EGF, VEGF, PDGF-AA; between RBC and EGF, VEGF,



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Figure 2 Platelet capture efficiency (%) of different preparation protocols. [a]*P* < 0.001 *vs* Mini GPS III; [b]*P* = 0.001 *vs* Mini GPS III. Arthrex ACP: Arthrex Autologous Conditioned Plasma.

PDGF-AA. In PRP samples prepared with Dr. PRP Kit, a significant correlation was found between PLT and EGF, FGF-basic; between WBC and IL-18, IL-23. All significant Spearman correlation values are presented in Supplementary Table 2. Selected differences in correlations obtained with different systems are shown in Figure 5.

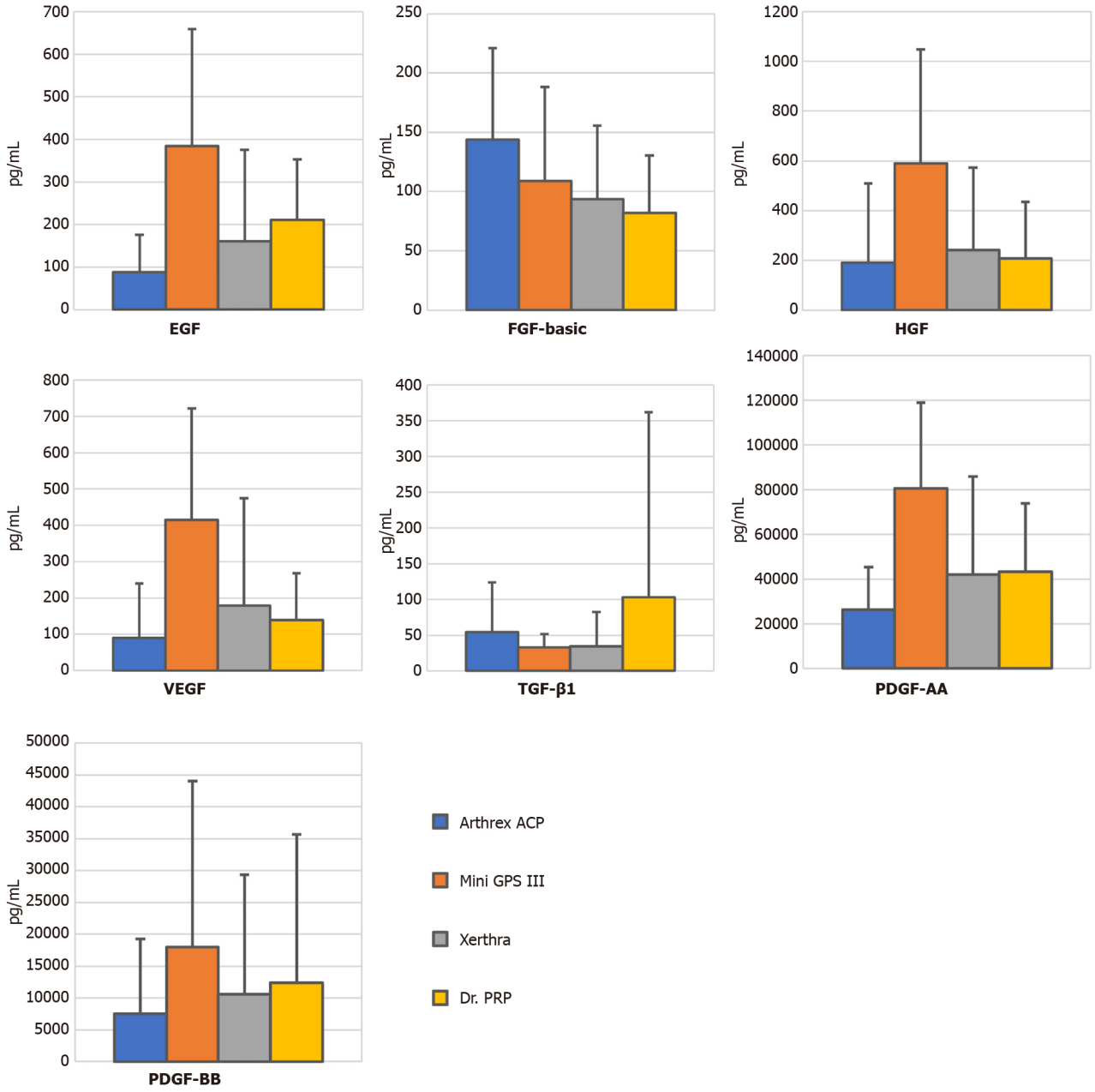
DISCUSSION

The results of the study revealed significant differences in PRP obtained with various commercial kits. Other studies had already confirmed the existence of such differences, therefore it was not the essence of the study[20]. The main goal was to highlight these differences, especially in the case of kits that have not been tested in this way before, such as Xerthra and Dr. PRP. Another novelty was the range of the investigated cytokines, significantly exceeding the ranges investigated in previous publications[10,20,23]. This study was also the first to pay attention to the repeatability of the quality of the obtained PRP, which is particularly important when planning a therapy or a clinical trial. This study also showed interesting differences in the results of PRP analysis and the correlations found as compared to the available literature.

It is believed that for therapeutic effect, PRP should have a platelet concentration above the baseline level. All PRP preparation systems were able to produce PRP with the mean platelet concentrations above this level but 4 samples prepared using Xerthra and 1 sample prepared using Dr. PRP did not meet this criterion. It seems to be due to the construction of separators in these systems. Immediately after centrifugation, the PRP is not physically separated from PPP and RBC which is why during the separation and extraction process it is not difficult to partially mix the content. The Arthrex ACP system uses a different approach because after centrifugation it has only two layers - RBC and easily removable plasma. That is probably why the manufacturer called its product Autologous Conditioned Plasma instead of Platelet-Rich Plasma. In his paper, L. Mazzucco considered PLT > 200 × 10^3/mL as sufficient for therapeutic effect, and all investigated systems reached this value[28]. The US Food and Drug Administration (FDA) requires a platelet concentration of at least 250 × 10^3/mL for PRP products which was also achieved by all systems. Other authors recommend a PLT concentration of about 1000 × 10^3[29]. Among systems included in this study, only Mini GPS III meets this criterion.

The content of PLT in PRP differed among systems but this difference was significant only when comparing Mini GPS III to other systems. The results of this study concerning PLT concentration for Mini GPS III and Arthrex ACP were similar to those obtained by other researchers[10,23,30,31]. The present authors found a positive correlation of PLT content with EGF, VEGF, HGF, PDGF-AA, PDGF-BB, IL-1β, MCP-1, IL-8 and IL-18 but not with FGF-basic, TGF-1β and the rest of the investigated inflammatory cytokines. Other authors support the correlation of PLT in PRP with PDGF[20], PDGF, VEGF [10], PDGF-AB, VEGF, EGF[23], PDGF-AB[31]. Contrary to the results presented in this study, J. Magalon and E.A Sundman found a positive correlation of PLT with TGF1β[23,31]. According to the present authors' knowledge, the positive correlations of PLT with MCP-1, IL-8 and IL-18 in PRP samples are presented in a scientific paper for the first time.

There are some controversies about leukocyte-rich platelet-rich plasma which is expected to have WBC concentration above the baseline. Its negative effect on tissue healing was demonstrated in *in vitro*

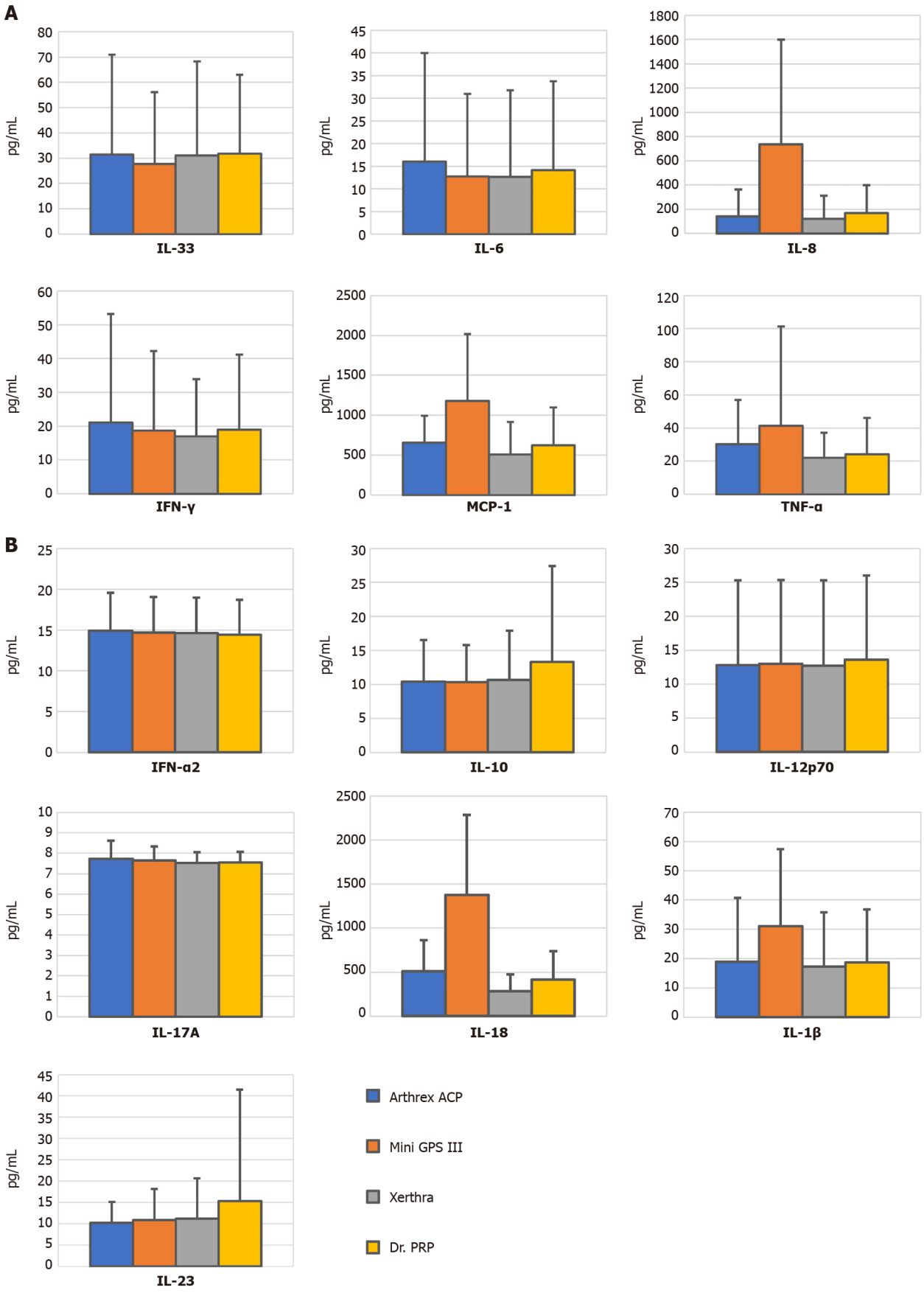


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Figure 3 Concentrations (pg/mL) of growth factors in platelet-rich plasma samples obtained by different systems (mean ± SD). EGF: Epidermal growth factor; FGF-basic: Fibroblast growth factor-basic; HGF: Hepatocyte growth factor; VEGF: Vascular endothelial growth factor; TGF-β1: Transforming growth factor-β1; PDGF-AA: Platelet-derived growth factor-AA; PDGF-BB: Platelet-derived growth factor-BB.

studies, which, however, was not confirmed by studies on living organisms. This effect may be due to the high content of proteinases and hydrolases in neutrophils and should be taken into consideration when planning the therapy[8,13,31,32]. WBC content could also have an antibacterial effect[33]. On the other hand, in the presented study, high leukocyte content positively correlates with the levels of important growth factors and cytokines such as EGF, VEGF, HGF, PDGF-AA, PDGF-BB, IL-1β, MCP-1, IL-8 and IL-18. Authors of similar papers do not frequently report results of correlations between WBC and GF. J. Magalon has shown a significant positive correlation of WBC content with EGF and VEGF but not with PDGF-AB and TGF-β1[23]. T. N. Castillo also found a positive correlation of WBC with VEGF and PDGF-ββ but not with PDGF-AB or TGF-β1[24]. The presented results support and greatly extend the above. The highest WBC content was found in PRP prepared using the Mini GPS III System as it is defined as leukocyte-rich platelet-rich plasma (L-PRP)[21,34].

There was also significantly higher content of RBC in Mini GPS III than in other systems. This is undesirable evidence of imperfect separation of PRP and may explain why other authors did not provide detailed information about RBC and its correlation with growth factors and cytokines. Surprisingly, a positive correlation was again demonstrated with EGF, VEGF, HGF, PDGF-AA, PDGF-BB, IL-1β, MCP-1, IL-8 and IL-18. This has never been reported by other authors in the context of PRP



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Figure 4 Concentrations (pg/mL) of inflammatory cytokines in platelet-rich plasma samples obtained by different systems (mean ± SD). A: Mini GPS III; B: Arthrex Autologous Conditioned Plasma. IFN-α2: Interferon-α2; IL-10: Interleukin-10; IL-12p70: Interleukin-12p70; IL-17A: Interleukin-17A; IL18: Interleukin-18; IL-1β: Interleukin-1β; IL-23: Interleukin-23; IL-33: Interleukin-33; Il-6: Interleukin-6; IL-8: Interleukin-8; IFN-γ: Interferon-γ; MCP-1: Monocyte

chemoattractant protein-1; TNF-α: Tumor necrosis factor α.

evaluation and requires further research.

Significant differences in the levels of EGF, VEGF, HGF, PDGF-AA, PDGF-BB, IL-8 and IL-18 were found between Mini GPS III and Arthrex, for EGF, IL-8 and IL-18 between Mini GPS III and Xerthra and for IL-18 between Mini GPS III and Dr. PRP. The presented results support and extend the current state of knowledge[10,23,24,30,31,35]. Further studies are needed to explain the origin of these differences in the cases in which the correlation between blood cell components and cytokines/growth factors cannot simply explain it.

For the first time in the literature, the repeatability of obtained concentrations of PLT, WBC and RBC in different PRP preparation systems was clearly evaluated. The presented study demonstrated considerable differences between systems. In the authors' opinion, especially Xerthra PRP kit requires some improvements in the provided protocol for better repeatability. Due to the fact that two PRP samples prepared with Xerthra had a PLT increase > 4x above the baseline level, the authors still believe that there is great potential in this system.

For clinical practice and further studies, the most important issue is what should be expected from differences in PRP cytokine levels. Multiple studies have demonstrated a beneficial effect of PDGF and FGF on the healing process, both in animal models and in patients with wound healing disorders. However, *in vivo* functions of many growth factors remain largely unconfirmed[12]. In this study, PDGF-AA and PDGF-BB were selected as representatives of the PDGF family which stimulates cell (neutrophil, monocyte, fibroblast) migration to the wound site, enhances the proliferation of fibroblasts and production of extracellular matrix[6,12]. FGF-basic, as an FGF family member has well described mitogenic activity, regulates migration and cell differentiation, and has a cytoprotective effect on cells under stress conditions[12]. VEGF is involved in the regulation of angiogenesis during wound healing, HGF was discovered as a stimulator of dissociation of epithelial cells, migration, proliferation and new blood vessel formation, EGF induces cell differentiation of both ectodermal and mesodermal origin, and TGF-β1 has an important role in controlling cell proliferation and differentiation during the repairing process[6,12]. Other important cytokines that play a positive role in tissue healing are MCP-1 as a major macrophage chemoattractant, IL-8 as a neutrophil chemoattractant and stimulant of reepithelialization, IL-10 as an inhibitor of inflammation and scar formation[12]. Proinflammatory cytokines such as IL-1α and β, IL-6 and TNF-α are also involved in the repairing process by stimulation of keratinocyte and fibroblast proliferation, synthesis and breakdown of extracellular matrix proteins, fibroblast chemotaxis and regulation of the immune response[12].

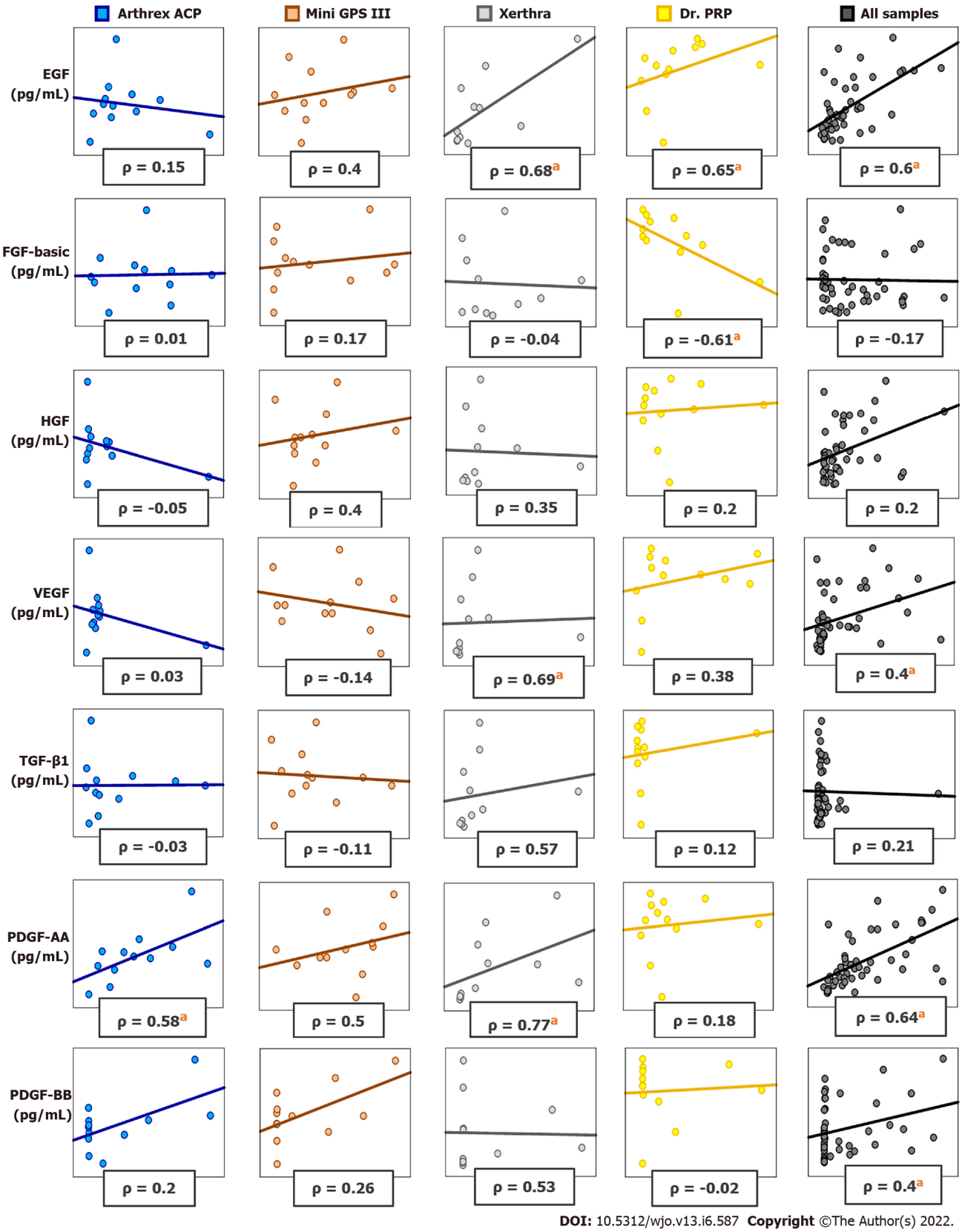
It is expected that high levels of the above cytokines in PRP should result in better wound healing. In the presented study, a positive but not always significant Spearman correlation was found between all blood cell components and growth factors such as PDGF-AA, PDGF-BB, EGF, VEGF, HGF, MCP-1, IL-8 and IL-1 β, however, their correlation with TGF-β1, FGF-basic, TNF-α, IL-6 and IL-10 was found to be negligible. These results suggest that the best clinical outcome should be expected from PRP with the highest concentration of blood cell components.

Proinflammatory cytokines such as IFN-α2, IFN-γ, IL-12p70, IL-17A, IL-18, IL-23 and IL-33 may play an additional role in wound healing by regulating the secretion of other cytokines, regulating the immune response and antimicrobial activity. However, their function in tissue repair is poorly understood. In the presented study, a significant correlation was found only between all blood cell components and IL-18. Since IL-18 is able to induce severe inflammatory reactions, the implications of its correlation with highly concentrated PRP require further investigation.

Significant differences in the content of blood cell components and growth factors between different methods of platelet-rich plasma separation have already been demonstrated in previous publications[10,20,23,24,30,35]. However, none of the studies analyzed the Xerthra and Dr. PRP systems in such great detail. The medical market offers much more commercially available PRP preparation systems than those included in the study. The present authors evaluated only four of them but still, most of similar studies analyzed a smaller or comparable number of different systems[10,23,24,30,35].

Another limitation of the study is the size of the population. However, the number of participants is larger compared to the majority of similar studies[20,23,24,30,35]. The group was kept as homogeneous as possible to eliminate additional factors that could distort the results, therefore the study included a group of healthy men of similar age. The post-hoc test power analysis showed a sufficient sample size for the PRP group comparison of PCE, blood cell components, EGF, PDGF-AA, IL-18 and slightly insufficient for VEGF, HGF, MCP-1 and IL-8. To achieve the test power level of 0.8 in order to compare most other cytokines, the sample size should be considerably increased from 3 (FGF-basic) to more than 100 times (IFN-α2, IL-12p70 or IL-33). This data may help other researchers to design their studies appropriately.

In the study presented in this paper, the degree of platelet activation was not tested. This was based on the available literature which showed no significant differences in platelet activation between different separation methods[23,36]. Moreover, according to the literature, the storage time of PRP in which there is no significant activation of the platelets, should not exceed 6 h at a temperature of 20°C



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Figure 5 Spearman correlations (ρ) between platelets and growth factors in platelet-rich plasma obtained with different protocols and combined. [a]*P* < 0.05. EGF: Epidermal growth factor; FGF-basic: Fibroblast growth factor-basic; HGF: Hepatocyte growth factor; VEGF: Vascular endothelial growth factor; TGF-β1: Transforming growth factor-β1; PDGF-AA: Platelet-derived growth factor-AA; PDGF-BB: Platelet-derived growth factor-BB.

[37]. All PRP samples obtained in this study were tested for the content of blood cell components immediately after production and then they were frozen at -80 °C waiting for cytokine analysis.

Not all of the known cytokines and growth factors that may affect the healing and regeneration processes occurring in platelet-rich plasma were analyzed. However, the focus was on the most important ones. This study analyzes a wider range of cytokines than most publications on this topic[10,20,23,24,30,35].

CONCLUSION

Significant differences were found in the content of biologically active components in PRP obtained with the use of different methods and considerable differences were demonstrated in their repeatability within each method. Significant correlations between blood cell components and growth factors/inflammatory cytokines were presented, contributing new data to the current state of knowledge.

Clinical relevance and recommendations

Due to the considerable heterogeneity of PRPs, the presented results support the recommendations for studies reporting the use of autologous blood-based therapies to provide detailed information about the characteristics of all PRP samples (MIBO)[27]. The study also provides detailed information about the desired content of growth factors and their correlation with blood cell components in four different commercially available systems for PRP preparation, which could help clinicians to choose one depending on their expectations. The results of this study also demonstrate the need for producers to improve the existing solutions in order to improve the provided protocols to increase the repeatability of the parameters of PRP samples.

In clinical practice, it seems reasonable to suggest the use of commercial PRP kits that allow obtaining the highest blood cell concentration with the highest predictable reproducibility. It is worth noting that not only the level of PLT but also WBC and RBC levels significantly correlated with cytokines involved in the healing process, which may encourage researchers to look for new "blood cell concentrate" treatment methods.

ARTICLE HIGHLIGHTS

Research background

Autologous platelet-rich plasma (PRP) therapy is a method used to treat a variety of diseases related to soft tissue degeneration. The main idea behind this is to improve local healing and stimulate regeneration by administering large amounts of platelet-derived growth factors and cytokines. There are many commercial kits available to assist in obtaining PRP in an outpatient setting.

Research motivation

Due to the wide variety of PRP preparation systems, there are justified doubts about the quality of the obtained samples. Differences in the content of biologically active compounds between some PRP systems have already been demonstrated. However, only a small number of available systems and a limited number of cytokines and growth factors have been investigated.

Research objectives

To compare PRP obtained using four different commercial preparation systems in terms of the content of biologically active components, correlations between those components and their repeatability in each method.

Research methods

After obtaining informed consent from participants, whole blood was collected from 12 young healthy male volunteers, and 4 different PRP samples were prepared from each of them in a single-donor model. PRP samples were prepared using different commercial kits: Arthrex Autologous Conditioned Plasma (ACP) Double Syringe System (Arthrex Inc., United States), the Mini GPS III Platelet Concentration System (Biomet Inc., United States), the Xerthra PRP kit (Biovico Sp. z o.o., Poland) and Dr. PRP (Rmedica, Republic of Korea). The content of cellular components in each sample was assessed using an automatic laboratory analyzer Mindray BC-5150 (Shenzhen Mindray Bio-Medical Electronics Co., PRC). To quantify the content of seven selected growth factors (Epidermal growth factor (EGF), Fibroblast Growth Factor- basic, Hepatocyte growth factor (HGF), vascular endothelial growth factor (VEGF), Transforming Growth Factor-β1, Platelet-Derived Growth Factor-AA, Platelet-Derived Growth Factor-BB and thirteen inflammatory cytokines [(Interferon-α2, Interleukin-10, Interleukin-12p70, Interleukin-17A, Interleukin-18 (IL-18), Interleukin-23 (IL-23), Interleukin-33, Interleukin-6, Interleukin-8, Interferon-γ, Monocyte Chemoattractant Protein-1 (MCP-1), Tumor Necrosis Factor α (TNF-α)], bead-based multiplex immunoassays LEGENDplexTM (BioLegend, United States) that use fluorescence-

encoded beads and flow cytometer measurements were performed.

Research results

Differences between PRPs obtained with various preparation systems were found in terms of cellular composition, repeatability, platelet capture efficiency, concentrations of growth factors and inflammatory cytokines. The highest ability to concentrate platelets (PLT) above the baseline was obtained with Mini GPS III (5.05 x) and the lowest with Arthrex ACP (1.47 x). Those two systems had the best repeatability of platelet concentrations assessed as the coefficient of variation of 13.25% and 12.18%, respectively. The highest concentrations of Epidermal growth factor, hepatocyte growth factor, vascular endothelial growth factor, platelet-derived growth factor-AA, platelet-derived growth factor-BB, IL-18, Interleukin-1β, Interleukin-8, MCP-1 and TNF-α were found in PRP with the highest PLT, white blood cells and red blood cells concentrations (obtained with Mini GPS III), and positive significant ($P < 0.05$) correlations between cell components and these paracrine factors (except TNF-α) were revealed.

Research conclusions

The study provided new data on the differences between PRP obtained with the various commercial systems. The range of analyzed cytokines far exceeded the ranges investigated in earlier publications. The presented findings should help researchers and clinicians choose the system that best meets their expectations.

Research perspectives

Further research should be focused on the comparison of PRPs obtained using different techniques in the context of their biological effect on soft tissues *in vitro* and their clinical efficacy in various diseases.

FOOTNOTES

Author contributions: Dejnek M, Reichert P, and Królikowska A designed and coordinated the study; Dejnek M, Witkowski J, Moreira H, and Płaczkowska S performed the experiments, acquired and analyzed data; Dejnek M, Reichert P, Królikowska A, and Morasiewicz P interpreted the data; Dejnek M wrote the manuscript; all authors approved the final version of the article.

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Informed consent statement: All study participants provided informed written consent prior to study enrollment.

Conflict-of-interest statement: The authors declare no conflict of interest. The founders had no role in the design of the study; in the collection, analyses, or interpretation of data; in the writing of the manuscript, or in the decision to publish the results.

Data sharing statement: The datasets used during the current study are available from the corresponding author on reasonable request.

ARRIVE guidelines statement: The authors have read the ARRIVE guidelines, and the manuscript was prepared and revised according to the ARRIVE guidelines.

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REFERENCES

1 **Creaney L**, Hamilton B. Growth factor delivery methods in the management of sports injuries: the state of play. *Br J Sports Med* 2008; **42**: 314-320 [PMID: 17984193 DOI: 10.1136/bjsm.2007.040071]

2 **Middleton KK**, Barro V, Muller B, Terada S, Fu FH. Evaluation of the effects of platelet-rich plasma (PRP) therapy involved in the healing of sports-related soft tissue injuries. *Iowa Orthop J* 2012; **32**: 150-163 [PMID: 23576936]

3 **Man D**, Plosker H, Winland-Brown JE. The use of autologous platelet-rich plasma (platelet gel) and autologous platelet-poor plasma (fibrin glue) in cosmetic surgery. *Plast Reconstr Surg* 2001; **107**: 229-37; discussion 238 [PMID: 11176628 DOI: 10.1097/00006534-200101000-00037]

4 **Tietze DC**, Geissler K, Borchers J. The effects of platelet-rich plasma in the treatment of large-joint osteoarthritis: a systematic review. *Phys Sportsmed* 2014; **42**: 27-37 [PMID: 24875970 DOI: 10.3810/psm.2014.05.2055]

5 **Dhillon RS**, Schwarz EM, Maloney MD. Platelet-rich plasma therapy - future or trend? *Arthritis Res Ther* 2012; **14**: 219 [PMID: 22894643 DOI: 10.1186/ar3914]

6 **Sánchez-González DJ**, Méndez-Bolaina E, Trejo-Bahena NI. Platelet-rich plasma peptides: key for regeneration. *Int J Pept* 2012; **2012**: 532519 [PMID: 22518192 DOI: 10.1155/2012/532519]

7 **Roh YH**, Kim W, Park KU, Oh JH. Cytokine-release kinetics of platelet-rich plasma according to various activation protocols. *Bone Joint Res* 2016; **5**: 37-45 [PMID: 26862077 DOI: 10.1302/2046-3758.52.2000540]

8 **Kobayashi Y**, Saita Y, Nishio H, Ikeda H, Takazawa Y, Nagao M, Takaku T, Komatsu N, Kaneko K. Leukocyte concentration and composition in platelet-rich plasma (PRP) influences the growth factor and protease concentrations. *J Orthop Sci* 2016; **21**: 683-689 [PMID: 27503185 DOI: 10.1016/j.jos.2016.07.009]

9 **Degen RM**, Conti MS, Camp CL, Altchek DW, Dines JS, Werner BC. Epidemiology and Disease Burden of Lateral Epicondylitis in the United States: Analysis of 85,318 Patients. *HSS J* 2018; **14**: 9-14 [PMID: 29398988 DOI: 10.1007/s11420-017-9559-3]

10 **Oh JH**, Kim W, Park KU, Roh YH. Comparison of the Cellular Composition and Cytokine-Release Kinetics of Various Platelet-Rich Plasma Preparations. *Am J Sports Med* 2015; **43**: 3062-3070 [PMID: 26473014 DOI: 10.1177/0363546515608481]

11 **Weibrich G**, Kleis WK, Hafner G, Hitzler WE. Growth factor levels in platelet-rich plasma and correlations with donor age, sex, and platelet count. *J Craniomaxillofac Surg* 2002; **30**: 97-102 [PMID: 12069512 DOI: 10.1054/jcms.2002.0285]

12 **Werner S**, Grose R. Regulation of wound healing by growth factors and cytokines. *Physiol Rev* 2003; **83**: 835-870 [PMID: 12843410 DOI: 10.1152/physrev.2003.83.3.835]

13 **Wasterlain AS**, Braun HJ, Dragoo JL. Contents and Formulations of Platelet-Rich Plasma. *Oper Tech Orthop* 2012; **22**: 33-42 [DOI: 10.1053/j.oto.2011.11.001]

14 **Monto RR**. Platelet rich plasma treatment for chronic Achilles tendinosis. *Foot Ankle Int* 2012; **33**: 379-385 [PMID: 22735279 DOI: 10.3113/FAI.2012.0379]

15 **Suthar M**, Gupta S, Bukhari S, Ponemone V. Treatment of chronic non-healing ulcers using autologous platelet rich plasma: a case series. *J Biomed Sci* 2017; **24**: 16 [PMID: 28241824 DOI: 10.1186/s12929-017-0324-1]

16 **Mi B**, Liu G, Zhou W, Lv H, Liu Y, Wu Q, Liu J. Platelet rich plasma *vs* steroid on lateral epicondylitis: meta-analysis of randomized clinical trials. *Phys Sportsmed* 2017; **45**: 97-104 [PMID: 28276986 DOI: 10.1080/00913847.2017.1297670]

17 **Shen L**, Yuan T, Chen S, Xie X, Zhang C. The temporal effect of platelet-rich plasma on pain and physical function in the treatment of knee osteoarthritis: systematic review and meta-analysis of randomized controlled trials. *J Orthop Surg Res* 2017; **12**: 16 [PMID: 28115016 DOI: 10.1186/s13018-017-0521-3]

18 **Lisi C**, Perotti C, Scudeller L, Sammarchi L, Dametti F, Musella V, Di Natali G. Treatment of knee osteoarthritis: platelet-derived growth factors vs. hyaluronic acid. A randomized controlled trial. *Clin Rehabil* 2018; **32**: 330-339 [PMID: 28783969 DOI: 10.1177/0269215517724193]

19 **Meheux CJ**, McCulloch PC, Lintner DM, Varner KE, Harris JD. Efficacy of Intra-articular Platelet-Rich Plasma Injections in Knee Osteoarthritis: A Systematic Review. *Arthroscopy* 2016; **32**: 495-505 [PMID: 26432430 DOI: 10.1016/j.arthro.2015.08.005]

20 **Kushida S**, Kakudo N, Morimoto N, Hara T, Ogawa T, Mitsui T, Kusumoto K. Platelet and growth factor concentrations in activated platelet-rich plasma: a comparison of seven commercial separation systems. *J Artif Organs* 2014; **17**: 186-192 [PMID: 24748436 DOI: 10.1007/s10047-014-0761-5]

21 **DeLong JM**, Russell RP, Mazzocca AD. Platelet-rich plasma: the PAW classification system. *Arthroscopy* 2012; **28**: 998-1009 [PMID: 22738751 DOI: 10.1016/j.arthro.2012.04.148]

22 **Graziani F**, Ivanovski S, Cei S, Ducci F, Tonetti M, Gabriele M. The *in vitro* effect of different PRP concentrations on osteoblasts and fibroblasts. *Clin Oral Implants Res* 2006; **17**: 212-219 [PMID: 16584418 DOI: 10.1111/j.1600-0501.2005.01203.x]

23 **Magalon J**, Bausset O, Serratrice N, Giraudo L, Aboudou H, Veran J, Magalon G, Dignat-Georges F, Sabatier F. Characterization and comparison of 5 platelet-rich plasma preparations in a single-donor model. *Arthroscopy* 2014; **30**: 629-638 [PMID: 24725317 DOI: 10.1016/j.arthro.2014.02.020]

24 **Castillo TN**, Pouliot MA, Kim HJ, Dragoo JL. Comparison of growth factor and platelet concentration from commercial platelet-rich plasma separation systems. *Am J Sports Med* 2011; **39**: 266-271 [PMID: 21051428 DOI: 10.1177/0363546510387517]

25 **Zimmermann R**, Arnold D, Strasser E, Ringwald J, Schlegel A, Wiltfang J, Eckstein R. Sample preparation technique and white cell content influence the detectable levels of growth factors in platelet concentrates. *Vox Sang* 2003; **85**: 283-289 [PMID: 14633254 DOI: 10.1111/j.0042-9007.2003.00361.x]

26 **Dejnek M**, Moreira H, Płaczkowska S, Morasiewicz P, Barg E, Witkowski J, Reichert P. Analysis and comparison of autologous platelet-rich plasma preparation systems used in the treatment of enthesopathies: A preliminary study. *Adv Clin Exp Med* 2021; **30**: 757-764 [PMID: 34118138 DOI: 10.17219/acem/135045]

27 **Murray IR**, Geeslin AG, Goudie EB, Petrigliano FA, LaPrade RF. Minimum Information for Studies Evaluating Biologics in Orthopaedics (MIBO): Platelet-Rich Plasma and Mesenchymal Stem Cells. *J Bone Joint Surg Am* 2017; **99**: 809-819 [PMID: 28509821 DOI: 10.2106/JBJS.16.00793]

28 **Mazzucco L**, Balbo V, Cattana E, Guaschino R, Borzini P. Not every PRP-gel is born equal. Evaluation of growth factor availability for tissues through four PRP-gel preparations: Fibrinet, RegenPRP-Kit, Plateltex and one manual procedure. *Vox Sang* 2009; **97**: 110-118 [PMID: 19392780 DOI: 10.1111/j.1423-0410.2009.01188.x]

29 **Marx RE**. Platelet-rich plasma (PRP): what is PRP and what is not PRP? *Implant Dent* 2001; **10**: 225-228 [PMID: 11813662 DOI: 10.1097/00008505-200110000-00002]

30 **Mazzocca AD**, McCarthy MB, Chowaniec DM, Cote MP, Romeo AA, Bradley JP, Arciero RA, Beitzel K. Platelet-rich plasma differs according to preparation method and human variability. *J Bone Joint Surg Am* 2012; **94**: 308-316 [PMID: 22336969 DOI: 10.2106/JBJS.K.00430]

31 **Sundman EA**, Cole BJ, Fortier LA. Growth factor and catabolic cytokine concentrations are influenced by the cellular composition of platelet-rich plasma. *Am J Sports Med* 2011; **39**: 2135-2140 [PMID: 21846925 DOI: 10.1177/0363546511417792]

32 **McCarrel TM**, Minas T, Fortier LA. Optimization of leukocyte concentration in platelet-rich plasma for the treatment of tendinopathy. *J Bone Joint Surg Am* 2012; **94**: e143(1-e1438) [PMID: 23032594 DOI: 10.2106/JBJS.L.00019]

33 **Cieślik-Bielecka A**, Bold T, Ziółkowski G, Pierchała M, Królikowska A, Reichert P. Antibacterial Activity of Leukocyte- and Platelet-Rich Plasma: An *In Vitro* Study. *Biomed Res Int* 2018; **2018**: 9471723 [PMID: 30050949 DOI: 10.1155/2018/9471723]

34 **Dohan Ehrenfest DM**, Rasmusson L, Albrektsson T. Classification of platelet concentrates: from pure platelet-rich plasma (P-PRP) to leucocyte- and platelet-rich fibrin (L-PRF). *Trends Biotechnol* 2009; **27**: 158-167 [PMID: 19187989 DOI: 10.1016/j.tibtech.2008.11.009]

35 **Everts PA**, Brown Mahoney C, Hoffmann JJ, Schönberger JP, Box HA, van Zundert A, Knape JT. Platelet-rich plasma preparation using three devices: implications for platelet activation and platelet growth factor release. *Growth Factors* 2006; **24**: 165-171 [PMID: 17079200 DOI: 10.1080/08977190600821327]

36 **Pignatelli P**, Pulcinelli FM, Ciatti F, Pesciotti M, Sebastiani S, Ferroni P, Gazzaniga PP. Acid citrate dextrose (ACD) formula A as a new anticoagulant in the measurement of *in vitro* platelet aggregation. *J Clin Lab Anal* 1995; **9**: 138-140 [PMID: 7714666 DOI: 10.1002/jcla.1860090211]

37 **Bausset O**, Giraudo L, Veran J, Magalon J, Coudreuse JM, Magalon G, Dubois C, Serratrice N, Dignat-George F, Sabatier F. Formulation and storage of platelet-rich plasma homemade product. *Biores Open Access* 2012; **1**: 115-123 [PMID: 23516671 DOI: 10.1089/biores.2012.0225]

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Retrospective Study

Evaluation of artificial intelligence models for osteoarthritis of the knee using deep learning algorithms for orthopedic radiographs

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Abstract

BACKGROUND

Deep learning, a form of artificial intelligence, has shown promising results for interpreting radiographs. In order to develop this niche machine learning (ML) program of interpreting orthopedic radiographs with accuracy, a project named deep learning algorithm for orthopedic radiographs was conceived. In the first phase, the diagnosis of knee osteoarthritis (KOA) as per the standard Kellgren-Lawrence (KL) scale in medical images was conducted using the deep learning algorithm for orthopedic radiographs.

AIM

To compare efficacy and accuracy of eight different transfer learning deep learning models for detecting the grade of KOA from a radiograph and identify the most appropriate ML-based model for the detecting grade of KOA.

METHODS

The study was performed on 2068 radiograph exams conducted at the Department of Orthopedic Surgery, Sir HN Reliance Hospital and Research Centre (Mumbai, India) during 2019-2021. Three orthopedic surgeons reviewed these independently, graded them for the severity of KOA as per the KL scale and settled disagreement through a consensus session. Eight models, namely ResNet50, VGG-16, InceptionV3, MobilnetV2, EfficientnetB7, DenseNet201, Xception and NasNetMobile, were used to evaluate the efficacy of ML in accurately classifying radiographs for KOA as per the KL scale. Out of the 2068 images, 70% were used initially to train the model, 10% were used subsequently to test the model, and 20% were used finally to determine the accuracy of and validate each model. The idea behind transfer learning for KOA grade image

classification is that if the existing models are already trained on a large and general dataset, these models will effectively serve as generic models to fulfill the study's objectives. Finally, in order to benchmark the efficacy, the results of the models were also compared to a first-year orthopedic trainee who independently classified these models according to the KL scale.

RESULTS

Our network yielded an overall high accuracy for detecting KOA, ranging from 54% to 93%. The most successful of these was the DenseNet model, with accuracy up to 93%; interestingly, it even outperformed the human first-year trainee who had an accuracy of 74%.

CONCLUSION

The study paves the way for extrapolating the learning using ML to develop an automated KOA classification tool and enable healthcare professionals with better decision-making.

Key Words: Osteoarthritis; Artificial intelligence; Knee; Computer vision; Machine leaning; Deep learning

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Core Tip: In this study, we evaluated different machine learning models to determine which model is best to classify the severity of knee osteoarthritis using the Kellgren-Lawrence grading system. The image set was composed of radiographs of native knees, in anteroposterior and lateral views. The radiographic exams were annotated by experts and tagged according to Kellgren-Lawrence grades. The findings of this study will pave the way for future development in the field, with the development of more accurate models and tools that can improve medical image classification by machine learning and will give valuable insight into orthopedic disease pathology.

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INTRODUCTION

Knee osteoarthritis (KOA) is a debilitating joint disorder that degrades the knee articular cartilage and is characterized by joint pain, stiffness, and deformity, and pathologically by cartilage wear and osteophyte formation. KOA has a high incidence among the elderly, obese, and sedentary. Early diagnosis is essential for clinical treatments and pathology[1,2]. The severity of the disease and the nature of bone deformation and intra-articular pathology impact decision-making. Radiographs form an essential element of preoperative planning and surgical execution.

Artificial intelligence (AI) is impacting almost every sphere of our lives today. We are pushing the boundaries of human capabilities with unmatched computing and analytical power. Newer technological advancements and recent progress of medical image analysis using deep learning (DL), a form of AI, has shown promising ways to improve the interpretation of orthopedic radiographs. Traditional machine learning (ML) has often put much effort into extracting features before training the algorithms. In contrast, DL algorithms learn the features from the data itself, leading to improvisation in practically every subsequent step. This has turned out to be a hugely successful approach and opens up new ways for experts in ML to implement their research and applications, such as medical image analysis, by shifting feature engineering from humans to computers.

DL can help radiologists and orthopedic surgeons with the automatic interpretation of medical images, potentially improving diagnostic accuracy and speed. Human error due to fatigue and inexperience, which causes strain on medical professionals, is overcome by DL, reducing their workload and, most importantly, providing objectivity to clinical assessment and decisions for need of surgical intervention. Moreover, DL methods trained based on the expertise of senior radiologists and orthopedic surgeons in major tertiary care centers could transfer that experience to smaller institutions and create more space in emergency care, where expert medical professionals might not be readily available. This could dramatically enhance access to care. DL has been successfully used in different orthopedic applications, such as fracture detection[3-6], bone tumor diagnosis[7], detecting hip implant mechanical loosening[8], and grading OA[9,10]. However, the implementation of DL in orthopedics is not without challenges and limitations.

While most of our orthopedic technological research remains focused on core areas like implant longevity and biomechanics, it is essential that orthopedic teams also invest their effort in an exciting area of research that is likely to have a long-lasting impact on the field of orthopedics. With this aim, we set up a project to determine the feasibility and efficacy of the DL algorithms for orthopedic radiographs (DLAOR). To the best of our knowledge, only few published studies have applied DL to KOA classification, but many of these involved application to preprocessed, highly optimized images[11]. In this study, radiographs from the Osteoarthritis Initiative staged by a team of radiologists using the Kellgren-Lawrence (KL) system were used. They were standardized and augmented automatically before using the images as input to a convolution neural network model.

The purpose of this study was to compare eight different transfer learning DL models for KOA grade detection from a radiograph and to identify the most appropriate model for detecting KOA grade.

MATERIALS AND METHODS

The study was approved by an institutional review committee as well as the institutional ethics committee (HNH/IEC/2021/OCS/ORTH 56). It involved a diagnostic method based on retrospectively collected radiographic examinations. The examinations had been performed by a neural network, for assessment of both presence and severity of KOA using the KL system[12]. AI identifies patterns in images based on input data and associated recurring learning. It is fed with both the input (the radiographic images) and the information of expected output label (classifications of OA grade) to establish a connection between the features of the different stages of KOA (*e.g.*, possible osteophytes, joint space narrowing, sclerosis of subchondral bone) and the corresponding grade[13]. Before being fed to the classification engine, images were manually annotated by a team of radiologists according to the KL grading.

Data group

All the medical images were de-identified, without personal details of patients. The inclusion and exclusion criteria were applied after de-identification, complying with international standards like the Health Insurance Portability and Accountability Act.

Inclusion criteria

The following inclusion criteria were used: age above 18 years; recorded patient complaint of chronic knee pain (pain most of the time for more than 3 mo) and presentation to the orthopedic department or following radiologic investigation; and recorded patient unilateral knee complaints and knee grading according to KL system classification.

Exclusion criteria

The following exclusion criteria were used: patients who had undergone operation for total knee arthroplasty in either of the knees; patients who had undergone operation for unicompartmental knee arthroplasty; or patients who had recorded bilateral knee complaints.

Standardized knee X-rays: For the anteroposterior view of the knee, the leg had been extended and centered to the central ray. The leg had then been rotated slightly inward, in order to place the knee and the lower leg in a true anterior-posterior position. The image receptor had then been centered on the central ray. For a lateral view, the patient had been positioned on the affected side, with the knee flexed 20-30 degrees.

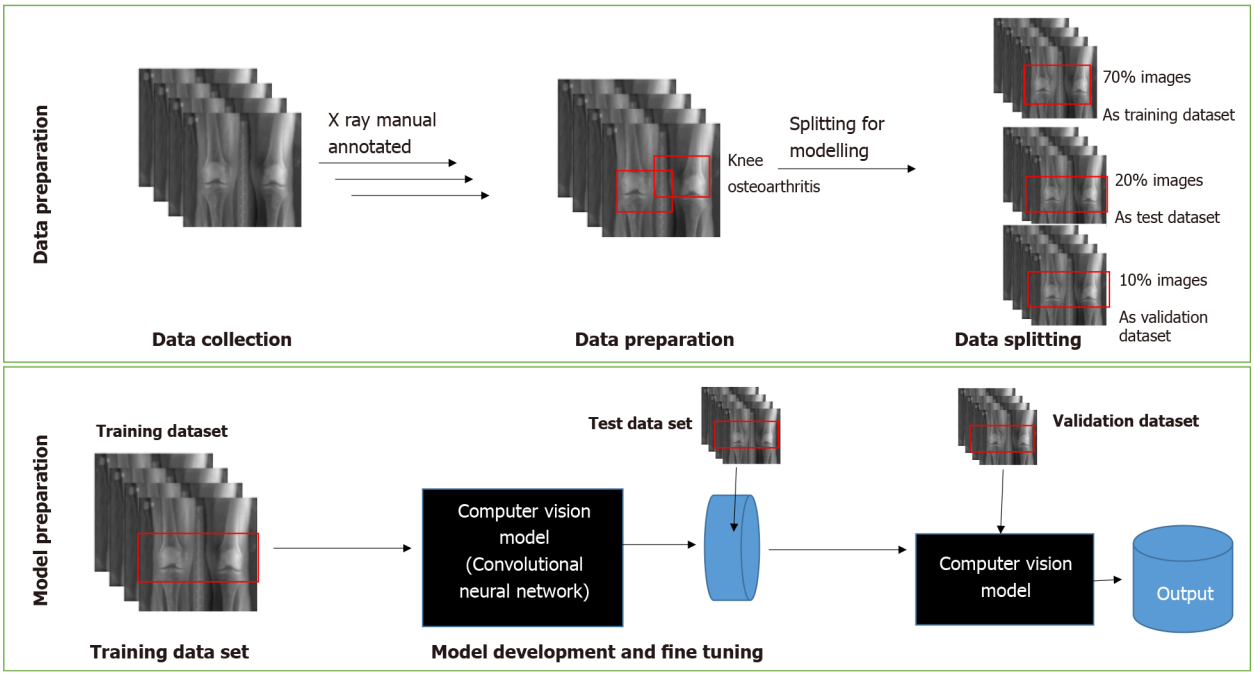
Assessment by orthopedic team: Three orthopedic surgeons reviewed these independently, graded them for the severity of KOA as per the KL scale and settled exams with disagreement through a consensus session. Finally, in order to benchmark the efficacy, the results of the models were also compared to a first-year orthopedic trainee who independently classified these models according to the KL scale.

Pre-processing

The models were trained with 2068 X-ray images. The dataset was split into three subsets used for training, testing, and validation, with a split ratio of 70-10-20. Initially, 70% of the images were used to train the model. Subsequently, 20% were used to test, and finally 10% were used for validation of the models. An end-to-end interpretable model took full knee radiographs as input and assessed KOA severity according to different grades (Figure 1).

Input images

The algorithm processed the images collected for each class. Each DICOM format radiograph was automatically cropped to the active image area, *i.e.* any black border was removed and reduced to a maximum of 224 pixels. Image dimensions were retained by padding the rectangular image to a square



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Figure 1 Architecture for deep learning algorithms for orthopedic radiographs.

format of 224 × 224 pixels. The training was carried out by cropping and rotating. Figure 2 shows the labelling of the KOA images in different classes as 0, 1, 2, 3 and 4, as per the KL grading scale and the knee severity from the X-ray images. The data were split into five different classes as per the KL grade shown in Figure 2. Table 1 shows the data splits in the training, testing and validation subsets, according to KL grades.

Need of transfer learning

A DL model is a program that has been trained on a set of data (called the training set) to recognize certain types of patterns. AI models use different algorithms to understand the information as part of a dataset and then learn from these data, with the definite goal of solving business challenges and overarching problems. The focus of traditional ML techniques used in image classification is acquiring knowledge from existing data and classifying. Most commonly, this means synthesizing practical concepts from historical data. However, another technique that encapsulates knowledge learned across many tasks and transfers it to new, unseen ones is transfer learning. Knowledge transfer can help speed up training and prevent overfitting, and improve the obtainable final performance. In transfer learning, knowledge is transferred from a trained model (or a set thereof) to a new model by encouraging the new model to have similar parameters. The trained models from which knowledge is transferred is not trained with this transfer in mind, and hence the task it was trained on must be very general for it to encode useful knowledge concerning other tasks. Transfer learning appeared to be helpful when there was a small training dataset with similar feature images. Thus, we have opted for a transfer learning approach to develop the DLAOR system. Figure 3 shows the traditional ML *vs* transfer learning.

DLAOR system

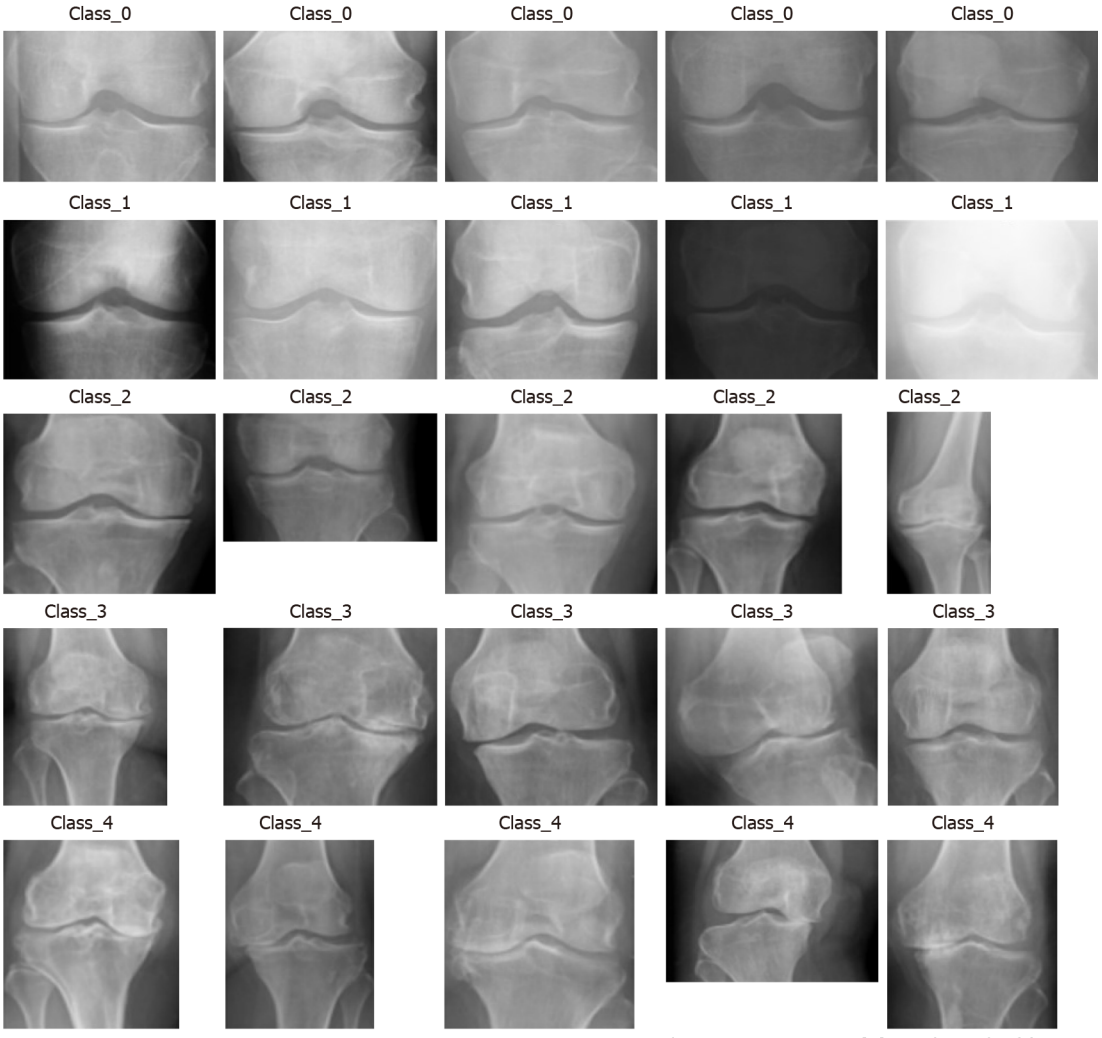
DLAOR is an image classification system where images are fed into the model to classify the KOA grade in medical images. It is built using a data ingestion pipeline, modelling engine, and classification system. The present study utilized a transfer learning technique for the effective classification of KOA grades using medical images. Since there are multiple well-established transfer learning models, we decided to use eight classification models. The selected models were reported to be the most efficient for image classification. All the selected models were compared to identify the best technique for the DLAOR system. The same set of images had been given to two OA surgeons to classify KL grades based on expert human interpretation and compared with models as part of the DLAOR system (Figure 4).

Model development

In this study, transfer ML models were developed using Python as Language; the Google Colab platform was used to run the code using GPU configuration to process models faster. Model development has the following steps: (1) Data augmentation and generators. There is the development of augmentation functions and data generator functions for training, testing, and validation datasets in

Table 1 Data splits in training, testing and validation subsets according to Kellgren-Lawrence grades

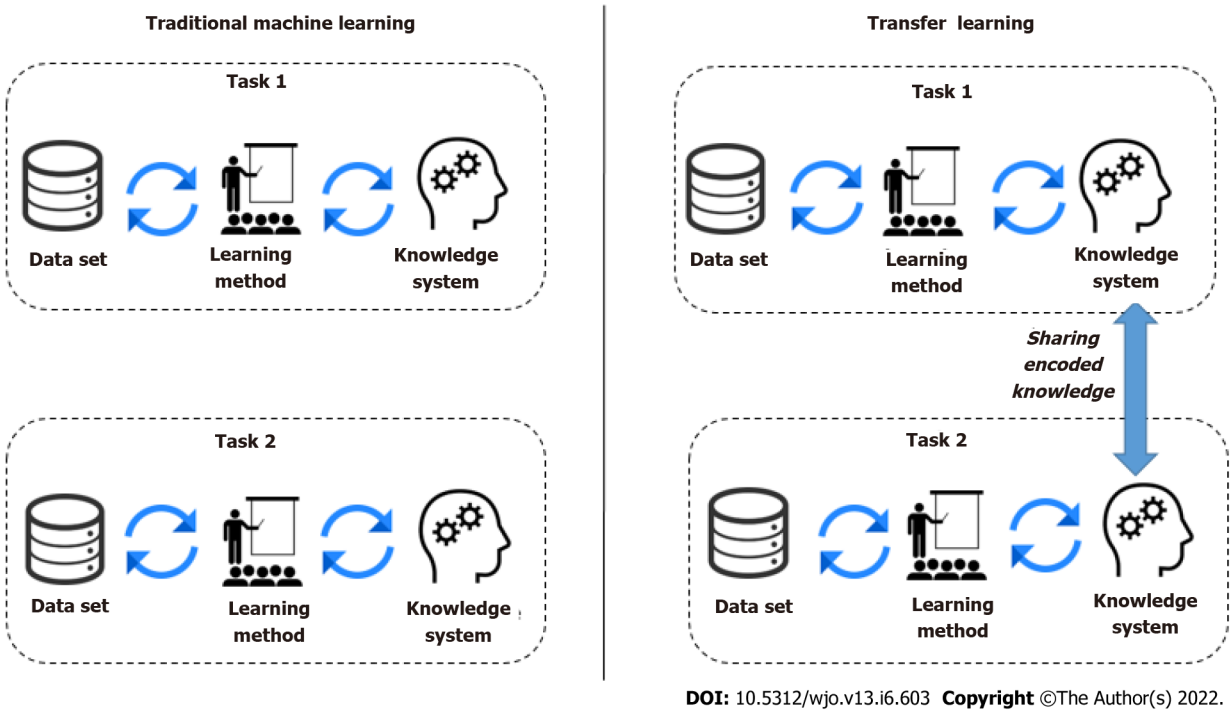
Osteoarthritis Kellgren-Lawrence grade	Training		Testing		Validation	
	Samples, *n*	Proportion, %	Samples, *n*	Proportion, %	Samples, *n*	Proportion, %
0	255	17.6	37	17.6	73	17.7
1	213	14.7	31	14.7	61	14.8
2	164	11.4	24	11.4	47	11.4
3	237	16.4	35	16.7	68	16.4
4	576	39.9	83	39.5	164	39.7
Total	1445	100	210	100	413	100



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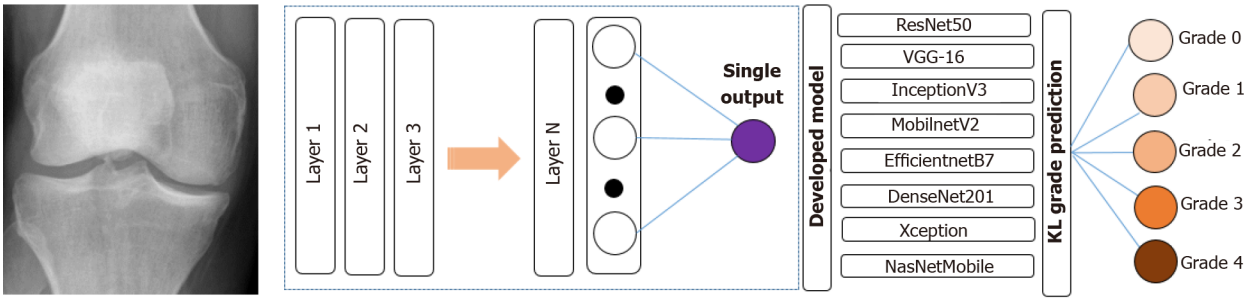
Figure 2 X-ray images of different Kellgren-Lawrence grades for knee osteoarthritis.

this stage; (2) Import the base transfer learning model. The next step is to import the base model from the TensorFlow/Keras library; (3) Build and compile the model. The base model was used just as a layer in a sequential model. After that, a single fully connected layer on top was added. Then, the model was compiled with Adam as an optimizer and categorical cross entropy as a loss mechanism; (4) Fit the model. In this step, the final model was fitted over the validation dataset. Then, with the help of 10 epochs, the model was finalized. This model was then evaluated over the test data; and (5) Fine-tune the model. We fine-tuned the model to improve the statistical order by giving a learning rate of 0.001 and additional epochs as 20.



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Figure 3 Traditional machine learning *vs* transfer learning.



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Figure 4 Multimodal pipeline, predicting the risk of osteoarthritis for a particular knee. We first used a deep convolutional neural network, trained different models in a multitask setting to predict the current stage of osteoarthritis defined according to the Kellgren-Lawrence (KL) grade scale.

RESULTS

In the present study, transfer ML was performed to compare the following parameters, to compare which model or human expert interpretation performed better regarding image classification of KOA grades: (1) Accuracy, which tells us what fractions are labeled correctly; (2) Precision, which is the number of true positives (TPs) over the sum of TPs and false positives. It shows what fraction of positive sides are correct; (3) Recall, which is the number of TPs over the sum of TPs and false negatives. It shows what fraction of actual positives is correct; and (4) Loss, which indicates the prediction error of the model.

Table 2 shows the performance comparison of the various models used for transfer learning models for KOA with the accuracy, precision, recall, and loss. It was observed that the highest accuracy was 92.87% and was achieved using DenseNet201. It had high precision and recall value as compared to all the other models.

This study leveraged cross-entropy multiple class loss. It is the measure of divergence of the predicted class from the actual class. It was calculated as a separate loss for each class label per observation and sums the result (Table 3).

Figure 5 shows the impact of iterations on the loss and accuracy of the eight different models. All the image clarification models had accuracy over 54%, while five models achieved accuracy over 80%, and one model achieved accuracy above 90%. High precision was achieved as 93.69% from the DenseNet model. The same model resulted in the highest accuracy of 92.87% and recall of 92.53%. Maximum loss was observed for the VGG-16 model. The minimum value for accuracy and precision was observed in

Table 2 Evaluation of parameters for knee osteoarthritis detection

Parameter	
Accuracy	Determines the accuracy of the standalone model inaccuracy to detect the presence of KOA and its classification in the input image
Precision	True positive/true positive + false positive
Recall	True positive/true positive + false negative
Loss	Determines the loss of the model

KOA: Knee osteoarthritis.

Table 3 Performance comparison of various transfer learning convolutional neural network models and eight expert human interpretations used for the development of deep learning algorithm for orthopedic radiographs

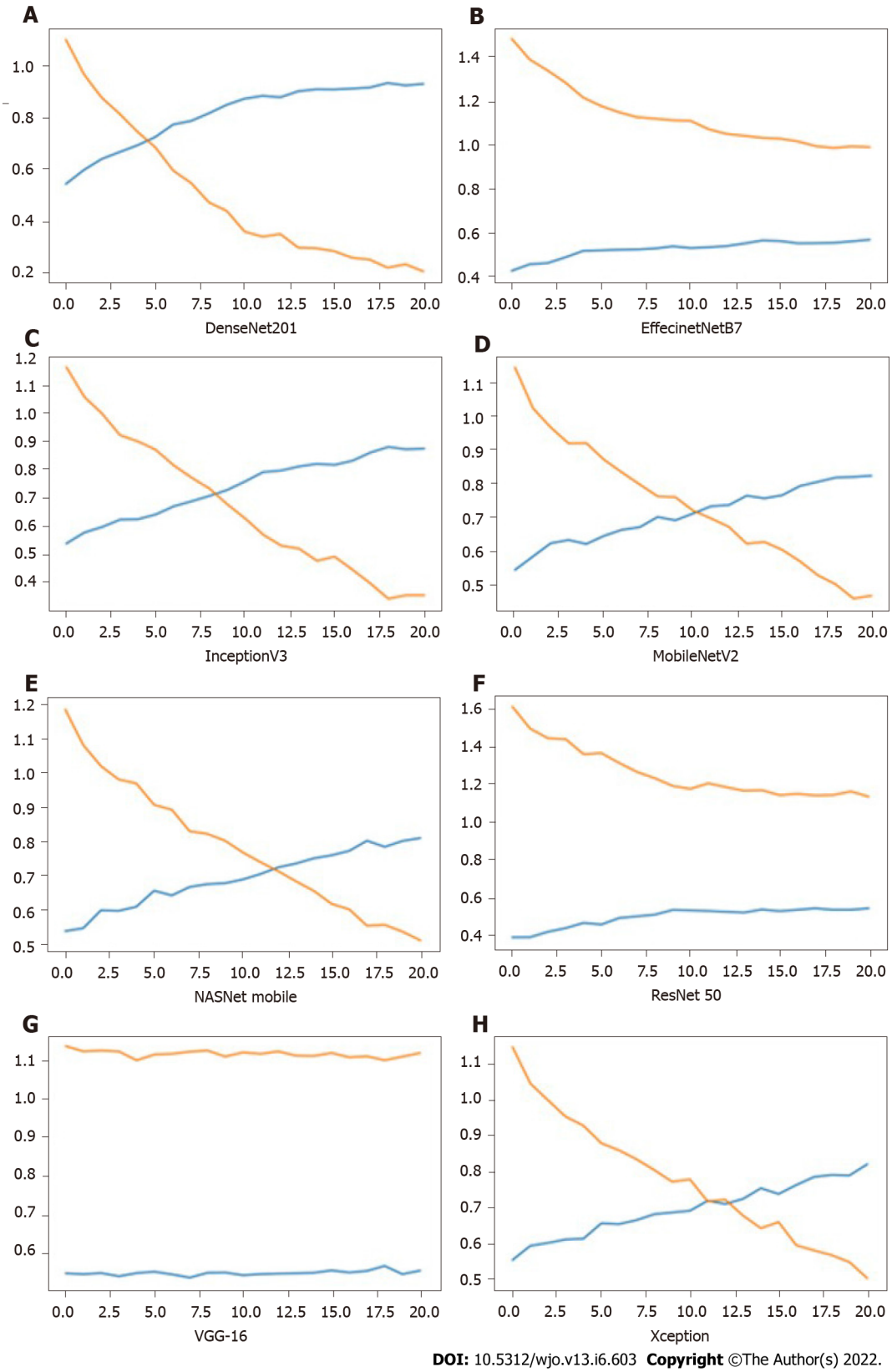
Model name	Accuracy	Precision	Recall	Loss	Outcome
ResNet50	54.29%	61.03%	39.52%	1.06	Average
VGG-16	56.68%	67.56%	35.02%	1.10	Average
InceptionV3	87.34%	89.19%	85.67%	0.35	Good
MobilnetV2	82.15%	84.66%	80.21%	0.46	Average
EfficientnetB7	56.61%	70.09%	38.27%	0.98	Average
DenseNet201	92.87%	93.69%	92.53%	0.20	Best
Xception	82.81%	85.03%	77.05%	0.50	Average
NasNetMobile	80.90%	83.98%	77.30%	0.50	Average
Surgeon	74.22%	79.50%	50.00%	0.25	Good

the ResNet50 model. The result showed that DenseNet was the best model to develop a DLAOR image classification system. The expert human interpretation for image classification was also captured for comparison. This was performed by two OA surgeons, and observed accuracy was 74.22%, with minimum loss value as second in comparison to all models.

DISCUSSION

Making the DL algorithm interpretable can benefit both the fields of computer science (to enable the development of improved AI algorithms) and medicine (to enable new medical discoveries). Interpreting and understanding cases of a machine's failure or when the machine is underperforming relative to the human expert can improve the DL algorithm itself. Understanding the AI decision-making process when the machine is outperforming the human expert can lead to new medical discoveries to extract the deep knowledge and insights that the AI utilizes to more optimal decisions than humans. DL in healthcare has already achieved wonders and improved the quality of treatment. Multiple organizations like Google, IBM, *etc* have spent a significant amount of time developing DL models that make predictions around hospitalized patients and support managing patient data and results. The future of healthcare has never been more intriguing, and both AI and ML have opened opportunities to craft solutions for particular needs within healthcare.

Standard radiographs of the hand, wrist, and ankle fractures were automatically diagnosed as a first step while identifying the examined view and body part[5]. A continuous, reliable, fast, effective, and most importantly accurate machine would be an asset without access to a radiology expert in the premise for preliminary diagnosis. AI solutions may incorporate both image data and the radiology text report for best judgment of an image or further learning of the network[14]. A recent study[15] revealed that with the help of isolating the subtle changes in cartilage texture of knee cartilage in a large number of magnetic resonance imaging T2-mapped images could effectively predict the onset of early symptomatic (WOMAC score) KOA, which may occur 3 years later. We are in a new era of orthopedic diagnostics where computers and not the human eye will comprehend the meaning of image data[16, 17], creating a paradigm shift for orthopedic surgeons and even more so for radiologists. The application of AI in orthopedics has mainly focused on the implementation of DL on clinical images.



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Figure 5 Depicting the loss and accuracy *vs* number of epochs for different models. Red line: Loss; Blue line: Accuracy; Y-axis: Depicting the loss and accuracy; X-axis: Number of epochs. A: DenseNet201; B: EffecinetNetB7; C: InceptionV3; D: MobileNetV2; E: NasNetMobile; F: ResNet 50; G: VGG-16; H: Xception.

DL algorithms will diagnose symptomatic OA needing treatment from radiological OA with no symptoms needing just observation. Both humans and machines make mistakes in applying their intelligence to solving problems. In ML, overfitting memorizes all examples, and an overfitted model lacks generalization and fails to work on never-before seen examples. In ML, transfer learning is a

method that reuses a model that has been developed through a system getting to know specialists and has already been reinforced on a huge dataset[18,19].

Transfer learning leverages data extracted from one set of distributions and uses it to leverage its learning to predict or classify others. In humans, the switch of expertise to college students is frequently performed with the aid of using instructors and training providers. This might not make the scholars smart. However, transfer learning makes the knowledge provider wise because of the knowledge-gathering party. In the case of humans, transferring expertise relies upon the inherent intelligence of the expert to improve the classification and prediction skills.

Future prospects

With the identification of top models for the classification of OA using a medical image, these models can be deployed for automating the process of preliminary X ray processing and determination of the next course of action. Any image classification project starts with a substantial number of images classified by an expert. This will provide inputs to the training of the model. There are multiple challenges that can result from this misclassification of data during validation of the model by a machine, such as intra-class variation, image scale variation, viewpoint variation, *i.e.* orientation of image, occlusion, multiple objects in the image, illumination, and background clutter. While humans can overcome some of these possible challenges with naked eyes, it will be difficult for a machine to reduce the impacts of such factors while classifying the images. This results in an increased amount of loss and effect on the outcome of the prediction.

Expert human interpretation accuracy comes with experience, and it was observed in this study. Both humans and machines are prone to overfitting, a curse that impacts preconceived notions while making decisions. AI is limited to the areas in which they are trained. Human intelligence and its interpretation, however, are independent of this domain of training. The key differentiator between human beings and machines is that humans will be able to solve problems related to unforeseen domains, while the latter will not have the capability to do that. The common solution suggested by experts to overcome overfitting or underfitting is cross-validation and regularization. This would be achieved by increasing the size or number of parameters in the ML model, increasing the exploration of complexity or type of the model, increasing the training time, and increasing the number of iterations until loss function in ML is minimized. Another major drawback of utilizing transfer learning models for image classification is negative transfer, where transfer learning ends up decreasing the accuracy or performance of the model. Thus, there is a need to customize the models and their parameters to see the impact of tuning and epochs on the performance or accuracy of the model.

This study is a preliminary step to the implementation of an end-to-end machine recommendation engine for the orthopedic department, which can provide sufficient inputs for OA surgeons to determine the requirement of OA surgery, patient treatment, and prioritization of patients based on engine output and related patient demographics.

CONCLUSION

The present study found that a neural network can be trained to classify and detect KOA severity and laterality as per the KL grading scale. The study reported excellent accuracy with the DenseNet model for the detection of the severity of KOA as per KL grading. Previously, it was challenging for healthcare professionals to collect and analyze large data for classification, analysis, and prediction of treatments since there were no such tools and techniques present. But now, with the advent of ML, it has been relatively available. ML may also help provide vital statistics, real-time data, and advanced analytics in terms of the patient's disease, lab test results, blood pressure, family history, clinical trial data, *etc* to doctors. The future of the technology in orthopedics and the application of this study's findings are multi-fold. We can also borrow from experience from other subspecialties.

Transfer learning techniques will not work when the image features learned by the classification layer, which are not enough nor appropriate to identify the classes for KL grades. When the medical images are not similar, then the KOA features are transferred poorly in the model as in the conventional model building, where layers for accuracy purposes have been adjusted as per convenience. If the same is applied in transfer learning, then it results in a reduction of trainable parameters and results in overfitting. Thus, it is important that a balance between overfitting and learning features is achieved.

This study also plans to improve the accuracy, which can be improved with more images, and the features of the algorithm. The implication of this study goes beyond the simple classification of KOA. The study paves the way for extrapolating the learning from KOA classification using ML to develop an automated KOA classification tool and enable healthcare professionals with better decision-making. This study helps in exploring trends and innovations and improving the efficiency of existing research and clinical trials associated with AI-based medical image classification. The Healthcare sector, including orthopedics, generates a large amount of real-time and non-real-time data. However, the challenge is to develop a pipeline that can collect these data effectively and use them for classification, analysis, prediction, and treatment in the most optimal manner. ML allows building models to quickly

analyze data and deliver results, leveraging historical and real-time data. Healthcare personnel can make better decisions on patients' diagnoses and treatment options using AI solutions, which leads to enhanced and effective healthcare services.

ARTICLE HIGHLIGHTS

Research background

Artificial intelligence (AI)-based on deep leaning (DL) has demonstrated promising results for the interpretation of radiographs. To develop a machine learning (ML) program capable of interpreting orthopedic radiographs with accuracy, a project called DL algorithm for orthopedic radiographs was initiated. It was used to diagnose knee osteoarthritis (KOA) using Kellgren-Lawrence scales in the first phase.

Research motivation

By using DL methods trained by senior radiologists and orthopedic surgeons in larger hospitals, smaller institutions could gain the expertise they need and create more space in emergency care, where medical professionals may not be readily available. Providing care in this manner would improve access dramatically.

Research objectives

This study aimed to explore the use of transfer learning convolutional neural network for medical image classification applications using KOA as a clinical scenario, comparing eight different transfer learning DL models for detecting the grade of KOA from a radiograph, to compare the accuracy between results from AI models and expert human interpretation, and to identify the most appropriate model for detecting the grade of KOA.

Research methods

As per the Kellgren-Lawrence scale, three orthopedic surgeons reviewed these independent cases, graded their severity for OA, and settled disagreements through consensus. To assess the efficacy of ML in accurately classifying radiographs for KOA, eight models were used, including ResNet50, VGG-16, InceptionV3, MobilnetV2, EfficientNetB7, DenseNet201, Xception, and NasNetMobile. A total of 2068 images were used, of which 70% were used initially to train the model, 10% were then used to test the model, and 20% were used for accuracy testing and validation of each model.

Research results

Overall, our network showed a high degree of accuracy for detecting KOA, ranging from 54% to 93%. Some networks were highly accurate, but few had an efficiency of more than 50%. The DenseNet model was the most accurate, at 93%, while expert human interpretation indicated accuracy of 74%.

Research conclusions

The study has compared the accuracy provided by expert human interpretation and AI models. It showed that an AI model can successfully classify and differentiate the knee X-ray image with the presence of different grades of KOA or by using various transfer learning convolution neural network models against human actions to classify the same. The purpose of the study was to pave the way for the development of more accurate models and tools, which can improve the classification of medical images by ML and provide insight into orthopedic disease pathology.

Research perspectives

AI can only operate within the areas in which it has been trained, whereas human intelligence and its interpretation are independent of the area in which it has been trained. One of the key differences between humans and machines is that humans will be able to solve problems related to unforeseen domains, while the latter will not have the capability to do that. It can be accomplished by increasing the size or number of parameters in the ML model, examining the complexity or type of the model, increasing the time spent training, and increasing the number of iterations until the loss function in ML is minimized.

FOOTNOTES

Author contributions: Tiwari A analyzed and evaluated the feasibility and accuracy of the artificial intelligence models with the interpretation of data; Poduval M was involved in critically revising the draft; Bagaria V designed and conceptualized the study and revised the manuscript for important intellectual content; All authors read and

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REFERENCES

1 **Hsu H**, Siwiec RM. Knee Arthroplasty. In: StatPearls [Internet]. Treasure Island: StatPearls Publishing, 2022 [PMID: 29939691]
2 **Aweid O**, Haider Z, Saed A, Kalairajah Y. Treatment modalities for hip and knee osteoarthritis: A systematic review of safety. *J Orthop Surg (Hong Kong)* 2018; **26**: 2309499018808669 [PMID: 30415598 DOI: 10.1177/2309499018808669]
3 **Urakawa T**, Tanaka Y, Goto S, Matsuzawa H, Watanabe K, Endo N. Detecting intertrochanteric hip fractures with orthopedist-level accuracy using a deep convolutional neural network. *Skeletal Radiol* 2019; **48**: 239-244 [PMID: 29955910 DOI: 10.1007/s00256-018-3016-3]
4 **Kim DH**, MacKinnon T. Artificial intelligence in fracture detection: transfer learning from deep convolutional neural networks. *Clin Radiol* 2018; **73**: 439-445 [PMID: 29269036 DOI: 10.1016/j.crad.2017.11.015]
5 **Olczak J**, Fahlberg N, Maki A, Razavian AS, Jilert A, Stark A, Sköldenberg O, Gordon M. Artificial intelligence for analyzing orthopedic trauma radiographs. *Acta Orthop* 2017; **88**: 581-586 [PMID: 28681679 DOI: 10.1080/17453674.2017.1344459]
6 **Lindsey R**, Daluiski A, Chopra S, Lachapelle A, Mozer M, Sicular S, Hanel D, Gardner M, Gupta A, Hotchkiss R, Potter H. Deep neural network improves fracture detection by clinicians. *Proc Natl Acad Sci U S A* 2018; **115**: 11591-11596 [PMID: 30348771 DOI: 10.1073/pnas.1806905115]
7 **Do BH**, Langlotz C, Beaulieu CF. Bone Tumor Diagnosis Using a Naïve Bayesian Model of Demographic and Radiographic Features. *J Digit Imaging* 2017; **30**: 640-647 [PMID: 28752323 DOI: 10.1007/s10278-017-0001-7]
8 **Langhorn J**, Borjali A, Hippensteel E, Nelson W, Raeymaekers B. Microtextured CoCrMo alloy for use in metal-on-polyethylene prosthetic joint bearings: multi-directional wear and corrosion measurements. *Tribol Int* 2018; **124**: 178-183 [PMID: 30778273 DOI: 10.1016/j.triboint.2018.04.007]
9 **Xue Y**, Zhang R, Deng Y, Chen K, Jiang T. A preliminary examination of the diagnostic value of deep learning in hip osteoarthritis. *PLoS One* 2017; **12**: e0178992 [PMID: 28575070 DOI: 10.1371/journal.pone.0178992]
10 **Tiulpin A**, Thevenot J, Rahtu E, Lehenkari P, Saarakkala S. Automatic Knee Osteoarthritis Diagnosis from Plain Radiographs: A Deep Learning-Based Approach. *Sci Rep* 2018; **8**: 1727 [PMID: 29379060 DOI: 10.1038/s41598-018-20132-7]
11 **Tiulpin A**, Klein S, Bierma-Zeinstra SMA, Thevenot J, Rahtu E, Meurs JV, Oei EHG, Saarakkala S. Multimodal Machine Learning-based Knee Osteoarthritis Progression Prediction from Plain Radiographs and Clinical Data. *Sci Rep* 2019; **9**: 20038 [PMID: 31882803 DOI: 10.1038/s41598-019-56527-3]
12 **Pai V**, Knipe H. Kellgren and Lawrence system for classification of osteoarthritis. [cited 23 Sep 2021]. Available from: https://radiopaedia.org/articles/27111
13 **Khan A**, Sohail A, Zahoora U, Qureshi AS. A survey of the recent architectures of deep convolutional neural networks. *Artif Intell Rev* 2020; **53**: 5455-5516 [DOI: 10.1007/s10462-020-09825-6]
14 **van Ginneken B**. Fifty years of computer analysis in chest imaging: rule-based, machine learning, deep learning. *Radiol Phys Technol* 2017; **10**: 23-32 [PMID: 28211015 DOI: 10.1007/s12194-017-0394-5]
15 **Ashinsky BG**, Bouhrara M, Coletta CE, Lehallier B, Urish KL, Lin PC, Goldberg IG, Spencer RG. Predicting early symptomatic osteoarthritis in the human knee using machine learning classification of magnetic resonance images from the

osteoarthritis initiative. *J Orthop Res* 2017; **35**: 2243-2250 [PMID: 28084653 DOI: 10.1002/jor.23519]

16 **Poduval M**, Ghose A, Manchanda S, Bagaria V, Sinha A. Artificial Intelligence and Machine Learning: A New Disruptive Force in Orthopaedics. *Indian J Orthop* 2020; **54**: 109-122 [PMID: 32257027 DOI: 10.1007/s43465-019-00023-3]

17 **Hamet P**, Tremblay J. Artificial intelligence in medicine. *Metabolism* 2017; **69S**: S36-S40 [PMID: 28126242 DOI: 10.1016/j.metabol.2017.01.011]

18 **Radford A**, Wu J, Amodei D, Clark J, Brundage M, Sutskever I. Better language models and their implications. OpenAI, 2018b. Available from: https://openai.com/blog/better-language-models

19 **Devlin J**, Chang M W, Lee K, Toutanova K. Bert: Pre-training of deep bidirectional transformers for language understanding. 2018 Preprint. Available from: arXiv:1810.04805 [DOI: 10.48550/arXiv.1810.04805]

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ORIGINAL ARTICLE

Retrospective Study

Role of joint aspiration before re-implantation in patients with a cement spacer in place

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Abstract

BACKGROUND

The usefulness of a mandatory joint aspiration before re-implantation in patients with a cement spacer already in place is unclear.

AIM

To evaluate the role of culturing synovial fluid obtained by joint aspiration before re-implantation in patients who underwent a two-stage septic revision.

METHODS

A retrospective observational study was conducted, including patients that underwent a two-stage septic revision (hip or knee) from 2010 to 2017. After the first stage revision and according to intraoperative culture results, all patients were treated with an antibiotic protocol for 6-8 wk. Following 2 wk without antibiotics, a culture of synovial fluid was obtained. The results of these cultures were recorded and compared with cultures obtained during re-implantation surgery.

RESULTS
Forty-one patients (20 hip and 21 knee spacers) were included in the final analysis. In 39 cases, the culture of synovial fluid was negative, while in the remaining 2 cases (knee spacers) no analysis was possible due to dry tap. In 5 of the patients, two or more intraoperative cultures taken during the re-implantation surgery were positive.

CONCLUSION
We found no evidence to support mandatory joint aspiration before re-implantation in patients with a cement spacer in place.

Key Words: Joint aspiration; Synovial fluid; Two-stage surgery; Revision surgery; Periprosthetic joint infection

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Core Tip: Many parameters and diagnostic methods have been analyzed to determine the optimal time to perform the second stage of a two-staged revision surgery. Synovial fluid culture after joint aspiration seems to be a reasonable test to evaluate the presence of microorganisms in the joint. However, the effectiveness of this diagnostic test is unclear. Despite the lack of validation, synovial aspiration is a common practice before prosthesis reimplantation. With our results, we found no evidence to support mandatory joint aspiration before re-implantation in patients with a cement spacer in place.

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INTRODUCTION

Periprosthetic joint infection (PJI) remains a challenging complication for all orthopedic surgeons. Despite the increase of a one-stage revision strategy, two-stage revision surgery remains the gold standard procedure for chronic PJI. Two-stage procedures using antibiotic-loaded cement spacers have reported eradication rates of over 73%[1-4]. To determine the optimal time to perform the second stage of the revision surgery, many parameters and diagnostic methods had been analyzed. Synovial fluid culture after a joint aspiration seems to be a reasonable test to evaluate the presence of microorganisms in the joint[5-7]. However, the effectiveness of this diagnostic test is unclear. Despite the lack of validation, synovial aspiration is a common practice before prosthesis reimplantation.

The purpose of our study was to evaluate the role of joint aspiration and synovial fluid culturing before re-implantation in patients with a cement spacer in place.

MATERIALS AND METHODS

A retrospective observational study was conducted. We analyzed all patients that underwent a two-stage revision surgery at our institution between 2010 and 2017 (inclusive).

The following variables were recorded for all patients: demographic parameters, results of first stage cultures, cultures of the synovial fluid between stages, results of second stage cultures, and the need for new procedures after the second stage.

All patients to whom arthrocentesis before the second stage of the surgery was not performed or the intraoperative cultures for the two stages of the surgery were not correctly analyzed were excluded from this study.

Treatment protocol

Our arthroplasty two-stage exchange protocol consisted of a first surgery where the prosthesis was explanted as well as all the cement and forage implants. A radical debridement was performed, and 5-7 samples were taken and analyzed by the microbiology laboratory. A cement spacer loaded with antibiotics (vancomycin and gentamicin), usually preformed (Vancogenx®-Space, Tecres), was then placed. After surgery, an empirical intravenous antibiotic treatment (teicoplanin, rifampin, and amikacin) was started and continued until definitive results for the microbiological cultures were

obtained. Once the causative microorganisms were isolated, antibiotic therapy was tailored to its sensitivity. This antibiotic treatment was then continued for 6 to 8 wk. After which, antibiotics were stopped for 2 wk (antibiotic holidays), and an arthrocentesis was performed. Blood tests were performed to quantify acute phase reactants, such as C-reactive protein. If the patient remained afebrile, without local clinical signs of infection, and with normalized serum C-reactive protein levels, we assumed that the infection was controlled and proceeded to the second stage. During the second-stage surgery, the cement spacer was removed and submitted to the microbiology laboratory for sonication. Another thorough debridement and sampling were performed before implantation of the definitive prosthesis. After the second stage surgery, patients received antibiotic therapy based on the sensitivity of the infecting organisms for 6 mo for total knee arthroplasty or 3 mo for total hip arthroplasty.

Joint aspiration protocol

The knee is a superficial joint where after adequate skin disinfection and with proper sterility measures we performed an arthrocentesis at the outpatient clinic. Synovial fluid obtained was sent for microbiological study. On the other hand, hip arthrocentesis was performed at the operating room with the assistance of sedation by the anesthesiologist and fluoroscopic aid to localize the correct space for joint puncture (Figure 1). Sterility measures and microbiological studies were the same as for the knee joint.

Microbiological protocol

Following the sampling protocol at our hospital, we took between 5 and 7 intraoperative samples. Each one was taken using a clean scalpel and clamp to avoid cross-contamination. Tissue samples were introduced in sterile plastic containers and sent to the microbiological laboratory without culture media. Once received in the laboratory, the tissue samples were homogenized in thioglycolate broth before plating in the following culture media (bioMérieux Marcy-l'Étoile, France): (1) 5% blood sheep agar: 7 d at 37 ^{o}C in 5% CO_2 atmosphere; (2) Chocolate agar: 7 d at 37 ^{o}C in 5% CO_2 atmosphere; (3) McConkey agar: 2 d in a normal atmosphere; (4) Sabouraud agar: 5 d at 37 ^{o}C in a normal atmosphere; (5) Anaerobic agar: 7 d in an anaerobic atmosphere; and (6) Thioglycolate broth: systematic spread after 5 d of incubation in a normal atmosphere, in 5% sheep blood agar, chocolate agar, and anaerobic agar with the incubation times previously described.

When the consistency of the samples did not allow homogenization, they were covered with thioglycolate broth and plated on agar plates (not in thioglycolate broth) after overnight incubation at 35 ^{o}C. Gram stains were performed from synovial fluid samples and then inoculated into a BacT/ALERT bottle (bioMérieux Marcy-l'Étoile, France) incubated for 7 d.

Results interpretation

The results of intraoperative cultures during first-stage surgery and synovial fluid were recorded and compared with cultures obtained during re-implantation surgery. According to culture results during the second stage, patients were classified as persistent infection when second stage cultures were positive for the same microorganism that was isolated during the first stage even if only one single culture was positive. Reinfection was considered when two or more of the second stage cultures were positive for the same microorganism but differ from the ones isolated during the first stage. The presence of only one positive culture from intraoperative samples for a low virulent microorganism not isolated in the first stage was considered as a contaminant.

RESULTS

A total of 50 patients diagnosed with PJI treated with a two-stage arthroplasty revision surgery were analyzed; nine patients were excluded because joint aspiration was not performed or the sample of synovial fluid was not correctly processed. The remaining 41 patients (20 hip and 21 knee joints) were included in the final analysis.

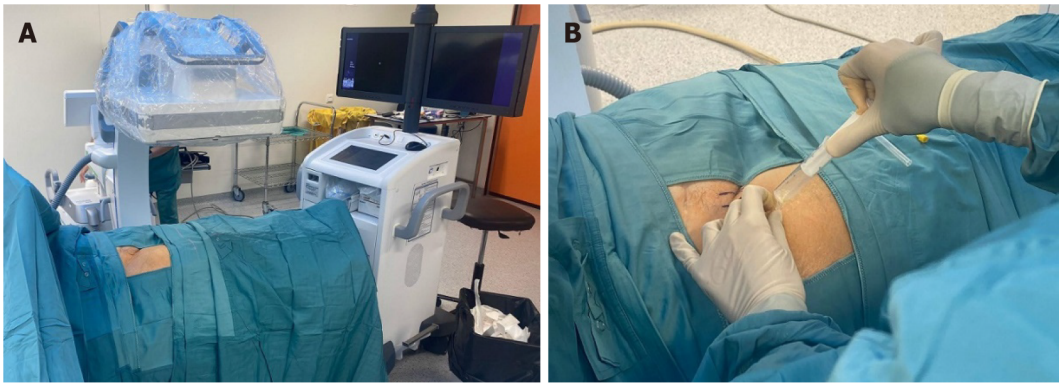
The mean age of patients was 70.4 years (range: 40-85 years). Twenty-four of them were females (61%), and sixteen were males (31%). In 39 patients, the synovial fluid culture was negative. In the remaining 2 cases, both knee spacers, no analysis was possible due to dry tap. Five patients had two or more positive intraoperative cultures during re-implantation surgery (Table 1). Only 1 patient, number 3, had a persistent infection. In this patient, the synovial fluid culture before the second-stage surgery failed to identify the infection. The other 4 cases had a reinfection, and in all of them the synovial fluid was negative. Three of these five patients (60%) required further surgeries after the second stage, and it was due to an infection in two cases (40%) (patients 1 and 2).

Thirty-six patients (87.8%) had negative cultures or one positive culture from a minimum of five intraoperative samples (considered contamination) during the second stage of the revision surgery. Of these patients, 17 (47.22%) needed new interventions after the second stage, and 12 of them (70.59%) were due to septic causes.

Table 1 Patients with more than two intraoperative cultures positive during second-stage surgery

Patient	Microorg. 1st stage	Spacer joint aspiration	Microorg. 2nd stage	Reinfection/Persistence	Reoperation after 2nd stage	Microorg. reoperation
1	Negative	Negative	*S. epidermidis; S. capitis*	Reinfection	Yes (Multiple)	*Klebsiella spp*
2	Negative	Negative	*S. epidermidis; S. cohnii*	Reinfection	Yes (Debridement)	Negative
3	*S. epidermidis; S. lugdunensis*	Negative	*S. epidermidis*	Persistence	No	-
4	Negative	Negative	*S. epidermidis; S. haemolyticus*	Reinfection	Yes (Periprosthetic fracture)	-
5	Negative	Negative	*S. epidermidis; C. acnes*	Reinfection	No	-

S. epidermidis: *Staphylococcus epidermidis*; *S. lugdunensis*: *Staphylococcus lugdunensis*; *S. haemolyticus*: *Staphylococcus haemolyticus*; *S. capitis*: *Staphylococcus capitis*; *S. cohni*: *Staphylococcus cohnii*; *C. acnes*: *Cutibacterium acnes*.



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Figure 1 Hip arthrocentesis procedure. A: Hip arthrocentesis setup; B: Hip arthrocentesis.

DISCUSSION

PJI is a challenging complication following orthopedic surgery. Two-stage revision surgery was first described by Insall *et al*[8], and it is considered the gold standard treatment for chronic PJI. The precise time to perform the second stage of the revision surgery remains uncertain. A combination of serum markers and synovial aspiration results is considered the best test for determining the presence of PJI persistence[5-7,9].

Although the majority of studies confirm low sensitivity for joint aspiration fluid culture before reimplantation surgery[10-14] (some as low as our data of 0%), other studies like Preininger *et al*[15] and Newman *et al*[16] reported higher rates (21% and 30%, respectively) with a maximum sensitivity of 83% in the study by Meermans *et al*[17]. All studies agree on its high specificity, above 90%[10-17].

Mont *et al*[18] and Aalirezaie *et al*[19] considered joint aspiration and synovial fluid culturing a useful tool. However, we found similarities in our results with other authors and agreed to not perform mandatory synovial fluid aspiration before the second stage[11-13,15].

An antibiotic-free interval before joint aspiration (antibiotic holiday) and the time until the culture result is available (a minimum of 2 wk) extends the duration between the first and second stage of the two-stage revision surgery. However, active antibiotic treatment can result in false negatives. In all the cases of our series, the cultures of the first stage, second stage, and synovial fluid obtained from joint aspiration were performed in patients without active antibiotic treatment. Despite this condition, we did not have any positive cultures. To reduce the time between stages, some authors such as Mühlhofer *et al*[10] and Boelch *et al*[11] recommend performing reimplantation surgery without antibiotic holiday.

There are some explanations for not having obtained any positive result in the synovial fluid culture in our patients. In the first place, the small sample size and the low sensitivity of the joint aspiration could explain our results. Second, the low bacterial load in the synovial fluid at the time of the joint aspiration. Third, the presence of local antibiotics due to elution of the antibiotic present in the cement spacer[20].

It is important to emphasize the differences between the knee and hip joint aspiration procedures. Knee joint aspiration is a much easier procedure as it is a more accessible joint and does not require guidance by fluoroscopy or ultrasound techniques. In some centers, when no fluid is obtained after joint aspiration, sterile saline is injected into the joint and then aspirated to obtain fluid to analyze. Injection of saline fluid into a joint that did not yield any synovial fluid (dry tap) was not recommended during the 2018 International Consensus Meeting on musculoskeletal infection.

The main limitations of our study are its retrospective nature and the limited number of cases. There are few articles published in the literature concerning the value of synovial aspiration before re-implantation surgery with a cement spacer in place. These papers present heterogeneous data and an inconsistent antibiotic-free interval, making them difficult to compare.

CONCLUSION

Although synovial fluid culture may provide useful information regarding the infection status of the joint, we found no evidence to support mandatory joint aspiration before re-implantation in patients with a cement spacer in place.

ARTICLE HIGHLIGHTS

Research background

There are few studies in the literature based on the usefulness of joint aspiration with a cement spacer in place. The importance of this type of study lies in finding useful methods for determining the appropriate timing of the second stage of revision surgery.

Research motivation

The main problem in this type of research is its heterogeneity, as the duration of antibiotic treatment, the presence of antibiotic holiday, the use or not of a physiological saline solution when a dry aspiration is obtained, *etc* vary according to each institution's protocol.

Research objectives

The objective of this study was to evaluate the role of culturing synovial fluid obtained by joint aspiration before re-implantation in patients who underwent a two-stage septic revision.

Research methods

This is a retrospective study, and the research method was to observe the results obtained in the joint aspiration performed before re-implantation in the knee/hip septic replacements in our center between 2010 and 2017.

Research results

The results obtained in the study showed low sensitivity of joint aspiration for detecting infection persistence when performed prior to the second stage in a two-stage replacement.

Research conclusions

The results obtained in our study lead us to not recommend the use of joint aspiration prior to the second stage of revision surgery due to its low sensitivity.

Research perspectives

Future research should focus on obtaining reliable markers to indicate the optimal time to perform the second stage of a two-stage septic revision.

FOOTNOTES

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REFERENCES

1 **Anagnostakos K**, Fürst O, Kelm J. Antibiotic-impregnated PMMA hip spacers: Current status. *Acta Orthop* 2006; **77**: 628-637 [PMID: 16929441 DOI: 10.1080/17453670610012719]
2 **Cui Q**, Mihalko WM, Shields JS, Ries M, Saleh KJ. Antibiotic-impregnated cement spacers for the treatment of infection associated with total hip or knee arthroplasty. *J Bone Joint Surg Am* 2007; **89**: 871-882 [PMID: 17403814 DOI: 10.2106/JBJS.E.01070]
3 **Kurd MF**, Ghanem E, Steinbrecher J, Parvizi J. Two-stage exchange knee arthroplasty: does resistance of the infecting organism influence the outcome? *Clin Orthop Relat Res* 2010; **468**: 2060-2066 [PMID: 20300903 DOI: 10.1007/s11999-010-1296-6]
4 **Biring GS**, Kostamo T, Garbuz DS, Masri BA, Duncan CP. Two-stage revision arthroplasty of the hip for infection using an interim articulated Prostalac hip spacer: a 10- to 15-year follow-up study. *J Bone Joint Surg Br* 2009; **91**: 1431-1437 [PMID: 19880885 DOI: 10.1302/0301-620X.91B11.22026]
5 **Trampuz A**, Hanssen AD, Osmon DR, Mandrekar J, Steckelberg JM, Patel R. Synovial fluid leukocyte count and differential for the diagnosis of prosthetic knee infection. *Am J Med* 2004; **117**: 556-562 [PMID: 15465503 DOI: 10.1016/j.amjmed.2004.06.022]
6 **Parvizi J**, Della Valle CJ. AAOS Clinical Practice Guideline: diagnosis and treatment of periprosthetic joint infections of the hip and knee. *J Am Acad Orthop Surg* 2010; **18**: 771-772 [PMID: 21119143 DOI: 10.5435/00124635-201012000-00007]
7 **Schinsky MF**, Della Valle CJ, Sporer SM, Paprosky WG. Perioperative testing for joint infection in patients undergoing revision total hip arthroplasty. *J Bone Joint Surg Am* 2008; **90**: 1869-1875 [PMID: 18762646 DOI: 10.2106/JBJS.G.01255]
8 **Insall JN**, Thompson FM, Brause BD. Two-stage reimplantation for the salvage of infected total knee arthroplasty. *J Bone Joint Surg Am* 1983; **65**: 1087-1098 [PMID: 6630253]
9 **Ghanem E**, Azzam K, Seeley M, Joshi A, Parvizi J. Staged revision for knee arthroplasty infection: what is the role of serologic tests before reimplantation? *Clin Orthop Relat Res* 2009; **467**: 1699-1705 [PMID: 19241115 DOI: 10.1007/s11999-009-0742-9]
10 **Mühlhofer HML**, Knebel C, Pohlig F, Feihl S, Harrasser N, Schauwecker J, von Eisenhart-Rothe R. Synovial aspiration and serological testing in two-stage revision arthroplasty for prosthetic joint infection: evaluation before reconstruction with a mean follow-up of twenty seven months. *Int Orthop* 2018; **42**: 265-271 [PMID: 29243060 DOI: 10.1007/s00264-017-3700-2]
11 **Boelch SP**, Weissenberger M, Spohn F, Rudert M, Luedemann M. Insufficient sensitivity of joint aspiration during the two-stage exchange of the hip with spacers. *J Orthop Surg Res* 2018; **13**: 7 [PMID: 29321073 DOI: 10.1186/s13018-017-0703-z]
12 **Boelch SP**, Roth M, Arnholdt J, Rudert M, Luedemann M. Synovial Fluid Aspiration Should Not Be Routinely Performed during the Two-Stage Exchange of the Knee. *Biomed Res Int* 2018; **2018**: 6720712 [PMID: 30009171 DOI: 10.1155/2018/6720712]
13 **Hoell S**, Moeller A, Gosheger G, Hardes J, Dieckmann R, Schulz D. Two-stage revision arthroplasty for periprosthetic joint infections: What is the value of cultures and white cell count in synovial fluid and CRP in serum before second stage reimplantation? *Arch Orthop Trauma Surg* 2016; **136**: 447-452 [PMID: 26757939 DOI: 10.1007/s00402-015-2404-6]
14 **Lonner JH**, Siliski JM, Della Valle C, DiCesare P, Lotke PA. Role of knee aspiration after resection of the infected total knee arthroplasty. *Am J Orthop (Belle Mead NJ)* 2001; **30**: 305-309 [PMID: 11334452]
15 **Preininger B**, Janz V, von Roth P, Trampuz A, Perka CF, Pfitzner T. Inadequacy of Joint Aspiration for Detection of Persistent Periprosthetic Infection During Two-Stage Septic Revision Knee Surgery. *Orthopedics* 2017; **40**: 231-234 [PMID: 28418574 DOI: 10.3928/01477447-20170411-04]
16 **Newman JM**, George J, Klika AK, Hatem SF, Barsoum WK, Trevor North W, Higuera CA. What is the Diagnostic

Accuracy of Aspirations Performed on Hips With Antibiotic Cement Spacers? *Clin Orthop Relat Res* 2017; **475**: 204-211 [PMID: 27672013 DOI: 10.1007/s11999-016-5093-8]

17 **Meermans G**, Haddad FS. Is there a role for tissue biopsy in the diagnosis of periprosthetic infection? *Clin Orthop Relat Res* 2010; **468**: 1410-1417 [PMID: 20131022 DOI: 10.1007/s11999-010-1245-4]

18 **Mont MA**, Waldman BJ, Hungerford DS. Evaluation of preoperative cultures before second-stage reimplantation of a total knee prosthesis complicated by infection. A comparison-group study. *J Bone Joint Surg Am* 2000; **82**: 1552-1557 [PMID: 11097443 DOI: 10.2106/00004623-200011000-00006]

19 **Aalirezaie A**, Bauer TW, Fayaz H, Griffin W, Higuera CA, Krenn V, Molano M, Moojen DJ, Restrepo C, Shahi A, Shubnyakov I, Sporer S, Tanavalee A, Teloken M, Velázquez Moreno JD. Hip and Knee Section, Diagnosis, Reimplantation: Proceedings of International Consensus on Orthopedic Infections. *J Arthroplasty* 2019; **34**: S369-S379 [PMID: 30343965 DOI: 10.1016/j.arth.2018.09.021]

20 **Anagnostakos K**, Meyer C. Antibiotic Elution from Hip and Knee Acrylic Bone Cement Spacers: A Systematic Review. *Biomed Res Int* 2017; **2017**: 4657874 [PMID: 28656144 DOI: 10.1155/2017/4657874]



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REVIEW

Septic arthritis of the hand: Current issues of etiology, pathogenesis, diagnosis, treatment

Konstantin V Lipatov, Arthur Asatryan, George Melkonyan, Aleksandr D Kazantcev, Ekaterina I Solov'eva, Urii E Cherkasov

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Abstract

Septic arthritis of the hand is a serious disease that often results in dysfunction of the joint or even the need to perform amputation of the finger. They rank second in the frequency of occurrence after lesions of the knee joint. Many points concerning the etiology, the timing of the development of cartilage destruction and the development of osteomyelitis, approaches to surgical treatment, the duration of antibiotic therapy, and the start of rehabilitation measures remain the subject of numerous discussions. Based on a search in the PubMed, Web of Science and Google Scholar databases down to 1990-2021, publications on septic arthritis of the hand were found and analyzed. The following inclusion criteria were used in our review: (1) Septic arthritis of the hand; (2) Published in a peer review journal; (3) Written in English; and (4) Full text version available. Studies were excluded if they met any of the following criteria: (1) Letters; (2) Articles published in abstract form only; and (3) Cadaveric studies. Septic arthritis of the hand was characterized by the most frequent damage to the joints of the index and middle fingers (> 50% of cases). Up to 90% of cases, the infection enters the joint as a result of penetrating trauma, animal bites, *etc.* Staphylococcus aureus became the most frequently isolated microorganism (30%-55%), and its polyanti-

biotic-resistant form Methicillin-resistant Staphylococcus aureus was found, according to various sources, from 0% to 73% among all isolated Staphylococcus aureus. In arthritis, Pasteurella multocida (6%-11%) is often isolated as a result of animal bites. Articular cartilage destruction in the experiment developed within 24-48 h after infection. In clinical studies, the development of osteomyelitis was noted when treatment was delayed by more than 10 d. X-ray data during the first two weeks were uninformative. Priority of surgical treatment of septic arthritis. Drainage and surgical treatment, and with the development of osteomyelitis, the implementation of arthrodesis. Antibacterial therapy for 2-4 wk and early start of rehabilitation measures. Timely surgical treatment in combination with antibiotic therapy and rehabilitation makes it possible to obtain a positive result in the treatment of septic arthritis of the hand.

Key Words: Septic arthritis; Hand; Staphylococcus aureus; Metacarpophalangeal joint; Interphalangeal joint; Rehabilitation

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Core Tip: Septic arthritis of the hand often occurs as a result of penetrating wounds. The most common causative agent is Staphylococcus aureus, often characterized by high antibiotic resistance. Delayed treatment of septic arthritis can lead to cartilage destruction and osteomyelitis. To achieve a positive result in the treatment of septic arthritis of the hand, timely surgery, adequate antibiotic therapy and early rehabilitation are necessary.

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INTRODUCTION

The hand is a unique anatomical formation of the human body, that determines its authenticity and individuality. Injuries and diseases of the hand can have the most tragic consequences, depriving the victims of the opportunity to continue their professional activities, causing irreparable cosmetic damage, and often causing disability[1,2]. Among the infectious pathologies of the hand, septic arthritis of the metacarpophalangeal and interphalangeal joints is characterized by particular severity. Delayed or inadequate treatment of these diseases can lead to loss of joint function or even to the need for finger amputation[3,4]. In addition, persistent infection, impaired function, and chronic pain after septic arthritis may warrant arthrodesis or amputation in 50%-75% of patients[1].

PREVALENCE AND CAUSES

The incidence of purulent arthritis of the hand joints is characterized by significant regional differences and ranges from 2 to 12 cases per 100000 people per year[5]. They rank second in prevalence (15%-20%) among purulent arthritis of other locations in adults after lesions of the knee joint[3]. However, according to other data, they are much less common than 5% among septic arthritis patients[6]. Among all hand infections, the proportion of bone and joint lesions ranges from 5% to 18%[3].

The joints of the index and middle fingers are most often affected (more than 50% of cases). Information about the involvement in the inflammatory process of the distal (DIP), proximal (PIP) interphalangeal joints and metacarpophalangeal (MCP) joints is contradictory according to various authors. Some of them indicate a higher frequency of DIP lesions, while others, on the contrary, indicate a more frequent involvement of PIP or MCP in the inflammatory process[2,6,7]. At the same time, it should be noted that the judgments of most authors are based on little clinical material.

As a rule, (85%-90% of all cases) the infection entered the joint directly as a result of tissue damage as a result of a domestic or industrial injury, animal or human bites, or medical manipulations[2]. Cat bites are significantly more likely than dog bites to cause infectious complications. This is due to differences in anatomy and bite mechanism. Dog bites are characterized by a crushing and tearing mechanism associated with naturally blunt dog teeth. The sharp teeth of cats, piercing tissues, leave behind a bacterial trail like an injection needle. This mechanism is characterized by slight tissue damage, contributing to the retention of bacteria in the deep layers, which leads to severe infectious complic-

ations[8]. Quite typical is the development of purulent arthritis of the metacarpophalangeal joint in traumatic injury, called clenched fist injury. It is dangerous not only because of tissue contamination with pathogenic microflora from the oral cavity, but also due to possible damage to the extensor tendon, MCP capsule, and metacarpal head[9]. It is possible to spread the infection to the joint with the development of septic arthritis from the surrounding soft tissues with felon, and pyogenic flexor tenosynovitis[10].

Much rare (up to 10%-12%) is the hematogenous route of infection penetration into the joint, and the source in most cases remains unidentified[2,4]. When trauma is not evident, the differential diagnosis should include degenerative arthritis, inflammatory arthritis, crystalline arthropathy, cellulitis and soft tissue abscess[11,12].

MICROBIOLOGY

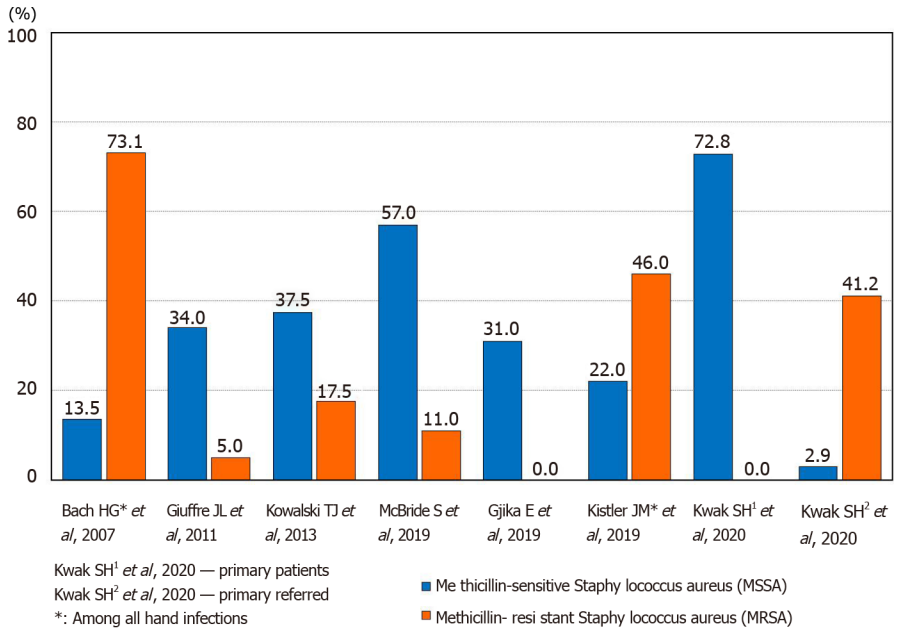
The microbiology of causative agents of septic arthritis of the hand has not been studied in sufficient detail. Data have been published that among the isolated microorganisms in septic arthritis, Staphylococcus aureus prevailed (30%-55%), and among its strains, the methicillin-resistant form was often found[7,13-15] (Figure 1). Various types of Streptococcus were also often isolated (up to 15%), including the most pathogenic Streptococcus pyogenes[16]. The level of gram-negative microorganisms remained relatively high (up to 13%)[3,16]. A feature of the microbial landscape of septic arthritis of the hand was the fairly frequent release of Pasteurella multocida (up to 6%-11%), the causative agent of zoonotic infections, which usually enter tissues with animal bites[7]. With septic arthritis of the fingers, monoinfection prevailed, although cases of isolation of associations of microorganisms (up to 5%-19%) were not uncommon[13,17]. The importance of identifying pathogens was not only in conducting scientific analysis, but also in the possibility of antibacterial therapy, taking into account the sensitivity of the isolated microflora. However, according to researchers, successful isolation of microorganisms in purulent arthritis of the hand occurred in only 50%-70% of cases[2,7,18].

PATHOGENESIS

Pathogenic microorganisms that have penetrated into the joint produce substances that promote their adhesion and protection from humoral and cellular immunity factors. The multiplication of bacteria leads to the spread of infection. In the initial stage of the immune response of the macroorganism, a cell wall is formed, including macrophages and polymorphonuclear leukocytes. The production of proinflammatory cytokines (interleukin 1-β, interleukin-6, tumor necrosis factor-α, *etc.*) begins along with the activation of the complement system. If it is impossible to eliminate the infection, the immunological response continues to develop with the formation of byproducts that lead to the release of matrix proteinases and lysosomal enzymes. They, in combination with bacterial toxins, cause the degradation of host collagen. The formed articular effusion disrupts the nutrition of chondrocytes, contributing to the occurrence of cartilage destruction[19-22]. Experimental studies have shown that cartilage surface erosion, degeneration and necrosis of chondrocytes appear starting from 24 h after intra-articular injection of bacteria[23,24]. An *in vivo* study showed the death of chondrocytes within 48 h of interaction with pathogenic microflora (S. aureus, E. coli)[23,25,26]. Clinical studies indicate that delaying treatment by more than 10 days leads to the development of osteomyelitis[4,27,28]. Other authors note even later periods of osteomyelitis − 1 mo or more after injury[3,29]. Undoubtedly, timely treatment is the most important factor preventing the occurrence of osteochondral destruction in purulent arthritis, which was proven by a study in which, with an average treatment delay of 5.4 d, osteomyelitis was not detected in any case[2]. Similar data are given by M. Sinha *et al*[10] (2006), who observed 26 patients with hand arthritis. The maximum treatment delay was up to 6 days. At the same time, cartilage destruction was not detected in any case.

CLASSIFICATION

Currently, a specialized classification of purulent arthritis of the hand has not been proposed, which would reflect important parameters such as the destruction of bone and cartilage structures, the tendons of the flexor and extensor of the finger, the presence of paraarticular wounds and fistulas. Septic arthritis of the fingers found some reflection in the classification of hand infections Brown[30] (1978). It includes such forms as: cellulitis, necrotizing fasciitis, paronychia, felon, pyogenic flexor tenosynovitis, deep space infections, septic arthritis, and osteomyelitis. The classification presents only two variants of purulent arthritis, one of which is accompanied by the development of osteomyelitis. Along with this, there is no information about the condition of the surrounding soft tissues, the patient's immune status, or clinical data. The generally accepted and recommended practice is to use the classifications



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Figure 1 The frequency of isolated microorganisms of Methicillin-sensitive Staphylococcus aureus and methicillin-resistant staphylococcus aureus.

developed for purulent arthritis of large joints. One of the most successful for clinical use is the classification by Tan *et al*[31] (1998), which includes a number of important parameters:

Joint name

Anatomic type: I: Periarticular soft-tissue infection without pyarthrosis; II: Isolated septic arthritis; III: Septic arthritis with soft-tissue extension, but no osteomyelitis; IV: Septic arthritis with contiguous osteomyelitis.

Host class: A: Normal immune system; B: Compromised system, B_L: Local tissue compromise, B_S: Systemic immune compromise; C: Risk associated with aggressive treatment unwarranted.

Clinical setting

(1) Less than 5 d of symptoms and nonvirulent organism; and (2) Symptoms for 5 d or more, or a virulent organism.

Clinical stage for the septic joint

Anatomic type + host class + clinical setting = stage.

DIAGNOSTICS

The diagnosis of septic arthritis of the hand is based on a set of clinical, instrumental and laboratory research methods. Among the clinical manifestations, there are symptoms such as pain, swelling, skin hyperemia, dysfunction of the joint, and signs of fluid accumulation in the joint cavity[13]. The severity of clinical symptoms may differ significantly depending on the acute or chronic course of the disease. A number of authors, extrapolating the data used in the classification of periprosthetic infections of large joints, highlight the acute or chronic course of arthritis of the hand. The acute course is associated with a duration of symptoms of < 3 wk with a hematogenous route of infection or < 4 wk with an exogenous source. In a chronic course, symptoms persist for ≥ 3 wk with a hematogenous route of infection of the joint or ≥ 4 wk with a nonhematogenous route[32].

Instrumental diagnostics may include radiography, ultrasound, computed tomography (CT) and magnetic resonance tomography (MRI). X-ray data are usually uninformative in the early stages, which can lead to diagnostic errors[1,3]. Less than 5% of acute cases of osteomyelitis of the hand are recognized on radiographs[33]. Signs characteristic of osteomyelitis, such as osteolysis (70%), osteopenia (10%), osteosclerosis (10%), periosteal reaction (10%), and sequestration (5%), appear on radiographs 2-3 wk after the onset of the disease[8]. Technetium-, gallium-, and indium-labeled white blood cell scans are helpful in identifying acute osteomyelitis before the aforementioned changes can be detected on

plain radiographs[33]. Ultrasound examination makes it possible to detect intra-articular effusion, and is also useful for pointing the needle when puncturing small joints of the hand[5,34,35]. MRI is a useful diagnostic tool to visualize joint effusion, its distribution, and the destruction of soft tissues and osteochondral structures of the joint. However, MRI is expensive and usually accompanied by a significant time delay and therefore can only be used in an acute situation to a limited extent[36,37]. CT makes it possible to examine bone structures in more detail than MRI, losing the visualization of soft tissues[5,38]. Both methods are necessary in the chronic course of the inflammatory process[39]. Laboratory diagnostics consisted of conducting a microbiological and cytological study of the articular effusion. Identification of the pathogen and determination of its sensitivity to antibiotics makes it possible to conduct effective antibiotic therapy[2,10,40].

TREATMENT

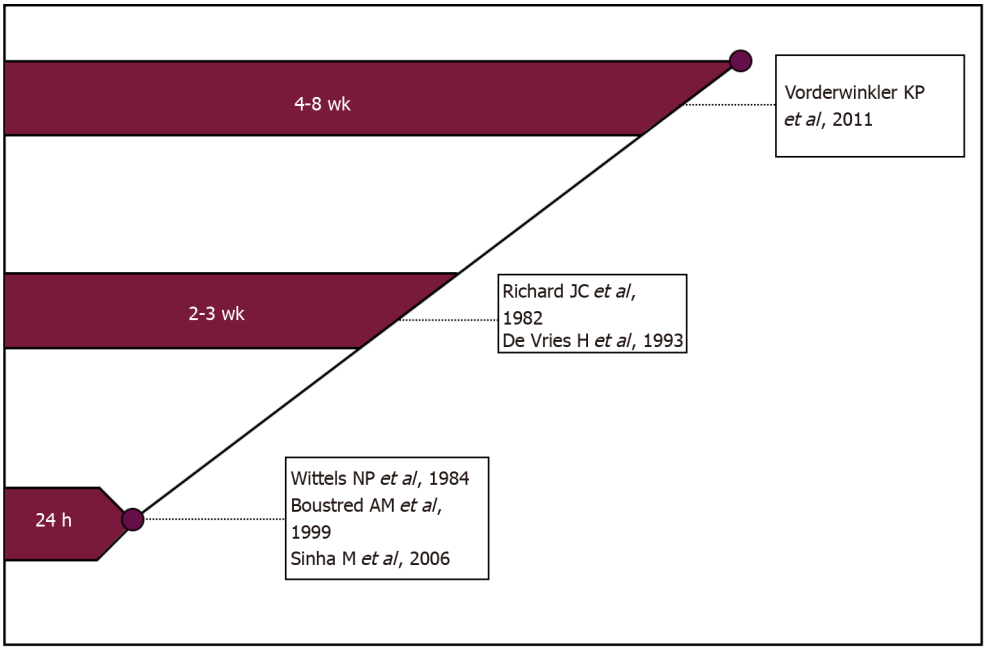
Recommendations for the treatment of patients with septic arthritis of the small joints of the hand are based on data from retrospective studies and expert opinion. The choice of sanitation method depends on the nature and severity of pathological changes and may include: repeated punctures, arthroscopic drainage and open sanitation[13,41]. Puncture treatment is effective only at the earliest stages of the disease, and arthroscopic sanitation of small joints of the hand is very difficult, so open sanitation of the joint is the most frequently performed surgical intervention[4,42]. In the absence of osteochondral destruction, the concept of continuous catheter irrigation, described by Wright[43] (1943) in the treatment of tendon sheath infections. Timely continuous irrigation of the joint cavity made it possible to prevent the destruction of cartilaginous tissue that accompanies septic arthritis. The authors noted such obligatory moments during irrigation as: axial traction along with passive flexion and extension of the joint[42]. The catheter was removed after the disappearance of edema and other clinical manifestations of inflammation, usually after 2-5 d. The start of rehabilitation was critical to joint function. Another treatment option has also been described: After surgical debridement, a collagen sponge with gentamicin was installed in the joint, and immobilization was performed for a period of 4 wk[44,45].

If signs of infection persist, a second operation is recommended within 24-48 h after the first operation[4,5,12]. There is only fragmentary information regarding the frequency of reoperations for septic arthritis of the hand. A number of authors report that in most cases (up to 80%) patients underwent 2 or more surgical interventions. The most common of these was surgical debridement[2,16,44]. Often, this was associated with suppuration of the paraarticular soft tissues and destruction of the flexor and extensor tendons of the finger[46]. Progression of the infection, despite surgical debridement and antibiotic therapy, may require amputation[1]. Along with this, data on the treatment of septic arthritis of the hand in two hospitals in Switzerland were published, where the number of surgical interventions in 1 patient was 1. At the same time, the average delay in surgical treatment from the onset of the disease was no more than 2-3 d[47].

In cases of detection of destruction of the articular cartilage and osteomyelitis, arthrodesis is recommended to prevent the formation of painful arthrosis or contracture in a functionally disadvantageous position[6,48]. Most of the experts prefer primary arthrodesis of the interphalangeal joints, while others favor secondary arthrodesis 4−6 wk after the primary revision with immobilization with an external fixator and the introduction of a cement spacer with gentamicin[4,13,16,45]. Single reports concern the possibility of using the Masquelet technique in the treatment of septic arthritis of the interphalangeal joints[38,49]. However, given the risk of purulent complications and rejection of the bone autograft, the expediency of such an operation may be questionable.

The course of septic arthritis of the hand in patients with diabetes mellitus is especially severe[9,50]. Published data indicate that the need for arthrodesis increased by 1.7 times. The risk of finger amputation increased even more, by 2.1 times[13]. Stiffness of the interphalangeal joints after purulent arthritis in patients with diabetes mellitus developed in more than 50% of cases, despite early activation and manual therapy started 24 h after surgery[13].

Antibacterial therapy, along with surgical treatment, is an essential component in purulent arthritis of the hand. Taking into account the data obtained in the study of the microbial landscape of purulent arthritis, the main antibacterial drugs used in their treatment are: amoxicillin/clavulanate, clindamycin, levofloxacin, vancomycin, cefazolin, and ceftriaxone[51,52]. Correction of empirical antibiotic therapy is carried out taking into account the results of microbiological studies. Based on an extensive systematic review evaluating the role of antimicrobials in the treatment of bone and joint infections, it was concluded that there is no evidence that any drug is superior to others[53]. However, if the nature of antibiotic therapy in general does not cause controversy among researchers, then its duration remains the subject of numerous discussions. A frequently encountered opinion of experts indicates the need for a course of antibiotic therapy for septic arthritis of the hand lasting approximately 1 mo[16]. As a rule, both the initial parenteral and subsequent oral routes of drug administration are included here[54]. On the other hand, Gjika *et al*[18] (2019) conducted a prospective randomized study (154 cases), which compared the effectiveness of 2 and 4 wk of antibiotic therapy after surgical treatment of septic arthritis of the hand in adults. The conclusion made proved the absence of any advantages of a 4-wk course over



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Figure 2 Review of beginning postoperative mobilisation of patients with the hand or wrist septic arthritis.

a 2-wk course. According to Kowalski *et al*[7] (2014) found that the combination of surgical treatment of a purulent focus with parenteral (less than 1 wk) and subsequent oral (2-3 wk) administration of antibacterial drugs is optimal. To date, a combined scheme (parenterally and then orally) for the administration of antibacterial drugs in the treatment of septic arthritis of the hand is optimal, since it is designed for both inpatient and outpatient treatment of patients[18,54].

REHABILITATION

It is known that one of the negative consequences of septic arthritis of the hand is stiffness of the joints [16]. In this regard, the question of the timing of the start of rehabilitation of patients who underwent surgery for septic arthritis of the metacarpophalangeal or interphalangeal joint remains important and controversial[5,7,42]. The duration of postoperative immobilization depends on the presence of articular cartilage destruction and is the subject of numerous discussions. The concept of supporters of early rehabilitation is that it contributes to the restoration of range of motion after inflammation. It is believed that "ideal" rehabilitation should begin 24 h after surgery[10]. Along with these, there is an opinion that it is advisable to apply a splint for several days or external fixation devices for 2-4 wk[4,44] (Figure 2).

The most important component in evaluating the results of treatment of septic arthritis of the hand is not only the elimination of the infection but also the restoration of the function of the affected joint, as well as the hand as a whole. Among the currently existing questionnaires and scales, Disabilities of the Arm, Shoulder, and Hand (DASH) and total active motion (TAM) are the most widely used in assessing hand function. Originally published in 1996 in the American Journal of Industrial Medicine, the DASH was a collaborative initiative between the American Academy of Orthopedic Surgeons, the Council of Musculoskeletal Specialty Societies, and the Institute for Work and Health. This outcome measure was designed to be a standardized assessment of the impact on function of a variety of musculoskeletal diseases and injuries in the upper extremities. The DASH is a 30-item self-report questionnaire in which the response options are presented on 5-point Likert scales. Scores range from 0 (no disability) to 100 (most severe disability). This score was designed to be useful in patients with any musculoskeletal disorder of the upper limb[55]. However, this questionnaire is characterized by a significant degree of subjectivity and reflects the function of the hand as a whole to a greater extent than a specific joint or finger.

TAM is described by the American Society for Surgery of the Hand as the sum of active MCP, PIP and DIP arc of motion in degrees of an individual digit. This calculation can then be compared to the TAM of the contralateral hand[56]. The TAM scale is objective and with high accuracy makes it possible to assess the degree of dysfunction of a particular finger. Complementing each other, DASH and TAM make it possible to obtain maximum information characterizing the functional result of the treatment of septic arthritis.

CONCLUSION

Thus, septic arthritis of the hand is a serious disease that can lead to the destruction of articular cartilage and the development of osteomyelitis, which, in turn, leads to loss of joint function or even the need for amputation of the finger. Even isolated septic arthritis is often accompanied by joint stiffness, which negatively affects the function of the hand as a whole. In the treatment of this disease, timely surgical treatment is of decisive importance, which, along with antibacterial therapy and a complex of rehabilitation measures, makes it possible to achieve a positive result.

FOOTNOTES

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REFERENCES

1 **McKay P**, Formby PM, Dickens J, Gibson M. Osteomyelitis and septic arthritis of the hand and wrist. *Curr Orthop Pract* 2010; **21**: 542-550 [DOI: 10.1097/BCO.0b013e3181f1f2c1]
2 **Meier R**, Wirth T, Hahn F, Vögelin E, Sendi P. Pyogenic Arthritis of the Fingers and the Wrist: Can We Shorten Antimicrobial Treatment Duration? *Open Forum Infect Dis* 2017; **4**: ofx058 [PMID: 28491895 DOI: 10.1093/ofid/ofx058]
3 **Sendi P**, Kaempfen A, Uçkay I, Meier R. Bone and joint infections of the hand. *Clin Microbiol Infect* 2020; **26**: 848-856 [PMID: 31917233 DOI: 10.1016/j.cmi.2019.12.007]
4 **Chenoweth B**. Septic Joints: Finger and Wrist. *Hand Clin* 2020; **36**: 331-338 [PMID: 32586459 DOI: 10.1016/j.hcl.2020.03.006]
5 **Lamou HJ**, Kim S, Kuchenbuch C, Thelen S, Eisenschenk A, Hakimi M. Septic Arthritis of the Hand and Wrist. *Handchir Mikrochir Plast Chir* 2021; **53**: 290-295 [PMID: 34134161 DOI: 10.1055/a-1512-0321]
6 **Angly B**, Steiger R, Zimmerli W. Septic arthritis of finger joints. *Handchir Mikrochir Plast Chir* 2007; **39**: 118-123 [PMID: 17497608 DOI: 10.1055/s-2007-965137]
7 **Kowalski TJ**, Thompson LA, Gundrum JD. Antimicrobial management of septic arthritis of the hand and wrist. *Infection* 2014; **42**: 379-384 [PMID: 24307329 DOI: 10.1007/s15010-013-0566-0]
8 **McDonald LS**, Bavaro MF, Hofmeister EP, Kroonen LT. Hand infections. *J Hand Surg Am* 2011; **36**: 1403-1412 [PMID: 21816297 DOI: 10.1016/j.jhsa.2011.05.035]
9 **Osterman M**, Draeger R, Stern P. Acute hand infections. *J Hand Surg Am* 2014; **39**: 1628-35; quiz 1635 [PMID: 25070032 DOI: 10.1016/j.jhsa.2014.03.031]
10 **Sinha M**, Jain S, Woods DA. Septic arthritis of the small joints of the hand. *J Hand Surg Br* 2006; **31**: 665-672 [PMID: 17046120 DOI: 10.1016/j.jhsb.2006.08.011]
11 **Flevas DA**, Syngouna S, Fandridis E, Tsiodras S, Mavrogenis AF. Infections of the hand: an overview. *EFORT Open Rev* 2019; **4**: 183-193 [PMID: 31191986 DOI: 10.1302/2058-5241.4.180082]
12 **Koshy JC**, Bell B. Hand Infections. *J Hand Surg Am* 2019; **44**: 46-54 [PMID: 30017648 DOI: 10.1016/j.jhsa.2018.05.027]
13 **Giuffre JL**, Jacobson NA, Rizzo M, Shin AY. Pyarthrosis of the small joints of the hand resulting in arthrodesis or amputation. *J Hand Surg Am* 2011; **36**: 1273-1281 [PMID: 21705153 DOI: 10.1016/j.jhsa.2011.05.022]
14 **Bach HG**, Steffin B, Chhadia AM, Kovachevich R, Gonzalez MH. Community-associated methicillin-resistant Staphylococcus aureus hand infections in an urban setting. *J Hand Surg Am* 2007; **32**: 380-383 [PMID: 17336847 DOI: 10.1016/j.jhsa.2007.01.006]

15 **Kistler JM**, Thoder JJ, Ilyas AM. MRSA Incidence and Antibiotic Trends in Urban Hand Infections: A 10-Year Longitudinal Study. *Hand (N Y)* 2019; **14**: 449-454 [PMID: 29322874 DOI: 10.1177/1558944717750921]

16 **McBride S**, Mowbray J, Caughey W, Wong E, Luey C, Siddiqui A, Alexander Z, Playle V, Askelund T, Hopkins C, Quek N, Ross K, Orec R, Mistry D, Coomarasamy C, Holland D. Epidemiology, Management, and Outcomes of Large and Small Native Joint Septic Arthritis in Adults. *Clin Infect Dis* 2020; **70**: 271-279 [PMID: 30941403 DOI: 10.1093/cid/ciz265]

17 **Houshian S**, Seyedipour S, Wedderkopp N. Epidemiology of bacterial hand infections. *Int J Infect Dis* 2006; **10**: 315-319 [PMID: 16483816 DOI: 10.1016/j.ijid.2005.06.009]

18 **Gjika E**, Beaulieu JY, Vakalopoulos K, Gauthier M, Bouvet C, Gonzalez A, Morello V, Steiger C, Hirsiger S, Lipsky BA, Uçkay I. Two weeks versus four weeks of antibiotic therapy after surgical drainage for native joint bacterial arthritis: a prospective, randomised, non-inferiority trial. *Ann Rheum Dis* 2019; **78**: 1114-1121 [PMID: 30992295 DOI: 10.1136/annrheumdis-2019-215116]

19 **Kanangat S**, Postlethwaite A, Hasty K, Kang A, Smeltzer M, Appling W, Schaberg D. Induction of multiple matrix metalloproteinases in human dermal and synovial fibroblasts by Staphylococcus aureus: implications in the pathogenesis of septic arthritis and other soft tissue infections. *Arthritis Res Ther* 2006; **8**: R176 [PMID: 17129374 DOI: 10.1186/ar2086]

20 **Nair R**, Schweizer ML, Singh N. Septic Arthritis and Prosthetic Joint Infections in Older Adults. *Infect Dis Clin North Am* 2017; **31**: 715-729 [PMID: 29079156 DOI: 10.1016/j.idc.2017.07.013]

21 **Ross K**, Mehr J, Carothers B, Greeley R, Benowitz I, McHugh L, Henry D, DiFedele L, Adler E, Naqvi S, Lifshitz E, Tan C, Montana B. Outbreak of Septic Arthritis Associated with Intra-Articular Injections at an Outpatient Practice - New Jersey, 2017. *MMWR Morb Mortal Wkly Rep* 2017; **66**: 777-779 [PMID: 28749922 DOI: 10.15585/mmwr.mm6629a3]

22 **Sultana S**, Dey R, Bishayi B. Dual neutralization of TNFR-2 and MMP-2 regulates the severity of S. aureus induced septic arthritis correlating alteration in the level of interferon gamma and interleukin-10 in terms of TNFR2 blocking. *Immunol Res* 2018; **66**: 97-119 [PMID: 29218573 DOI: 10.1007/s12026-017-8979-y]

23 **Curtiss PH Jr**. The pathophysiology of joint infections. *Clin Orthop Relat Res* 1973; 129-135 [PMID: 16999001]

24 **Roy S**, Bhawan J. Ultrastructure of articular cartilage in pyogenic arthritis. *Arch Pathol* 1975; **99**: 44-47 [PMID: 1111494]

25 **Smith RL**, Merchant TC, Schurman DJ. In vitro cartilage degradation by Escherichia coli and Staphylococcus aureus. *Arthritis Rheum* 1982; **25**: 441-446 [PMID: 7041916 DOI: 10.1002/art.1780250413]

26 **Wang J**, Wang L. Novel therapeutic interventions towards improved management of septic arthritis. *BMC Musculoskelet Disord* 2021; **22**: 530 [PMID: 34107951 DOI: 10.1186/s12891-021-04383-6]

27 **de Vries H**, van der Werken C. Septic arthritis of the hand. *Injury* 1993; **24**: 32-34 [PMID: 8432571 DOI: 10.1016/0020-1383(93)90079-L]

28 **Boustred AM**, Singer M, Hudson DA, Bolitho GE. Septic arthritis of the metacarpophalangeal and interphalangeal joints of the hand. *Ann Plast Surg* 1999; **42**: 623-8; discussion 628 [PMID: 10382798 DOI: 10.1097/00000637-199906000-00007]

29 **Reilly KE**, Linz JC, Stern PJ, Giza E, Wyrick JD. Osteomyelitis of the tubular bones of the hand. *J Hand Surg Am* 1997; **22**: 644-649 [PMID: 9260620 DOI: 10.1016/S0363-5023(97)80122-0]

30 **Brown H**. Hand infections. *Am Fam Physician* 1978; **18**: 79-85 [PMID: 685801]

31 **Tan V**, Pepe MD, Esterhai JL. Sepsis of the shoulder girdle. In: Disoders of the shoulder: diagnosis and management. Edited by J. Iannotti, G.R. Williams. Philadelphia, Baltimore, New York, London, Buenos Aires, Hong Kong, Sydney, Tokyo. Lippincott Williams and Wilkins, 1998.-P.951-976.

32 **Osmon DR**, Berbari EF, Berendt AR, Lew D, Zimmerli W, Steckelberg JM, Rao N, Hanssen A, Wilson WR; Infectious Diseases Society of America. Diagnosis and management of prosthetic joint infection: clinical practice guidelines by the Infectious Diseases Society of America. *Clin Infect Dis* 2013; **56**: e1-e25 [PMID: 23223583 DOI: 10.1093/cid/cis803]

33 **Barbieri RA**, Freeland AE. Osteomyelitis of the hand. *Hand Clin* 1998; **14**: 589-603, ix [PMID: 9884897]

34 **Hillman D**, Rheinboldt M, Petraszko A. Sonographic imaging of hand and wrist injuries: applications in the ER setting. *Emerg Radiol* 2019; **26**: 227-240 [PMID: 30327891 DOI: 10.1007/s10140-018-1649-0]

35 **Kim S**, Baradia H, Sambasivan A. The Use of Ultrasonography in Expediting Septic Joint Identification and Treatment: A Case Report. *Am J Phys Med Rehabil* 2020; **99**: 449-451 [PMID: 31361617 DOI: 10.1097/PHM.0000000000001284]

36 **Yu JS**, Habib P. MR imaging of urgent inflammatory and infectious conditions affecting the soft tissues of the musculoskeletal system. *Emerg Radiol* 2009; **16**: 267-276 [PMID: 19132424 DOI: 10.1007/s10140-008-0786-2]

37 **Patel DB**, Emmanuel NB, Stevanovic MV, Matcuk GR Jr, Gottsegen CJ, Forrester DM, White EA. Hand infections: anatomy, types and spread of infection, imaging findings, and treatment options. *Radiographics* 2014; **34**: 1968-1986 [PMID: 25384296 DOI: 10.1148/rg.347130101]

38 **Saito T**, Noda T, Kondo H, Demiya K, Nezu S, Yokoo S, Matsuhashi M, Uehara T, Shimamura Y, Kodama M, Ozaki T. The Masquelet technique for septic arthritis of the small joint in the hands: Case reports. *Trauma Case Rep* 2020; **25**: 100268 [PMID: 31890833 DOI: 10.1016/j.tcr.2019.100268]

39 **Unglaub F**, Langer MF, Unglaub JM, Hohendorff B, Müller LP, Hahn P, Löw S, Spies CK. Joint infections of the hand. *Unfallchirurg* 2016; **119**: 943-953 [PMID: 27785520 DOI: 10.1007/s00113-016-0261-6]

40 **Kennedy N**, Chambers ST, Nolan I, Gallagher K, Werno A, Browne M, Stamp LK. Native Joint Septic Arthritis: Epidemiology, Clinical Features, and Microbiological Causes in a New Zealand Population. *J Rheumatol* 2015; **42**: 2392-2397 [PMID: 26523022 DOI: 10.3899/jrheum.150434]

41 **Kwak SH**, Bae JY, Oh Y, Jang HS, Ahn TY, Lee SH. Primarily treated patients versus referred patients in the treatment of native septic arthritis of digits: a retrospective comparative study. *BMC Musculoskelet Disord* 2020; **21**: 780 [PMID: 33246444 DOI: 10.1186/s12891-020-03770-9]

42 **Chung SR**, Kang YC, McGrouther DA. Techniques for Continuous Irrigation of Septic Joints of the Hand. *Tech Hand Up Extrem Surg* 2019; **23**: 133-137 [PMID: 30973488 DOI: 10.1097/BTH.0000000000000241]

43 **Wright DA**. Tendon sheath infection. *Proc R Soc Med* 1943; **37**: 504-505

44 **Vorderwinkler KP**, Mühldorfer M, Pillukat T, van Schoonhoven J. Treatment of bacterial infection in the interphalangeal joints of the hand. *Oper Orthop Traumatol* 2011; **23**: 192-203 [PMID: 21735254 DOI: 10.1007/s00064-011-0024-z]

45 **Allieu Y**, Chammas M, Hixson ML. External fixation for treatment of hand infections. *Hand Clin* 1993; **9**: 675-682 [PMID: 8300736]

46 **Richard JC**, Vilain R. Acute septic arthritis of the fingers. A clinical study of 87 cases. *Ann Chir Main* 1982; **1**: 214-220 [PMID: 9336613 DOI: 10.1016/s0753-9053(82)80004-5]

47 **Rotunno T**, Müller C, Heidekrueger P, Gjika E, Gauthier M, Lauper N, Beaulieu J-Y, Erba P, Christen T, Uçkay I. Outcomes of Septic Joint Arthritis of the Hand: A DualCenter Study. *Clin Surg* 2019; **4**: 2356 [DOI: 10.5167/uzh-183928]

48 **Spies CK**, Hohendorff B, Löw S, Müller LP, Oppermann J, Hahn P, Unglaub F. Arthrodesis of the distal interphalangeal joint using the headless compression screw. *Oper Orthop Traumatol* 2017; **29**: 374-384 [PMID: 28616779 DOI: 10.1007/s00064-017-0507-7]

49 **Ono R**, Komura S, Hirakawa A, Hirose H, Tsugita M, Masuda T, Ito Y, Akiyama H. Staged arthrodesis using the Masquelet technique for osteomyelitis of the finger with articular destruction: a report of two cases. *Arch Orthop Trauma Surg* 2019; **139**: 1025-1031 [PMID: 31093754 DOI: 10.1007/s00402-019-03197-5]

50 **Jalil A**, Barlaan PI, Fung BK, Ip JW. Hand infection in diabetic patients. *Hand Surg* 2011; **16**: 307-312 [PMID: 22072465 DOI: 10.1142/S021881041100559X]

51 **Clerc O**, Prod'hom G, Greub G, Zanetti G, Senn L. Adult native septic arthritis: a review of 10 years of experience and lessons for empirical antibiotic therapy. *J Antimicrob Chemother* 2011; **66**: 1168-1173 [PMID: 21393124 DOI: 10.1093/jac/dkr047]

52 **Türker T**, Capdarest-Arest N, Bertoch ST, Bakken EC, Hoover SE, Zou J. Hand infections: a retrospective analysis. *PeerJ* 2014; **2**: e513 [PMID: 25210653 DOI: 10.7717/peerj.513]

53 **Stengel D**, Bauwens K, Sehouli J, Ekkernkamp A, Porzsolt F. Systematic review and meta-analysis of antibiotic therapy for bone and joint infections. *Lancet Infect Dis* 2001; **1**: 175-188 [PMID: 11871494 DOI: 10.1016/S1473-3099(01)00094-9]

54 **Pinder R**, Barlow G. Osteomyelitis of the hand. *J Hand Surg Eur Vol* 2016; **41**: 431-440 [PMID: 26482914 DOI: 10.1177/1753193415612373]

55 **Hudak PL**, Amadio PC, Bombardier C. Development of an upper extremity outcome measure: the DASH (disabilities of the arm, shoulder and hand) [corrected]. The Upper Extremity Collaborative Group (UECG). *Am J Ind Med* 1996; **29**: 602-608 [PMID: 8773720 DOI: 10.1002/(SICI)1097-0274(199606)29:6<602::AID-AJIM4>3.0.CO;2-L]

56 American Society for Surgery of the Hand. Clinical Assessment Committee Report, IL, Rosemont, 1976 [DOI: 10.1016/s0363-5023(76)80027-5]

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ORIGINAL ARTICLE

Retrospective Cohort Study

Outcomes after arthroscopic repair of rotator cuff tears in the setting of mild to moderate glenohumeral osteoarthritis

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Abstract

BACKGROUND

Rotator cuff pathology is a very common source of shoulder pain. Similarly, osteoarthritis of the glenohumeral joint can cause shoulder pain and produce similar symptoms. Surgical management can be indicated for both pathologies, however, outcomes data is limited when examining rotator cuff repair (RCR) in the setting of glenohumeral arthritis (GHOA). Thus, this study sought to determine outcomes for patients who undergo RCR in the setting of GHOA.

AIM

To evaluate if a relationship exists between outcomes of RCR in the setting of GHOA.

METHODS

This was a retrospective analysis of patients who underwent arthroscopic rotator cuff repair with concurrent glenohumeral osteoarthritis between 2010-2017.

Patients were stratified based on rotator cuff tear size and glenohumeral osteoarthritis severity. Cohorts were paired 1:1 with patients without glenohumeral osteoarthritis. Patients included had a minimum two year follow-up. Rate of conversion to total shoulder arthroplasty, complication rates following initial surgery, and patient-reported outcome measures were collected.

RESULTS

A total of 142 patients were included. The number of patients that required total shoulder arthroplasty within two years after index surgery was low. 2/71 (2.8%) patients with GHOA, and 1/71 (1.4%) without GHOA. Following rotator cuff repair, both groups showed favorable patient-reported outcomes.

CONCLUSION

Patients with glenohumeral osteoarthritis who underwent arthroscopic rotator cuff repair showed comparable outcomes to patients without glenohumeral osteoarthritis.

Key Words: Rotator cuff repair; Rotator cuff tear; Glenohumeral osteoarthritis; Shoulder; Arthroscopic; Outcomes

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Core Tip: We evaluated a cohort of patients with mild to moderate glenohumeral arthritis who underwent rotator cuff repair. We retrospectively reviewed 71 patients with glenohumeral osteoarthritis (GHOA) (Glenohumeral Arthritis) who underwent concomitant rotator cuff repair, and matched these patients to 71 patients who underwent rotator cuff repair without GHOA. We evaluated patient reported outcomes and demographic information for both cohorts.

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INTRODUCTION

Rotator cuff pathology is a common source of shoulder pain. A significant proportion of individuals have rotator cuff tears with increasing age and can become disabled[1-3]. In older patients, onset of new symptoms correlate to the progression of rotator cuff tear size and increasing morbidity[3].

Like rotator cuff pathology, glenohumeral osteoarthritis (GHOA) is related to advancing age and is estimated to affect 16%-20% of adults over age 65[4,5]. It can be debilitating and a source of shoulder dysfunction, pain, and loss of motion[6,7].

Although rotator cuff pathology and GHOA are two prevalent shoulder pathologies, there are limited studies evaluating the relationship of GHOA to outcomes after rotator cuff repair (RCR)[8-11]. Cases of severe GHOA accompanied by rotator cuff pathology are most appropriately managed with either reverse total shoulder arthroplasty (RTSA) or total SA (TSA) with RCR. However, a recent study by Jeong *et al*[8] suggests that patients with mild GHOA and repair of large rotator cuff tears fare similarly to their counterparts without GHOA in terms of clinical outcomes and progression to GHOA. In contrast, another study found that GHOA was associated with lower outcome scores after RCR at 1-year follow-up[10].

Studies have shown that patients with concomitant GHOA and rotator cuff tears can range from 13%-27% of patients treated for rotator cuff tears; to our knowledge, the outcomes of these patients after RCR are lacking within literature[12,13]. This study evaluated the effect of the presence or absence of GHOA on short and mid-term clinical outcomes after arthroscopic repair of small to large rotator cuff tears, comparing the rates of conversion to shoulder arthroplasty (TSA or RTSA) as well as PROM's at follow-up > 2 years from their RCR surgery. We hypothesized there would be no significant differences in clinical outcomes or rates of subsequent conversion to shoulder arthroplasty in patients with small to large rotator cuff tears undergoing arthroscopic repair with or without concurrent GHOA.

MATERIALS AND METHODS

Following International Review Board approval, patients who underwent arthroscopic RCR of small (< 1 cm), medium (1-3 cm), or large (3-5 cm) rotator cuff tears with GHOA were identified at a large single-center academic orthopedic group. All patients treated between January 2010 and June 2017 were identified using Current Procedural Terminology code 29827 for "arthroscopy, shoulder, surgical, with rotator cuff repair." Patients with GHOA were initially identified and paired with patients without GHOA. The three criteria for matching the patients involved: Age ± 3 years, clinical follow-up ± 1 year, and same sex (Figure 1A).

Inclusion criteria consisted of patients who: (1) Were 18 years old at the time of index surgery; (2) Had a rotator cuff tear measuring 0-5 cm; (3) Had a preoperative plain radiograph; (4) Had a preoperative magnetic resonance imaging (MRI); and (5) Had a minimum of 2 year follow-up after their index RCR procedure. Patients were excluded if they had any of the following: (1) Open physes; (2) Post-traumatic osteoarthritis; (3) Post-dislocation glenohumeral arthropathy; (4) Avascular necrosis; (5) Prior surgical intervention on the ipsilateral shoulder; and/or (6) Autoimmune conditions such as rheumatoid arthritis. The data was collected and stored using REDCap electronic data capture tools hosted at OrthoCarolina Research Institute[4].

The primary outcome variable was the rate of conversion to TSA or RTSA within 2 years from the index surgery. Secondary outcomes were clinical patient-reported outcome measures (PROs) including American Shoulder and Elbow Surgeons (ASES) score, Single Assessment Numeric Evaluation (SANE), VAS for pain, and Veterans RAND 12-Item Health Survey (VR-12).

Demographical information such as age, sex, body mass index (BMI), smoking history, diabetes, and injury mechanism (ultra-low *vs* low *vs* high energy) where applicable was obtained. Using preoperative plain radiographs and MRI, the Samilson-Priesto Classification (Figure 2**)**, Goutallier classification, and Warner atrophy grade were obtained to assess GHOA severity, fatty degeneration of rotator cuff muscles, and muscle atrophy, respectively. Each patient was classified based on the presence of GHOA in the setting of a small, medium, or large rotator cuff tear (Figure 3**)**. The different rotator cuff tear sizes, largely based on level of retraction, were determined by two independent fellowship trained sports medicine and shoulder orthopedic surgeons using MRI imaging. Coronal oblique images were obtained and used to identify the tears, and were classified as either small (< 1 cm) medium (1-3 cm) and massive (< 5 cm).

The procedural variables captured using operative notes included: surgical technique, fixation technique, and concomitant procedures (*e.g.*, distal clavicle excision, subacromial decompression, capsular release, debridement, chondroplasty, biceps tenotomy, and/or biceps tenodesis). Postoperative variables were measured: complications, re-operation (s) and the type of secondary procedure. PROs following surgery were collected during routine clinical follow-up at 2 or more years. Patients without the standard of care 2-year follow-up were contacted *via* phone or email to answer questions regarding PROs, subsequent rotator cuff re-tear, or re-operation outside of our institution.

Statistical analysis

All data underwent descriptive statistical analysis using SAS version 9.4 (SAS Institute, Cary, NC; http://www.sas.com/software/sas9). Two groups were defined based on presence or absence of primary GHOA and stratified based on rotator cuff tear size. For normally distributed continuous data, mean and standard deviation, were reported. For non-parametric continuous data, median and interquartile range were reported. Frequencies and proportions were reported for categorical variables. A Wilcoxon rank sum test was used for non-parametric continuous variables and a two-sample t test was used for normally distributed data. For categorical variables, a chi-square test (or Fisher's exact test, where appropriate) was used for comparisons between groups. Significance was determined by an alpha level of 0.05.

RESULTS

Between January 2010 and June 2017, 71 patients were identified that underwent arthroscopic RCR of small to large tears with the presence of GHOA. These patients were subsequently matched with 71 patients without GHOA that underwent the same procedure.

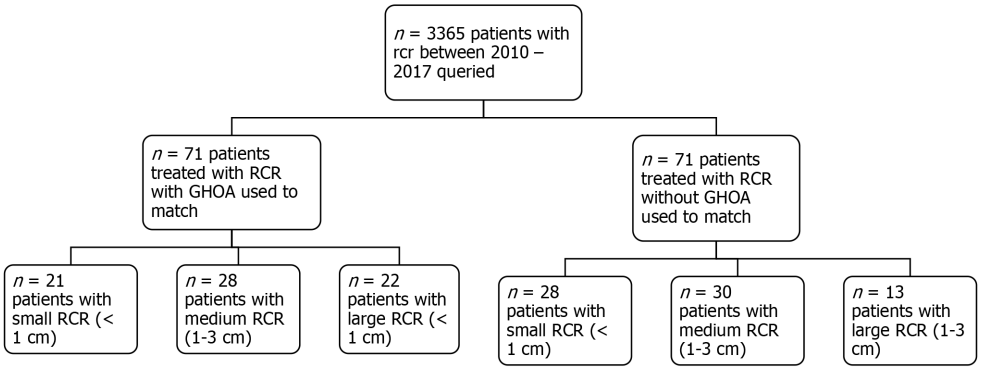
The demographics of the comparison study groups can be found in Table 1. The median age at time of rotator cuff repair was 64 years (IQR 60, 70) for patients in both groups. They had an exact match by sex and 57.7% (41/71) of repairs were performed in males in each respective group. Median BMI at the time of repair was 29.8 (IQR 26.7, 33.2) and 28.5 (IQR 25.5, 31) respectively. In patients with GHOA, 57.7% (41/71) reported having never smoked tobacco products, 40.8% (29/71) have smoked previously and 1.4% (1/71) were actively smoking. In patients without GHOA, 60.6% (43/71) reported having never smoked tobacco products, 33.8% (24/71) have smoked previously and 5.6% (4/71) were actively smoking.

Table 1 Demographic information

		With GHOA				Without GHOA			
		Tear size group				Tear size group			
	Overall (*n* = 142)	Case overall (*n* = 71)	Small (0-1 cm) (*n* = 21)	Medium (1-3 cm) (*n* = 28)	Large (3-5 cm) (*n* = 22)	Control overall (*n* = 71)	Small (0-1 cm) (*n* = 28)	Medium (1-3 cm) (*n* = 30)	Large (3-5 cm) (*n* = 13)
Age (in yr) at surgery, median (IQR)	64 (60, 70)	64 (60, 70)	63 (62, 67)	63 (58, 67.5)	66 (62, 71)	64 (60, 70)	63 (59.5, 68.5)	65 (61, 70)	63 (61, 69)
BMI, median (IQR)	29.2 (25.8, 32.9)	29.8 (26.7, 33.2)	32.9 (29.4, 35.9)	28.1 (24.5, 30.8)	29 (27.3, 33.2)	28.5 (25.5, 31)	29.9 (27, 31)	27.2 (24.5, 30.4)	27.5 (24.7, 32.1)
Time (in yr) since DOS, median (IQR)	8.1 (6.9, 9.3)	8.2 (6.9, 9.3)	8 (7.1, 9.4)	8 (6.4, 9.3)	8.3 (7.1, 8.9)	8.1 (6.8, 9.3)	8.3 (6.8, 9.6)	8 (7.5, 8.8)	7.8 (6.9, 9.3)
Tear size, median (IQR)	2 (1, 3)	2 (1, 3.5)	1 (1, 1)	2 (1.7, 2.6)	4 (3.5, 4)	1.5 (1, 2.5)	.5 (.5, 1)	2 (1.5, 2.5)	4 (3.7, 4.3)
Male	82 (57.7)	41 (57.7)	10 (47.6)	13 (46.4)	18 (81.8)	41 (57.7)	13 (46.4)	19 (63.3)	9 (69.2)
Sex, *n* (%)									
Female	60 (42.3)	30 (42.3)	11 (52.4)	15 (53.6)	4 (18.2)	30 (42.3)	15 (53.6)	11 (36.7)	4 (30.8)
Smoking, *n* (%)									
Never	84 (59.2)	41 (57.7)	16 (76.2)	14 (50.0)	11 (50.0)	43 (60.6)	19 (67.9)	19 (63.3)	5 (38.5)
Previous	53 (37.3)	29 (40.8)	5 (23.8)	13 (46.4)	11 (50.0)	24 (33.8)	7 (25.0)	10 (33.3)	7 (53.8)
Current	5 (3.5)	1 (1.4)	0 (0)	1 (3.6)	0 (0)	4 (5.6)	2 (7.1)	1 (3.3)	1 (7.7)
Diabetes, *n* (%)									
No	115 (81.0)	57 (80.3)	18 (85.7)	24 (85.7)	15 (68.2)	58 (81.7)	22 (78.6)	27 (90.0)	9 (69.2)
Yes	27 (19.0)	14 (19.7)	3 (14.3)	4 (14.3)	7 (31.8)	13 (18.3)	6 (21.4)	3 (10.0)	4 (30.8)
Preoperative samilson-prieto score, *n* (%)									
None	71 (50.0)	1 (1.4)	0 (0)	1 (3.6)	0 (0)	70 (98.6)	28 (100.0)	29 (96.7)	13 (100.0)
Mild (< 3 mm)	62 (43.7)	61 (85.9)	18 (85.7)	27 (96.4)	16 (72.7)	1 (1.4)	0 (0)	1 (3.3)	0 (0)
Moderate (3 mm-7 mm)	9 (6.3)	9 (12.7)	3 (14.3)	0 (0)	6 (27.3)	0 (0)	0 (0)	0 (0)	0 (0)
Goutallier classification, *n* (%)									
Grade 0 (normal muscle)	95 (66.9)	47 (66.2)	18 (85.7)	19 (67.9)	10 (45.5)	48 (67.6)	23 (82.1)	20 (66.7)	5 (38.5)
Grade 1 (some fattys-treaks)	36 (25.4)	18 (25.4)	2 (9.5)	7 (25.0)	9 (40.9)	18 (25.4)	5 (17.9)	8 (26.7)	5 (38.5)
Grade 2 (< 50% fattymuscle atrophy)	11 (7.7)	6 (8.5)	1 (4.8)	2 (7.1)	3 (13.6)	5 (7.0)	0 (0)	2 (6.7)	3 (23.1)
Muscle atrophy (warner grading system), *n* (%)									0 (0)
None	107 (75.4)	50 (70.4)	18 (85.7)	21 (75.0)	11 (50.0)	57 (80.3)	24 (85.7)	24 (80.0)	9 (69.2)
Mild	29 (20.4)	17 (23.9)	2 (9.5)	5 (17.9)	10 (45.5)	12 (16.9)	4 (14.3)	5 (16.7)	3 (23.1)
Moderate	6 (4.2)	4 (5.6)	1 (4.8)	2 (7.1)	1 (4.5)	2 (2.8)	0 (0)	1 (3.3)	1 (7.7)
Primary GHOA, *n* (%)									
No	71 (50.0)	0 (0)	0 (0)	0 (0)	0 (0)	71 (100.0)	28 (100.0)	30 (100.0)	13 (100.0)
Yes	71 (50.0)	71 (100.0)	21 (100.0)	28 (100.0)	22 (100.0)	0 (0)	0 (0)	0 (0)	0 (0)

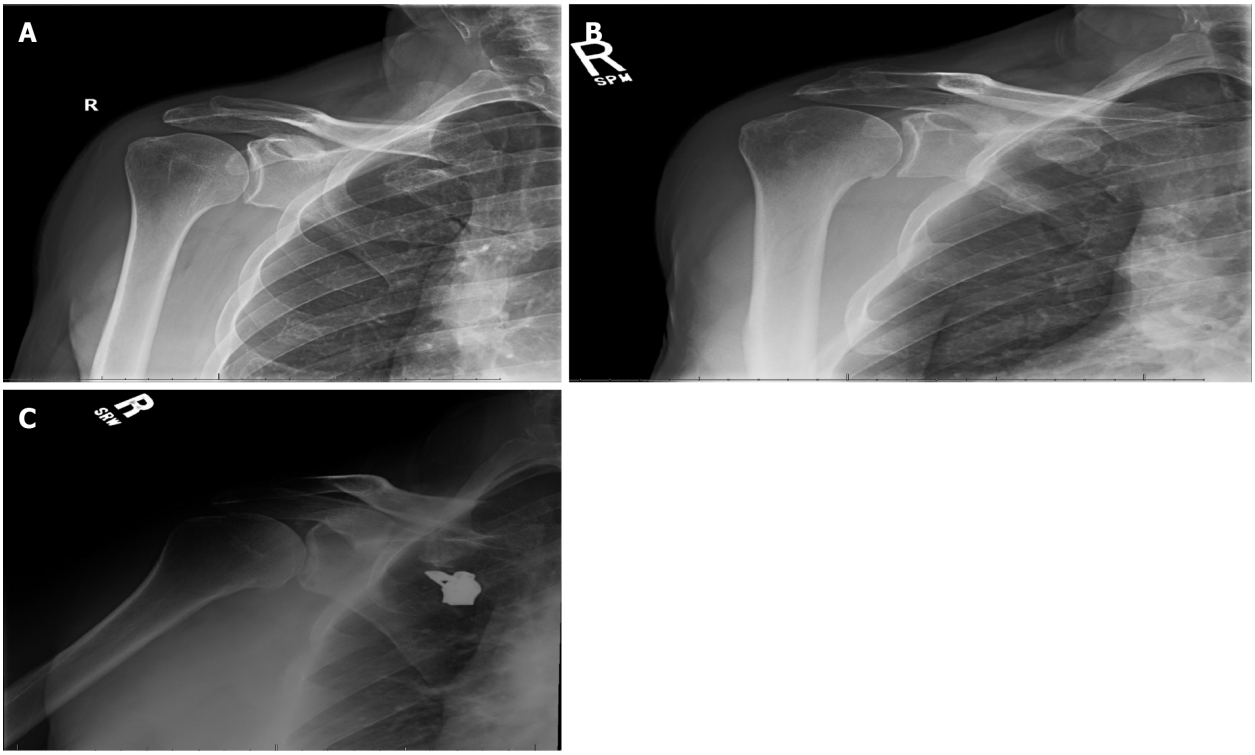
GHOA: Glenohumeral osteoarthritis; BMI: Body mass index; DOS: Date of surgery.

Using the Samilson-Prieto classification to grade GHOA severity, 85.9% (61/71) had a grade of 1 (mild or < 3 mm), and 12.7% (9/71) had a grade of 2 (moderate or 3 mm - 7 mm). Goutallier classification of the rotator cuff revealed that patients with GHOA: 66.2% (47/71) had a grade of 0 (normal muscle), 25.4% (18/71) had a grade of 1 (some fatty streaks), and 8.5% (6/71) had a grade of 2 (less than



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Figure 1 CONSORT flow diagram of patients included in study. RCR: Rotator cuff repair; GHOA: Glenohumeral osteoarthritis.



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Figure 2 Anteroposterior radiograph. A: Anteroposterior radiograph of right shoulder demonstrating Samilson-Prieto grade 0 (normal); B: Anteroposterior radiograph of right shoulder demonstrating Samilson-Prieto grade 1 (mild); C: Anteroposterior radiograph of right shoulder demonstating Samilson-Prieto grade 2 (moderate).

50% fatty muscle atrophy). In comparison, the Goutallier classification of the rotator cuff for patients without GHOA revealed: 67.6% (48/71) with grade of 0, 25.4% (18/71) with a grade of 1, and 7.0% (5/71) with a grade of 2. Finally, in patients with GHOA the Warner grading system for muscle atrophy revealed: 70.4% (50/71) with no atrophy, 23.9% (17/71) with mild atrophy, and 5.6% (4/71) with moderate atrophy. For patients without GHOA, the Warner grading system for muscle atrophy revealed: 80.3% (57/71) with no atrophy, 16.9% (12/71) with mild atrophy, and 2.8% (2/71) with moderate atrophy.

Detailed data regarding RCR surgical technique, type of anchors used, fixation method and concurrent procedures for patients with or without GHOA stratified by rotator cuff tear size can be found in Table 2.

The re-operation rate was 15.5% (11/71) and 8.5% (6/71) in patients with GHOA and without GHOA respectively. The mean follow-up period for both groups was 12.45 mo, with a range from 0-104 mo for the GHOA group, and 0-94 mo for the patients without GHOA. Within two years after rotator cuff repair, 2.8% (2/71) patients with GHOA underwent TSA or RTSA in the ipsilateral shoulder compared to 1.4% (1/71) patients without GHOA. Both patients developed rotator cuff arthropathy and pain with range of motion, and eventually underwent RTSA. The non GHOA patient eventually underwent an

Table 2 Operative data and type of operation

	With GHOA				Without GHOA			
		Tear size group				Tear size group		
	Overall (*n* = 142)	Overall Case (*n* = 71)	Small (0-1 cm) (*n* = 21)	Medium (1-3 cm) (*n* = 28)	Large (3-5 cm) (*n* = 22)	Overall Control (*n* = 71)	Small (0-1 cm) (*n* = 28)	Medium (1-3 cm) (*n* = 30)	Large (3-5 cm) (*n* = 13)
Single row, *n* (%)									
No	124 (87.3)	60 (84.5)	16 (76.2)	24 (85.7)	20 (90.9)	64 (90.1)	26 (92.9)	26 (86.7)	12 (92.3)
Yes	18 (12.7)	11 (15.5)	5 (23.8)	4 (14.3)	2 (9.1)	7 (9.9)	2 (7.1)	4 (13.3)	1 (7.7)
Double row, *n* (%)									
Yes	122 (85.9)	60 (84.5)	17 (81.0)	23 (82.1)	20 (90.9)	62 (87.3)	24 (85.7)	26 (86.7)	12 (92.3)
No	20 (14.1)	11 (15.5)	4 (19.0)	5 (17.9)	2 (9.1)	9 (12.7)	4 (14.3)	4 (13.3)	1 (7.7)
Medial row, *n* (%)									
Yes	138 (97.2)	69 (97.2)	19 (90.5)	28 (100.0)	22 (100.0)	69 (97.2)	28 (100.0)	28 (93.3)	13 (100.0)
No	4 (2.8)	2 (2.8)	2 (9.5)	0 (0)	0 (0)	2 (2.8)	0 (0)	2 (6.7)	0 (0)
Lateral row, *n* (%)									
Yes	120 (84.5)	61 (85.9)	18 (85.7)	23 (82.1)	20 (90.9)	59 (83.1)	24 (85.7)	24 (80.0)	11 (84.6)
No	22 (15.5)	10 (14.1)	3 (14.3)	5 (17.9)	2 (9.1)	12 (16.9)	4 (14.3)	6 (20.0)	2 (15.4)
Arthrotunneler, *n* (%)									
No	139 (97.9)	71 (100.0)	21 (100.0)	28 (100.0)	22 (100.0)	71 (100.0)	28 (100.0)	28 (93.3)	12 (92.3)
Yes	3 (2.1)		0 (0)	0 (0)	0 (0)		0 (0)	2 (6.7)	1 (7.7)
Medial row fixation type, *n* (%)									
Missing for 6 patients									
Suture tied	135 (95.1)	67 (94.4)	19 (90.5)	26 (92.9)	22 (100.0)	68 (95.8)	28 (100.0)	28 (93.3)	12 (92.3)
Knotless	1 (0.7)	0 (0)	0 (0)	0 (0)	0 (0)	1 (1.4)	0 (0)	0 (0)	1 (7.7)
Medial row anchor type, *n* (%)									
Missing for 11 patients									
PEEK	86 (60.6)	53 (74.6)	16 (76.2)	21 (75.0)	16 (72.7)	33 (46.5)	16 (57.1)	12 (40.0)	5 (38.5)
Knotted	35 (24.6)	10 (14.1)	2 (9.5)	5 (17.9)	3 (13.6)	25 (35.2)	10 (35.7)	11 (36.7)	4 (30.8)
Knotless	7 (4.9)	0 (0)	0 (0)	0 (0)	0 (0)	7 (9.9)	1 (3.6)	5 (16.7)	1 (7.7)
Plastic	3 (2.1)	3 (4.2)	1 (4.8)	0 (0)	2 (9.1)	0 (0)	0 (0)	0 (0)	0 (0)
Lateral row fixation type, *n* (%)									
Missing for 23 patients									
Knotless	90 (63.4)	46 (64.8)	13 (61.9)	16 (57.1)	17 (77.3)	44 (62.0)	20 (71.4)	18 (60.0)	6 (46.2)
Suture tied	29 (20.4)	15 (21.1)	5 (23.8)	7 (25.0)	3 (13.6)	14 (19.7)	4 (14.3)	6 (20.0)	4 (30.8)
Lateral row anchor type, n (%)									
Missing for 29 patients									
PEEK	70 (49.3)	28 (39.4)	12 (57.1)	8 (28.6)	8 (36.4)	42 (59.2)	21 (75.0)	15 (50.0)	6 (46.2)
Plastic	20 (14.1)	20 (28.2)	3 (14.3)	8 (28.6)	9 (40.9)	0 (0)	0 (0)	0 (0)	0 (0)
Knotted	17 (12.0)	6 (8.5)	1 (4.8)	4 (14.3)	1 (4.5)	11 (15.5)	3 (10.7)	4 (13.3)	4 (30.8)

Knotless	6 (4.2)	3 (4.2)	1 (4.8)	1 (3.6)	1 (4.5)	3 (4.2)	0 (0)	3 (10.0)	0 (0)
Concurrent procedures									
Distal clavicle excision, *n* (%)									
Yes	79 (55.6)	41 (57.7)	15 (71.4)	16 (57.1)	10 (45.5)	38 (53.5)	16 (57.1)	17 (56.7)	5 (38.5)
No	63 (44.4)	30 (42.3)	6 (28.6)	12 (42.9)	12 (54.5)	33 (46.5)	12 (42.9)	13 (43.3)	8 (61.5)
Subacromial decompression, *n* (%)									
Yes	142 (100.0)	71 (100.0)	21 (100.0)	28 (100.0)	22 (100.0)	71 (100.0)	28 (100.0)	30 (100.0)	13 (100.0)
Capsular release, *n* (%)									
No	133 (93.7)	66 (93.0)	20 (95.2)	25 (89.3)	21 (95.5)	67 (94.4)	26 (92.9)	30 (100.0)	11 (84.6)
Yes	9 (6.3)	5 (7.0)	1 (4.8)	3 (10.7)	1 (4.5)	4 (5.6)	2 (7.1)	0 (0)	2 (15.4)
Labral debridement, *n* (%)									
No	125 (88.0)	63 (88.7)	20 (95.2)	24 (85.7)	19 (86.4)	62 (87.3)	24 (85.7)	26 (86.7)	12 (92.3)
Yes	17 (12.0)	8 (11.3)	1 (4.8)	4 (14.3)	3 (13.6)	9 (12.7)	4 (14.3)	4 (13.3)	1 (7.7)
Chondroplasty, *n* (%)									
No	120 (84.5)	54 (76.1)	14 (66.7)	20 (71.4)	20 (90.9)	66 (93.0)	25 (89.3)	28 (93.3)	13 (100.0)
Yes	22 (15.5)	17 (23.9)	7 (33.3)	8 (28.6)	2 (9.1)	5 (7.0)	3 (10.7)	2 (6.7)	0 (0)
Biceps tenotomy, *n* (%)									
No	92 (64.8)	44 (62.0)	11 (52.4)	20 (71.4)	13 (59.1)	48 (67.6)	18 (64.3)	23 (76.7)	7 (53.8)
Yes	50 (35.2)	27 (38.0)	10 (47.6)	8 (28.6)	9 (40.9)	23 (32.4)	10 (35.7)	7 (23.3)	6 (46.2)
Biceps tenodesis, *n* (%)									
No	99 (69.7)	54 (76.1)	20 (95.2)	19 (67.9)	15 (68.2)	45 (63.4)	18 (64.3)	17 (56.7)	10 (76.9)
Yes	43 (30.3)	17 (23.9)	1 (4.8)	9 (32.1)	7 (31.8)	26 (36.6)	10 (35.7)	13 (43.3)	3 (23.1)
If biceps tenodesis, *n* (%)									
Suprapectoral	37 (26.1)	11 (15.5)	0 (0)	5 (17.9)	6 (27.3)	26 (36.6)	10 (35.7)	13 (43.3)	3 (23.1)
Subpectoral	6 (4.2)	6 (8.5)	1 (4.8)	4 (14.3)	1 (4.5)	0 (0)	0 (0)	0 (0)	0 (0)

GHOA: Glenohumeral osteoarthritis; PEEK: Polyether ether ketone.

RTSA for rotator cuff arthropathy. Beyond the two year follow-up 4 patients with GHOA and 2 patients without GHOA underwent the conversion to TSA or RTSA. Complication rates after initial rotator cuff repair was 23.9% (17/71) and 18.3% (13/71) for patients with GHOA and without GHOA respectively and 12.7% (9/71) of patients with GHOA experienced rotator cuff re-tear after RCR compared to 11.3% (8/71) of patients without GHOA as determined by post op MRI or intra-operative findings (Table 3).

The Median VR-12 mental health component summary scores were 58.3 (IQR 44.8, 61.3) and 56.5 (IQR 47.5, 61.7) and the median VR-12 physical health component summary scores were 49.6 (IQR 40.2, 52.4) and 47.6 (IQR 36.6, 53.7) in patients with and without GHOA respectively. The overall median ASES score for the right shoulder was 98.3 (IQR 93.3, 100) in patients with or without GHOA; overall median ASES score for the left shoulders were 100 (IQR 91.7, 100) and 96.7 (86.7, 100) respectively. Finally, the overall median SANE score was 95 (IQR 90, 100) and 95 (IQR 85, 100) in patients with or without GHOA respectively. PROs did not show any significant difference according to rotator cuff tear size when patients with GHOA were compared with patients without GHOA (Table 4).

Table 3 Postoperative complications

	With GHOA					Without GHOA			
		Tear size group				Tear size group			
	Overall (*n* = 142)	Case Overall (*n* = 71)	Small (0-1cm) (*n* = 21)	Medium (1-3cm) (*n* = 28)	Large (3-5cm) (*n* = 22)	Control Overall (*n* = 71)	Small (0-1cm) (*n* = 28)	Medium (1-3cm) (*n* = 30)	Large (3-5cm) (*n* = 13)
Reoperation post RCR, *n* (%)									
No	125 (88.0)	60 (84.5)	19 (90.5)	23 (82.1)	18 (81.8)	65 (91.5)	26 (92.9)	28 (93.3)	11 (84.6)
Yes	17 (12.0)	11 (15.5)	2 (9.5)	5 (17.9)	4 (18.2)	6 (8.5)	2 (7.1)	2 (6.7)	2 (15.4)
Complications, *n* (%)									
Missing for 1 patient									
No	111 (78.2)	53 (74.6)	16 (76.2)	22 (78.6)	15 (68.2)	58 (81.7)	22 (78.6)	24 (80.0)	12 (92.3)
Yes	30 (21.1)	17 (23.9)	4 (19.0)	6 (21.4)	7 (31.8)	13 (18.3)	6 (21.4)	6 (20.0)	1 (7.7)
Wound issues, *n* (%)									
Missing for 131 patients									
No	11 (7.7)	9 (12.7)	2 (9.5)	3 (10.7)	4 (18.2)	2 (2.8)	0 (0)	2 (6.7)	0 (0)
Infection, *n* (%)									
Missing for 131 patients									
No	11 (7.7)	9 (12.7)	2 (9.5)	3 (10.7)	4 (18.2)	2 (2.8)	0 (0)	2 (6.7)	0 (0)
Stiffness, *n* (%)									
Missing for 126 patients									
Yes	8 (5.6)	5 (7.0)	3 (14.3)	1 (3.6)	1 (4.5)	3 (4.2)	1 (3.6)	2 (6.7)	0 (0)
No	8 (5.6)	7 (9.9)	0 (0)	3 (10.7)	4 (18.2)	1 (1.4)	0 (0)	1 (3.3)	0 (0)
Rotator cuff retear, *n* (%)									
Missing for 122 patients									
Yes	17 (12.0)	9 (12.7)	0 (0)	4 (14.3)	5 (22.7)	8 (11.3)	3 (10.7)	4 (13.3)	1 (7.7)
No	3 (2.1)	2 (2.8)	2 (9.5)	0 (0)	0 (0)	1 (1.4)	0 (0)	1 (3.3)	0 (0)
Other complication, *n* (%)									
Missing for 128 patients									
No	8 (5.6)	4 (5.6)	1 (4.8)	2 (7.1)	1 (4.5)	4 (5.6)	1 (3.6)	2 (6.7)	1 (7.7)
Yes	6 (4.2)	3 (4.2)	1 (4.8)	1 (3.6)	1 (4.5)	3 (4.2)	2 (7.1)	1 (3.3)	0 (0)
Other complication description, *n* (%)									
Pain	1 (0.7)	1 (1.4)	1 (4.8)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Block related neuropraxia	1 (0.7)	1 (1.4)	0 (0)	1 (3.6)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Weakness	1 (0.7)	1 (1.4)	0 (0)	0 (0)	1 (4.5)	0 (0)	0 (0)	0 (0)	0 (0)
Median nerve neuropathy	1 (0.7)	0 (0)	0 (0)	0 (0)	0 (0)	1 (1.4)	1 (3.6)	0 (0)	0 (0)
Greater tuberosity fx	1 (0.7)	0 (0)	0 (0)	0 (0)	0 (0)	1 (1.4)	1 (3.6)	0 (0)	0 (0)
Heterotopic ossification	1 (0.7)	0 (0)	0 (0)	0 (0)	0 (0)	1 (1.4)	0 (0)	1 (3.3)	0 (0)
1st reoperation diagnosis, *n* (%)									
Other	13 (9.2)	9 (12.7)	2 (9.5)	4 (14.3)	3 (13.6)	4 (5.6)	1 (3.6)	1 (3.3)	2 (15.4)
Stiffness	3 (2.1)	2 (2.8)	0 (0)	1 (3.6)	1 (4.5)	1 (1.4)	0 (0)	1 (3.3)	0 (0)
Hardware pain	1 (0.7)	0 (0)	0 (0)	0 (0)	0 (0)	1 (1.4)	1 (3.6)	0 (0)	0 (0)
1st reoperation other diagnosis, *n*									

(%)									
Rotator cuff arthropathy	4 (2.8)	3 (4.2)	0 (0)	2 (7.1)	1 (4.5)	1 (1.4)	0 (0)	0 (0)	1 (7.7)
Rotator cuff retear	4 (2.8)	3 (4.2)	0 (0)	2 (7.1)	1 (4.5)	1 (1.4)	0 (0)	1 (3.3)	0 (0)
Inflammatory arthritis	1 (0.7)	1 (1.4)	1 (4.8)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Glenohumeral arthritis	1 (0.7)	1 (1.4)	1 (4.8)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Retear RTC, rotator cuffarthropathy	1 (0.7)	1 (1.4)	0 (0)	0 (0)	1 (4.5)	0 (0)	0 (0)	0 (0)	0 (0)
Greater tuberosity fracture	1 (0.7)	0 (0)	0 (0)	0 (0)	0 (0)	1 (1.4)	1 (3.6)	0 (0)	0 (0)
Rotator cuff arthropathy	1 (0.7)	0 (0)	0 (0)	0 (0)	0 (0)	1 (1.4)	0 (0)	0 (0)	1 (7.7)
1st reoperation procedure, *n* (%)									
Conversion to RTSA	8 (5.6)	5 (7.0)	1 (4.8)	2 (7.1)	2 (9.1)	3 (4.2)	1 (3.6)	0 (0)	2 (15.4)
Other	6 (4.2)	3 (4.2)	0 (0)	2 (7.1)	1 (4.5)	3 (4.2)	1 (3.6)	2 (6.7)	0 (0)
Lysis of adhesions	2 (1.4)	2 (2.8)	0 (0)	1 (3.6)	1 (4.5)	0 (0)	0 (0)	0 (0)	0 (0)
Conversion to TSA	1 (0.7)	1 (1.4)	1 (4.8)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
1st reoperation other procedure, *n* (%)									
Revision rotator cuff repair	4 (2.8)	3 (4.2)	0 (0)	2 (7.1)	1 (4.5)	1 (1.4)	0 (0)	1 (3.3)	0 (0)
Removal of heterotopicossification	1 (0.7)	0 (0)	0 (0)	0 (0)	0 (0)	1 (1.4)	0 (0)	1 (3.3)	0 (0)
Removal of hardware, RTC debridement	1 (0.7)	0 (0)	0 (0)	0 (0)	0 (0)	1 (1.4)	1 (3.6)	0 (0)	0 (0)
2nd reoperation post RCR, *n* (%)									
Missing for 1 patient									
No	14 (9.9)	10 (14.1)	1 (4.8)	5 (17.9)	4 (18.2)	4 (5.6)	1 (3.6)	2 (6.7)	1 (7.7)
Yes	2 (1.4)	1 (1.4)	1 (4.8)	0 (0)	0 (0)	1 (1.4)	0 (0)	0 (0)	1 (7.7)
2nd reoperation diagnosis, *n* (%)									
Other	2 (1.4)	1 (1.4)	1 (4.8)	0 (0)	0 (0)	1 (1.4)	0 (0)	0 (0)	1 (7.7)
2nd reoperation other diagnosis, *n* (%)									
Insufficiency due to subscapularis failure	1 (0.7)	1 (1.4)	1 (4.8)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Instability	1 (0.7)	0 (0)	0 (0)	0 (0)	0 (0)	1 (1.4)	0 (0)	0 (0)	1 (7.7)
2nd reoperation procedure, *n* (%)									
Other	2 (1.4)	1 (1.4)	1 (4.8)	0 (0)	0 (0)	1 (1.4)	0 (0)	0 (0)	1 (7.7)
Conversion to TSA/RTSA within 2 yr post index DOS, *n* (%)									
No	139 (97.9)	69 (97.2)	20 (95.2)	28 (100.0)	21 (95.5)	70 (98.6)	28 (100.0)	30 (100.0)	12 (92.3)
Yes	3 (2.1)	2 (2.8)	1 (4.8)	0 (0)	1 (4.5)	1 (1.4)	0 (0)	0 (0)	1 (7.7)

GHOA: Glenohumeral osteoarthritis; RCR: Rotator cuff repair; RTSA: Reverse tota shoulder arthroplasty; TSA: Total shoulder arthroplasty.

DISCUSSION

The results demonstrate the conversion to shoulder arthroplasty, patient-reported clinical outcome scores, and rates of re-operation were no different when comparing RCR done in the setting of GHOA *vs* without GHOA in short-term follow-up. Our results indicate that the presence of GHOA at the time of RCR did not seem to influence the progression of GHOA. There is general agreement within literature that severe primary GHOA is an appropriate indication for TSA or RTSA[14,15]. Additionally, rotator cuff tear arthropathy, rotator cuff insufficiency, and superior migration of humeral head - is considered another indication for RTSA[14-16]. While GHOA and rotator cuff tears both contribute to morbidity due to decreased shoulder function, there are limited studies evaluating the outcomes of

Table 4 Patient-reported outcomes

	Overall (*n* = 142)	With GHOA, Small tear (0-1 cm) (*n* = 21)	Without GHOA, Small tear (0-1 cm) (*n* = 28)	*P* value	With GHOA, Medium tear (1-3 cm) (*n* = 28)	Without GHOA, Medium tear (1-3 cm) (*n* = 30)	*P* value	With GHOA, Large tear (3-5 cm) (*n* = 22)	Without GHOA, Large tear (3-5 cm) (*n* = 13)	*P* value
MCS, median (IQR)	57.1 (46.5, 61.6)	60.9 (37.6, 64.1)	56.3 (44.4, 61.5)	> 0.99	59.3 (44.6, 61.3)	58.3 (50, 62.8)	> 0.99	54.4 (48, 57.9)	51 (47.3, 60.2)	> 0.99
PCS, median (IQR)	49.1 (40, 52.6)	40.2 (29.6, 49.1)	51.4 (42.4, 55)	0.148	50 (44.9, 51.8)	46.4 (35.1, 50.8)	> 0.99	52.7 (49.7, 55.4)	41.8 (34.4, 53.3)	> 0.99
VAS pain, median (IQR)	0.0 (0.0, 0.0)	0.0 (0.0, 0.0)	0.0 (0.0, 0.0)	> 0.99	0.0 (0.0, 1.0)	0.0 (0.0, 1.0)	> 0.99	0.0 (0.0, 0.0)	0.0 (0.0, 0.0)	> 0.99
VAS instability, median (IQR)	0.0 (0.0, 0.0)	0.0 (0.0, 0.0)	0.0 (0.0, 0.0)	> 0.99	0.0 (0.0, 0.0)	0.0 (0.0, 0.0)	-	0.0 (0.0, 0.0)	0.0 (0.0, 0.0)	-
ASES shoulder right, median (IQR)	98.3 (93.3, 100)	100 (95, 100)	99.2 (95, 100)	> 0.99	98.3 (91.7, 100)	95 (91.7, 100)	> 0.99	98.3 (93.3, 98.3)	100 (95, 100)	> 0.99
ASES shoulder left, median (IQR)	98.3 (90, 100)	100 (85, 100)	98.3 (91.7, 100)	> 0.99	100 (93.3, 100)	95.8 (87.5, 100)	> 0.99	100 (91.7, 100)	90 (66.7, 100)	> 0.99
SANE, median (IQR)	95 (85, 100)	96.5 (90, 100)	100 (92.5, 100)	> 0.99	100 (95, 100)	95 (80, 100)	> 0.99	90 (85, 95)	85 (50, 100)	> 0.99

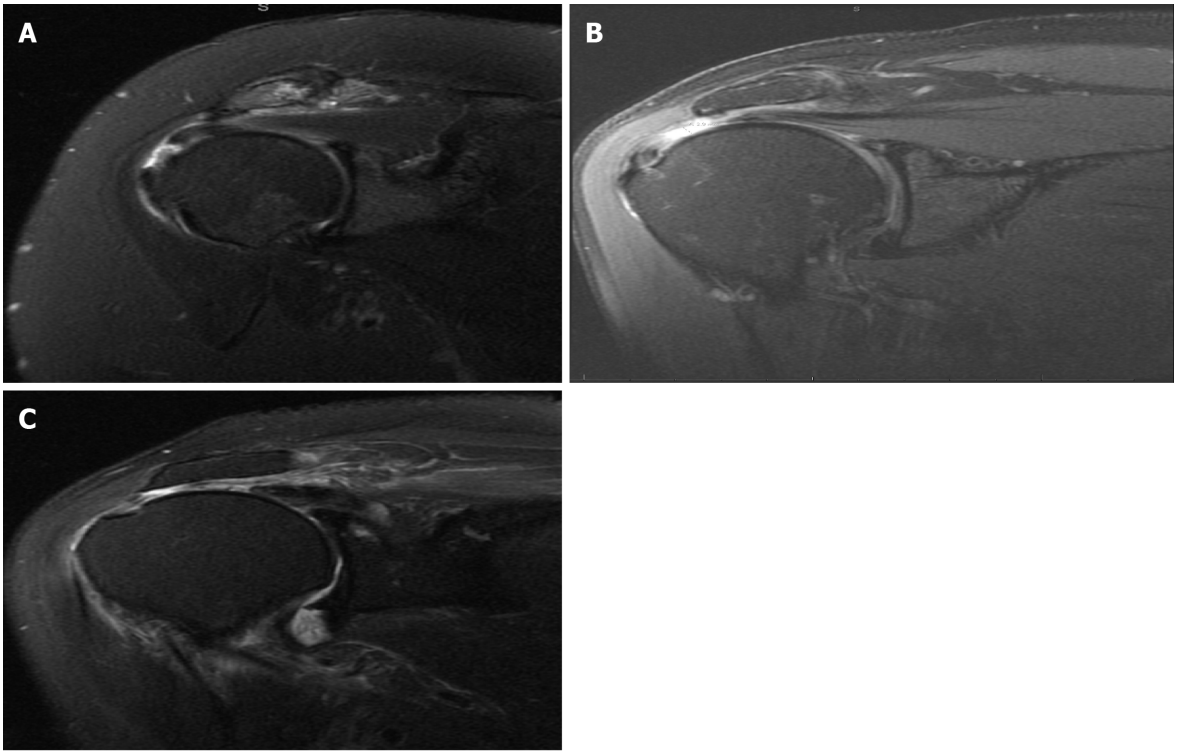
MCS: Veterans RAND 12-Item Health Survey mental health component summary scores; PCS: Veterans RAND 12-Item Health Survey physical health component summary score; VAS: Visual analogue scale; ASES: American shoulder and elbow surgeons score; SANE: Single assessment numeric evaluation.

joint-preserving treatment *via* RCR in the setting of GHOA.

A recent study by Jeong *et al*[8] retrospectively evaluated the clinical outcomes of large to massive RCR in patients with and without mild GHOA. The authors found that preoperative and postoperative variables (VAS scores, ROM, muscle strength, University of California, Los Angeles (UCLA) scores, and Constant scores) at final follow-up (2 years) showed no significant differences between the two groups. Our study also included VAS and similarly did not show any significant difference between groups at final follow up period of 2 years. Jeong *et al*[8] reported mean VAS scores in patients with large to massive tears with mild GHOA and without mild GHOA to be 0.3 ± 0.7 and 0.3 ± 0.8, respectively which are similar to our overall median VAS score of 0.0 (IQR 0.0, 0.0). These combined results indicate that patients with small to large rotator cuff repairs in the setting of mild to moderate GHOA can expect to have a pain score close to 0 after a minimum of 2 years after RCR.

A study by Kukkonen *et al*[10] evaluated outcomes using Constant scores in patients with or without GHOA after undergoing supraspinatus tendon repair with tear sizes ranging from 0.5 cm to 2.5 cm. Both pre and post-operative Constant scores were significantly lower in patients with GHOA. These results differ from ours and Jeong *et al*'s which showed no difference in PROs in patients with or without GHOA[8]. Kukkonen *et al*'s study only included males, had final follow-up of 1 year, and used the Kellgren-Lawrence classification to determine GHOA severity and status[10]. In contrast, our study and the study by Jeong *et al*[8] included males and females with a follow-up of 2 years and used the Samilson-Priesto classification for GHOA grading. A study of radiographic classifications of GHOA found that the Kellgren-Lawrence provided inferior inter-observer agreement in diagnosis of GHOA compared to Samilson-Priesto due to the challenge of identifying minor joint space narrowing in the non-weight bearing shoulder joint[17]. The aforementioned finding may limit comparative value of studies using different radiographic classification methods.

Overall, the results of our PROs after a short to medium term follow-up period show favorable results in VR-12, VAS, ASES, and SANE regardless of tear size or presence of GHOA. In patients with mild to moderate GHOA, there were no significant differences in all categories of PROs when comparing to patients without GHOA stratified by small to large rotator cuff tears. The minimal clinical important difference (MCID) was established to define minimum difference in PROs that is required to provide a clinically relevant benefit for patients rather than relying on statistically significant differences. The MCID for VR-12 PCS, MCS, VAS pain, ASES, and SANE following RCR has been reported to be 4.94, 5.99, 1.4, 21.0, and 11.80 respectively[18,19]. VR-12 PCS was the only PROs that showed MCID when patients with small or large rotator cuff tears were compared by presence or absence of GHOA. Surprisingly, patients with mild to moderate GHOA and small RCR had worse VR-



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Figure 3 Magnetic resonance imaging. A: Magnetic resonance imaging demonstrating small (0-1 cm) tear of rotator cuff; B: Magnetic resonance imaging demonstrating medium (1-3 cm) tear of rotator cuff; C: Magnetic resonance imaging demonstrating large (3-5 cm) tear of rotator cuff.

12 PCS scores. A literature review of histopathology of rotator cuff tears showed that inflammatory cell infiltrate and number of blood vessels are inversely correlated with tear size[20]. Immunochemistry has also shown torn rotator cuff tendons with lower vascularity have fewer new nerve fibers and is linked to lower chronic pain[21].

The rate of conversion to TSA or RTSA within 2 years after RCR were low for patients with and without GHOA at 2.8% (2/71) and 1.4% (1/71), respectively. This is the first study to report conversion to TSA or RTSA as an outcome variable while comparing outcomes following RCR in patients with or without GHOA. Results of previous studies, which showed that the progression of GHOA did not negatively affect PROs at final follow-up in patients who underwent RCR or arthroscopic debridement of massive irreparable rotator cuff tears[8,22,23], led us to hypothesize patients with GHOA would have conversion rate to TSA or RTSA are comparable with patients without GHOA. The results of our study report good PROs and very low conversion rates to shoulder arthroplasty after RCR with concomitant GHOA.

Due to the retrospective design, there are aspects to patient selection and classification that may introduce confounding biases. The heterogeneous nature of the patients with regard to demographics, surgical technique, and being treated by multiple surgeons at a single academic institution may limit the ability to make accurate comparisons between groups. Furthermore, no preoperative PROs were obtained which may have served as a baseline measure to observe any improvements or exacerbations following RCR. Our follow-up period may be reflective of short- term outcomes with a lack of findings for longer-term outcomes (greater than 5 years or 10 years). However, a recent study by Manderle *et al* [24] showed that the vast majority of RCR patients achieve MCID, substantial clinical benefit and patient acceptable symptomatic state for various PROs within 1 year. Therefore, our minimum 2-year follow-up period may be sufficient to evaluate and make comparisons of the postoperative PROs following RCR in this patient population.

CONCLUSION

This study reveals comparable outcomes in patients following small, medium, and large RCR with or without GHOA. Within a clinical follow-up period of 2 years, there were low rates of conversion to TSA or RTSA and no significant statistical differences found in PROs between patients with and without GHOA. In patients with mild to moderate GHOA and small to large rotator cuff tears, RCR is an effective means of surgical intervention that allows for joint-preservation and satisfactory PROs at short and medium-term follow-up.

ARTICLE HIGHLIGHTS

Research background

This study showed that patient reported outcomes in patients that have undergone a rotator cuff repair procedure, in the setting of Glenohumeral Osteoarthritis (GHOA) are favorable at short term (IE less than 2 year) follow-up. The rate of conversion to arthroplasty for these patients was also very low, indicating satisfaction with their outcomes.

Research motivation

There is a paucity of literature surrounding this topic, rotator cuff repair (RCR) in the setting of GHOA, so we felt it necessary to add to the literature with our own set of data in hopes of providing clinicians with more data surrounding this topic.

Research objectives

To determine patient report outcomes and rate of conversion to arthroplasty for patients with GHOA after undergoing a rotator cuff repair procedure. With favorable outcomes, and low conversion rates to arthroplasty, these objectives were realized in our data set.

Research methods

This was a retrospective cohort study with patient follow-up *via* questionnaire by phone, email, or in person *via* clinic visits.

Research results

Our results showed a low rate of conversion to arthroplasty in both subgroups after undergoing RCR. Patient reported outcomes using standardized scales were also quite favorable in both subgroups.

Research conclusions

Our study showed favorable outcomes with regards to patient reported outcomes. A low conversion rate to arthroplasty was also noted in the short term follow-up.

Research perspectives

The future direction of our research will include longer term patient follow-up (IE greater than 5-10 years) to ascertain data on conversion to arthroplasty in the GHOA patient.

FOOTNOTES

Author contributions: Saltzman BM, Fleischli JE, Connor PM and Hamid N developed the idea for the project; Hong IS, Rao AJ, CarlLee TL, and Meade JD contributed to formulating, writing, and revising the documents; Hurwit DJ, Scarola G, Trofa DP, and Schiffern SC contributed to development of the data analysis, manuscript revisions and formulation of project; all authors have agreed to be responsible for the final version of the manuscript.

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Informed consent statement: All study participants or their legal guardian provided informed written consent about personal and medical data collection prior to study enrolment.

Conflict-of-interest statement: All authors have no conflict of interest related to the manuscript.

Data sharing statement: Dataset can be made available upon request per the corresponding author at Bryan.Saltzman@orthocarolina.com.

STROBE statement: The authors have read the STROBE Statement—checklist of items, and the manuscript was prepared and revised according to the STROBE Statement—checklist of items.

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REFERENCES

1 **Yamaguchi K**, Ditsios K, Middleton WD, Hildebolt CF, Galatz LM, Teefey SA. The demographic and morphological features of rotator cuff disease. A comparison of asymptomatic and symptomatic shoulders. *J Bone Joint Surg Am* 2006; **88**: 1699-1704 [PMID: 16882890 DOI: 10.2106/JBJS.E.00835]
2 **Keener JD**, Steger-May K, Stobbs G, Yamaguchi K. Asymptomatic rotator cuff tears: patient demographics and baseline shoulder function. *J Shoulder Elbow Surg* 2010; **19**: 1191-1198 [PMID: 21030274 DOI: 10.1016/j.jse.2010.07.017]
3 **Minagawa H**, Yamamoto N, Abe H, Fukuda M, Seki N, Kikuchi K, Kijima H, Itoi E. Prevalence of symptomatic and asymptomatic rotator cuff tears in the general population: From mass-screening in one village. *J Orthop* 2013; **10**: 8-12 [PMID: 24403741 DOI: 10.1016/j.jor.2013.01.008]
4 **Ansok CB**, Muh SJ. Optimal management of glenohumeral osteoarthritis. *Orthop Res Rev* 2018; **10**: 9-18 [PMID: 30774456 DOI: 10.2147/ORR.S134732]
5 **Oh JH**, Chung SW, Oh CH, Kim SH, Park SJ, Kim KW, Park JH, Lee SB, Lee JJ. The prevalence of shoulder osteoarthritis in the elderly Korean population: association with risk factors and function. *J Shoulder Elbow Surg* 2011; **20**: 756-763 [PMID: 21530320 DOI: 10.1016/j.jse.2011.01.021]
6 **Ibounig T**, Simons T, Launonen A, Paavola M. Glenohumeral osteoarthritis: an overview of etiology and diagnostics. *Scand J Surg* 2021; **110**: 441-451 [PMID: 32662351 DOI: 10.1177/1457496920935018]
7 **Zhang Y**, Jordan JM. Epidemiology of osteoarthritis. *Clin Geriatr Med* 2010; **26**: 355-369 [PMID: 20699159 DOI: 10.1016/j.cger.2010.03.001]
8 **Jeong HY**, Jeon YS, Lee DK, Rhee YG. Rotator cuff tear with early osteoarthritis: how does it affect clinical outcome after large to massive rotator cuff repair? *J Shoulder Elbow Surg* 2019; **28**: 237-243 [PMID: 30337266 DOI: 10.1016/j.jse.2018.07.022]
9 **Kerr R**, Resnick D, Pineda C, Haghighi P. Osteoarthritis of the glenohumeral joint: a radiologic-pathologic study. *AJR Am J Roentgenol* 1985; **144**: 967-972 [PMID: 3872581 DOI: 10.2214/ajr.144.5.967]
10 **Kukkonen J**, Joukainen A, Lehtinen J, Äärimaa V. The effect of glenohumeral osteoarthritis on the outcome of isolated operatively treated supraspinatus tears. *J Orthop Sci* 2013; **18**: 405-409 [PMID: 23512014 DOI: 10.1007/s00776-013-0369-2]
11 **Yamamoto A**, Takagishi K, Osawa T, Yanagawa T, Nakajima D, Shitara H, Kobayashi T. Prevalence and risk factors of a rotator cuff tear in the general population. *J Shoulder Elbow Surg* 2010; **19**: 116-120 [PMID: 19540777 DOI: 10.1016/j.jse.2009.04.006]
12 **Gartsman GM**, Taverna E. The incidence of glenohumeral joint abnormalities associated with full-thickness, reparable rotator cuff tears. *Arthroscopy* 1997; **13**: 450-455 [PMID: 9276051 DOI: 10.1016/s0749-8063(97)90123-7]
13 **Hsu HC**, Luo ZP, Stone JJ, Huang TH, An KN. Correlation between rotator cuff tear and glenohumeral degeneration. *Acta Orthop Scand* 2003; **74**: 89-94 [PMID: 12635800 DOI: 10.1080/00016470310013725]
14 **Lin DJ**, Wong TT, Kazam JK. Shoulder Arthroplasty, from Indications to Complications: What the Radiologist Needs to Know. *Radiographics* 2016; **36**: 192-208 [PMID: 26761537 DOI: 10.1148/rg.2016150055]
15 **Mattei L**, Mortera S, Arrigoni C, Castoldi F. Anatomic shoulder arthroplasty: an update on indications, technique, results and complication rates. *Joints* 2015; **3**: 72-77 [PMID: 26605254 DOI: 10.11138/jts/2015.3.2.072]
16 **Nam D**, Maak TG, Raphael BS, Kepler CK, Cross MB, Warren RF. Rotator cuff tear arthropathy: evaluation, diagnosis, and treatment: AAOS exhibit selection. *J Bone Joint Surg Am* 2012; **94**: e34 [PMID: 22438007 DOI: 10.2106/JBJS.K.00746]
17 **Brox JI**, Lereim P, Merckoll E, Finnanger AM. Radiographic classification of glenohumeral arthrosis. *Acta Orthop Scand* 2003; **74**: 186-189 [PMID: 12807327 DOI: 10.1080/00016470310013932]
18 **Kim DM**, Kim TH, Kholinne E, Park JH, Shin MJ, Kim H, Park D, Jeon IH, Koh KH. Minimal Clinically Important Difference, Substantial Clinical Benefit, and Patient Acceptable Symptomatic State After Arthroscopic Rotator Cuff Repair. *Am J Sports Med* 2020; **48**: 2650-2659 [PMID: 32813985 DOI: 10.1177/0363546520943862]
19 **Zhou L**, Natarajan M, Miller BS, Gagnier JJ. Establishing Minimal Important Differences for the VR-12 and SANE Scores in Patients Following Treatment of Rotator Cuff Tears. *Orthop J Sports Med* 2018; **6**: 2325967118782159 [PMID: 30090834 DOI: 10.1177/2325967118782159]
20 **Longo UG**, Berton A, Khan WS, Maffulli N, Denaro V. Histopathology of rotator cuff tears. *Sports Med Arthrosc Rev* 2011; **19**: 227-236 [PMID: 21822106 DOI: 10.1097/JSA.0b013e318213bccb]
21 **Xu Y**, Bonar F, Murrell GA. Neoinnervation in rotator cuff tendinopathy. *Sports Med Arthrosc Rev* 2011; **19**: 354-359 [PMID: 22089285 DOI: 10.1097/JSA.0b013e318229d7e3]
22 **Liem D**, Lengers N, Dedy N, Poetzl W, Steinbeck J, Marquardt B. Arthroscopic debridement of massive irreparable rotator cuff tears. *Arthroscopy* 2008; **24**: 743-748 [PMID: 18589261 DOI: 10.1016/j.arthro.2008.03.007]
23 **Harris PA**, Taylor R, Thielke R, Payne J, Gonzalez N, Conde JG. Research electronic data capture (REDCap)--a metadata-driven methodology and workflow process for providing translational research informatics support. *J Biomed Inform* 2009; **42**: 377-381 [PMID: 18929686 DOI: 10.1016/j.jbi.2008.08.010]
24 **Manderle BJ**, Gowd AK, Liu JN, Beletsky A, Nwachukwu BU, Nicholson GP, Bush-Joseph C, Romeo AA, Forsythe B, Cole BJ, Verma NN. Time Required to Achieve Clinically Significant Outcomes After Arthroscopic Rotator Cuff Repair. *Am J Sports Med* 2020; **48**: 3447-3453 [PMID: 33079576 DOI: 10.1177/0363546520962512]

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ORIGINAL ARTICLE

Retrospective Cohort Study

Association between tourniquet use and intraoperative blood loss during below-knee amputation

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Abstract

BACKGROUND

Despite over 150000 amputations of lower limbs annually, there remains a wide variation in tourniquet practice patterns and no consensus on their necessity, especially among orthopedic patient populations. The purpose of this study was to determine whether tourniquet use in orthopedic patients undergoing below knee amputation (BKA) was associated with a difference in calculated blood loss relative to no tourniquet use.

AIM

To determine if tourniquet use in orthopedic patients undergoing BKA was associated with a difference in calculated blood loss relative to no tourniquet use.

METHODS

We performed a retrospective review of consecutive patients undergoing BKA by orthopedic surgeons at a tertiary care hospital from 2008 through 2018. Blood loss was calculated using a combination of the Nadler equation for preoperative blood volume and a novel formula utilizing preoperative and postoperative hemoglobin levels and transfusions. Univariate and forwards step-wise multivariate linear regressions were performed to determine the association between tourniquet use and blood loss. A Wilcoxon was used to determine the univariate relationship between tourniquet use and blood loss for in the restricted subgroups of patients who underwent BKA for trauma, tumor, and infection.

RESULTS

Of 97 eligible patients identified, 67 underwent surgery with a tourniquet and 30 did not. In multivariate regression, tourniquet use was associated with a 488 mL decrease in calculated blood loss (CI 119-857, P = 0.01). In subgroup analysis, no

individual group showed a statistically significant decrease in blood loss with tourniquet use. There was no significant association between tourniquet use and either postoperative transfusions or reoperation at one year.

CONCLUSION

We found that tourniquet use during BKA is associated with decreased calculated intraoperative blood loss. We recommend that surgeons performing this procedure use a tourniquet to minimize blood loss.

Key Words: Amputation; Tourniquet; Blood loss; Hemostasis

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Core Tip: We retrospectively evaluated 138 patients who underwent a below knee amputation by an orthopedic surgeon and compared the calculated intraoperative blood loss between patients who received or did not receive a tourniquet. We found that patients who did receive a tourniquet had significantly lower blood loss than those who did not.

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INTRODUCTION

Since its 2nd century introduction to amputation surgery by Heliodorus, the tourniquet has been nearly as enduring as the knife itself[1,2]. Yet despite the amputation of over 150000 Lower limbs annually in the United States, there are wide variations in tourniquet practice patterns and no consensus on their necessity during limb removal[3].

Tourniquet application during limb amputation is controversial. Historically, the high rate of mortality associated with early amputations was attributed to both delayed septicemia and immediate blood loss, leading surgeons such as Esmarch, Lister, and Cushing to improve upon early designs during the 19th and 20th centuries[2]. Today, tourniquet use is associated with decreased intraoperative blood loss and fewer transfusions in below knee amputations performed primarily in vascular surgery settings[4,5]. However, this has hardly settled the question of whether they should be used routinely for hemorrhage control during orthopedic limb removal. Throughout the dissection, use of a tourniquet may provide a drier surgical field by slowing intraoperative bleeding, but at the same time may limit the palpation of neurovascular structures[6-8]. Additionally, blood loss continues beyond the intraoperative period, and application of a tourniquet may prevent the surgeon from identifying damage to small vessels that continue to ooze postoperatively. There is also a theoretical risk of damaging fragile atherosclerotic vessels as pneumatic pressure increases, leading to swelling and blood loss in the perioperative period after the tourniquet has been removed[9]. This may explain studies finding no difference in total blood loss or transfusions with tourniquet use in studies of both below knee amputation and total knee arthroplasty[9-12].

There is a paucity of literature describing the association between tourniquet use and blood loss during below knee amputation in orthopedic populations, which include patients undergoing surgery for neoplastic disease, trauma, and infection[11]. Furthermore, blood loss in prior studies has typically been recorded using surgeon estimation, which is subjective, imprecise, and does not account for perioperative "hidden" blood loss that continues after closure of the wound[10,13,14].

The primary purpose of this study was to determine whether tourniquet use in orthopedic patients undergoing below knee amputation was associated with a difference in calculated blood loss relative to no tourniquet use. Secondarily, we assessed whether tourniquet application was associated with postoperative transfusions during the inpatient stay or reoperation within one year. We hypothesized that tourniquet use would not be associated with decreased blood loss, postoperative transfusions, or reoperation within one year.

Table 1 Demographic characteristics of patients undergoing below knee amputation with and without tourniquet

	No tourniquet	Tourniquet	*P* value
n	30	67	
Age, mean (SD)	43.31 (18.53)	56.05 (14.02)	< 0.001
Gender = M (%)	19 (63.3)	43 (64.2)	1
Height (mean (SD))	1.73 (0.10)	1.75 (0.10)	0.423
Weight (mean (SD))	90.63 (31.57)	98.78 (32.46)	0.252
BMI (mean (SD))	29.96 (9.62)	32.12 (9.81)	0.315
Diabetes (%)	7 (23.3)	27 (40.3)	0.165
Hepatitis C (%)	0 (0.0)	4 (6.0)	0.415
Smoking (%)	6 (20.0)	26 (38.8)	0.112
IV drug use (%)	1 (3.3)	5 (7.5)	0.746
Alcoholism (%)	2 (6.7)	10 (14.9)	0.419
Outside hospital transfer (%)	3 (10.0)	13 (19.4)	0.391
ASA score (%)			0.433
1	1 (3.3)	0 (0.0)	
2	12 (40.0)	20 (29.9)	
3	15 (50.0)	40 (59.7)	
4	2 (6.7)	6 (9.0)	
5	0 (0.0)	1 (1.5)	
Homeless (%)	0 (0.0)	1 (1.5)	1
Preoperative hemoglobin (mean (SD))	11.91 (2.64)	11.78 (2.74)	0.82
Platelets (mean (SD))	270.83 (153.50)	315.09 (114.02)	0.117
Indication for surgery (%)			< 0.001
Infection	14 (46.7)	53 (79.1)	
Trauma	2 (6.7)	9 (13.4)	
Tumor	14 (46.7)	5 (7.5)	

BMI: Body mass index.

MATERIALS AND METHODS

With Institutional Review of Board approval, we retrospectively reviewed consecutive patients undergoing below knee amputation by orthopedic surgeons at a single academic institution over a ten-year period from January 1, 2008 to December 31, 2018. The hospital is a tertiary referral center for soft tissue sarcomas and a Level 1 trauma center. This study was conducted following STROBE guidelines [15].

Patients were identified by CPT code for below-knee amputation. To prevent confounding by other sources of bleeding, patients were excluded if the indication for below-knee amputation was a trauma that had occurred within one week, if they had active gastrointestinal bleeding, or if they had a diagnosed bleeding disorder. We excluded patients with through-knee amputations.

Data for identified patients was collected from chart review including demographic characteristics (*e.g.*, age, sex), known or potential modifiers of blood loss (*e.g.*, kidney dysfunction, platelet count), and surgical data (*e.g.*, indication for surgery, intraoperative transfusions). A full list of variables that were collected can be found in Supplementary Table 1. Tourniquet use and tourniquet time were taken from surgeon operative reports. Post-operative hemoglobin and hematocrit results were taken within 72 h of the operation. We used the first post-operative hemoglobin in blood loss calculations.

Blood loss was determined using a series of calculations. Preoperative blood volume was calculated using patient height, weight, and gender by the Nadler formula[16]:

Table 2 Results of multivariate regression modeling

Variable	Estimate (95%CI)	*P* value
Tourniquet use	-488 mL (-857, -119)	0.01
Indication (*vs* infection)		
Trauma	12 mL (-474, 498)	0.96
Tumor	-190 mL (-624, 245)	0.39

CI: Confidence interval.

Blood volume (Male) = $0.3669 \times H^3 + 0.03219 \times W + 0.6041$.

Blood volume (Female) = $0.3561 \times H^3 + 0.03308 \times W + 0.1833$.

Total blood loss was then determined using calculated blood volume, change in hemoglobin concentration, and the mass of hemoglobin transfused intraoperatively, based on modification of the formula by Wied *et al*[10]: Total mass of Hgb lost = Blood volume (L) × (Hgb preop - Hgb postop) × 10 + mass of transfused Hgb. Where mass of transfused Hgb = 61.25g × intraoperative units transfused[16]. Blood loss (L)= total mass of Hgb lost/ (Hgb preop × 10).

We excluded five variables with > 5% data missingness (functional capacity, erythrocyte sedimentation rate, C-reactive protein, A1c, and albumin). The only remaining variable with missing data (creatinine, 2%) was included in regression analysis. Characteristics of patients undergoing below knee amputation with and without tourniquet were compared using t tests or chi square tests as appropriate.

For our primary outcome, we performed a univariate linear regression to determine the association between tourniquet use and blood loss. We also ran subgroup analyses by indication for surgery, using a Wilcoxon due to the non-parametric distribution of blood loss and the low number of observations in each subgroup. We then performed a forward stepwise regression with potential modifiers of the association between tourniquet use and blood loss, sequentially retaining variables that changed the estimation of the association by greater than 10 percent. We excluded the surgeon as a variable from this analysis as it was thought to lie on a causal pathway between indication and blood loss and was not generalizable. We also excluded operative time due to the directionality of its association with tourniquet use and because it likely lies along the causal pathway between tourniquet use and blood loss[11]. To avoid spurious associations, we only included variables that were logically associated tourniquet use and blood loss, and limited the variables tested to 10% of the number of observations. We included interaction terms for variables of interest.

We then performed two logistic regressions in a similar fashion using postoperative transfusion and reoperation in one year as outcomes. Postoperative transfusions were only included if administered during the immediate inpatient stay. Reoperations included stump revisions, revision to a higher-level amputation (*e.g.*, above-the-knee), and irrigation and debridement.

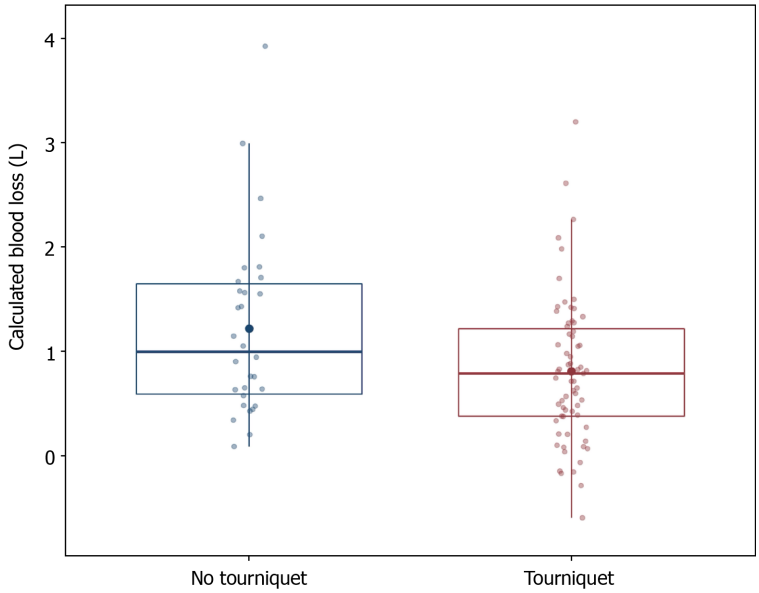
All statistical analysis was performed using R version 3.6.3 including the packages tableone, dplyr, ggplot2, and chest. Statistical significance was determined at 0.05. The study was reviewed by our statistician Dr. Erik Woelber.

RESULTS

138 patients undergoing below knee amputation were identified by chart review. 41 patients were excluded because they sustained a trauma within the prior week, leaving 97 patients for analysis. Of the patients identified, 67 underwent surgery with a tourniquet and 30 did not. Indications included infection (69%, $n = 67$), trauma (11%, $n = 11$), and tumor (20%, $n = 19$). Demographic characteristics are shown in Table 1. The tourniquet group was older (56 *vs* 43 years, $P < 0.001$) and had categorical differences in indication for surgery ($P < 0.001$).

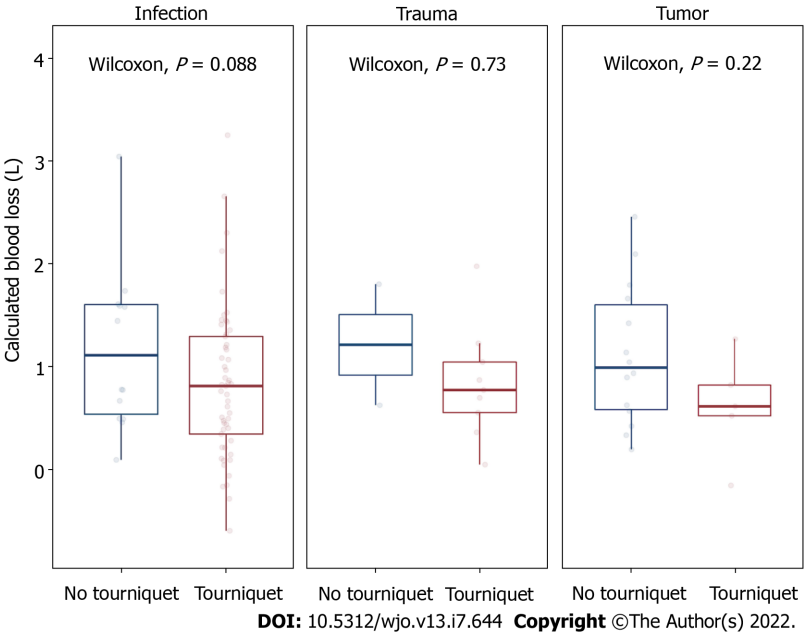
In simple linear regression, tourniquet use was associated with significantly decreased blood loss (-0.41 Liters, SE 0.17, $P = 0.01$) (Figure 1). The calculation allowed for negative blood loss values to occur for 6 patients (6%). The plots reveal a right-skewed distribution of calculated blood loss for both tourniquet and non-tourniquet patients. In the analysis of restricted subgroups, no individual group showed a statistically significant decrease in blood loss with tourniquet use (Figure 2).

Results of multivariate regression are shown in Table 2. Of the tested variables, only the indication for surgery modified the association between tourniquet use and blood loss above the 10% threshold for inclusion. Though it differed significantly between tourniquet and non-tourniquet groups, age did not significantly modify the association between tourniquet use and blood loss. Two patients with missing data for creatinine were excluded from stepwise regression modelling but were included in the final multivariate model. The interaction term between tourniquet use and indication for surgery was not



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Figure 1 Tourniquet use was associated with significantly decreased blood loss.



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Figure 2 No individual group showed a statistically significant decrease in blood loss with tourniquet use.

significant (P = 0.84 for trauma and P = 0.99 for tumor, relative to infection).

Thirteen patients in the tourniquet group (19%) and six patients in the non-tourniquet group (20%) received a postoperative transfusion. Twenty patients in the tourniquet group (30%) and 13 patients in the non-tourniquet group (43%) underwent an unplanned reoperation within one year of the index surgery. Adjusted secondary analyses showed no statistically significant association between tourniquet use and either inpatient blood transfusion after the first postoperative lab draw (OR 0.83, CI 0.25-2.72, P = 0.75) or reoperation at one year (OR 0.84, CI 0.26-2.79, P = 0.78).

DISCUSSION

Our results indicate that tourniquet use during below knee amputations performed on orthopedic surgery patients is associated with significantly decreased surgical blood loss. The magnitude of the as

sociation is noteworthy, as a 488 mL decrease with use of a tourniquet equates to an approximately ten percent difference in total blood volume lost.

Our findings are consistent with the results of prior studies in non-orthopedic populations. A non-randomized study found that tourniquet use in vascular patients undergoing below-knee amputation is associated with decreased surgical blood loss, fewer postoperative transfusions, and fewer complications[4]. Similarly, a prospective, randomized, blinded study found that tourniquet use in peripheral arterial disease patients is associated with less intraoperative blood loss, a smaller perioperative drop in hemoglobin, fewer transfusions, and similar complication rates[5].

Our secondary analysis did not demonstrate a statistically significant association between tourniquet use and inpatient postoperative transfusions. A prior study found that as much blood is lost following above-knee amputations postoperatively as during the procedure, which could explain this result[10]. Another study echoed the finding that tourniquet use during BKA is associated with less intraoperative blood loss, but no difference in total blood loss (including the postoperative period)[11]. In the joint arthroplasty literature, tourniquet use is not associated with a difference in transfusions or total blood loss[12]. In our study, it is also possible that we did not have adequate power to detect a difference in transfusions due to their rarity.

Our secondary analysis also did not demonstrate a statistically significant association between tourniquet use and reoperations at one year. At least one study comparing reoperation rates with and without a tourniquet found no difference in the rate of conversion to a higher-level amputation at 30 days[11].

This study had multiple limitations. First, the calculation of intraoperative blood loss relies on several assumptions: It assumes that all patients are adequately resuscitated following their operation at the time of their first postoperative blood draw (and thus may have underestimated total blood loss), and it does not account for changes in intravascular volume cause by vasoconstriction or fluid shifts. The calculation also does not account for any blood volume in the amputated limb. In theory, the equation overestimates blood loss because it is based off of a pre-operative patient weight, but this impact is negligible and should be equal in both groups. Patients taking anticoagulation or antiplatelet medications could also have increased blood loss and this was not taken into account in our analysis. However, patients are usually instructed to stop such medications before an operation. These calculations impose rigid mathematical formulas on patients representing a range of body compositions and physiologic responses to surgery that are dynamic and idiosyncratic. This may be particularly relevant in tertiary referral centers that see a non-representative range of body habitus and patients with impaired compensatory responses to hemorrhage. However, calculated blood loss has several advantages over surgeon estimation, including its standardization and immunity to the bias of a surgeon's visual assessment. It is also easily replicable at other centers and avoids the logistical hassles of alternative methods such as weighing surgical drapes and sponges.

A second limitation is that our patient population was heterogenous and derived from an academic center, and therefore potentially less generalizable. This fact is offset by our study being the first to approach this question in an orthopedic patient population, which differs from the more commonly studied general surgery population in terms of indications and patient characteristics. Second, the patients underwent procedures by a diverse group of surgeons employing a range of surgical techniques, increasing the external validity of our results.

Another limitation is that in the patients with an infectious etiology, which was primarily due to diabetes, the presence of peripheral vascular disease was not taken into account, which could affect blood loss.

Our study found no evidence of effect modification by the indication for surgery, indicating that use of a tourniquet does not have a variable effect on blood loss in oncology, infection, and trauma patients. However, the subgroup analysis was not powered to detect a difference in blood loss; comparisons within these groups were affected by small sample sizes, particularly in the group undergoing amputation due to trauma (n = 11). Thus, both the individual subgroup analyses and the lack of evidence for effect modification should be interpreted with caution.

CONCLUSION

We found that tourniquet use during below knee amputation is associated with decreased calculated intraoperative blood loss. The decision to use a tourniquet depends on multiple factors related to the individual patient, the underlying pathology being treated, and surgeon preferences. However, based on these results, we recommend that surgeons performing this procedure use a tourniquet if they wish to minimize blood loss. Analysis of a larger database may provide supporting evidence for tourniquet use in specific patient subgroups including patients with malignant tumors and those who sustained acute traumatic injury.

ARTICLE HIGHLIGHTS

Research background

Below-knee amputation (BKA) is common procedure in the orthopedic population. Etiology for patients requiring this surgery are primarily trauma, infection, and neoplastic disease. There is currently no consensus among orthopedic surgeons regarding the use of a tourniquet in these patients.

Research motivation

The motivation behind this study is to determine a possible method to minimize blood loss in BKA operations.

Research objectives

To compare blood loss between patients who received a tourniquet during their BKA procedure and those who did not.

Research methods

We performed a retrospective cohort study on consecutive patients who underwent BKA over a ten-year period at a tertiary care hospital. Blood loss was estimated using the Nadler equation for preoperative blood volume and a novel formula that utilizes preoperative and postoperative hemoglobin levels and transfusions. Univariate and forwards stepwise multivariate linear regression were utilized to determine an association between tourniquet use and blood loss.

Research results

We found that patients undergoing a BKA operation with tourniquet use were associated with a 488 mL decrease in calculated blood loss. This is significant for orthopedic surgeons wanting to minimize blood loss in BKA operations.

Research conclusions

This study utilized a calculated blood loss rather than the commonly utilized estimated blood loss, and proposes that a tourniquet should be used if orthopedic surgeons wish to minimize blood loss in BKA operation.

Research perspectives

Research should be conducted on a larger population across multiple centers to determine a stronger association and increase external validity.

FOOTNOTES

Author contributions: Woelber E, Meeker J and Working Z contributed the study conception and design; Wyland AE, Wong LH and Arakawa J contributed the generation, collection of the data; Wyland AE and Woelber E contributed the assembly, analysis and/or interpretation of the data; Wyland A, Woelber E, Meeker J and Working Z contributed to drafting and revising the manuscript.

Institutional review board statement: This study was approved by the Institutional Review Board (STUDY00020406).

Informed consent statement: All study participants or their legal guardian provided informed written consent about personal and medical data collection prior to study enrolment.

Conflict-of-interest statement: Each author certifies that he or she has no commercial associations (*e.g.*, consultancies, stock ownership, equity interest, patent/Licensing arrangements, *etc.*) that might pose a conflict of interest in connection with the submitted article.

Data sharing statement: Data and study materials are available upon reasonable request from the corresponding author at meekerj@ohsu.edu. Consent was not obtained, but the data are anonymous and the risk of identification is low.

STROBE statement: The authors have read the STROBE Statement—checklist of items, and the manuscript was prepared and revised according to the STROBE Statement—checklist of items.

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REFERENCES

1 **Kirkup J**. A History of Limb Amputation. London: Springer, 2007: 1-12 [DOI: 10.1002/bjs.6331]
2 **Bowker JH**, Pritham CH. The history of amputation surgery and prosthetics. In: Smith DG, editor. Atlas of Amputation and Limb Deficiencies: Surgical, Prosthetic and Rehabilitation Principles, 3rd edition. Rosemont, IL: AAOS, 2004: 3-21 [DOI: 10.1007/s10016-006-9117-9]
3 **Dillingham TR**, Pezzin LE, MacKenzie EJ. Limb amputation and limb deficiency: epidemiology and recent trends in the United States. *South Med J* 2002; **95**: 875-883 [PMID: 12190225 DOI: 10.1097/00007611-200208000-00018]
4 **Wolthuis AM**, Whitehead E, Ridler BM, Cowan AR, Campbell WB, Thompson JF. Use of a pneumatic tourniquet improves outcome following trans-tibial amputation. *Eur J Vasc Endovasc Surg* 2006; **31**: 642-645 [PMID: 16427337 DOI: 10.1016/j.ejvs.2005.11.018]
5 **Choksy SA**, Lee Chong P, Smith C, Ireland M, Beard J. A randomised controlled trial of the use of a tourniquet to reduce blood loss during transtibial amputation for peripheral arterial disease. *Eur J Vasc Endovasc Surg* 2006; **31**: 646-650 [PMID: 16750790 DOI: 10.1016/j.ejvs.2006.03.008]
6 **Jarolem KL**, Scott DF, Jaffe WL, Stein KS, Jaffe FF, Atik T. A comparison of blood loss and transfusion requirements in total knee arthroplasty with and without arterial tourniquet. *Am J Orthop (Belle Mead NJ)* 1995; **24**: 906-909 [PMID: 8776080]
7 **Aglietti P**, Baldini A, Vena LM, Abbate R, Fedi S, Falciani M. Effect of tourniquet use on activation of coagulation in total knee replacement. *Clin Orthop Relat Res* 2000; 169-177 [DOI: 10.1097/00003086-200002000-00021]
8 **Streichenberger R**, Barjoud H, Konieczny M, Elias W. Surgical management of major varicose veins of the lower limb using a pneumatic tourniquet. *Ann Vasc Surg* 1991; **5**: 559-560 [PMID: 1772766 DOI: 10.1007/BF02015285]
9 **Silver R**, de la Garza J, Rang M, Koreska J. Limb swelling after release of a tourniquet. *Clin Orthop Relat Res* 1986; 86-89 [DOI: 10.1097/00003086-198605000-00017]
10 **Wied C**, Tengberg PT, Kristensen MT, Holm G, Kallemose T, Troelsen A, Foss NB. Total Blood Loss After Transfemoral Amputations Is Twice the Intraoperative Loss: An Observational Cohort Study of 81 Nontraumatic Amputations. *Geriatr Orthop Surg Rehabil* 2017; **8**: 123-127 [PMID: 28835867 DOI: 10.1177/2151458517706595]
11 **Wied C**, Tengberg PT, Holm G, Kallemose T, Foss NB, Troelsen A, Kristensen MT. Tourniquets do not increase the total blood loss or re-amputation risk in transtibial amputations. *World J Orthop* 2017; **8**: 62-67 [PMID: 28144581 DOI: 10.5312/wjo.v8.i1.62]
12 **Smith TO**, Hing CB. Is a tourniquet beneficial in total knee replacement surgery? *Knee* 2010; **17**: 141-147 [PMID: 19616954 DOI: 10.1016/j.knee.2009.06.007]
13 **Wied C**, Foss NB, Kristensen MT, Holm G, Kallemose T, Troelsen A. Surgical apgar score predicts early complication in transfemoral amputees: Retrospective study of 170 major amputations. *World J Orthop* 2016; **7**: 832-838 [PMID: 28032037 DOI: 10.5312/wjo.v7.i12.832]
14 **Rothermel LD**, Lipman JM. Estimation of blood loss is inaccurate and unreliable. *Surgery* 2016; **160**: 946-953 [PMID: 27544540 DOI: 10.1016/j.surg.2016.06.006]
15 **von Elm E**, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP; STROBE Initiative. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. *PLoS Med* 2007; **4**: e296 [PMID: 17941714 DOI: 10.1371/journal.pmed.0040296]
16 **Nadler SB**, Hidalgo JH, Bloch T. Prediction of blood volume in normal human adults. *Surgery* 1962; **51**: 224-232 [PMID: 21936146]

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ORIGINAL ARTICLE

Randomized Controlled Trial

Does orthotics use improve comfort, speed and injury rate during running? Preliminary analysis of a randomised control trial

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Abstract

BACKGROUND

Evidence regarding the effectiveness of using orthotics in improving comfort, increasing running speed and helping to reduce injury rate during running is limited and mixed. Alongside the increasing popularity of running is the increasing rate of running-related injuries (RRIs). Further research into whether orthotics could be used to help reduce RRIs would be highly beneficial for those affected. Additionally, there is a need to clarify whether orthotics use increases comfort during running and helps improve running speed.

AIM

To investigate whether running with Aetrex Orthotics improves comfort and performance and reduces injury whilst running.

METHODS

Runners were recruited on a voluntary basis if they were 18 or older with no serious health conditions, ongoing foot pain or deformity, previous foot surgery in their lifetime or any surgery in the past 6 mo. Participants were randomly assigned to either an intervention group or a control group. All participants were asked to complete runs and provide quantitative data regarding comfort during running, running time and distance, and any RRIs over an 8-wk study period. Participants in the intervention group ran with Aetrex L700 Speed Orthotics, whilst participants in the control group ran without orthotics. Other than the addition of orthotics for participants in the intervention group, all participants were asked to run as they usually would. This report presents preliminary data from the first 47 participants recruited for this study. Running speed was calculated from running distance and time and given in miles per hour. For each outcome variable, the mean for each group, effect size and 95% confidence

interval were calculated, and a t-test was performed to determine if between-group differences were statistically significant.

RESULTS

Data for all three primary outcomes was provided from a total of 254 runs by the 23 participants in the intervention group and a total of 289 runs by the 24 participants in the control group. Participants in the intervention group reported higher comfort scores (8.00 ± 1.41 *vs* 6.96 ± 2.03, $P \leq 0.0001$), faster running speeds (6.27 ± 1.03 *vs* 6.00 ± 1.54, $P = 0.013$), and lower RRI rates (0.70 ± 1.01 *vs* 1.21 ± 1.53, $P = 0.18$) than those in the control group. These findings were statistically significant for comfort and running speed but not for RRI rate, with statistical significance considered if $P < 0.05$. No adjustments were made for group differences in age, gender, tendency for RRIs or usual running speed.

CONCLUSION

This preliminary report provides evidence for orthotics use in increasing comfort levels and running speed, but no significant difference in RRI rate.

Key Words: Running; Foot orthoses; Running related injuries; Pain; Patient comfort; Athletic performance

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Core Tip: Running-related injuries are becoming increasingly prevalent due to the increasing popularity of this sport. Foot orthotics have been suggested to increase comfort and speed whilst running, as well as reduce injury rate. However, current evidence is limited and mixed. This article, presenting preliminary randomised control trial data, finds significant evidence that running with Aetrex L700 Speed Orthotics, compared to running with no orthotics, in 'participants' regular running shoes, improves comfort and running speed. Participants running with Aetrex L700 Speed Orthotics, on average, reported lower injury rates than those running without orthotics. However, this difference was not significant.

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INTRODUCTION

Running is becoming an increasingly popular sport, likely due to it being easily accessible, low cost and having multiple physical and mental health benefits. However, alongside this, there is also an increase in running-related injuries (RRIs). These usually affect the lower limb, the most common site being the knee, with almost half of RRIs occurring here[1-5]. Other common areas include the lower leg, ankle and foot due to injuries such as Achilles Tendonitis, Plantar Fasciitis and Tibial Stress Syndrome[3]. RRIs result in pain and discomfort and often cause individuals to take time off running. Reported rates of RRIs vary between 19.4% to 79.3% - partly due to the variation in the definition for RRI used by different studies, and therefore, it is important that studies clarify which definition they use. The risk of RRIs when running, alongside the rising popularity of the sport, necessitates research to find ways to prevent injury.

For many years foot orthotics have been used by runners to correct the alignment of the lower leg, improve arch support and increase cushioning of the foot. Orthotics are inserts which fit into the shoe in place of the removable insole. There are many different types, including off-the-shelf and custom-made. Previous research into the use of orthotics has found that they can improve comfort, provide better arch support and decrease the incidence of certain lower limb injuries such as stress fractures[6-9]. However, some studies have found no statistically significant difference in the Incidence of certain RRIs, such as soft-tissue injuries, when comparing the use of orthotics to no orthotics[9,10]. One study suggested that orthotics were a risk factor for RRIs, although the runners using orthotics in this study may have been more prone to injury than those who were not[5].

Previous research into the impact that orthotics have on running performance is limited and gives no clear conclusion. Some studies have shown a small significant increase in running economy with cushioned shoes[11], whereas others have found orthotics to have a negative impact on running economy[12]. Whether or not an improvement in running economy leads to a subsequent increase in performance is also unclear[13].

Overall, previous research regarding the effect of orthotics on running comfort, RRI rate and running performance is not clear. There are conflicting issues creating a lack of guidance for both professional and amateur runners concerning whether orthotics should or should not be used. Further research is required to clarify the effectiveness of orthotics in increasing comfort during running, improving running performance and preventing RRIs. The aim of this study is to assess comfort during running, running performance and RRI rate for recreational runners using prefabricated Aetrex[14] Orthotics compared to recreational runners not using orthotics. The results from this study will add to the existing knowledge surrounding the effect of orthotics on running and may provide evidence of a useful tool to prevent RRIs.

This article presents preliminary data from this study, followed by a discussion of how this data confers, conflicts with, and expands the current evidence base.

MATERIALS AND METHODS

This is a randomised control trial. The primary objective is to investigate whether inserting prefabricated orthotics into running shoes will increase comfort and speed and help decrease injury during recreational running as compared to running shoes without orthotics.

Recruitment

Participants were recruited on a voluntary basis through local running clubs and social media advertisements. Posters were distributed containing contact details for the Principal Investigator. Participants who got in contact were provided with the participant information sheet *via* email or post by a member of the research team. Potential participants were asked to read the information sheet fully and given time for consideration. Subsequently, all participants had either a phone or Zoom call, depending on their preference, with the Principal Investigator to discuss any queries they had about the study. Once participants had understood all the information and were happy to proceed, written informed consent was obtained, either online *via* legalesign.com or by post.

To be eligible, participants had to be aged 18 or over and be used to completing runs of at least 5km distance during the last 1 year. Participants were excluded if they were using prescription orthotics, had any ongoing pain or deformity in the foot or any serious health condition which has led to a doctor advising them not to exercise. They were also excluded if they had undergone any surgery in the last 6 months or any surgery to the feet during their lifetime. Participants were informed of their ability to withdraw from the study at any time if they wished, without needing to give a reason.

Randomisation

Once recruited, participants were randomised into one of two groups: an intervention group, who ran with Aetrex[14] L700 Speed Orthotics in their usual running shoes (Group A), and a control group, who ran with no orthotics (Group B). The Aetrex[14] L700 Speed Orthotics are pictured in Figure 1. Group allocation occurred by the opening of pre-filled and sealed envelopes containing notes to assign them either to Group A or to Group B. These envelopes were shuffled, and an individual independent of the study picked an envelope at random to assign a participant to a group. There was no blinding of either participants or researchers to group allocations following randomisation.

Those in Group A received Aetrex[14] L700 Speed Orthotics *via* post, according to their shoe size, along with an instruction sheet on how to use the orthotics. Participants in Group B were asked to run as they usually would, with no adjustments made to their regular running shoes.

Data collection

Basic demographic information was collected from participants upon recruitment to the study. All participants were asked to complete runs and provide quantitative data over an 8-wk data collection period. Participants provided data remotely *via* an online or paper survey, depending on their preference. Other than the addition of orthotics for participants in Group A, all participants were asked to run without altering their regular running routine, thereby keeping confounding variables to a minimum.

The following data was collected by participants immediately after each run: (1) Comfort - collected on a self-report visual analogue scale (VAS) of 0 to 10, where 0 is "No comfort" and 10 is "Maximum comfort"[15]; and (2) Running duration (measured in hours and minutes) and running distance (measured in miles) – used to calculate running speed.

Once per week, participants were asked to provide data relating to any RRIs experienced in the previous seven days *via* a self-report 'fill me in' section of the survey. The consensus definition for an RRI presented by Yamato and co-workers[16] was used in this study which is: "Running-related musculoskeletal pain in the lower limbs that causes a restriction or stoppage of running (distance, speed, duration, or training) for at least 7 d or 3 consecutive scheduled training sessions, or that which requires the runner to consult a physician or other health professional." Participants were provided with an RRI information sheet to inform them of this definition, and the common sites, symptoms and causes



Figure 1 Image of Aetrex L700 Speed Orthotics.

of RRIs, to help them provide accurate, consistent data relating to the injury.

Weeks 1 and 2 of data collection were an 'acclimatisation period', and weeks 7 and 8 were a 'de-acclimatisation period'; during these weeks, only injury data was collected. Comfort during running, running time and running distance data was collected during weeks 3, 4, 5 and 6.

The preliminary data presented in this article relates to the first 47 participants recruited for the study. However, recruitment is still ongoing in order to obtain a larger study cohort of 106 participants to maximise the reliability and reproducibility of results. This number is based on a sample size calculation performed using a target significance level of 5%, target power of 80% and allowing for a 20% dropout rate.

Statistical analysis

Once collected, data was stored appropriately, and statistical testing was performed[17]. The standard deviations, effect size (mean difference) and 95% confidence interval for each outcome variable were calculated to determine the direction and strength of any correlations in the results. An unpaired two-tailed t-test was performed from the data for each outcome variable to determine if between-group differences were statistically significant. Standard deviations differed between the two groups, and so all *t*-tests used Welch's correction to adjust for this.

The statistical methods of this study were reviewed by Steven Lane from the Department of Biostatistics, University of Liverpool.

The full trial protocol can be accessed at: https://clinicaltrials.gov/ct2/show/NCT04901442?term=orthotic%2C+running+related+injury%2C+comfort&cntry=GB&draw=2&rank=1.

RESULTS

This article presents preliminary data from the first 47 participants recruited to this randomised control trial (intervention group = 23, control group = 24). The details of participant flow, including numbers of participants recruited, randomly allocated to a group, and included in analysis, as well as withdrawals, are provided in Figure 2.

Recruitment began in July 2021 and is planned to finish in October 2022. Participants ranged in age from 19 to 67 years old (mean age = 39.9 years old). Participants in the intervention group were, on average, older than participants in the control group, with a mean age of 42.2 and 37.8 years old, respectively. 61.7% of study participants were male, and both groups contained more males than females. Basic demographic data and clinical characteristics for the 47 participants included in the preliminary analysis are provided in Table 1.

All participants were analysed within their original assigned groups, and all participants in the intervention group ran with the orthotics for the entire study period. Data for all three primary outcomes were provided from a total of 254 runs by the 23 participants in the intervention group (an average of 11 runs per participant) and a total of 289 runs by the 24 participants in the control group (an average of 12 runs per participant). Results for each primary outcome in each group are provided in Table 2, along with the mean difference and its precision. Results show positive effects between the use of Aetrex[14] Orthotics and comfort and running speed compared with using no orthotic. The effect size for the use of the orthotics on comfort was 1.10 (95%CI 0.81-1.40), larger than for running speed, which showed an effect size of 0.28 (95%CI 0.06–0.50). These differences in comfort and running speed are statistically significant, with P values of < 0.0001 and 0.013, respectively.

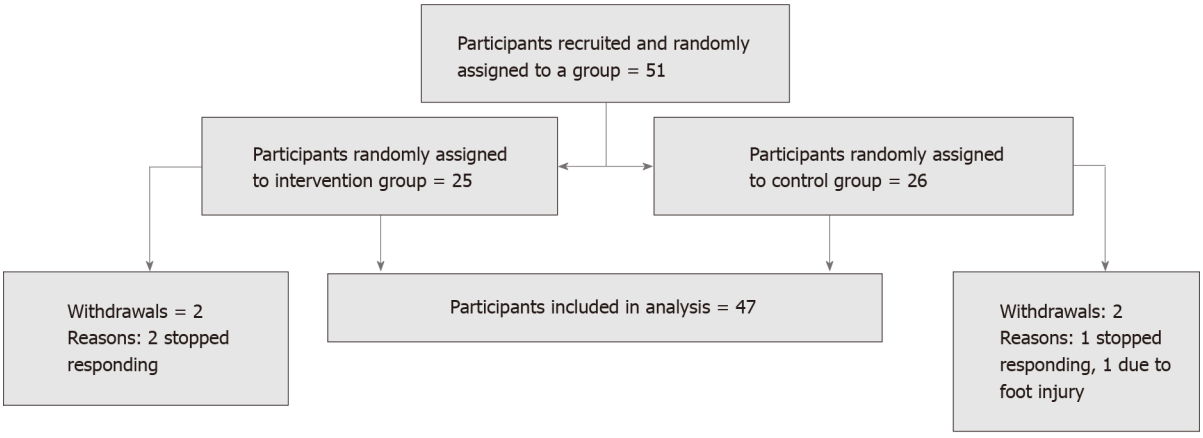
Table 1 Basic demographic information for participants included in preliminary analysis

	Orthotic group (%)	Control (no orthotic) group (%)	Total (%)
Sex			
Male	13 (56.5)	16 (66.7)	29 (61.7)
Female	10 (43.5)	8 (33.4)	18 (38.3)
Age (years)			
< 20	1 (4.3)	0 (0)	1 (2.1)
20-29	1 (4.3)	3 (12.5)	4 (8.5)
30-39	6 (26)	9 (37.5)	15 (31.9)
40-49	10 (43.5)	10 (41.7)	20 (42.6)
50-59	3 (13)	1 (4.2)	4 (8.5)
60-69	2 (8.7)	1 (4.2)	3 (6.4)
Total	23	24	47

Table 2 Data on all primary outcomes for both groups

	Intervention group	Control group	Mean difference (95%CI)	*P* value
Comfort	8.06 ± 1.41	6.96 ± 2.03	1.10 (0.81 to 1.40)	< 0.0001
Injury rate	0.70 ± 1.01	1.21 ± 1.53	-0.51 (-1.28 to 0.25)	0.18
Running speed (miles per hour)	6.27 ± 1.03	6.00 ± 1.54	0.28 (0.06 to 0.50)	0.013

Values for the intervention group and control group are expressed as mean ± standard deviation. Statistical analysis used *P* values from unpaired two-tailed t-tests with Welch's correction. Significant difference was considered if $P < 0.05$. CI: Confidence interval. Injury rate: Number of injuries reported per participant over the 8-wk study period.



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Figure 2 Participant flow, including randomised group assignment and any withdrawals.

Participants in the intervention group reported a lower RRI rate than the control group, with an average of 0.70 injuries per participant running with the orthotics during the study period, compared to 1.21 injuries per participant running with no orthotics. This corresponds to a negative effect of -0.51 (95%CI -1.28 to 0.25) for RRI rate with the orthotics compared with no orthotics. This difference, however, is not statistically significant ($P = 0.18$).

Table 2 also shows standard deviations for each mean value. These are generally large relative to mean values, demonstrating widespread data. As a result, 95% confidence intervals for effect sizes are also wide. Interestingly, standard deviations and confidence intervals for all outcome measures data were larger for the control group, indicating that the intervention group generally produced more consistent data.

Despite injury being measured in the study, it was ensured that no participants experienced any additional harm or injury as a result of taking part by asking all participants to run as they normally would, without changing their running frequency, duration or speed. The only intervention was the addition of orthotics in the running shoes of participants in the intervention group, which demonstrated a lower RRI rate than the control group. One participant withdrew from the study due to injury. However, they were assigned to the control group meaning their injury was not due to the study intervention. This participant did not require any medical intervention other than cessation of running.

DISCUSSION

This article presents preliminary results from a randomised control trial study investigating the impact of running with Aetrex[14] Orthotics inserted into normal running shoes on comfort, running speed and RRI rate compared with running in normal running shoes with no orthotics. It finds that participants who ran with Aetrex[14] Orthotics reported higher comfort scores and running speeds and lower RRI rates than those who ran with no orthotics. This confers with other studies that have tested prefabricated orthotics[8,9] and adds to the current evidence for orthotics improving these parameters. The working principle of orthotics in benefitting comfort and reducing injury relates to their function in distributing pressure across the soles of the feet and decreasing overpronation. This subsequently reduces the internal rotation of the lower limb joints, which in turn reduces the risk of pressure- and overpronation-associated lower limb injuries[18-20]. This working principle is illustrated in Figures 3 and 4.

In this preliminary report, the relationship between improved comfort during running with Aetrex [14] Orthotics showed the largest effect size, whereas improvements in running speed and reductions in RRI rate showed smaller effects. Improvements in comfort and running speed when running with the orthotics were statistically significant in this study. This is relevant and advances current evidence for orthotics in improving these parameters, as many previous studies have been unable to find significant improvements[9,10]. In contrast, the reduction in RRI rate with orthotics in this study was not significant. These findings suggest that orthotics may be a cost-benefit. However, a full cost analysis will be provided in the final study report.

The spread of data was high for all outcome measures; this may be partly due to the nature of the variables, as running speed varies greatly between different runners, likewise tendency for injury. This may partly explain why many previous studies have found benefits in comfort, running performance and injury reduction with orthotics use[17,21], but that was not statistically significant, and additionally why the reduction in RRI rate with orthotics in this study was not significant.

Strengths and limitations

A limitation of the data in this preliminary report is the small number of participants. Further analysis, once the study has recruited its target sample size (106 participants), will provide more reliable and reproducible results. Another limitation is the lack of blinding of participants following group assignment due to the nature of the study. Some improvements in comfort and performance reported by participants who were provided with an orthotic may have been due to the placebo effect if participants had expectations that the orthotic would improve these parameters. VAS was selected for comfort scoring as it has been shown to have high inter-session reliability when used for a comfort rating of footwear[15], but it is still a subjective measurement, creating the potential for bias.

The study sample demonstrates a wide range of ages (19 to 67 years old), adding to the generalisability of the results. It also reflects the 2017 Sport England Active Lives Survey[22] estimate of the characteristics of the UK running population, in that it contains a greater number of men than women, adding to the validity of the results. However, the voluntary nature of recruitment in this study means that its sample cannot be said to be representative of the general population.

No adjustments were made for group differences in certain variables, such as tendency to become injured and usual running speed, and these may have had confounding effects on the results. One way to improve reliability in this study could be to collect quantitative data from participants for normal injury tendency (e.g. number of weeks spent injured, or number of RRIs in the past one year) and running speed (e.g., average running speed overall runs in the past six months) and adjust for group differences in these parameters.

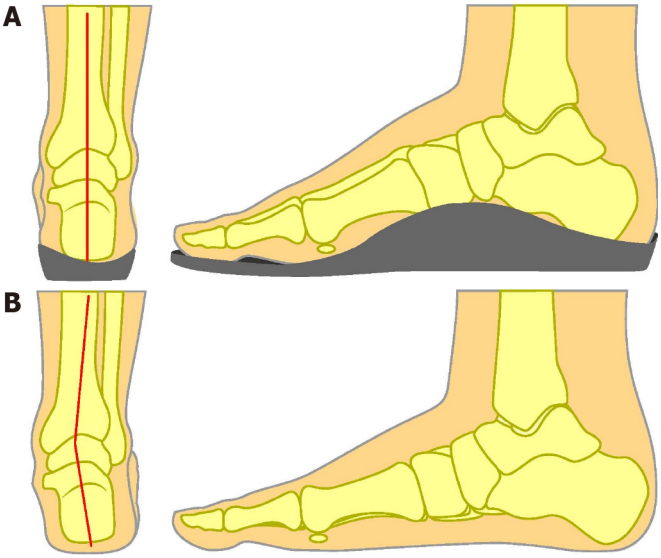
CONCLUSION

This preliminary report of randomised control trial data provides evidence that using Aetrex[14] Orthotics in normal running shoes increases comfort levels and speed during running and decreases RRI rates, with the relationship between orthotics use and improved comfort showing the largest effect size. However, only improvements in comfort and running performance were significant. The sample



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Figure 3 Internal rotation of lower limb joints and opposing external rotation of the patella caused by overpronation during running, which can lead to injuries.



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Figure 4 Working principle of orthotics. A: The correction of lower limb alignment by orthotics, by reducing overpronation; B: Compared to the lower limb misalignment present without orthotics, due to overpronation.

size included in this preliminary analysis is small (n = 47). Further analysis, once recruitment and data collection in this study is complete, will expand on the findings given in this report and provide a full analysis of the cost-benefit.

ARTICLE HIGHLIGHTS

Research background

There is currently mixed and limited evidence regarding the effectiveness of orthotics use in increasing comfort and speed and reducing injury rate during running.

Research motivation

Further research into the effect of orthotics use on running-related injury (RRI) rates would be helpful for the ever-growing population of runners, who frequently suffer from RRIs. Additionally, there is a need to clarify whether orthotics use increases comfort during running and helps improve running speed.

Research objectives

To investigate whether running with Aetrex Orthotics improves comfort and performance and reduces injury whilst running.

Research methods

A randomised control trial study design was used. Participants were regular runners over 18 with no serious health conditions, ongoing foot pain or deformity, previous foot surgery in their lifetime or any surgery in the past 6 months, recruited on a voluntary basis through local running clubs and social media advertisements. Participants were randomly assigned to either an intervention group or a control group. Participants in the intervention group ran with Aetrex orthotics inserted into their normal running shoes, whilst participants in the control group ran in their normal running shoes with no orthotics. All participants were asked to complete runs as they usually would and provide data regarding comfort during running, running time and distance, and any RRIs over an 8-wk study period. For each outcome variable, the mean for each group, effect size and 95% confidence interval were calculated, and a t-test was performed to determine if between-group differences were statistically significant.

Research results

This article presents the interim results from the first 47 participants recruited to this study (intervention group = 23, control group = 24), who provided data for all three primary outcomes from a total of 543 runs. Participants in the intervention group reported higher comfort scores (8.00 ± 1.41 *vs* 6.96 ± 2.03, $P \leq 0.0001$), faster running speeds (6.27 ± 1.03 *vs* 6.00 ± 1.54, $P = 0.013$), and lower RRI rates (0.70 ± 1.01 *vs* 1.21 ± 1.53, $P = 0.18$) than participants in the control group. Statistical significance was considered if $P < 0.05$. The findings were statistically significant for comfort and running speed but not for RRI rate.

Research conclusions

This interim report finds that using Aetrex Orthotics whilst running significantly increases comfort and speed. Using Aetrex Orthotics also reduces the rate of RRIs. However, this was not significant.

Research perspectives

Further analysis, once recruitment and data collection in this study is complete, is needed to expand on the findings given in this report and provide a full analysis of the cost-benefit of using orthotics for running.

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FOOTNOTES

Author contributions: Fortune AE, Sims JMG, Rhodes SJ, and Ampat G contributed equally to the study; Fortune AE, Sims JMG and Ampat G designed the research study; Sims JMG and Rhodes SJ were involved in recruitment and data collection; Ampat G performed telephone consultations with all participants on enrolment to the study; Fortune AE analysed the data and wrote the manuscript; all authors have read and approved the final manuscript.

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Institutional review board statement: This study was reviewed and approved by Wales Research Committee 5 (reference number: 21/WA/0098).

Clinical trial registration statement: This study is registered at https://clinicaltrials.gov/ct2/show/NCT04901442. The registration identification number is: NCT04901442.

Informed consent statement: All study participants gave their informed, written consent (via an online e-form) prior to study inclusion.

Conflict-of-interest statement: George Ampat, Jonathan M G Sims and Samantha J Rhodes are Directors/employees of Talita Cumi Ltd. Talita Cumi Ltd has a commercial relationship with Aetrex, Inc. 414 Alfred Avenue Teaneck, NJ 07666, USA. Alice E Fortune has no conflict of interest.

Data sharing statement: The anonymised dataset is available from the corresponding author at g.ampat@liverpool.ac.uk. Participants gave informed consent for sharing of anonymised data.

CONSORT 2010 statement: The authors have read the CONSORT 2010 Statement, and the manuscript was prepared and revised according to the CONSORT 2010 Statement.

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REFERENCES

1 **Koplan JP**, Rothenberg RB, Jones EL. The natural history of exercise: a 10-yr follow-up of a cohort of runners. *Med Sci Sports Exerc* 1995; **27**: 1180-1184 [PMID: 7476063]
2 **van Gent RN**, Siem D, van Middelkoop M, van Os AG, Bierma-Zeinstra SM, Koes BW. Incidence and determinants of lower extremity running injuries in long distance runners: a systematic review. *Br J Sports Med* 2007; **41**: 469-80; discussion 480 [PMID: 17473005 DOI: 10.1136/bjsm.2006.033548]
3 **Taunton JE**, Ryan MB, Clement DB, McKenzie DC, Lloyd-Smith DR, Zumbo BD. A retrospective case-control analysis of 2002 running injuries. *Br J Sports Med* 2002; **36**: 95-101 [PMID: 11916889 DOI: 10.1136/bjsm.36.2.95]
4 **Kemler E**, Blokland D, Backx F, Huisstede B. Differences in injury risk and characteristics of injuries between novice and experienced runners over a 4-year period. *Phys Sportsmed* 2018; **46**: 485-491 [PMID: 30071170 DOI: 10.1080/00913847.2018.1507410]
5 **van der Worp MP**, ten Haaf DS, van Cingel R, de Wijer A, Nijhuis-van der Sanden MW, Staal JB. Injuries in runners; a systematic review on risk factors and sex differences. *PLoS One* 2015; **10**: e0114937 [PMID: 25706955 DOI: 10.1371/journal.pone.0114937]
6 **Finestone A**, Giladi M, Elad H, Salmon A, Mendelson S, Eldad A, Milgrom C. Prevention of stress fractures using custom biomechanical shoe orthoses. *Clin Orthop Relat Res* 1999; 182-190 [PMID: 10101324 DOI: 10.1097/00003086-199903000-00022]
7 **Gerych D**, Tvrznik A, Prokesova E, Nemeckova Z, Jelen K. Analysis of peak pressure, maximal force, and contact area changes during walking and running with conventional and shock-absorbing insoles in the combat boots of the Czech army. *J Mech Med Biol* 2013; **13** [DOI: 10.1142/s0219519413500425]
8 **Mündermann A**, Stefanyshyn DJ, Nigg BM. Relationship between footwear comfort of shoe inserts and anthropometric and sensory factors. *Med Sci Sports Exerc* 2001; **33**: 1939-1945 [PMID: 11689747 DOI: 10.1097/00005768-200111000-00021]
9 **Bonanno DR**, Landorf KB, Munteanu SE, Murley GS, Menz HB. Effectiveness of foot orthoses and shock-absorbing insoles for the prevention of injury: a systematic review and meta-analysis. *Br J Sports Med* 2017; **51**: 86-96 [PMID: 27919918 DOI: 10.1136/bjsports-2016-096671]
10 **Larsen K**, Weidich F, Leboeuf-Yde C. Can custom-made biomechanic shoe orthoses prevent problems in the back and lower extremities? *J Manipulative Physiol Ther* 2002; **25**: 326-331 [PMID: 12072853 DOI: 10.1067/mmt.2002.124419]
11 **Fuller JT**, Bellenger CR, Thewlis D, Tsiros MD, Buckley JD. The effect of footwear on running performance and running economy in distance runners. *Sports Med* 2015; **45**: 411-422 [PMID: 25404508 DOI: 10.1007/s40279-014-0283-6]
12 **Crago D**, Bishop C, Arnold JB. The effect of foot orthoses and insoles on running economy and performance in distance runners: A systematic review and meta-analysis. *J Sports Sci* 2019; **37**: 2613-2624 [PMID: 31423908 DOI: 10.1080/02640414.2019.1651582]
13 **O Sullivan IJ**, Johnson MI, Hind K, Breen S, Francis P. Are changes in running economy associated with changes in performance in runners? *J Sports Sci* 2019; **37**: 1521-1533 [PMID: 30810467 DOI: 10.1080/02640414.2019.1575177]
14 **Aetrex**. Aetrex.com [Internet]. Aetrex.com: Aetrex Worldwide, Inc.; 2022 [DOI: 10.1089/glre.2016.201011]
15 **Lindorfer J**, Kröll J, Schwameder H. Comfort assessment of running footwear: Does assessment type affect inter-session

reliability? *Eur J Sport Sci* 2019; **19**: 177-185 [PMID: 30044208 DOI: 10.1080/17461391.2018.1502358]

16 **Yamato TP**, Saragiotto BT, Lopes AD. A consensus definition of running-related injury in recreational runners: a modified Delphi approach. *J Orthop Sports Phys Ther* 2015; **45**: 375-380 [PMID: 25808527 DOI: 10.2519/jospt.2015.5741]

17 **Richter RR**, Austin TM, Reinking MF. Foot orthoses in lower limb overuse conditions: a systematic review and meta-analysis--critical appraisal and commentary. *J Athl Train* 2011; **46**: 103-106 [PMID: 21214358 DOI: 10.4085/1062-6050-46.1.103]

18 **Bonanno DR**, Landorf KB, Menz HB. Pressure-relieving properties of various shoe inserts in older people with plantar heel pain. *Gait Posture* 2011; **33**: 385-389 [PMID: 21256025 DOI: 10.1016/j.gaitpost.2010.12.009]

19 **Albert S**, Rinoie C. Effect of custom orthotics on plantar pressure distribution in the pronated diabetic foot. *J Foot Ankle Surg* 1994; **33**: 598-604 [PMID: 7894408]

20 **Desmyttere G**, Hajizadeh M, Bleau J, Begon M. Effect of foot orthosis design on lower limb joint kinematics and kinetics during walking in flexible pes planovalgus: A systematic review and meta-analysis. *Clin Biomech (Bristol, Avon)* 2018; **59**: 117-129 [PMID: 30227277 DOI: 10.1016/j.clinbiomech.2018.09.018]

21 **Hume P**, Hopkins W, Rome K, Maulder P, Coyle G, Nigg B. Effectiveness of foot orthoses for treatment and prevention of lower limb injuries : a review. *Sports Med* 2008; **38**: 759-779 [PMID: 18712943 DOI: 10.2165/00007256-200838090-00005]

22 **SportEngland**. Active Lives Adult Survey: May 16/17 Report [Internet]. England: Sport England; 2017 [DOI: 10.1093/ww/9780199540884.013.u225130]

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SYSTEMATIC REVIEWS

Clinical and mechanical outcomes in isolated anterior cruciate ligament reconstruction *vs* additional lateral extra-articular tenodesis or anterolateral ligament reconstruction

Nikhil Agarwal, Jaibaji Monketh, Andrea Volpin

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Abstract

BACKGROUND

Anterior cruciate ligament (ACL) reconstruction has been a successful treatment for ACL rupture. However ongoing rotational instability can be an issue. Several surgical techniques have been recommended to overcome this including lateral extra-articular tenodesis (LET) and more recently anterolateral ligament reconstruction (ALLR).

AIM

To compare the clinical outcomes following ACL reconstruction (ACLR) alone or ACLR with either LET or ALLR.

METHODS

A systematic review was conducted by means of four databases (MEDLINE, EMBASE, Cochrane and Clinical.Trials.Gov), and the *Reference Citaion Analysis* (https://www.referencecitationanalysis.com/) to identify all studies investigating either or both of LET and ALLR. The Critical Appraisal Skills Programme checklist for cohort studies was employed for critical appraisal and evaluation of all twenty-four studies which met the inclusion criteria.

RESULTS

Pooled meta-analyses illustrated that ACLR with additional LET or ALLR results in improved pivot shift test scores, compared to isolated ACLR. There was no statistically significant difference in International Knee Documentation Committee (IKDC) clinical scores with addition of either LET or ALLR. ACL re-rupture

rates were compared between LET and ALLR techniques. There was a statistically significant difference between techniques, with a 1.14% rupture rate in ACLR +ALLR, and 4.03% rupture rate in ACLR + LET. Isolated ACLR re-rupture rates were 12.59%, significantly higher than when augmented with either ALLR or LET ($P < 0.0001$ for both groups). There were no statistical differences in pivot shift test or IKDC scores between LET and ALLR techniques.

CONCLUSION

This meta-analysis has found that use of either LET or ALLR in addition to ACLR results in improved mechanical outcomes suggesting surgeons should consider augmenting ACLR with an extra-articular procedure in patients with rotatory instability. Furthermore, both anterolateral extra articular procedures in addition to ACLR lead to reduced ACL re-rupture rates compared to isolated ACLR. Moreover, ALLR results in reduced ACL re-rupture rates, compared to LET. More research is needed to compare the two respective extra-articular procedures.

Key Words: Anterior cruciate ligament; Knee; Systematic review; Lateral extra tenodesis; Anterolateral ligament; Knee surgery

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Core Tip: Either lateral extra-articular tenodesis (LET) or anterolateral ligament reconstruction (ALLR) should be utilized with anterior cruciate ligament (ACL) reconstruction (ACLR) in patients with rotational instability, to confer greater stability. Either technique, together with ACLR, leads to superior mechanical outcomes, in comparison to ACLR alone. Both techniques reduce risk of ACL re-rupture, compared to isolated ACLR, with ALLR having lower rates than LET.

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INTRODUCTION

Rupture of the anterior cruciate ligament (ACL) is one of the most common sporting injuries affecting the knee joint. In the United Kingdom, the National Ligament Registry has noted over 15304 cases of ACL rupture between 2012 and 2019[1].

Those with symptomatic instability have traditionally been treated with arthroscopic ACL reconstruction (ACLR). Numerous studies demonstrate excellent short term functional outcomes however some questions remain regarding this treatment[2,3]. ACLR has demonstrated to be effective in restoring translational stability, however the capacity to restore rotational stability is limited[4,5]. Patient reported outcome measures tend to correlate with improvements in translational rather than rotational stability. Moreover, rotational instability has been implicated in the development of knee osteoarthritis. Despite technical improvements, such as single or double bundle reconstructions and more accurate tunnel placement, the rates of positive pivot-shift test remain unacceptably high.

The role of the anterolateral soft tissue restraints (including the anterolateral ligament (ALL)) in rotational stability are increasingly being recognized[6,7]. Historically, several anterolateral extra articular procedures (AEAP) had been developed to tackle anterolateral instability, including lateral extra-articular tenodesis (LET), originally described by Lemaire[8]. There is conflicting evidence in the literature surrounding LET. Some studies have shown that LET provides no additional benefit when performed in combination with ACLR, compared to isolated ACLR[9,10]. Other studies have found that in high-risk patients, such as those with additional laxity, LET results in reduced graft rupture and reduces rotatory laxity[11,12]. More recently, with the newfound understanding of biomechanics and anatomy, another procedure, anterolateral ligament reconstruction (ALLR) has been developed. Biomechanical studies have shown variable restoration of knee kinematics in addition to concerns that the technique may lead to over constraint of the lateral compartment; thus, actually accelerating degenerative changes[13,14].

The aim of this systematic review and meta-analysis was to firstly compare the clinical effectiveness of ACLR combined with LET or ALLR, to ACLR alone. Secondly, to compare the clinical and mechanical outcomes of the two AEAPs discussed.

MATERIALS AND METHODS

Database and inclusion criteria

A systematic review in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRSIMA) was conducted[15]. Using the PICO model, inclusion and exclusion criteria were set[16]. Only randomized control trials (RCTs) cohort, cross-sectional studies and case control studies were included. Reviews, conference abstracts, case series, case reports and editorials were excluded. Only studies which investigated either ACL reconstruction with additional ALLR or LET were included. Studies which investigated revision ACLR were excluded. The references of the final studies were checked for any additional studies that would meet the inclusion criteria.

A literature search was carried out by A. N. Four databases were searched for studies which were relevant to this systematic review: MEDLINE (2000 to Week 4 November 2021), EMBASE (2000 to 29 November 2021), Cochrane library (2000 to November 2021) and clinical trials.gov (2000 to November 2021). The *Reference Citaion Analysis* (https://www.referencecitationanalysis.com/) software was also utilized to identify any additional studies.

A comprehensive strategy was developed, upon which the databases were searched. This was designed on the basis of the guidelines provided by the Cochrane Highly Sensitive Search Strategy[17]. This included but was not restricted to the following MeSH terms: "Anterior Cruciate Ligament", or "tenodesis" or "iliotibial band" or "extra articular" and "reconstruction" or "Anterior Cruciate Ligament Reconstruction". Full MeSH terms used can be found in Appendix 1 (Supplementary material). Only *in vivo* studies were included. In addition, it was decided that only studies from 2000 onwards should be included, since studies before this time could be considered outdated, considering the novel developments in orthopaedic surgery. The authors only wanted to examine novel techniques which are currently in use in clinical practice. The overall results of the comprehensive search are shown in Figure 1. The structure of this table was incorporated from Page *et al*[18].

Quality assessment

All studies included in this review were independently appraised by two authors A. N and J. M. The critical appraisal was conducted by the Critical Appraisal Skills Programme (CASP) checklists for randomized controlled trials, cohort studies and case control studies[19]. The appraisals for each RCT can be found in Table 1 and appraisals for cohort studies can be found in Table 2. One study was of case control study design. This was assessed accordingly by the CASP checklist for case control studies. The questions in each of the checklists are listed in Appendix 2 (Supplementary material). Any disagreements were solved by discussion.

Data extraction

The following study characteristics were extracted from each study after full text analysis: study design, number of patients included in the study, country of origin, mean follow up time, type of AEAP investigated, outcomes measured, and year published.

Statistical analysis

All statistical analysis was conducted using JASP (version 0.16, University of Amsterdam). A restricted maximum likelihood random effects model was used to generate a pooled estimate of the odds ratio of an "event" for analysis of post-operative pivot shift test and International Knee Documentation Committee (IKDC) score. I^2 test was used as a measure of between study heterogeneity. The pivot shift test is a validated tool to assess rotatory instability, is highly sensitive and specific for ACL rupture and the presence of a positive results does correlate well with clinical outcomes[20]. The IKDC score has also been shown to have a high criterion validity in assessment of treatment outcome and is widely used [21]. As these two measures could be recorded as categorical variables they were selected for meta-analysis. For the purpose of the analysis and in line with previous published literature we considered a pivot shift test grades 1, 2 or 3 was defined as an event[22]. For the IKDC score an overall grade C (abnormal) or D (severely abnormal) was considered an event. Statistical analysis on categorical data was performed using cross tabulation and Chi squared testing for categorical data, or Fisher's exact test if the sample size did not permit Chi Squared testing. A P value of < 0.05 was considered statistically significant.

RESULTS

Study characteristics

Table 3 displays the study characteristics of all 24 studies encompassed in this review. Most studies were cohort studies, with 6 retrospective, 5 prospective and 2 matched cohort studies (n = 2). Ten studies were RCTs. One study was a case control study.

Table 1 Critical appraisal of randomised control trials, using Critical Appraisal Skills Programme checklist for randomised control trials, *n* = 10

Ref.	Q1	Q2	Q3	Q4a	Q4b	Q4c	Q5	Q6	Q7	Q8	Q9	Q10	Q11
Chiba *et al*[23]	Yes	Yes	Yes	Yes	No	No	Yes	Yes	Yes	Yes	Yes	Yes	No
Getgood *et al*[12]	Yes	Yes	Yes	No	No	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Hamido *et al*[39]	Yes	Yes	Yes	No	No	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Ibrahim *et al*[40]	Yes	Yes	Yes	No	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No
Mogoş *et al*[24]	Yes	Yes	Yes	No	No	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Porter *et al*[41]	Yes	Yes	Yes	No	No	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Sonnery-Cottet *et al*[25]	Yes	Yes	Yes	No	No	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Stensbirk *et al*[42]	Yes	Yes	Yes	No	No	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Trichine *et al*[43]	Yes	Yes	Yes	Yes	No	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Vadalà *et al*[44]	Yes	Yes	Yes	No	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes

Table 2 Critical appraisal of cohort studies, using Critical Appraisal Skills Programme checklist for cohort studies, *n* = 13: Questions 7, 8 and 12 were left out of the table due to the fact they are not yes/no questions

Ref.	Q1	Q2	Q3	Q4	Q5a	Q5b	Q6a	Q6b	Q9	Q10	Q11
Ahn *et al*[45]	Yes	Yes	Yes	Yes	No	Can't tell	Yes	Yes	Yes	Yes	Yes
Dejour *et al*[46]	Yes	Yes	Yes	Yes	Yes	Can't tell	Yes	No	Yes	Yes	Yes
Erden *et al*[47]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes
Ferretti *et al*[33]	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes
Giraud *et al*[48]	Yes	Yes	Yes	Yes	No	Can't tell	Yes	No	Yes	Yes	Yes
Goncharov *et al*[49]	Yes	Yes	Yes	Yes	No	No	Yes	No	Yes	Yes	Yes
Lee *et al*[50]	Yes	Yes	Yes	Yes	Yes	Can't tell	Yes	No	Yes	Yes	Yes
Mahmoud *et al*[11]	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes
Rowan *et al*[51]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes
Sonnery-Cottet *et al*[52]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes
Sonnery-Cottet *et al*[53]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes
Sonnery-Cottet *et al*[36]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Ventura *et al*[54]	Yes	Yes	Yes	Yes	No	Can't tell	Yes	Yes	Yes	Yes	Yes

Thirteen studies compared ACLR to ACLR + LET. The remaining 11 were studies which compared ACLR to ACLR + ALLR.

The most common range of follow up times was 37-60 mo (*n* = 7). Six studies had a follow up time between 13 and 24 mo. Only 5 of studies used follow up times greater than 60 mo. Thirteen of the studies included in this review, had a follow up duration time less than 37 mo.

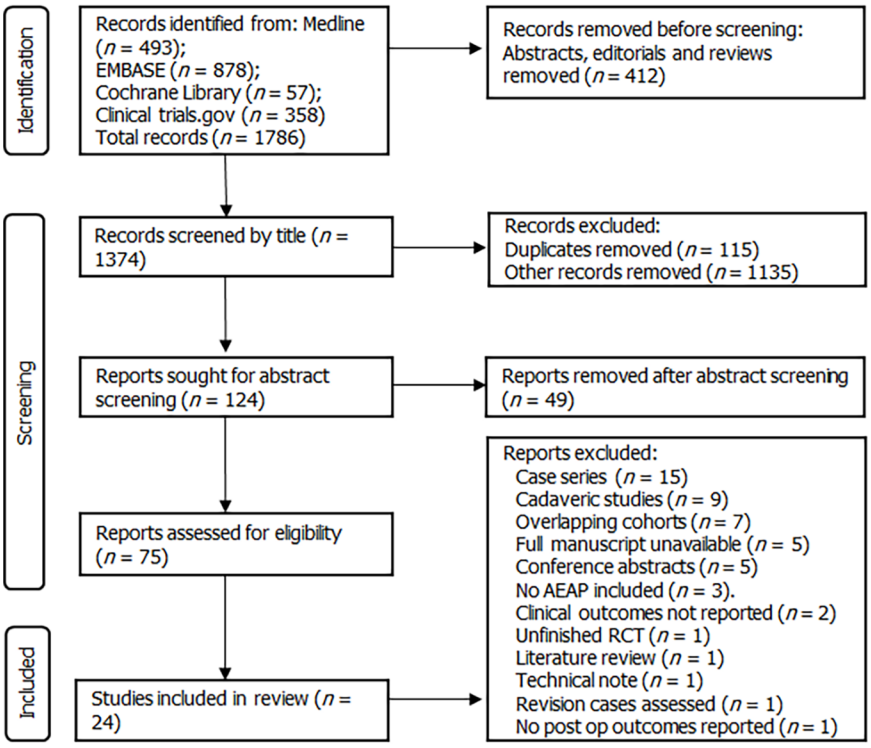
Upon critical appraisal of the studies included in this review, using the appropriate CASP tools, it was established that very few RCTs included in this review were blinded. This was however, recognized by most studies, who considered it unfeasible to blind the patients, and impractical to blind the surgeons. Some of the cohort studies included in this review did not account for or did not mention confounding variables, which could have led to unforeseen biases. Three of the studies also were deemed to have short follow up (< 24 mo). While it was recognized the reliably of the meta-analysis would be improved by only including studies with longer follow up (> 24 mo), it was the consensus of the authors that the large number of patients and the overall quality of the studies meant the data present in these three studies would add robustness to the meta-analysis as such they were included[23-25]. Overall, the quality of all studies included in this review was high. Tables 1 and 2 demonstrate the full methodological quality assessment of the included studies.

Table 3 Characteristics of the studies included in the review, *n* = 24

Study characteristic	*n* (%)
Study design	
Randomised controlled trial	10 (42)
Prospective cohort study	5 (21)
Retrospective cohort study	6 (25)
Matched cohort study	2 (8)
Case control study	1 (4)
Country of origin	
France	6 (25)
Italy	4 (17)
Australia	2 (8)
South Korea	2 (8)
United States	1 (4)
Kuwait	2 (8)
Turkey	1 (4)
United Kingdom	1 (4)
Brazil	1 (4)
Russia	1 (4)
Canada	1 (4)
Denmark	1 (4)
Algeria	1 (4)
Year published	
2006	1 (4)
2012	1 (4)
2013	1 (4)
2014	2 (8)
2016	1 (4)
2017	2 (8)
2018	1 (8)
2019	4 (17)
2020	4 (17)
2021	7 (29)
Number of patients	
< 50	2 (8)
50-100	10 (42)
100-250	8 (33)
250-500	2 (8)
> 500	2 (8)
Mean follow-up time	
1-12 mo	2 (8)
13 -24 mo	6 (25)
25-36 mo	4 (17)

37-60 mo	7 (29)
61-120 mo	4 (17)
> 120 mo	1 (4)
Type of AEAP	
LET	13 (54)
ALLR	11 (46)

AEAP: Anterolateral extra articular procedures; LET: Lateral extra articular tenodesis; ALLR: Anterolateral ligament reconstruction.



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Figure 1 Results from the comprehensive literature search.

Clinical outcomes

Table 4 summarizes the main characteristics of all the studies included in this systematic review.

Forest plots were created to analyze clinical and mechanical outcomes most utilized by all studies in ACLR only patient groups *vs* ACLR + AEAP patient groups (Figure 2).

Figure 2A shows analysis of all nine studies which used pivot shift test scores to analyze mechanical outcomes in ACLR only patient groups *vs* ACLR + AEAP patient groups. The nine studies that could be used in analysis encompassed 961 knees. Six of the nine studies demonstrated a statistically significant difference in pivot shift test scores between ACLR only patient groups and ACLR + AEAP patient groups. The pooled estimates of odds ratio were -1.54 (95%CI -2.02 to -1.06, $P < 0.001$) in favor of ACLR + AEAP. This suggests that the addition of AEAP to ACLR results in statistically significantly better pivot shift test scores and therefore greater rotational stability.

Comparison of clinical outcomes between ACLR only and ACLR + AEAP patient groups was conducted using IKDC scores. Five studies were eligible for pooled analysis, which encompassed 878 knees (Figure 2B). There was no statistically significant difference in IKDC scores between the ACLR only and ACLR + AEAP patient groups in any of the five studies. The pooled estimates of log ratio were -0.34 (95%CI -1.04 to 0.37). This demonstrated that the addition of AEAP to ACLR did not result in any statistically significant improvement in IKDC clinical scores ($Z = -0.938$, $P = 0.348$).

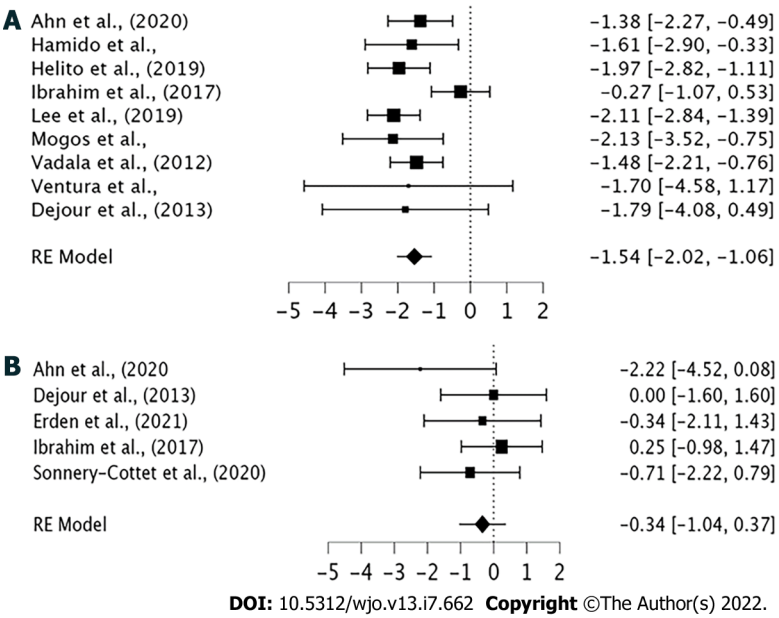
Following statistical analysis of ACLR alone *vs* ACLR + AEAP, analysis was then conducted to determine whether there was a difference in clinical and mechanical outcomes between the two AEAPs included: LET and ALLR. The chi squared test was performed which demonstrated that there was no statistically significant difference in pivot shift tests between ACLR + LET and ACLR + ALLR groups ($P = 0.39$). The chi squared test also showed that there was no statistically significant difference in IKDC

Table 4 Main characteristics of studies included in this systematic review, *n* = 24

Ref.	Design of study	AEAP used	Number of patients involved	Mean follow up	Outcome measures used	Technique favoured
Ahn *et al*[45]	Retrospective cohort study	LET	171	49.7 ± 5.7 mo	IKDC, KL grade, graft maturation score and revision rates	ACLR with LET favoured over ACLR alone
Chiba *et al*[23]	RCT	LET	18	12 mo	Anterior tibial translation, KOOS, tibial rotation relative to the femur	ACLR with LET is not superior to ACLR alone
Dejour *et al*[46]	Prospective cohort study	LET	75	25 mo	Anterior tibial translation, IKDC, pivot shift grading	ACLR with LET favoured over ACLR alone
Erden *et al*[47]	Retrospective cohort study	ALLR	63	24 mo	Cincinnati knee score, IKDC, Lysholm scores, graft rupture rate, anterior tibial translation, pivot shift test	ACLR with ALLR is not superior to ACLR alone
Ferretti *et al*[33]	Retrospective cohort study	LET	140	120 mo	Lysholm score, IKDC, Tegner score, anterior tibial translation	ACLR with LET favoured over ACLR alone
Getgood *et al*[12]	RCT	LET	618	24 mo	P4, KOOS, Marx Activity Rating scale, IKDC, ACL QOL	ACLR with LET favoured over ACLR alone
Giraud *et al*[48]	Prospective cohort study	LET	63	84 mo	IKDC, anterior tibial translation, radiological medial and lateral compartment laxity	ACLR with LET is not superior to ACLR alone
Goncharov *et al*[49]	Prospective cohort study	ALLR	50	24 mo	Tegner Lysholm score, IKDC, Lachmann test, Pivot shift test	ACLR with ALLR is not superior to ACLR alone
Hamido *et al*[39]	RCT	ALLR	107	60 mo	IKDC, anterior tibial translation, Tegner score, Lysholm score	ACLR with ALLR favoured over ACLR alone
Helito *et al*[55]	Case control study	ALLR	90	29.6 ± 6.2 mo for group 1; 28.1 ± mo for group 2	Anterior tibial translation, IKDC, Lysholm, Tegner score Pivot shift test, rupture rates	ACLR with ALLR favoured over ACLR alone
Ibrahim *et al*[40]	RCT	ALLR	103	27 mo	Anterior tibial translation, IKDC, Lysholm score, Tegner score, Pivot shift test	ACLR with ALLR is not superior to ACLR alone
Lee *et al*[50]	Retrospective cohort study	ALLR	87	36 mo	ACL-RSI, Anterior tibial translation, IKDC, Lysholm score, Tegner score	ACLR with ALLR is not superior to ACLR alone
Mahmoud *et al*[11]	Matched cohort study	LET	144	120 mo	IKDC, Lysholm score, OKS, Tegner score	ACLR with LET favoured over ACLR alone
Mogoş *et al*[24]	RCT	ALLR	57	12 mo	IKDC, Lysholm score, Pivot shift test, Rolimeter test, Tegner score	ACLR with ALLR favoured over ACLR alone
Porter *et al*[41]	RCT	LET	55	24 mo	IKDC, Lysholm score, KOOS, Tegner score	ACLR with LET favoured over ACLR alone
Rowan *et al*[51]	Prospective cohort study	LET	273	52 mo	Lysholm score, Tegner score	ACLR with LET favoured over ACLR alone
Sonnery-Cottet *et al*[52]	Prospective cohort study	ALLR	502	38.4 ± 8.5 mo	IKDC, Lysholm score, Side to side laxity, Tegner score	ACLR with ALLR favoured over ACLR alone
Sonnery-Cottet *et al*[53]	Retrospective cohort study	ALLR	383	37.4 mo	Lysholm score, Side to side laxity, Tegner score	ACLR with ALLR favoured over ACLR alone
Sonnery-Cottet *et al*[25]	RCT	ALLR	224	12.3 ± 1.9 mo	IKDC, Lysholm score, KOOS, Range of motion, Tegner score	ACLR with ALLR favoured over ACLR alone

Sonnery-Cottet *et al*[36]	Matched cohort study	ALLR	172	104.33 ± 3.74 mo	IKDC, Lysholm score, KOOS, Side to side laxity, Tegner score	ACLR with ALLR favoured over ACLR alone
Stensbirk *et al* [42]	RCT	LET	60	180 mo	AKP questionnaire, Lysholm score, Tegner score	ACLR with LET is not superior to ACLR alone
Trichine *et al*[43]	Single blinded RCT	LET	120	24 mo	IKDC, Objective laxity	Inconclusive
Vadalà *et al*[44]	RCT	LET	60	44.6 mo	Anterior tibial translation, IKDC, Lysholm score, Tegner score, VAS	ACLR with LET favoured over ACLR only
Ventura *et al*[54]	Retrospective cohort study	LET	24	54 mo	Anterior tibial translation, IKDC, Lysholm score, Tegner score	ACLR with LET favoured over ACLR alone

AEAP: Anterolateral extra articular procedures; ACL-RSI: Anterior cruciate ligament – return to sport after injury; ALLR: Anterolateral ligament reconstruction; AKP: Anterior knee pain; IKDC: International Knee Documentation Committee; KOOS: Knee injury and Osteoarthritis Outcome Score; LET: Lateral extra articular tenodesis; OKS: Oxford Knee Score; RCT: Randomised controlled trial; VAS: Visual analogue scale.



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Figure 2 Forest plot. A: The effect size of pivot shift test scores in patients who underwent anterolateral extra articular procedures (AEAP) in addition to anterior cruciate ligament reconstruction (ACLR), compared to ACLR alone. I^2 = 47.192; B: The effect size of International Knee Documentation Committee scores in patients who underwent AEAP in addition to ACLR, compared to ACLR alone. I^2 = 6.432e-6. RE: Random effects.

scores between ACLR + LET and ACLR + ALLR groups (P = 0.90). This indicates that there are no differences in rotational stability or clinical outcomes with regards to the specific AEAP (LET or ALLR) utilized with ACLR.

ACL re rupture rates were also compared between ACLR + LET and ACLR + ALLR techniques. There was a statistically significant difference between techniques, with a 1.14% re rupture rate in ACLR + ALLR, and 4.03% re rupture rate in ACLR + LET (P = 0.015). This indicated that ACL re-rupture rates were higher in ACLR + LET compared ACLR + ALLR. The re-rupture rate for ACLR alone across all studies was 12.59%, significantly higher than when augmented with either ALLR or LET (P < 0.0001 for both groups).

DISCUSSION

ACLR has shown excellent results in restoring translational stability. The capacity to restore rotational stability, however, remains an issue. This review has focused on the clinical and mechanical outcomes which follow treatment of primary ACL injuries with AEAPs, in addition to ACLR. The supplementation of an AEAP does appear to improve mechanical outcomes compared to ACLR alone. This suggests that patients with rotatory instability should be offered an AEAP with the ACLR

reconstruction. However, there appears to be no difference in mechanical outcomes between AEAPs, which suggests that either LET or ALLR can be used with ACLR to reduce rotational instability. Our results did not show any benefits in clinical outcomes with the addition of AEAP to ACLR. An important consideration to note is that, since we have demonstrated there may not necessarily be direct clinical benefit in all patients, the challenge will be to identify patients where the risk-benefit analysis would favour AEAP. Both LET and ALLR can cause issue over constraint with poor graft placement which may worsen patient outcomes.

The most common mechanical outcome measured in the studies included in this review was the pivot shift test scores. Other mechanical outcomes investigated by studies included; KT 1000/-2000 arthrometry side to side laxity, anterior tibial translation, Lachmann test, Rolimeter test scores and radiological medial and lateral compartment laxities. Analysis of instability using the latter techniques mentioned was not conducted due to the inconsistent use of these scoring systems between studies, and the small number of studies which employed each. The combined analyses of pivot shift test scores demonstrated that use of AEAP in addition to ACLR results in better pivot shift test scores, compared to ACLR alone. However, upon comparison of the ACLR + LET *vs* ACLR + ALLR there is no statistically significant difference in mechanical outcomes between these two groups. This suggests that though ACLR + AEAPs confers greater rotational stability than ACLR alone, neither technique confers more rotational stability than the other.

Studies have shown that poorer pivot shift test scores correlate to poorer clinical outcomes and patient satisfaction following ACLR[26,27]. Moreover, recent cadaveric studies have demonstrated that ACLR alone does not restore normal knee kinematics, and that an AEAP is required to restore anterior tibial translation and tibiofemoral motion[28,29].

The most common clinical outcome utilized by studies was IKDC scores. Other clinical scores used were: Lysholm score, Tegner score, KOOS score and Cincinnati knee score. Analysis of clinical outcomes, using these latter scoring systems was not conducted due to the small number of studies which employed each one. The pooled analyses of the IKDC scores demonstrated that use of an AEAP with ACLR does not result in any statistical improvements in outcomes. There are several possibilities for this. There may be a ceiling effect to IKDC score making it insensitive in detecting improvements in rotatory stability. We also utilized overall scores and dichotomized the outcomes; this may have also reduced the sensitivity of the analysis.

When directly comparing ALLR with LET, re-rupture rates were higher with LET (1.14% *vs* 4.03%, $P = 0.015$). The re-rupture rate for ACLR alone across all studies was 12.59%, significantly higher than when augmented with either ALLR or LET ($P < 0.0001$ for both groups). Studies that evaluated ACLR + LET were then compared with studies which assessed ACLR + ALLR. Direct analysis shows that ACL re-rupture rates were higher in ACLR + LET than with ACLR + ALLR. This suggests that LET techniques have a higher ACL re rupture rate. However, existing literature suggests that ACL re-rupture rates are higher in ACLR alone compared with ACLR with AEAPs. A study conducted by Marom *et al*[30], found that the addition of LET to ACLR reduces stress on the graft, by transferring loads to the LET. In addition, this reduces anterior tibial translation when pivoting loads are applied [30]. The reduced strain on the graft would explain why AEAPs lead to reduced re-rupture rates.

There were no studies in the literature which directly compared LET with ALLR. This is understandable given the recent growing interest in ALLR. Certainly, randomized controlled trials are required to assess the two techniques. As ALLR becomes more common practice in the future this will likely become feasible. Ra *et al*[31] did compare the studies using ACLR + LET with ACLR + ALLR in 2020. Their meta-analysis of non-comparative could not demonstrate a significant difference in rotational stability between ALLR and LET.

There are risks associated with LET procedure. LET is a non-anatomical reconstructive procedure potentially giving it inherent disadvantages over ALLR. While there is evidence to suggest it does help restore normal knee kinematics following ACL injury, there are concerns in the literature that the knee may become over constrained[28,32]. Biomechanical studies have investigated the effects of over constraining[28,32]. Several studies reporting on LET have recommended the graft be fixed with the knee in extension. This could interfere with the "screw home" mechanism of the knee by acting as a restraint to tibial internal rotation[28]. Tibiofemoral contact pressures could increase, thus accelerating the development of osteoarthritis. In addition, this would increase tensile forces the knee is subjected to through the action of the extensor mechanism, potentially increasing the risk of graft rupture. This could explain why our date shows increased risk of graft rupture in LET compared to ALLR. However, these same studies have noted that if the graft is tensioned in neutral, risk of overstraining decreases and there is little risk of accelerated osteoarthritis[28,32]. The study by Ferretti *et al*[33] demonstrated that at a 10 year follow up, ACLR with LET did not result in increased osteoarthritic rates. This perhaps underscores the importance of sound surgical technique, as more experience is gained with LET, we may see improved outcomes with respect to over constraining of the lateral compartment. Longer term follow-up studies are needed to examine the risk of osteoarthritis further.

Similar concerns have been voiced for ALLR techniques. A recent cadaveric study demonstrated that over constraining is possible with ALLR[34]. A separate study by Neri *et al*[35] illustrated that ALLR does not lead to increased contact pressures in the lateral compartment. Sonnery-Cottet *et al*[36] commented that they considered the reason that ALLR avoids over constraint is because the grafts are

fixed such that they behave an isometrically. In their technique they identify an isometric point close to the lateral femoral condyle. This point is drilled in an outside-in technique. The tunnel is used for both the ACL reconstruction and ALLR. Once the ACL reconstruction is completed the remaining strand of the graft is used to complete the ALLR by tunnelling it under the ilio-tibial band but superficial to the fibular collateral ligament. The graft is then passed though the tibial tunnel and then brought back proximally towards the femur. This creates an inverted Y shaped acting as a double bundle graft. Whether this behaves isometrically has yet to be proven.

LET is also associated with donor site cosmesis problems[37,38]. It is possible this can be overcome with new minimally invasive techniques which involve tunnelling the grafts deeper.

The strengths of this review include the breadth of studies included. Studies from 13 countries were included in this review. Multiple languages were included, meaning we were less likely to miss relevant datasets. To the best of our knowledge this first meta-analysis to include randomized control studies and case-control studies ALLR with ACLR and the largest to include ALLR.

There were limitations to this review. There was significant heterogeneity amongst the studies included in this review, and thus several studies could not be included in the pooled analysis. This is a common problem encountered when attempting to conduct a meta-analysis. Moreover, there was a wide variation in the techniques used for each procedure of ACLR, ALLR and LET. Regarding extra articular procedures, no consensus has been reached regarding the optimal graft type, location of fixation or the fixation angle.

Another limitation was that only studies conducted after 2000 were included in this review. The reason for this was we wanted to examine novel techniques that were currently in use. However, we acknowledge that this may bias the outcomes of this review. Moreover, this analysis did not search the grey literature, and so there are potentially other studies which are relevant but were not included in this review.

There were also limitations of the studies included in this review. The mean follow duration was 50.8 mo across all studies. The mean follow-up for LET studies was 62.2 mo, compared with 36.8 mo for ALLR. As a result, these studies could not effectively compare rates of osteoarthritis between techniques. Though as previously mentioned, Ferretti *et al*[33] which conducted a 10-year follow up study, found no increases in osteoarthritic rates with ACLR with LET. Since ALLR is a relatively new technique, it is possible that more studies with longer follow up times may be available over the coming years. While it was recognized the reliably of the meta-analysis would be improved by only including studies with longer follow up (> 24 mo). We did include three studies that had a mean follow up period of approximately 12 mo[23-25]. It was the consensus of the authors that the large number of patients and the overall quality of the studies meant the data present in these two studies would add robustness to the meta-analysis as such they were included. The authors also felt it would be of value to the reader for the review to be more comprehensive to make the reader aware of the breadth of evidence available on the subject matter. This strengthened the consensus for the inclusion of these studies.

CONCLUSION

The addition of AEAPs to primary ACLR appears to result in improved rates of rotatory stability when comparing pivot shift test results, however it remains unclear whether this translates to improved functional outcomes. Our results suggest that surgeons should consider offering AEAPs in patients with rotatory instability following ACL rupture. More work is needed to identify patients who would benefit most. Both techniques appear to result in reduced rates of graft failure, compared to isolated ACLR, though ALLR has lower re-rupture rates than LET. Mechanical outcomes appear equivocal between the two AEAPs. A randomized controlled trial comparing the two techniques would be of value.

ARTICLE HIGHLIGHTS

Research background

Anterior cruciate ligament (ACL) reconstruction surgery has shown excellent outcomes, however the restoration of rotational stability remains limited. The role of the reconstruction of the lateral soft tissue restraints or the supplement of the ACL reconstruction with a lateral extra-articular tenodesis have gain popularity and they are now routinely procedures following an ACL reconstruction.

Research motivation

The research motivation of this systematic review and meta-analysis was to clarify how ACL reconstruction surgery combined with lateral extra-articular tenodesis (LET) or anterolateral ligament reconstruction (ALLR) can improve rotational stability and how this can prevent possible failure and instability symptoms.

Research objectives

The aim of this review article was to compare the clinical effectiveness of ACL reconstruction surgery combined with LET or ALLR to ACLR alone.

Research methods

A systematic review to include all the studies investigation either or both of LET and ALLR was conducted. A literature search was carried out on 4 databases for studies from 2000 to November 2021. All studies included in this review were independently appraised by two authors. The critical appraisal was conducted by the Critical Appraisal Skills Programme. Statistical analysis was performed on the collected data.

Research results

Thirteen studies compared ACLR to ACLR + LET. The remaining eleven were studies which compared ACLR to ACLR + ALLR.The nine studies that could be used in analysis encompassed 961 knees. Six of the nine studies demonstrated a statistically significant difference in pivot shift test scores between ACLR only patient groups and ACLR + AEAP patient groups.

Research conclusions

This systematic review has demonstrated that the use of either LET or ALLR in addition to ACLR results in improved mechanical outcomes suggesting surgeons should consider augmenting ACLR with an extra-articular procedure in patients with rotatory instability.

Research perspectives

A randomized controlled trial comparing the two techniques would be of value for clarifying which technique would give the better outcomes regarding the rotational stability following an ACL reconstruction surgery.

FOOTNOTES

Author contributions: Monketh J and Agarwal N analyzed the data and wrote the manuscript; Volpin A designed the research study and reviewed the manuscript; and All authors have read and approve the final manuscript.

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Country/Territory of origin: United Kingdom

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REFERENCES

1 **National Ligament Registry**. The Sixth Annual Report. 2020. Available from: https://www.uknlr.co.uk/

2 **Chouliaras V**, Ristanis S, Moraiti C, Stergiou N, Georgoulis AD. Effectiveness of reconstruction of the anterior cruciate ligament with quadrupled hamstrings and bone-patellar tendon-bone autografts: an in vivo study comparing tibial internal-external rotation. *Am J Sports Med* 2007; **35**: 189-196 [PMID: 17251174 DOI: 10.1097/BLO.0b013e31802b4a0a]

3 **Tashman S**, Collon D, Anderson K, Kolowich P, Anderst W. Abnormal rotational knee motion during running after anterior cruciate ligament reconstruction. *Am J Sports Med* 2004; **32**: 975-983 [PMID: 15150046 DOI: 10.1177/0363546503261709]

4 **Luc B**, Gribble PA, Pietrosimone BG. Osteoarthritis prevalence following anterior cruciate ligament reconstruction: a systematic review and numbers-needed-to-treat analysis. *J Athl Train* 2014; **49**: 806-819 [PMID: 25232663 DOI:

10.4085/1062-6050-49.3.35]
5 **Lien-Iversen T**, Morgan DB, Jensen C, Risberg MA, Engebretsen L, Viberg B. Does surgery reduce knee osteoarthritis, meniscal injury and subsequent complications compared with non-surgery after ACL rupture with at least 10 years follow-up? *Br J Sports Med* 2020; **54**: 592-598 [PMID: 31732650 DOI: 10.1136/bjsports-2019-100765]
6 **Caterine S**, Litchfield R, Johnson M, Chronik B, Getgood A. A cadaveric study of the anterolateral ligament: re-introducing the lateral capsular ligament. *Knee Surg Sports Traumatol Arthrosc* 2015; **23**: 3186-3195 [PMID: 24929656 DOI: 10.1007/s00167-014-3117-z]
7 **Claes S**, Vereecke E, Maes M, Victor J, Verdonk P, Bellemans J. Anatomy of the anterolateral ligament of the knee. *J Anat* 2013; **223**: 321-328 [PMID: 23906341 DOI: 10.1111/joa.12087]
8 **Schindler OS**. Surgery for anterior cruciate ligament deficiency: a historical perspective. *Knee Surg Sports Traumatol Arthrosc* 2012; **20**: 5-47 [PMID: 22105976 DOI: 10.1007/s00167-011-1756-x]
9 **Castoldi M**, Magnussen RA, Gunst S, Batailler C, Neyret P, Lustig S, Servien E. A Randomized Controlled Trial of Bone-Patellar Tendon-Bone Anterior Cruciate Ligament Reconstruction With and Without Lateral Extra-articular Tenodesis: 19-Year Clinical and Radiological Follow-up. *Am J Sports Med* 2020; **48**: 1665-1672 [PMID: 32368935 DOI: 10.1177/0363546520914936]
10 **Marcacci M**, Zaffagnini S, Giordano G, Iacono F, Presti ML. Anterior cruciate ligament reconstruction associated with extra-articular tenodesis: A prospective clinical and radiographic evaluation with 10- to 13-year follow-up. *Am J Sports Med* 2009; **37**: 707-714 [PMID: 19193599 DOI: 10.1177/0363546508328114]
11 **Mahmoud A**, Torbey S, Honeywill C, Myers P. Lateral Extra-Articular Tenodesis Combined With Anterior Cruciate Ligament Reconstruction Is Effective in Knees With Additional Features of Lateral, Hyperextension, or Increased Rotational Laxity: A Matched Cohort Study. *Arthroscopy* 2022; **38**: 119-124 [PMID: 34090996 DOI: 10.1016/j.arthro.2021.04.068]
12 **Getgood AMJ**, Bryant DM, Litchfield R, Heard M, McCormack RG, Rezansoff A, Peterson D, Bardana D, MacDonald PB, Verdonk PCM, Spalding T; STABILITY Study Group, Willits K, Birmingham T, Hewison C, Wanlin S, Firth A, Pinto R, Martindale A, O'Neill L, Jennings M, Daniluk M, Boyer D, Zomar M, Moon K, Pritchett R, Payne K, Fan B, Mohan B, Buchko GM, Hiemstra LA, Kerslake S, Tynedal J, Stranges G, Mcrae S, Gullett L, Brown H, Legary A, Longo A, Christian M, Ferguson C, Mohtadi N, Barber R, Chan D, Campbell C, Garven A, Pulsifer K, Mayer M, Simunovic N, Duong A, Robinson D, Levy D, Skelly M, Shanmugaraj A, Howells F, Tough M, Spalding T, Thompson P, Metcalfe A, Asplin L, Dube A, Clarkson L, Brown J, Bolsover A, Bradshaw C, Belgrove L, Millan F, Turner S, Verdugo S, Lowe J, Dunne D, McGowan K, Suddens CM, Declercq G, Vuylsteke K, Van Haver M. Lateral Extra-articular Tenodesis Reduces Failure of Hamstring Tendon Autograft Anterior Cruciate Ligament Reconstruction: 2-Year Outcomes From the STABILITY Study Randomized Clinical Trial. *Am J Sports Med* 2020; **48**: 285-297 [PMID: 31940222 DOI: 10.1177/0363546519896333]
13 **Sonnery-Cottet B**, Thaunat M, Freychet B, Pupim BH, Murphy CG, Claes S. Outcome of a Combined Anterior Cruciate Ligament and Anterolateral Ligament Reconstruction Technique With a Minimum 2-Year Follow-up. *Am J Sports Med* 2015; **43**: 1598-1605 [PMID: 25740835 DOI: 10.1177/0363546515571571]
14 **Hopper GP**, Aithie JMS, Jenkins JM, Wilson WT, Mackay GM. Combined Anterior Cruciate Ligament Repair and Anterolateral Ligament Internal Brace Augmentation: Minimum 2-Year Patient-Reported Outcome Measures. *Orthop J Sports Med* 2020; **8**: 2325967120968557 [PMID: 33415174 DOI: 10.1177/2325967120968557]
15 Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA). 2015. Available from: http://www.prisma-statement.org/
16 **O'Connor D**, Green S HJ. Defining the Review Question and Developing Criteria for Including Studies. In: Cochrane Handbook for Systematic Reviews of Interventions: Cochrane Book Series. 2008. Available from: https://training.cochrane.org/handbook
17 **Lefebvre C**, Manheimer E, Glanville J. Searching for Studies. In: Cochrane Handbook for Systematic Reviews of Interventions. John Wiley and Sons; 2008; 95–150 [DOI: 10.1002/9780470712184.ch6]
18 **Page MJ**, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, Shamseer L, Tetzlaff JM, Akl EA, Brennan SE, Chou R, Glanville J, Grimshaw JM, Hróbjartsson A, Lalu MM, Li T, Loder EW, Mayo-Wilson E, McDonald S, McGuinness LA, Stewart LA, Thomas J, Tricco AC, Welch VA, Whiting P, Moher D. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *BMJ* 2021; **372**: n71 [PMID: 33782057 DOI: 10.1136/bmj.n71]
19 **Critical Appraisal Skills Programme**. CASP Cohort Study Checklist. 2018. Available from: https://casp-uk.net/wp-content/uploads/2018/01/CASP-Cohort-Study-Checklist_2018.pdf
20 **Vaudreuil NJ**, Rothrauff BB, de Sa D, Musahl V. The Pivot Shift: Current Experimental Methodology and Clinical Utility for Anterior Cruciate Ligament Rupture and Associated Injury. *Curr Rev Musculoskelet Med* 2019; **12**: 41-49 [PMID: 30706283 DOI: 10.1007/s12178-019-09529-7]
21 **Irrgang JJ**, Ho H, Harner CD, Fu FH. Use of the International Knee Documentation Committee guidelines to assess outcome following anterior cruciate ligament reconstruction. *Knee Surg Sports Traumatol Arthrosc* 1998; **6**: 107-114 [PMID: 9604196 DOI: 10.1007/s001670050082]
22 **Hewison CE**, Tran MN, Kaniki N, Remtulla A, Bryant D, Getgood AM. Lateral Extra-articular Tenodesis Reduces Rotational Laxity When Combined With Anterior Cruciate Ligament Reconstruction: A Systematic Review of the Literature. *Arthroscopy* 2015; **31**: 2022-2034 [PMID: 26116497 DOI: 10.1016/j.arthro.2015.04.089]
23 **Chiba D**, Gale T, Nishida K, Suntaxi F, Lesniak BP, Fu FH, Anderst W, Musahl V. Lateral Extra-articular Tenodesis Contributes Little to Change In Vivo Kinematics After Anterior Cruciate Ligament Reconstruction: A Randomized Controlled Trial. *Am J Sports Med* 2021; **49**: 1803-1812 [PMID: 33872056 DOI: 10.1177/03635465211003298]
24 **Mogoş Ş**, D'Ambrosi R, Antonescu D, Stoica IC. Combined Anterior Cruciate Ligament and Anterolateral Ligament Reconstruction Results in Superior Rotational Stability Compared with Isolated Anterior Cruciate Ligament Reconstruction in High Grade Pivoting Sport Patients: A Prospective Randomized Clinical Trial. *J Knee Surg* 2021 [PMID: 33932949 DOI: 10.1055/s-0041-1729621]
25 **Sonnery-Cottet B**, Pioger C, Vieira TD, Franck F, Kajetanek C, Fayard JM, Thaunat M, Saithna A. Combined ACL and Anterolateral Reconstruction Is Not Associated With a Higher Risk of Adverse Outcomes: Preliminary Results From the

SANTI Randomized Controlled Trial. *Orthop J Sports Med* 2020; **8**: 2325967120918490 [PMID: 32490026 DOI: 10.1177/2325967120918490]

26 **Ayeni OR**, Chahal M, Tran MN, Sprague S. Pivot shift as an outcome measure for ACL reconstruction: a systematic review. *Knee Surg Sports Traumatol Arthrosc* 2012; **20**: 767-777 [PMID: 22218828 DOI: 10.1007/s00167-011-1860-y]

27 **Kocher MS**, Steadman JR, Briggs K, Zurakowski D, Sterett WI, Hawkins RJ. Determinants of patient satisfaction with outcome after anterior cruciate ligament reconstruction. *J Bone Joint Surg Am* 2002; **84**: 1560-1572 [PMID: 12208912 DOI: 10.2106/00004623-200209000-00008]

28 **Geeslin AG**, Moatshe G, Chahla J, Kruckeberg BM, Muckenhirn KJ, Dornan GJ, Coggins A, Brady AW, Getgood AM, Godin JA, LaPrade RF. Anterolateral Knee Extra-articular Stabilizers: A Robotic Study Comparing Anterolateral Ligament Reconstruction and Modified Lemaire Lateral Extra-articular Tenodesis. *Am J Sports Med* 2018; **46**: 607-616 [PMID: 29268024 DOI: 10.1177/0363546517745268]

29 **Inderhaug E**, Stephen JM, Williams A, Amis AA. Biomechanical Comparison of Anterolateral Procedures Combined With Anterior Cruciate Ligament Reconstruction. *Am J Sports Med* 2017; **45**: 347-354 [PMID: 28027653 DOI: 10.1177/0363546516681555]

30 **Marom N**, Ouanezar H, Jahandar H, Zayyad ZA, Fraychineaud T, Hurwit D, Imhauser CW, Wickiewicz TL, Pearle AD, Nawabi DH. Lateral Extra-articular Tenodesis Reduces Anterior Cruciate Ligament Graft Force and Anterior Tibial Translation in Response to Applied Pivoting and Anterior Drawer Loads. *Am J Sports Med* 2020; **48**: 3183-3193 [PMID: 33017168 DOI: 10.1177/0363546520959322]

31 **Ra HJ**, Kim JH, Lee DH. Comparative clinical outcomes of anterolateral ligament reconstruction versus lateral extra-articular tenodesis in combination with anterior cruciate ligament reconstruction: systematic review and meta-analysis. *Arch Orthop Trauma Surg* 2020; **140**: 923-931 [PMID: 32140829 DOI: 10.1007/s00402-020-03393-8]

32 **Novaretti JV**, Arner JW, Chan CK, Polamalu S, Harner CD, Debski RE, Lesniak BP. Does Lateral Extra-articular Tenodesis of the Knee Affect Anterior Cruciate Ligament Graft In Situ Forces and Tibiofemoral Contact Pressures? *Arthroscopy* 2020; **36**: 1365-1373 [PMID: 32057987 DOI: 10.1016/j.arthro.2020.01.051]

33 **Ferretti A**, Monaco E, Ponzo A, Basiglini L, Iorio R, Caperna L, Conteduca F. Combined Intra-articular and Extra-articular Reconstruction in Anterior Cruciate Ligament-Deficient Knee: 25 Years Later. *Arthroscopy* 2016; **32**: 2039-2047 [PMID: 27157658 DOI: 10.1016/j.arthro.2016.02.006]

34 **Schon JM**, Moatshe G, Brady AW, Cruz RS, Chahla J, Dornan GJ, Turnbull TL, Engebretsen L, LaPrade RF. Anatomic Anterolateral Ligament Reconstruction Leads to Overconstraint at Any Fixation Angle: Response. *Am J Sports Med* 2016; **44**: NP58-NP59 [PMID: 27694611 DOI: 10.1177/0363546516669314]

35 **Neri T**, Cadman J, Beach A, Grasso S, Dabirrahmani D, Putnis S, Oshima T, Devitt B, Coolican M, Fritsch B, Appleyard R, Parker D. Lateral tenodesis procedures increase lateral compartment pressures more than anterolateral ligament reconstruction, when performed in combination with ACL reconstruction: a pilot biomechanical study. *J ISAKOS* 2021; **6**: 66-73 [PMID: 33832979 DOI: 10.1136/jisakos-2019-000368]

36 **Sonnery-Cottet B**, Haidar I, Rayes J, Fradin T, Ngbilo C, Vieira TD, Freychet B, Ouanezar H, Saithna A. Long-term Graft Rupture Rates After Combined ACL and Anterolateral Ligament Reconstruction Versus Isolated ACL Reconstruction: A Matched-Pair Analysis From the SANTI Study Group. *Am J Sports Med* 2021; **49**: 2889-2897 [PMID: 34351825 DOI: 10.1177/03635465211028990]

37 **Roth JH**, Kennedy JC, Lockstadt H, McCallum CL, Cunning LA. Intra-articular reconstruction of the anterior cruciate ligament with and without extra-articular supplementation by transfer of the biceps femoris tendon. *J Bone Joint Surg Am* 1987; **69**: 275-278 [PMID: 3805091]

38 **Bylski-Austrow DI**, Grood ES, Hefzy MS, Holden JP, Butler DL. Anterior cruciate ligament replacements: a mechanical study of femoral attachment location, flexion angle at tensioning, and initial tension. *J Orthop Res* 1990; **8**: 522-531 [PMID: 2355292 DOI: 10.1002/jor.1100080408]

39 **Hamido F**, Habiba AA, Marwan Y, Soliman ASI, Elkhadrawe TA, Morsi MG, Shoaeb W, Nagi A. Anterolateral ligament reconstruction improves the clinical and functional outcomes of anterior cruciate ligament reconstruction in athletes. *Knee Surg Sports Traumatol Arthrosc* 2021; **29**: 1173-1180 [PMID: 32617609 DOI: 10.1007/s00167-020-06119-w]

40 **Ibrahim SA**, Shohdy EM, Marwan Y, Ramadan SA, Almisfer AK, Mohammad MW, Abdulsattar WS, Khirat S. Anatomic Reconstruction of the Anterior Cruciate Ligament of the Knee With or Without Reconstruction of the Anterolateral Ligament: A Randomized Clinical Trial. *Am J Sports Med* 2017; **45**: 1558-1566 [PMID: 28293966 DOI: 10.1177/0363546517691517]

41 **Porter M**, Shadbolt B. Modified Iliotibial Band Tenodesis Is Indicated to Correct Intraoperative Residual Pivot Shift After Anterior Cruciate Ligament Reconstruction Using an Autologous Hamstring Tendon Graft: A Prospective Randomized Controlled Trial. *Am J Sports Med* 2020; **48**: 1069-1077 [PMID: 32182127 DOI: 10.1177/0363546520910148]

42 **Stensbirk F**, Thorborg K, Konradsen L, Jørgensen U, Hölmich P. Iliotibial band autograft versus bone-patella-tendon-bone autograft, a possible alternative for ACL reconstruction: a 15-year prospective randomized controlled trial. *Knee Surg Sports Traumatol Arthrosc* 2014; **22**: 2094-2101 [PMID: 23974633 DOI: 10.1007/s00167-013-2630-9]

43 **Trichine F**, Alsaati M, Chouteau J, Moyen B, Bouzitouna M, Maza R. Patellar tendon autograft reconstruction of the anterior cruciate ligament with and without lateral plasty in advanced-stage chronic laxity. A clinical, prospective, randomized, single-blind study using passive dynamic X-rays. *Knee* 2014; **21**: 58-65 [PMID: 23810648 DOI: 10.1016/j.knee.2013.06.001]

44 **Vadalà AP**, Iorio R, De Carli A, Bonifazi A, Iorio C, Gatti A, Rossi C, Ferretti A. An extra-articular procedure improves the clinical outcome in anterior cruciate ligament reconstruction with hamstrings in female athletes. *Int Orthop* 2013; **37**: 187-192 [PMID: 22623063 DOI: 10.1007/s00264-012-1571-0]

45 **Ahn JH**, Kim J, Mun JW. A Retrospective Comparison of Single-Bundle Anterior Cruciate Ligament Reconstruction With Lateral Extra-Articular Tenodesis With Double-Bundle Anterior Cruciate Ligament Reconstruction. *Arthroscopy* 2021; **37**: 976-984 [PMID: 33188853 DOI: 10.1016/j.arthro.2020.11.011]

46 **Dejour D**, Vanconcelos W, Bonin N, Saggin PR. Comparative study between mono-bundle bone-patellar tendon-bone, double-bundle hamstring and mono-bundle bone-patellar tendon-bone combined with a modified Lemaire extra-articular

procedure in anterior cruciate ligament reconstruction. *Int Orthop* 2013; **37**: 193-199 [PMID: 23180103 DOI: 10.1007/s00264-012-1718-z]

47 **Erden T**, Toker B, Toprak A, Taşer Ö. Comparison of the outcomes of isolated anterior cruciate ligament reconstruction and combined anterolateral ligament suture tape augmentation and anterior cruciate ligament reconstruction. *Jt Dis Relat Surg* 2021; **32**: 129-136 [PMID: 33463428 DOI: 10.5606/ehc.2020.78201]

48 **Giraud B**, Besse JL, Cladière F, Ecochard R, Moyen B, Lerat JL. [Intra-articular reconstruction of the anterior cruciate ligament with and without extra-articular supplementation by quadricipital tendon plasty: seven-year follow-up]. *Rev Chir Orthop Reparatrice Appar Mot* 2006; **92**: 788-797 [PMID: 17245238 DOI: 10.1016/s0035-1040(06)75947-5]

49 **Goncharov EN**, Koval OA, Dubrov VE, Bezuglov EN, Filimonova AM, Goncharov NG. Clinical experience with combined reconstruction of the anterior cruciate and anterolateral ligaments of the knee in sportsmen. *Int Orthop* 2019; **43**: 2781-2788 [PMID: 31511952 DOI: 10.1007/s00264-019-04409-8]

50 **Lee DW**, Kim JG, Cho SI, Kim DH. Clinical Outcomes of Isolated Revision Anterior Cruciate Ligament Reconstruction or in Combination With Anatomic Anterolateral Ligament Reconstruction. *Am J Sports Med* 2019; **47**: 324-333 [PMID: 30640514 DOI: 10.1177/0363546518815888]

51 **Rowan FE**, Huq SS, Haddad FS. Lateral extra-articular tenodesis with ACL reconstruction demonstrates better patient-reported outcomes compared to ACL reconstruction alone at 2 years minimum follow-up. *Arch Orthop Trauma Surg* 2019; **139**: 1425-1433 [PMID: 31297583 DOI: 10.1007/s00402-019-03218-3]

52 **Sonnery-Cottet B**, Saithna A, Cavalier M, Kajetanek C, Temponi EF, Daggett M, Helito CP, Thaunat M. Anterolateral Ligament Reconstruction Is Associated With Significantly Reduced ACL Graft Rupture Rates at a Minimum Follow-up of 2 Years: A Prospective Comparative Study of 502 Patients From the SANTI Study Group. *Am J Sports Med* 2017; **45**: 1547-1557 [PMID: 28151693 DOI: 10.1177/0363546516686057]

53 **Sonnery-Cottet B**, Saithna A, Blakeney WG, Ouanezar H, Borade A, Daggett M, Thaunat M, Fayard JM, Delaloye JR. Anterolateral Ligament Reconstruction Protects the Repaired Medial Meniscus: A Comparative Study of 383 Anterior Cruciate Ligament Reconstructions From the SANTI Study Group With a Minimum Follow-up of 2 Years. *Am J Sports Med* 2018; **46**: 1819-1826 [PMID: 29741400 DOI: 10.1177/0363546518767659]

54 **Ventura A**, Legnani C, Boisio F, Borgo E, Peretti GM. The association of extra-articular tenodesis restores rotational stability more effectively compared to contralateral hamstring tendon autografts ACL reconstruction alone in patients undergoing ACL revision surgery. *Orthop Traumatol Surg Res* 2021; **107**: 102739 [PMID: 33390331 DOI: 10.1016/j.otsr.2020.06.022]

55 **Helito CP**, Sobrado MF, Giglio PN, Bonadio MB, Pécora JR, Camanho GL, Demange MK. Combined Reconstruction of the Anterolateral Ligament in Patients With Anterior Cruciate Ligament Injury and Ligamentous Hyperlaxity Leads to Better Clinical Stability and a Lower Failure Rate Than Isolated Anterior Cruciate Ligament Reconstruction. *Arthroscopy* 2019; **35**: 2648-2654 [PMID: 31421960 DOI: 10.1016/j.arthro.2019.03.059]

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LETTER TO THE EDITOR

Risk of methicillin-resistant *Staphylococcus aureus* prosthetic joint infection in elective total hip and knee arthroplasty following eradication therapy

Jayaweera Arachchige Asela Sampath Jayaweera

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Abstract

Re-screening following methicillin-resistant *Staphylococcus aureus* (MRSA) decolonization will be helpful to minimize the development of prosthetic joint infection among MRSA colonizers.

Key Words: Methicillin-resistant *Staphylococcus aureus* colonization; MRSA decolonization; Prosthetic joint implantation; Prosthetic joint infections

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Core Tip: Patients with methicillin-resistant *Staphylococcus aureus* (MRSA) colonization have a high risk of contracting prosthetic joint infections, and MRSA screening and decolonization are essential to minimize the development of prosthetic joint infection. However, studies showed that re-screening following MRSA decolonization is important before planned prosthetic joint surgery to minimize infections.

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TO THE EDITOR

I read the important retrospective study by Kapur *et al*[1] on the risk of methicillin-resistant *Staphylococcus aureus* (MRSA) prosthetic joint infection in elective total hip and knee arthroplasty following eradication therapy. MRSA is a virulent pathogen that causes infections among healthy and immunocompromised individuals. The spectrum of MRSA infection varies from cellulitis, necrotizing fasciitis, bone and joint infections, bacteremia, and infective endocarditis to pneumonia[2].

That article provides a crucial insight into the importance of screening and re-screening following eradication of MRSA prior to prosthetic joint implant in orthopedic surgery. The authors have compared the incidence of prosthetic joint infection (PJI) among MRSA colonizers and non-colonizers, and following follow-up, found that PJI risk is high among MRSA colonizers. As we know, the associated financial burden following PJI is substantial.

The authors have mentioned the method of MRSA decolonization and some practice instead of prontoderm nasal spray and octenisan for 4% chlorhexidine and mupirocin ointment. The IDSA guidelines explain the importance of the latter regime, but different formulae have similar decolonization ability and differ in cost as the latter is cheaper[3]. Use of povidone-iodine and rifampin has shown efficient and low cost MRSA decolonization. Simor *et al*[4] showed that the use of topical germicide and antibiotic plus oral agents and rifampin achieved a 92% eradication rate for MRSA. Moreover, the duration of decolonization was given as 5-10 d of mupirocin and 5-14 d of 4% chlorhexidine body wash. Here the authors have discussed the mupirocin use.

The authors mentioned the use of teicoplanin prophylaxis among MRSA positive patients. In emergency surgery, the advice is to provide vancomycin or teicoplanin prophylactically while replacing cefuroxime. However, routine use of anti-MRSA antibiotic prophylaxis for MRSA positives following decolonization is questionable. The expectation would be to minimize the occurrence of MRSA bacteremia. Most studies have discussed the failure of the MRSA decolonization procedure. Almost all prosthetic joint implantation is done as a planned procedure; this would signify the importance of employing the re-screening strategy following decolonization prior to the surgery[5].

A study conducted by Garvey *et al*[6] showed the possibility of having MRSA colonization following decolonization. Following repeated decolonization, the MRSA colonization has been reduced from 7.2% to 4.7%. Several methods were employed by different research groups for MRSA screening. In addition to molecular methods, the use of chromogenic agar is also costly, but the use of mannitol salt agar and swabs into 7.5% NaCl in brain-heart infusion broth and phenotypic detection including tube and slide coagulase testing is cost effective to isolate MRSA[2]. Over the period, I have seen many patients with repeated MRSA colonization following MRSA decolonization. However, almost all isolates were mupirocin susceptible. Therefore, it may be associated with a lack of compliance and a lack of highlighting the importance of decolonization to the patient or the family. Since most patients are morbid and probably have mobility problems, adherence to a 5-d regular body wash and nasal spraying is questionable[7].

The authors have highlighted the importance of re-screening while relating the financial and social burden following PJI. Another thing is that, if possible, re-screening following MRSA eradication would minimize the prophylactic use of teicoplanin.

Re-screening following MRSA decolonization will be helpful to minimize the development of PJI among MRSA colonizers.

FOOTNOTES

Author contributions: Sampath Jayaweera JAA designed the study, analyzed the data, and wrote the manuscript.

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REFERENCES

1 **Kapur BP**, Tonge X, Kumar G. Risk of methicillin-resistant staphylococcus aureus prosthetic joint infection in elective total hip and knee arthroplasty following eradication therapy. *World J Orthop* 2021; **12**: 842-849 [PMID: 34888144 DOI: 10.5312/wjo.v12.i11.842]

2 **Sampath Jayaweera JAA**, Karunarathne M, Kumbukgolla WW. The importance of the timely introduction of vancomycin therapy against methicillin-resistant Staphylococcus aureus (MRSA) bacteremia and severity of MRSA bacteremia at Teaching Hospital, Anuradhapura, Sri Lanka. *Int J One Health* 2017; **3**: 7 [DOI: 10.14202/ijoh.2017.7-11]

3 Lambert H. IDSA Guidelines on the Treatment of MRSA Infections in Adults and Children. *Am Fam Physician* 2011; **84**: 455-463

4 **Simor AE**, Phillips E, McGeer A, Konvalinka A, Loeb M, Devlin HR, Kiss A. Randomized controlled trial of chlorhexidine gluconate for washing, intranasal mupirocin, and rifampin and doxycycline versus no treatment for the eradication of methicillin-resistant Staphylococcus aureus colonization. *Clin Infect Dis* 2007; **44**: 178-185 [PMID: 17173213 DOI: 10.1086/510392]

5 **Sai N**, Laurent C, Strale H, Denis O, Byl B. Efficacy of the decolonization of methicillin-resistant Staphylococcus aureus carriers in clinical practice. *Antimicrob Resist Infect Control* 2015; **4**: 56 [PMID: 26688720 DOI: 10.1186/s13756-015-0096-x]

6 **Garvey MI**, Winfield J, Wiley C, Reid M, Cooper M. Reduction in methicillin-resistant *Staphylococcus aureus* colonisation: impact of a screening and decolonisation programme. *J Infect Prev* 2016; **17**: 294-297 [PMID: 28989493 DOI: 10.1177/1757177416661406]

7 **Zhu X**, Sun X, Zeng Y, Feng W, Li J, Zeng J. Can nasal Staphylococcus aureus screening and decolonization prior to elective total joint arthroplasty reduce surgical site and prosthesis-related infections? *J Orthop Surg Res* 2020; **15**: 60 [PMID: 32075670 DOI: 10.1186/s13018-020-01601-0]



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REVIEW

Anterolateral complex of the knee: State of the art

Luigi Sabatini, Marcello Capella, Daniele Vezza, Luca Barberis, Daniele Camazzola, Salvatore Risitano, Luca Drocco, Alessandro Massè

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Abstract

Rotatory instability of the knee represents the main reason for failure and poor clinical outcomes regarding anterior cruciate ligament (ACL) reconstruction techniques. It is now clear that the anterolateral complex (ALC) of the knee possesses a fundamental role, in association with the ACL, in controlling internal rotation. Over the past decade, ever since the anterolateral ligament has been identified and described as a distinct structure, there has been a renewed interest in the scientific community about the whole ALC: Lateral extra-articular tenodesis have made a comeback in association with ACL reconstructions to improve functional outcomes, reducing the risks of graft failure and associated injuries. Modern ACL reconstruction surgery must therefore investigate residual instability and proceed, when necessary, to extra-articular techniques, whether functional tenodesis or anatomical reconstruction.This review aims to investigate the latest anatomical and histological descriptions, and the role in rotational control and knee biomechanics of the ALC and its components. The diagnostic tools for its identification, different reconstruction techniques, and possible surgical indications are described.. In addition, clinical and functional results available in the literature are reported.

Key Words: Knee; Knee dislocation; Anterior cruciate ligament reconstruction; Fascia lata; Tenodesis; Joint instability

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Core Tip: Residual rotatory instability is present in a significant percentage of patients who underwent anterior cruciate ligament (ACL) reconstruction. Regardless of the injured structure of the anterolateral complex involved, whether the anterolateral ligament itself or different iliotibial band layers, the combination of a lateral extra-articular tenodesis technique has proven to be a safe, easily reproducible, and effective practice in reducing tibial internal rotation, improving ACL graft survival, reducing the overall reintervention rate, and improving the rate of return to previous athletic activity.

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INTRODUCTION

Anterior cruciate ligament (ACL) reconstruction techniques have sought to restore knee kinematics and reduce rotational instability. Since the 1970s[1] the idea that anterolateral rotatory instability (ALRI) was due not only to ACL injury, but also to the structures of the anterolateral complex (ALC), began to catch on. Over the last decade, awareness of the ALC has increased, especially since the anterolateral ligament (ALL) has been described and identified[2]. Several biomechanical studies have been carried out and different reconstruction techniques have been proposed.

The anterolateral ligament of the knee is a distinct ligamentous structure about which there is no consensus regarding its function and existence. Some authors deny the existence of such a structure, emphasizing the importance of other anatomical structures, such as the deeper portion of the iliotibial band (ITB) and the anterolateral capsule[3,4]. In contrast, other studies have identified the ALL as a ligament in its own right[5,6]. This disagreement originates from the anatomic dissection techniques that are performed[7,8].

Associated ACL and ALL injury have been shown to significantly increase knee rotational laxity and tibial internal rotation (IR), posing as the background for suboptimal outcomes, potential failure of an isolated ACL reconstruction (ACLR), and secondary meniscal or cartilage injury, as well as for early development of arthritic degeneration[9]. Controlling rotational laxity in ACLR still remains a challenge, with evidence of ALRI persistence in up to 25% of patients regardless of the ACLR technique used[10]. Several studies, in the last years, have identified the ALC as responsible for this residual instability and have pointed at the ALL and the ITB as the main players to internal tibial rotation restrain.

To improve residual rotational instability, more anatomical ACLR techniques have been developed, seeking a more oblique path of the femoral tunnel using the medial portal technique. Recently, the addition of a posterolateral bundle to the anteromedial bundle in double-bundle ACLR has been proposed; however, the technique did not improve rotatory stability and it has now been almost abandoned[11].

HISTORY

Although there have been sporadic references before 2013 about the existence of a capsuloligamentous structure connecting the femur and tibia in the anterolateral region, descriptions have been vague and often in disagreement. The first reference to the ALL date back more than 100 years. Segond[12], in 1879, described an avulsion fracture of the anterolateral margin of the tibia. He reported a "pearly band extending in an oblique fashion from the femur inserting into the avulsed tibial bone" without elaborating further on the details and anatomical relationships of this structure. However, this finding was ignored until it was rediscovered in a study by Hughston *et al*[1] in the 1970s in which they illustrated different patterns of rotational instability. They described a structure, called the "mid-third lateral capsular ligament", that was intimately connected to the lateral meniscus and how it could be involved in rotational instability. This structure, however, was not mentioned again, except sporadically in subsequent studies. In the same year, Johnson[13] described "the anterior oblique band of the lateral collateral ligament." On the other hand, Terry *et al*[14] pointed out that the main players in the antero-lateral region were the deep, capsulo-osseous and superficial layers of the ITB without making references to distinct structures that could refer to the ALL.

In 2007, Vieira *et al*[15] described how the capsulo-osseous layer acts as "an anterolateral ligament". This term was used a few years later by Vincent *et al*[16] who identified, during TKA implantation, a ligamentous structure with connections to the distal femur, proximal tibia, and lateral meniscus in the anterolateral region of the knee. Nevertheless, before the study by Claes *et al*[2] in 2013 that was the first to provide a detailed description of ALL, this term was used to identify likely different structures and to

describe their role in the rotational control.

ANATOMY

According to Claes *et al*[2], a distinct anatomical structure connecting the distal femur and proximal tibia can be distinguished on the anterolateral portion of the knee. The structure is entirely extracapsular. The proximal insertion point lies on the prominence of the lateral femoral epicondyle, anterior to the fibular collateral ligament (FCL) insertion and proximal and posterior to the insertion of the popliteus tendon; the distal insertion of the ALL is located posterior to Gerdy's tubercle and anterior to the head of the fibula[17-19]. However, it is possible to recognize more superficial fibers that continue into the lateral intermuscular septum of the thigh and more posterior fibers that are closely connected to the more proximal portion of the FCL[2]. Connections to the body of the lateral meniscus also belong to the ALL, divided into meniscofemoral and meniscotibial portions. The lateral inferior geniculate artery and the vein invariably run between the ALL and the lateral meniscus.

Since the femoral insertion points of ALL and FCL are in close relationship, both structures can be described with the term "lateral collateral ligament complex." Likewise, the ALL could be the lateral counterpart of the deep medial collateral ligament[2]. However, some studies, have emphasized how the ALL structure and location can vary[20]. While several authors agree in identifying the tibial insertion, the disagreement about the femoral insertion is of particular interest. This discordance has biomechanical implications: The femoral insertion has been described as anterior and distal to the insertion of the FCL[2] or posterior and proximal with the fibers overlapping the FCL itself[18,21]. It is unclear whether this difference is due to interindividual differences or different dissection techniques.

In contrast, another model described by Helito *et al*[22] shows the existence of 2 distinct bundles: A more superficial one with femoral insertion posterior and proximal to the epicondyle and a deeper one with insertion in the center of the epicondyle. It is also likely that the ALL has an intimate relationship with the ITB, supported by a high association of lesions of the ALL and distal ITB[23].

The latest evidence emphasizes that the control of the ALRI is due to the entire anterolateral complex. The ALC works together with the ACL to restrain internal tibial rotation. The ALC consists of the ALL, the superficial and deep portion of the ITB, the capsulo-osseous layer, and the anterolateral capsule. Indeed, the deep part of the ITB and its complex insertion points at the distal femur contribute significantly to rotational control. Kaplan's fibers (KFs) play a role, along with the ITB, as a secondary passive stabilizer after the ACL[24]. They are described as a deep, posterior portion of the ITB connected to distal femur, divided into two bundles, the proximal fibers (PKF) and the distal fibers (DKF).

The capsulo-osseous layer has been described by Lobenhoffer *et al*[25] as a deep portion of the ITB, an arcuate retrograde fiber tract extending from the intermuscular septum of the femur in the lateral supracondylar region to the Gerdy's tubercle. This ligament-like unit forms a sling around the postero-lateral aspect of the distal femur. More recent studies[26] have confirmed the presence of this layer as a distinct anatomic entity separated from the ALL and have also suggested a synergistic role of these structures in restraining IR.

HISTOLOGY

The histologic analysis provides evidence of particular interest in demonstrating the existence of the ALL as a distinct ligamentous structure with the presence of dense, well-arranged connective tissue and not as a simple capsular thickening that would have less organized and less cellular tissue[6]. The primary composition is type I collagen (90%) with a fibroblast concentration of 121/m^2 in adults and 1631/m^2 in fetal preparations[27]. In a study, by Caterine *et al*[28], the ALL shows fascicular organization in cross-section and also mechanoreceptors and nerve terminal fibers. Likewise, in an *in vivo* study of patients undergoing TKA, it was shown that the structure of ALL, compared to ACL, owned a similar pattern of collagen fibers orientation, nuclei's form, and a similar cellularity[29]. Furthermore, a clear distinction between ALL and capsule is present since the joint capsule resembles a loose connective tissue. Additionally, the ALL femoral insertion shows a transition from ligamentous tissue to mineralized cartilage and bone; this transition indicates ligamentous tissue[28].

IDENTIFICATION OF ALL

Although ALRI must be clinically assessed, there are diagnostic tools that allow visualization of the ALL.

Magnetic resonance imaging

Scientific studies that have investigated anterolateral complex lesions in patients with ACL injuries with

magnetic resonance imaging (MRI) often highlight conflicting results with association rates from 40% to 80%[30,31]. These discrepancies may be due to inclusion criteria, in some studies, of patients with chronic ACL injuries.

To visualize more easily a thin structure, such as the ALL, the use of a 3 T MRI with 0.4-mm slice and fat-suppressed acquisition is recommended[28] (Figure 1). In a study by Helito[32], MRIs of patients with acute ACL lesions were analyzed to point out the injured structures that were most frequently associated with an ALL lesion: FCL (P = 0.004), popliteal tendon (P = 0.005), MCL (P = 0.011), anterolateral capsule (P = 0.000034), and ITB with an increased correlation with a greater degree of injury (P = 0.000021). Tears of the ALL are found in 40% of acute ACL injuries, whereas no association was found with meniscal injuries. There was also no association between ALL injury and partial ACL injury, suggesting that the ALL is torn only in major traumas or that its integrity is a protective factor for ACL [32].

A systematic review by Puzzitiello *et al*[33] concluded that at least a portion of the ALL is visualizable on MRI in 76-100% of knees, and its possible injury in patients with acute ACL injury is identifiable from 10.8% to 62.5% of cases. Additionally, the level of inter- and intra-observer reliability varies from moderate to almost perfect. A higher prevalence of ALL lesions has been identified in MRI in patients with acute ACL injury and high-grade pivot shift with a positive correlation between pivot shift grade and lesion severity (P < 0.013)[34]. The finding of these injury associations helps to delineate how the anterolateral rotational stability of the knee is due to the synergistic work of these structures.

Arthroscopy

Several authors have described the possibility of arthroscopic identification of ALL and have provided step-by-step descriptions[35]. According to Zein[35], it is possible to identify it with a 30° scope through the AL portal. It is necessary to place the limb in a figure of-4-position. In the lateral compartment, the popliteal tendon (PT), popliteal hiatus and synovial bulge anterior to the meniscal bare area are identified. By advancing the arthroscope into the lateral gutter above the synovial bulge, PT, FCL, and ALL can be identified, which run in different planes and directions. Applying an internal rotation, a tensioning of ALL can be observed. It is also possible to identify the meniscotibial attachment of the ALL below the lateral meniscus, anterior to the PT.

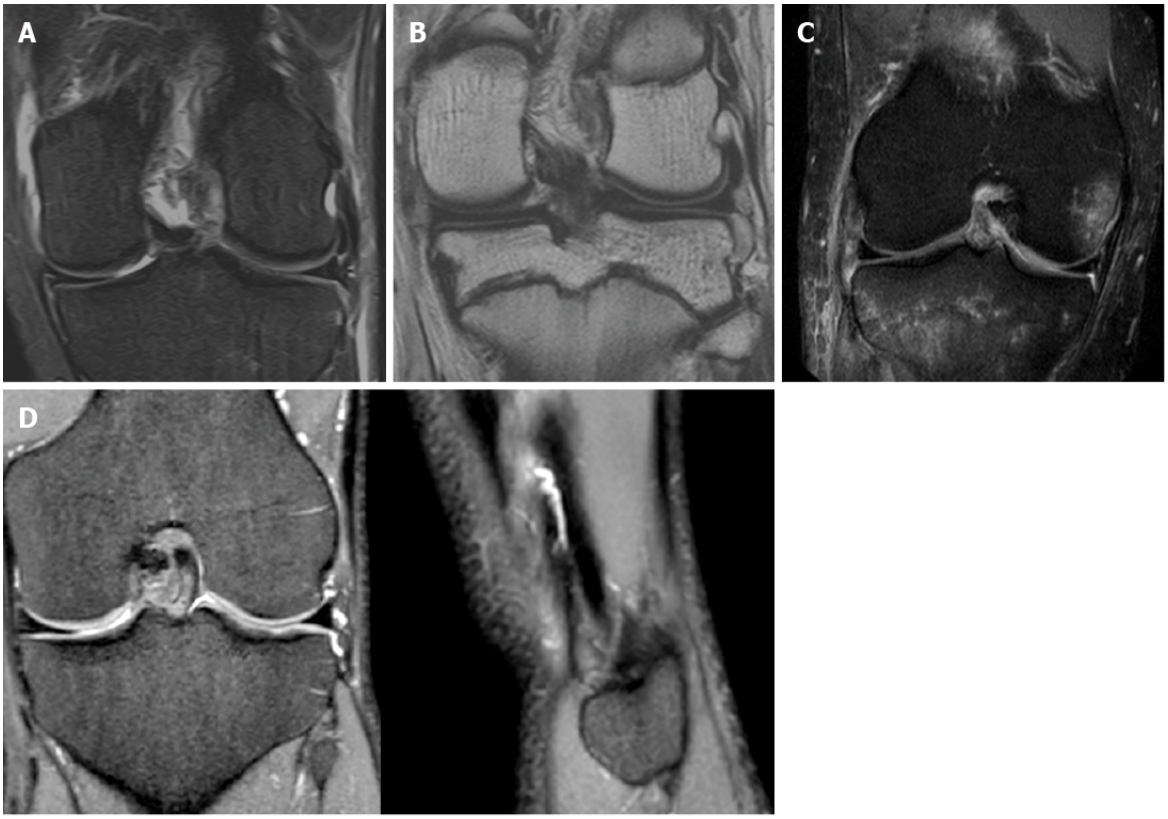
BIOMECHANICS

Regarding the ALL, there is no agreement in the literature regarding its role in knee biomechanics. While in some studies it has been shown that the ALL possesses a stabilizing role in an extension and internal rotation position[36], in a cadaveric study[37], the ALL limits internal rotation only at flexion angles greater than 35°, while providing minimal resistance to anteroposterior translation. However, it must be pointed out that the differences reported in these studies may be due to the dissection techniques adopted. In the study by Rasmussen *et al*[36], the ALL was not dissected but all anterolateral structures, from Gerdy's tubercle to the head of the fibula, were sectioned not considering that additional structures of the ALC might affect stabilization. Given that additional evidence points to the ITB as the main restrain to internal rotation[38], having it removed may have overestimated the role of the ALL.

It must be remembered that the ligamentous structures of the knee are unlikely to possess isometric behavior, and the various surgical techniques that seek isometric reconstruction fail to achieve anatomic positioning. Although the geometry of the condyles would make the area through which the transepicondylar axis passes a relatively isometric insertion zone, the roll-glide mechanism of the lateral condyle makes it impossible to find isometric femorotibial connections[39]. Structures, that therefore insert posteriorly to the epicondyle, are strained in extension, whereas anterior structures are strained in flexion.

In agreement with previous studies, Sonnery-Cottet *et al*[40] demonstrated how a section of the ALL did not lead to an increase in tibial IR at 20° of flexion angle but increased it at 90° and also showed that the ITB also participates in rotational control. In a study by Noyes *et al*[41], after sectioning of the ALL and the ITB, in agreement with evidence demonstrating a synergistic role of these structures in limiting IR, an increase of 5.1° at 60° of flexion and 6.7° at 90° of flexion has been observed. The latest evidence (in cadaver biomechanical studies) agrees that the ALL possesses an IR stabilizing function only at high degrees of flexion. Only at flexion angles of 60° and 90° a restriction to the IR by the ALL can be observed[42]. These results indicate that the ALL does not own a role in the pivot shift phenomenon that occurs at flexion degrees of 20°-30°[43], and one must therefore look for the ALRI responsible not in a single structure, but in the entire ALC. Terry *et al*[14] showed, in a cadaveric study of 82 knees, an anterolateral capsular lesion in 93% of patients with ACL injury and that this damage was significantly correlated with the degree of pivot shift.

It must be pointed out, however, that this evidence come from *in vitro* studies. Since anatomical dissections demonstrate connections between the ALL and ITB by Kaplan fibers, the actual function *in vivo* might prove to be different as the ITB might dynamically influence the ALL tension[42]. Zens *et al*



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Figure 1 Magnetic resonance imaging. A: Coronal T2 magnetic resonance imaging (MRI) showing a partial anterolateral ligament (ALL) lesion; B: Coronal T1 MRI showing a partial ALL lesion; C: Coronal STIR MRI showing a complete ALL lesion; D: Coronal and Sagittal T2 MRI showing an intact ALL.

[44] observed, in a cadaveric study, a progressive increase in the length of the ALL in the passive range of motion from 0° to 90° with an average increase of 0.15% per degree of flexion. They also observed that the greatest change in length (+33.77% ± 9.62%) was observed at 90° flexion in 25° internal rotation.

Through biomechanical studies, the failure of the ALL has also been demonstrated to occur in: Ligamentous tear at the tibial or femoral insertion point, intrasubstance tear, or complete tibial detachment with bone fragment avulsion (Segond fracture)[45].

In contrast, according to a robotic study by Kittl *et al*[46], it is the ITB that provides the greatest resistance to tibial IR (44%). The deep fibers of the ITB, Kaplan fibers, act as an IR stabilizing ligament, fixing the ITB against the lateral epicondyle[47]. Indeed, after a section of the KFs, it's been observed that the ITB is no longer attached to the lateral epicondyle, thus losing its effectiveness in rotational control[48]. The role of the KFs was also confirmed by Geeslin *et al*[49], demonstrating that sectioning of the KFs resulted in an IR control loss from 30° to 90° of flexion.

In summary, anterolateral soft tissues contribute to rotational stability in ACL-deficient knees, with the deep ITB possibly playing a more important role closer to extension than the ALL, which has a greater control of IR at higher flexion angles.

ALC STIFFNESS

A study by Wytrykowski *et al*[50] analyzed the stiffness of the ALL (21 N/mm) and the load at failure (141 N), and also described the load at failure of the gracilis tendon (200.7 N) and ITB (161.1 N). Other biomechanical studies have measured the mean maximum load during pull-to-failure testing of KFs (170 N for DKF and 71.3 N for PKF), and thus, suggest an important role for resistant structures like the ALL[26]. It follows that both LETs and anterolateral ligament reconstructions (ALLRs) with ITB strips and gracilis grafts own sufficient strength for anterolateral procedures.

INDICATIONS

The clinical indications for ALLR or LET are not clearly defined, and level one clinical studies are currently lacking. It has not yet been established whether there is significant clinical knee instability that

requires correction with an additional procedure.

Currently, the indication to perform an extra articular procedure associated with ACL reconstruction is based on preoperative clinical evaluation and patient characteristics. Radiologic investigation is not routinely used as an objective assessment of ALL stability because relatively small lesions can be easily missed in a setting of more obvious associated injuries. Some authors recommend the routine use of such procedures in all ACL reconstruction[51,52].

In contrast, other authors recommend an associated procedure only in selected cases[41] based on comparative studies that have demonstrated significant benefits in specific populations, such as: ACL revisions[53,54], chronic ACL injuries[55], patients with high-grade pivot shift[10,56], patients with Segond's fracture[10], patients with hyperlaxity[55], or in high demanding patients with a need to return to high levels of sports activity and pivoting activities[52] (Table 1).

LATERAL EXTRA-ARTICULAR TENODESIS (LET)

Lateral extra-articular tenodesis was originally used as an isolated technique in patients with ACL deficiency. Several LET techniques showed good clinical results in the short term[57]. However, long-term results highlighted that isolated LETs tended to fail, returning again to a condition of rotatory instability[58].

After performing LETs extensively in the early 1980s, there is now renewed interest in these techniques as combined procedures for ACL reconstruction. These procedures were initially abandoned because of concerns about excessive constraint of the lateral compartment and potential development of osteoarthritis.

More than 12 LETs (Table 2) have been described, most of which use a variable-length ITB strip passed underneath the FCL and attached at various points on the lateral femoral condyle or at Gerdy's tubercle. The FCL acts as a pulley above the graft while maintaining a relative isometry of the graft itself. However, clinical studies to determine the superiority of one technique over the others are lacking. A correlation can be established on the biomechanical function of KF and LET techniques since both provide a connection between the ITB and the distal femur to control IR.

Recently, some authors have described a "more anatomical" extra-articular tenodesis that aims to tension the capsulo-osseous layer and reconstruct the distal KFs[59]. An ITB strip is elevated, maintaining the distal insertion, passed over the FCL, and then fixed into a tunnel drilled at the level of a bony prominence 31.4 mm proximal to the lateral epicondyle (DKF insertion point).

Over the past few years, the authors have tried the use of different LETs and have decided to use mainly the Cocker-Arnold technique. It is a simple technique, easily reproducible, and does not require the preparation of tunnels or the use of suture anchors. The Cocker Arnold technique has proven effective in patients with a preoperative pivot shift 2+ or 3+ at decreasing the phenomenon and reducing the ALRI[60]. Good results were also found in ACLR revisions in high function demand patients with an excellent return to sport rate[61].

Cocker Arnold Mod. Technique[62]

A longitudinal, 10-cm, slightly curved incision is made just posterior to the lateral femoral epicondyle. Dissection continues by identifying the posterior margin of the ITB and removing any fascial attachments down to the level of Gerdy's tubercle. A 1-cm-wide, 8 to 10-cm-long strip of ITB is elevated from the anterior aspect of the posterior half of the ITB. The insertion of the ITB strip to Gerdy's tubercle is preserved, removing any deep attachments of the strip from the vastus lateralis. Identification of the FCL is performed by palpation, facilitated by placing the knee in a figure-of-4 position, which stretches the ligament. Once the FCL has been identified, a blunt dissection is made anteriorly and posteriorly to the proximal portion of the ligament. Efforts should be made to remain extracapsular in order not to damage the popliteal tendon. The ITB graft is then guided under the FCL from distal to proximal, flipped over the Gerdy's tubercule, and sutured to itself using a high resistance non adsorbable suture, with the knee in near full extension and neutral rotation (Figure 2).

ANTEROLATERAL LIGAMENT RECONSTRUCTION

The concepts of ALLR and LET are sometimes used synonymously, since these procedures share conceptual similarities in terms of technique and goals. However, in ALLRs an anatomical reconstruction of the ALL is sought, while in LETs a functional and not an anatomical reconstruction is performed.

Several studies have shown that isometry of the graft used in ALLRs is achieved by fixing it distal to Gerdy's tubercle and very proximal and posterior to the distal metaepiphyseal junction of the femur [63]. However, this positioning does not match the anatomic insertions of the ALL. The ALL is an anisometric structure: the length and tension of the ligament changes with knee flexion. The best

Table 1 Indications for an extra-articular procedure

Patients with specific characteristics:
ACL revisions
Chronic ACL injuries
High-grade pivot shifts
Segond's fracture
Hyperlaxity
High demanding patients

ACL: Anterior cruciate ligament.

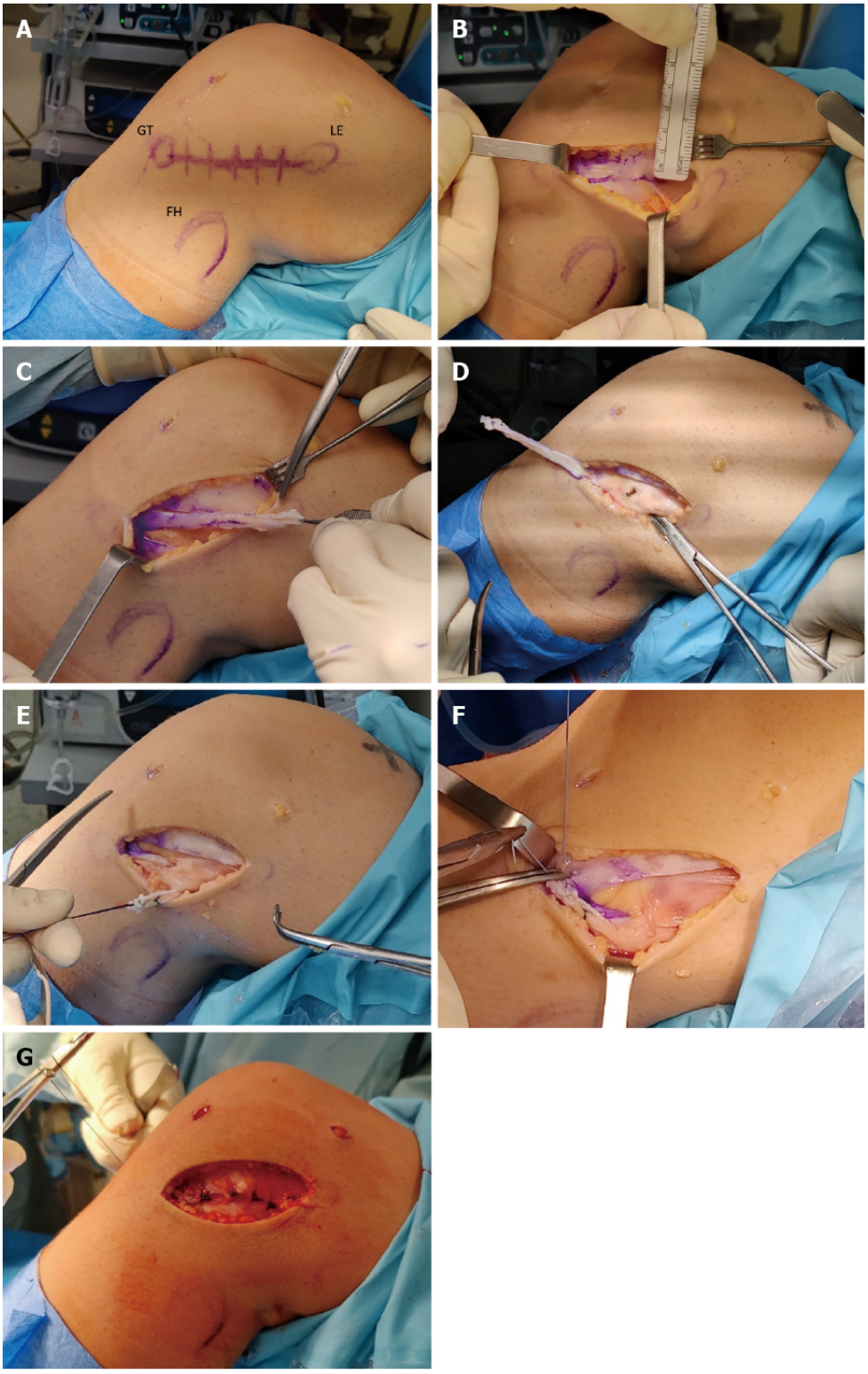
Table 2 The most performed lateral extra-articular tenodesis

Technique	Description
Lemaire *et al*[87], 1967	An ITB strip is harvested while maintaining the distal insertion, and then passed under the FCL and through a semi-circular tunnel created on the lateral aspect of the distal femur. The strip is then reflected and sutured onto itself.
Mod. Lemaire[21,88,89]	An ITB strip is harvested while maintaining the distal insertion, passed under the FCL, and secured to the lateral condyle with an interference screw or a staple.
MacIntosh *et al*[90], 1976	An ITB strip is harvested while maintaining the distal insertion, passed under the FCL, through a subperiosteal tunnel, through the intermuscular septum, back under the FCL, and sutured onto itself.
Losee *et al*[91], 1978	An ITB strip is harvested while maintaining the distal insertion, passed under the FCL, through a femoral tunnel originating at the gastrocnemius insertion point and ending anterior to the FCL. The strip is then sutured onto itself.
Ellison *et al*[92], 1979	A strip of ITB is elevated distally with a bony bract, passed under the FCL, and attached anteriorly to the original insertion.
Arnold and Coker *et al*[62], 1979	An ITB strip is harvested while maintaining the distal insertion, passed under the FCL, reflected, and sutured to itself at Gerdy's tubercle.
Benum[93], 1982	A lateral portion of the patellar tendon is harvested while maintaining the distal insertion, passed under the FCL, and secured with a staple to the lateral condyle.
Andrews and Sanders[94], 1983	Two ITB strips are elevated proximally, whipstitched with sutures that are passed through two parallel tunnels from the lateral condyle to the medial condyle, and then tied together.
Zarins and Rowe[95], 1986	The semitendinosus tendon is harvested while maintaining the insertion, passed through a tibial tunnel, through the joint, and over the lateral condyle below the FCL ,and sutured to the ITB. Similarly, a strip of ITB is harvested proximally, passed under the FCL, over the lateral condyle, through the tibial tunnel, and sutured to the semitendinosus tendon.
Wilson and Scranton[96], 1990	An ITB strip is harvested while maintaining the distal insertion, passed under the FCL and lateral gastrocnemius tendon, and sutured onto itself.
Marcacci and Zaffagnini[97], 1998	The semitendinosus and gracilis tendons are harvested while maintaining the insertion, sutured together, passed through a tibial tunnel, through the femoral notch, and over the top of the lateral condyle. The graft is then passed deep to the ITB, over the FCL, and attached distally to Gerdy's tubercle.

FCL: Fibular collateral ligament; ITB: Iliotibial band.

compromise[64,65] between the anatomic reconstruction and the ideal location of the graft insertions is as follows: At the femur, fixation proximal and posterior to the lateral epicondyle; at the tibia, fixation midway between Gerdy's tubercle and the ALL insertion. Fixation should also be done with the knee extended and the foot in neutral rotation. It is critical not to tension the graft in external rotation to avoid stiffening the knee and increasing stress.

The ALLR technique with the most clinical data available in the literature is reported by Sonnery-Cottet *et al*[10]: They described a combined ACL and ALL reconstruction technique using a 3-strand semitendinosus graft coupled with a free gracilis tendon graft. That resulted in a graft that, therefore, had a quadruple section, used for ACL reconstruction, that continues into a single gracilis strand used for ALL reconstruction. An isometric point near the femoral condyle is identified and drilled with an outside-in technique to serve as both the femoral tunnel for the intra-articular ACL and the femoral attachment for the extra-articular ALL reconstruction. The gracilis strand is then advanced distally into a tibial tunnel with an entry point superolateral to Gerdy's tubercle and then flipped back on itself, resulting in an inverted Y shape. This distal double bundle technique differs from most other ALL reconstruction techniques, which tend to use a free graft and a single tibial fixation point[66,67].



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Figure 2 Cocker Arnold Mod Technique. A: Bony landmarks on the anterolateral aspect of the knee: Gerdy's tubercle, lateral epicondyle, fibular head; B: An iliotibial band (ITB) strip 1cm-wide, 8 cm-long is prepared; C: ITB strip harvesting maintaining the distal insertion; D: Identification of the fibular collateral ligament (FCL) and blunt dissection; E: The graft is passed under the FCL and reflected to itself; F: The graft is sutured to Gerdy's tubercle with knee in extension and neutral rotation; G: The ITB is sutured in a standard fashion.

ALLR *VS* LET

Biomechanical studies explain that LET procedures have an advantageous lever arm in resisting IR compared to ALLR techniques. This is due to the more anterior point of fixation at Gerdy's tubercle, which provides a more efficient force vector[68].

Since a major concern lies in the overconstraint of the lateral compartment[69], several studies have been concerned with analyzing the effectiveness of different techniques at different degrees of tension [70]. The authors verified the optimal graft tension by applying different fixation tensions. The results show that a modified Lemaire tenodesis (in which an ITB strip is elevated, passed under the FCL, and fixed to the distal femur with a suture anchor) can restore proper knee kinematics with a tension of 20 N regardless of the degree of flexion (0°, 30°, and 60°) while maintaining the foot in neutral rotation. An ALL-anatomical reconstruction, on the other hand, cannot sufficiently reduce rotational laxity even at 40 N tension. According to the research of Inderhaug *et al*[71], a double-bundle ALLR (with one femoral attachment point and two distinct tibial attachment point) procedure can restore rotatory laxity when the graft is fixed in full extension. However, it has been reported that flexion-extension of the knee leads to the detensioning of one of the 2 bundles, and therefore the use of a stronger single bundle, has been recommended.

Long-term effects on articular cartilage wear in outcomes of LET or ALLR procedures do not yet have high levels of evidence[72]; however, it makes sense to opt for effective procedures at lower levels of tension in order not to increase the contact pressure of the articular surfaces. In a study by Marcacci *et al* [52], in which patients who underwent ACLR and LET were prospectively followed for up to 13 years, there was no evidence of increased arthritic degeneration when comparing patients who underwent ACLR alone.

Previous studies recommended fixation of the graft (in LET procedures) by maintaining the tibia in an external rotation position. However, more recent studies recommend fixing the graft while keeping the tibia in a neutral rotation position so as not to inhibit physiologic rotational motion[73]. Since anterolateral structures are thought to affect ALRI, it is reasonable to assume that fixation while keeping the knee in extension (at a flexion angle where pivot shift occurs) is favorable for seeking normal knee kinematics[71]. Additionally, the ALL or LET graft is stretched and fixed after ACL graft fixation to minimize the overconstraint.

Regarding the choice of graft, both an ITB strip and a gracilis graft own sufficient strength to vicariate the function of the ALL. In a study by Kittl *et al*[64], patterns of change in length and isometry in lateral extra-articular reconstructions were analyzed. Of the variables examined, only two effectively and reproducibly predicted a relative isometric graft behavior in different degrees of flexion: a graft path below the FCL and a femoral graft fixation proximal and posterior to the lateral epicondyle. In a biomechanical study, it was shown that an anatomic reconstruction of the ALL did not significantly reduce IR or anterior translation. In contrast, a LET procedure significantly improved anterior translation and rotational laxity[21].

Several *in vitro* biomechanical studies have attempted to quantify the efficacy of LET procedures. However, it is difficult to reach objective conclusions of superiority and durability given the large variability in different surgical techniques, graft selection, and type of fixation.

RESULTS

The indication for performing an anterolateral procedure is based on the concept of reducing stress forces on the ACL graft and more accurately restoring normal knee kinematics[74]. Improved knee stability results in a protective effect of the ACL graft and on the menisci[75]. These biomechanical advantages translate into clinical benefits, including reduced risk of ACL graft rupture, higher rates of return to previous sports physical activity, and lower risk of meniscal repair failure[76].

As early as 1990, LET combined with ACLR was shown to reduce graft stress by 43%[77] and combined use is being sought to improve joint kinematics and reduce graft failure rates[78].

Combining an ALLR reduces IR compared to isolated ACLR while having no significant effect on anterior translation. The resulting decrease in IR is more pronounced by increasing the degree of flexion. Specifically, applying a torque of 6 N/m decreased internal rotation of 1.64° ($P < 0.001$) in patients undergoing ACLR + ALLR compared to patients undergoing isolated ACLR[79].

Historically, several ACL reconstruction techniques have been proposed to restore rotational instability. Isolated ACL reconstructions, whether single or double bundle, have failed in the attempt by resulting in a residual rotational laxity. In a study by Monaco *et al*[51], it was demonstrated "*in vivo*" that the combination of a LET with a single-bundle ACLR procedure was significantly more effective than an isolated double-bundle technique ($P = 0.0001$) in reducing tibial IR.

In a study with 2-year follow-up in 502 patients[80], it was shown that the combination of ACLR (with hamstring graft) and ALLR had a 2.5-fold lower rate of ACL graft failure than isolated ACLR with BTPB and 3.1-fold lower rate than isolated ACLR with hamstring graft.

In a recent study by Sonnery-Cottet *et al*[81], it was shown at an average follow-up of 104 mo that patients undergoing ACLR combined with ALLR experienced significantly better ACL graft survival ($P = 0.0027$), lower overall revision rates ($P < 0.05$), lower ACLR revision rates ($P < 0.05$), and comparable complication rates to patients undergoing isolated ACLR. Overall, patients undergoing isolated ACLR had a 5-fold increased risk of ACL revision.

Regarding the concern of developing osteoarthritis in patients undergoing ALLR, there are two possible opposing scenarios to consider. The first factor relates to a possible overconstraint of the lateral compartment resulting in increased contact forces. The second factor, in contrast, concerns the possible residual rotational instability in case an ALLR is not performed, resulting in poor tibial rotation control and the consequent risk of secondary meniscal and chondral injuries. Several studies, however, state that there is no association between ALLR and early development of osteoarthritis compared with patients undergoing isolated ACLR[52,82]. In a multicenter study with 675 patients at 12 years of follow-up[83], there was no evidence of an association between ALLR and arthritic degeneration, which was instead reported mainly in cases of medial meniscectomy.

Recent literature states that, in agreement with biomechanical studies, associating an anterolateral procedure significantly improves a high-grade pivot shift, ensuring better clinical functional outcomes [84,85]. Additionally, subjective scores, such as IKDC and Lysholm and objective tests, such as the KT-1000, are also significantly better ($P < 0.05$) in patients who underwent a combined procedure[86].

ACTUAL LIMITS AND FUTURE PERSPECTIVES

A more complete and comprehensive understanding of ALC has encouraged surgeons to perform combined reconstructions to improve clinical results and long-term outcomes. It should be noted, however, that the heterogeneity of the techniques used in the studies examined cannot provide valid data and results for each anterolateral procedure. Although recent studies have shown the efficacy and safety of these techniques[80,81], randomized clinical trials and level one studies are required to analyze the superiority of a LET or ALLR technique over the others in terms of ALRI reduction and total revision rate.

CONCLUSION

From the latest evidence, it appears that it is not a single anterolateral structure that determines rotational stability, but rather that several structures act synergistically: the ALL, the superficial and deep layers of the ITB, the capsulo-osseous layer, and the Kaplan fibers. Regardless of the distinct structures that are injured and cause an ALRI, the authors consider it important to obtain a careful clinical evaluation of the patient, repeated just before the surgical procedure under anesthesia. In a scenario where there is no demonstrated superiority of one technique over the others, the authors opted to use the Cocker Arnold Modified Tenodesis as a combined procedure in ACLR deciding to perform it according to […] patient's characteristics (such as a high-grade pivot shift, hyperlaxity, Segond's fracture) and functional demands. They also use it in any revision surgery where there has been a previous ACL graft failure in order to reduce the ACL graft stress and the risk rate of a new failure.

FOOTNOTES

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REFERENCES

1 **Hughston JC**, Andrews JR, Cross MJ, Moschi A. Classification of knee ligament instabilities. Part II. The lateral compartment. *J Bone Joint Surg Am* 1976; **58**: 173-179 [PMID: 1254620 DOI: 10.2106/00004623-197658020-00002]
2 **Claes S**, Vereecke E, Maes M, Victor J, Verdonk P, Bellemans J. Anatomy of the anterolateral ligament of the knee. *J Anat* 2013; **223**: 321-328 [PMID: 23906341 DOI: 10.1111/joa.12087]
3 **Urban S**, Pretterklieber B, Pretterklieber ML. The anterolateral ligament of the knee and the lateral meniscotibial ligament - Anatomical phantom *vs* constant structure within the anterolateral complex. *Ann Anat* 2019; **226**: 64-72 [PMID: 31330303 DOI: 10.1016/j.aanat.2019.06.005]
4 **Sheean AJ**, Shin J, Patel NK, Lian J, Guenther D, Musahl V. The Anterolateral Ligament is Not the Whole Story: Reconsidering the Form and Function of the Anterolateral Knee and its Contribution to Rotatory Knee Instability. *Tech Orthop* 2018; **33**: 219-224 [PMID: 30542220 DOI: 10.1097/BTO.0000000000000303]
5 **Cho HJ**, Kwak DS. Anatomical Consideration of the Anterolateral Ligament of the Knee. *Biomed Res Int* 2019; **2019**: 5740473 [PMID: 31111059 DOI: 10.1155/2019/5740473]
6 **Helito CP**, Demange MK, Bonadio MB, Tírico LE, Gobbi RG, Pécora JR, Camanho GL. Anatomy and Histology of the Knee Anterolateral Ligament. *Orthop J Sports Med* 2013; **1**: 2325967113513546 [PMID: 26535259 DOI: 10.1177/2325967113513546]
7 **Herbst E**, Albers M, Burnham JM, Fu FH, Musahl V. The Anterolateral Complex of the Knee. *Orthop J Sports Med* 2017; **5**: 2325967117730805 [PMID: 29051903 DOI: 10.1177/2325967117730805]
8 **Ariel de Lima D**, Helito CP, Lacerda de Lima L, de Castro Silva D, Costa Cavalcante ML, Dias Leite JA. Anatomy of the Anterolateral Ligament of the Knee: A Systematic Review. *Arthroscopy* 2019; **35**: 670-681 [PMID: 30612770 DOI: 10.1016/j.arthro.2018.09.006]
9 **Stergiou N**, Ristanis S, Moraiti C, Georgoulis AD. Tibial rotation in anterior cruciate ligament (ACL)-deficient and ACL-reconstructed knees: a theoretical proposition for the development of osteoarthritis. *Sports Med* 2007; **37**: 601-613 [PMID: 17595155 DOI: 10.2165/00007256-200737070-00004]
10 **Sonnery-Cottet B**, Thaunat M, Freychet B, Pupim BH, Murphy CG, Claes S. Outcome of a Combined Anterior Cruciate Ligament and Anterolateral Ligament Reconstruction Technique With a Minimum 2-Year Follow-up. *Am J Sports Med* 2015; **43**: 1598-1605 [PMID: 25740835 DOI: 10.1177/0363546515571571]
11 **Ferretti A**, Monaco E, Labianca L, Conteduca F, De Carli A. Double-bundle anterior cruciate ligament reconstruction: a computer-assisted orthopaedic surgery study. *Am J Sports Med* 2008; **36**: 760-766 [PMID: 17702998 DOI: 10.1177/0363546507305677]
12 **Segond P**. Recherches cliniques et expérimentales sur les épanchements sanguins du genou par entorse. Aux Bureaux du Progrès médical [DOI: 10.1192/bjp.42.177.369]
13 **Johnson LL**. Lateral capsualr ligament complex: anatomical and surgical considerations. *Am J Sports Med* 1979; **7**: 156-160 [PMID: 464170 DOI: 10.1177/036354657900700302]
14 **Terry GC**, Hughston JC, Norwood LA. The anatomy of the iliopatellar band and iliotibial tract. *Am J Sports Med* 1986; **14**: 39-45 [PMID: 3752345 DOI: 10.1177/036354658601400108]
15 **Vieira EL**, Vieira EA, da Silva RT, Berlfein PA, Abdalla RJ, Cohen M. An anatomic study of the iliotibial tract. *Arthroscopy* 2007; **23**: 269-274 [PMID: 17349469 DOI: 10.1016/j.arthro.2006.11.019]
16 **Vincent JP**, Magnussen RA, Gezmez F, Uguen A, Jacobi M, Weppe F, Al-Saati MF, Lustig S, Demey G, Servien E, Neyret P. The anterolateral ligament of the human knee: an anatomic and histologic study. *Knee Surg Sports Traumatol Arthrosc* 2012; **20**: 147-152 [PMID: 21717216 DOI: 10.1007/s00167-011-1580-3]
17 **Patel RM**, Brophy RH. Anterolateral Ligament of the Knee: Anatomy, Function, Imaging, and Treatment. *Am J Sports Med* 2018; **46**: 217-223 [PMID: 28320209 DOI: 10.1177/0363546517695802]
18 **Ariel de Lima D**, Helito CP, Daggett M, Neto FMM, de Lima LL, Leite JAD, Cavalcante MLC. Anterolateral ligament of the knee: a step-by-step dissection. *BMC Musculoskelet Disord* 2019; **20**: 142 [PMID: 30947710 DOI: 10.1186/s12891-019-2517-0]
19 **De Carli A**, Monaco E, Mazza D, Argento G, Redler A, Proietti L, Gaj E, Ferretti A. Assessment of the Anterolateral Ligament of the Knee by Magnetic Resonance Imaging. *Joints* 2018; **6**: 153-156 [PMID: 30582102 DOI: 10.1055/s-0038-1675163]
20 **Sonnery-Cottet B**, Daggett M, Fayard JM, Ferretti A, Helito CP, Lind M, Monaco E, de Pádua VBC, Thaunat M, Wilson A, Zaffagnini S, Zijl J, Claes S. Anterolateral Ligament Expert Group consensus paper on the management of internal rotation and instability of the anterior cruciate ligament - deficient knee. *J Orthop Traumatol* 2017; **18**: 91-106 [PMID: 28220268 DOI: 10.1007/s10195-017-0449-8]
21 **Spencer L**, Burkhart TA, Tran MN, Rezansoff AJ, Deo S, Caterine S, Getgood AM. Biomechanical analysis of simulated clinical testing and reconstruction of the anterolateral ligament of the knee. *Am J Sports Med* 2015; **43**: 2189-2197 [PMID: 26093007 DOI: 10.1177/0363546515589166]
22 **Helito CP**, do Amaral C Jr, Nakamichi YD, Gobbi RG, Bonadio MB, Natalino RJ, Pécora JR, Cardoso TP, Camanho GL, Demange MK. Why Do Authors Differ With Regard to the Femoral and Meniscal Anatomic Parameters of the Knee Anterolateral Ligament? *Orthop J Sports Med* 2016; **4**: 2325967116675604 [PMID: 28203587 DOI: 10.1177/2325967116675604]
23 **Mansour R**, Yoong P, McKean D, Teh JL. The iliotibial band in acute knee trauma: patterns of injury on MR imaging. *Skeletal Radiol* 2014; **43**: 1369-1375 [PMID: 24902510 DOI: 10.1007/s00256-014-1918-2]
24 **Getgood A**, Brown C, Lording T, Amis A, Claes S, Geeslin A, Musahl V; ALC Consensus Group. The anterolateral complex of the knee: results from the International ALC Consensus Group Meeting. *Knee Surg Sports Traumatol Arthrosc* 2019; **27**: 166-176 [PMID: 30046994 DOI: 10.1007/s00167-018-5072-6]
25 **Lobenhoffer P**, Posel P, Witt S, Piehler J, Wirth CJ. Distal femoral fixation of the iliotibial tract. *Arch Orthop Trauma Surg* 1987; **106**: 285-290 [PMID: 3632313 DOI: 10.1007/BF00454335]
26 **Godin JA**, Chahla J, Moatshe G, Kruckeberg BM, Muckenhirn KJ, Vap AR, Geeslin AG, LaPrade RF. A Comprehensive

Reanalysis of the Distal Iliotibial Band: Quantitative Anatomy, Radiographic Markers, and Biomechanical Properties. *Am J Sports Med* 2017; **45**: 2595-2603 [PMID: 28609131 DOI: 10.1177/0363546517707961]

27 **Helito CP**, do Prado Torres JA, Bonadio MB, Aragão JA, de Oliveira LN, Natalino RJ, Pécora JR, Camanho GL, Demange MK. Anterolateral Ligament of the Fetal Knee: An Anatomic and Histological Study. *Am J Sports Med* 2017; **45**: 91-96 [PMID: 27624543 DOI: 10.1177/0363546516664888]

28 **Caterine S**, Litchfield R, Johnson M, Chronik B, Getgood A. A cadaveric study of the anterolateral ligament: re-introducing the lateral capsular ligament. *Knee Surg Sports Traumatol Arthrosc* 2015; **23**: 3186-3195 [PMID: 24929656 DOI: 10.1007/s00167-014-3117-z]

29 **Sabatini L**, Risitano S, Atzori F, Volante M, Aprato A, Indelli PF, Massè A. Histological analysis of the anterolateral ligament of the knee. *J Orthop* 2019; **16**: 368-372 [PMID: 31011250 DOI: 10.1016/j.jor.2019.03.019]

30 **Claes S**, Bartholomeeusen S, Bellemans J. High prevalence of anterolateral ligament abnormalities in magnetic resonance images of anterior cruciate ligament-injured knees. *Acta Orthop Belg* 2014; **80**: 45-49 [PMID: 24873084]

31 **Helito CP**, Helito PVP, Costa HP, Demange MK, Bordalo-Rodrigues M. Assessment of the Anterolateral Ligament of the Knee by Magnetic Resonance Imaging in Acute Injuries of the Anterior Cruciate Ligament. *Arthroscopy* 2017; **33**: 140-146 [PMID: 27324971 DOI: 10.1016/j.arthro.2016.05.009]

32 **Helito CP**, Helito PVP, Leão RV, Demange MK, Bordalo-Rodrigues M. Anterolateral ligament abnormalities are associated with peripheral ligament and osseous injuries in acute ruptures of the anterior cruciate ligament. *Knee Surg Sports Traumatol Arthrosc* 2017; **25**: 1140-1148 [PMID: 28293698 DOI: 10.1007/s00167-017-4498-6]

33 **Puzzitiello RN**, Agarwalla A, Zuke WA, Garcia GH, Forsythe B. Imaging Diagnosis of Injury to the Anterolateral Ligament in Patients With Anterior Cruciate Ligaments: Association of Anterolateral Ligament Injury With Other Types of Knee Pathology and Grade of Pivot-Shift Examination: A Systematic Review. *Arthroscopy* 2018; **34**: 2728-2738 [PMID: 30037574 DOI: 10.1016/j.arthro.2018.04.025]

34 **Song GY**, Zhang H, Wu G, Zhang J, Liu X, Xue Z, Qian Y, Feng H. Patients with high-grade pivot-shift phenomenon are associated with higher prevalence of anterolateral ligament injury after acute anterior cruciate ligament injuries. *Knee Surg Sports Traumatol Arthrosc* 2017; **25**: 1111-1116 [PMID: 28243704 DOI: 10.1007/s00167-017-4492-z]

35 **Zein AM**. Step-by-Step Arthroscopic Assessment of the Anterolateral Ligament of the Knee Using Anatomic Landmarks. *Arthrosc Tech* 2015; **4**: e825-e831 [PMID: 27284519 DOI: 10.1016/j.eats.2015.08.002]

36 **Rasmussen MT**, Nitri M, Williams BT, Moulton SG, Cruz RS, Dornan GJ, Goldsmith MT, LaPrade RF. An In Vitro Robotic Assessment of the Anterolateral Ligament, Part 1: Secondary Role of the Anterolateral Ligament in the Setting of an Anterior Cruciate Ligament Injury. *Am J Sports Med* 2016; **44**: 585-592 [PMID: 26684663 DOI: 10.1177/0363546515618387]

37 **Parsons EM**, Gee AO, Spiekerman C, Cavanagh PR. The biomechanical function of the anterolateral ligament of the knee. *Am J Sports Med* 2015; **43**: 669-674 [PMID: 25556221 DOI: 10.1177/0363546514562751]

38 **Kittl C**, El-Daou H, Athwal KK, Gupte CM, Weiler A, Williams A, Amis AA. The Role of the Anterolateral Structures and the ACL in Controlling Laxity of the Intact and ACL-Deficient Knee. *Am J Sports Med* 2016; **44**: 345-354 [PMID: 26657572 DOI: 10.1177/0363546515614312]

39 **Sidles JA**, Larson RV, Garbini JL, Downey DJ, Matsen FA 3rd. Ligament length relationships in the moving knee. *J Orthop Res* 1988; **6**: 593-610 [PMID: 3379513 DOI: 10.1002/jor.1100060418]

40 **Sonnery-Cottet B**, Lutz C, Daggett M, Dalmay F, Freychet B, Niglis L, Imbert P. The Involvement of the Anterolateral Ligament in Rotational Control of the Knee. *Am J Sports Med* 2016; **44**: 1209-1214 [PMID: 26865395 DOI: 10.1177/0363546515625282]

41 **Noyes FR**, Huser LE, Jurgensmeier D, Walsh J, Levy MS. Is an Anterolateral Ligament Reconstruction Required in ACL-Reconstructed Knees With Associated Injury to the Anterolateral Structures? *Am J Sports Med* 2017; **45**: 1018-1027 [PMID: 28056513 DOI: 10.1177/0363546516682233]

42 **Drews BH**, Kessler O, Franz W, Dürselen L, Freutel M. Function and strain of the anterolateral ligament part I: biomechanical analysis. *Knee Surg Sports Traumatol Arthrosc* 2017; **25**: 1132-1139 [PMID: 28258329 DOI: 10.1007/s00167-017-4472-3]

43 **Galway HR**, MacIntosh DL. The lateral pivot shift: a symptom and sign of anterior cruciate ligament insufficiency. *Clin Orthop Relat Res* 1980; 45-50 [PMID: 7371314 DOI: 10.1097/00003086-198003000-00008]

44 **Zens M**, Niemeyer P, Ruhhammer J, Bernstein A, Woias P, Mayr HO, Südkamp NP, Feucht MJ. Length Changes of the Anterolateral Ligament During Passive Knee Motion: A Human Cadaveric Study. *Am J Sports Med* 2015; **43**: 2545-2552 [PMID: 26264771 DOI: 10.1177/0363546515594373]

45 **Kennedy MI**, Claes S, Fuso FA, Williams BT, Goldsmith MT, Turnbull TL, Wijdicks CA, LaPrade RF. The Anterolateral Ligament: An Anatomic, Radiographic, and Biomechanical Analysis. *Am J Sports Med* 2015; **43**: 1606-1615 [PMID: 25888590 DOI: 10.1177/0363546515578253]

46 **Kittl C**, Inderhaug E, Williams A, Amis AA. Biomechanics of the Anterolateral Structures of the Knee. *Clin Sports Med* 2018; **37**: 21-31 [PMID: 29173554 DOI: 10.1016/j.csm.2017.07.004]

47 **Lutz C**, Sonnery-Cottet B, Niglis L, Freychet B, Clavert P, Imbert P. Behavior of the anterolateral structures of the knee during internal rotation. *Orthop Traumatol Surg Res* 2015; **101**: 523-528 [PMID: 26183087 DOI: 10.1016/j.otsr.2015.04.007]

48 **Kennedy MI**, LaPrade CM, Geeslin AG, LaPrade RF. An Overview of Clinically Relevant Biomechanics of the Anterolateral Structures of the Knee. *Tech Orthop* 2018; **33**: 213-218 [PMID: 30542219 DOI: 10.1097/BTO.0000000000000300]

49 **Geeslin AG**, Moatshe G, Chahla J, Kruckeberg BM, Muckenhirn KJ, Dornan GJ, Coggins A, Brady AW, Getgood AM, Godin JA, LaPrade RF. Anterolateral Knee Extra-articular Stabilizers: A Robotic Study Comparing Anterolateral Ligament Reconstruction and Modified Lemaire Lateral Extra-articular Tenodesis. *Am J Sports Med* 2018; **46**: 607-616 [PMID: 29268024 DOI: 10.1177/0363546517745268]

50 **Wytrykowski K**, Swider P, Reina N, Murgier J, Laffosse JM, Chiron P, Cavaignac E. Cadaveric Study Comparing the Biomechanical Properties of Grafts Used for Knee Anterolateral Ligament Reconstruction. *Arthroscopy* 2016; **32**: 2288-

2294 [PMID: 27161509 DOI: 10.1016/j.arthro.2016.03.004]
51 **Monaco E**, Labianca L, Conteduca F, De Carli A, Ferretti A. Double bundle or single bundle plus extraarticular tenodesis in ACL reconstruction? *Knee Surg Sports Traumatol Arthrosc* 2007; **15**: 1168-1174 [PMID: 17589826 DOI: 10.1007/s00167-007-0368-y]
52 **Marcacci M**, Zaffagnini S, Giordano G, Iacono F, Presti ML. Anterior cruciate ligament reconstruction associated with extra-articular tenodesis: A prospective clinical and radiographic evaluation with 10- to 13-year follow-up. *Am J Sports Med* 2009; **37**: 707-714 [PMID: 19193599 DOI: 10.1177/0363546508328114]
53 **Ferretti A**, Conteduca F, Monaco E, De Carli A, D'Arrigo C. Revision anterior cruciate ligament reconstruction with doubled semitendinosus and gracilis tendons and lateral extra-articular reconstruction. Surgical technique. *J Bone Joint Surg Am* 2007; **89** Suppl 2: 196-213 [PMID: 17768215 DOI: 10.2106/JBJS.G.00310]
54 **Lee DW**, Kim JG, Cho SI, Kim DH. Clinical Outcomes of Isolated Revision Anterior Cruciate Ligament Reconstruction or in Combination With Anatomic Anterolateral Ligament Reconstruction. *Am J Sports Med* 2019; **47**: 324-333 [PMID: 30640514 DOI: 10.1177/0363546518815888]
55 **Helito CP**, Sobrado MF, Giglio PN, Bonadio MB, Pécora JR, Camanho GL, Demange MK. Combined Reconstruction of the Anterolateral Ligament in Patients With Anterior Cruciate Ligament Injury and Ligamentous Hyperlaxity Leads to Better Clinical Stability and a Lower Failure Rate Than Isolated Anterior Cruciate Ligament Reconstruction. *Arthroscopy* 2019; **35**: 2648-2654 [PMID: 31421960 DOI: 10.1016/j.arthro.2019.03.059]
56 **Monaco E**, Ferretti A, Labianca L, Maestri B, Speranza A, Kelly MJ, D'Arrigo C. Navigated knee kinematics after cutting of the ACL and its secondary restraint. *Knee Surg Sports Traumatol Arthrosc* 2012; **20**: 870-877 [PMID: 21877296 DOI: 10.1007/s00167-011-1640-8]
57 **Andrews JR**, Sanders RA, Morin B. Surgical treatment of anterolateral rotatory instability. A follow-up study. *Am J Sports Med* 1985; **13**: 112-119 [PMID: 3985258 DOI: 10.1177/036354658501300206]
58 **Amirault JD**, Cameron JC, MacIntosh DL, Marks P. Chronic anterior cruciate ligament deficiency. Long-term results of MacIntosh's lateral substitution reconstruction. *J Bone Joint Surg Br* 1988; **70**: 622-624 [PMID: 3403611 DOI: 10.1302/0301-620X.70B4.3403611]
59 **Gali JC**, Gali Filho JC, Marques MF, Almeida TA, Cintra da Silva PA, LaPrade RF. Capsulo-osseous Layer Retensioning and Distal Kaplan Fiber Surgical Reconstruction: A Proposed Anatomical Lateral Extra-articular Tenodesis Approach. *Arthrosc Tech* 2021; **10**: e159-e164 [PMID: 33532223 DOI: 10.1016/j.eats.2020.09.021]
60 **Vadalà AP**, Iorio R, De Carli A, Bonifazi A, Iorio C, Gatti A, Rossi C, Ferretti A. An extra-articular procedure improves the clinical outcome in anterior cruciate ligament reconstruction with hamstrings in female athletes. *Int Orthop* 2013; **37**: 187-192 [PMID: 22623063 DOI: 10.1007/s00264-012-1571-0]
61 **Alessio-Mazzola M**, Formica M, Russo A, Sanguineti F, Capello AG, Lovisolo S, Felli L. Outcome after Combined Lateral Extra-articular Tenodesis and Anterior Cruciate Ligament Revision in Professional Soccer Players. *J Knee Surg* 2019; **32**: 906-910 [PMID: 30227449 DOI: 10.1055/s-0038-1672120]
62 **Arnold JA**, Coker TP, Heaton LM, Park JP, Harris WD. Natural history of anterior cruciate tears. *Am J Sports Med* 1979; **7**: 305-313 [PMID: 507265 DOI: 10.1177/036354657900700601]
63 **Kurosawa H**, Yasuda K, Yamakoshi K, Kamiya A, Kaneda K. An experimental evaluation of isometric placement for extraarticular reconstructions of the anterior cruciate ligament. *Am J Sports Med* 1991; **19**: 384-388 [PMID: 1897654 DOI: 10.1177/036354659101900411]
64 **Kittl C**, Halewood C, Stephen JM, Gupte CM, Weiler A, Williams A, Amis AA. Length change patterns in the lateral extra-articular structures of the knee and related reconstructions. *Am J Sports Med* 2015; **43**: 354-362 [PMID: 25540293 DOI: 10.1177/0363546514560993]
65 **Imbert P**, Lutz C, Daggett M, Niglis L, Freychet B, Dalmay F, Sonnery-Cottet B. Isometric Characteristics of the Anterolateral Ligament of the Knee: A Cadaveric Navigation Study. *Arthroscopy* 2016; **32**: 2017-2024 [PMID: 27157662 DOI: 10.1016/j.arthro.2016.02.007]
66 **Chahla J**, Menge TJ, Mitchell JJ, Dean CS, LaPrade RF. Anterolateral Ligament Reconstruction Technique: An Anatomic-Based Approach. *Arthrosc Tech* 2016; **5**: e453-e457 [PMID: 27656361 DOI: 10.1016/j.eats.2016.01.032]
67 **Smith JO**, Yasen SK, Lord B, Wilson AJ. Combined anterolateral ligament and anatomic anterior cruciate ligament reconstruction of the knee. *Knee Surg Sports Traumatol Arthrosc* 2015; **23**: 3151-3156 [PMID: 26387120 DOI: 10.1007/s00167-015-3783-5]
68 **Amis AA**. Anterolateral knee biomechanics. *Knee Surg Sports Traumatol Arthrosc* 2017; **25**: 1015-1023 [PMID: 28299387 DOI: 10.1007/s00167-017-4494-x]
69 **Slette EL**, Mikula JD, Schon JM, Marchetti DC, Kheir MM, Turnbull TL, LaPrade RF. Biomechanical Results of Lateral Extra-articular Tenodesis Procedures of the Knee: A Systematic Review. *Arthroscopy* 2016; **32**: 2592-2611 [PMID: 27324970 DOI: 10.1016/j.arthro.2016.04.028]
70 **Inderhaug E**, Stephen JM, Williams A, Amis AA. Biomechanical Comparison of Anterolateral Procedures Combined With Anterior Cruciate Ligament Reconstruction. *Am J Sports Med* 2017; **45**: 347-354 [PMID: 28027653 DOI: 10.1177/0363546516681555]
71 **Inderhaug E**, Stephen JM, Williams A, Amis AA. Anterolateral Tenodesis or Anterolateral Ligament Complex Reconstruction: Effect of Flexion Angle at Graft Fixation When Combined With ACL Reconstruction. *Am J Sports Med* 2017; **45**: 3089-3097 [PMID: 28898106 DOI: 10.1177/0363546517724422]
72 **Dodds AL**, Gupte CM, Neyret P, Williams AM, Amis AA. Extra-articular techniques in anterior cruciate ligament reconstruction: a literature review. *J Bone Joint Surg Br* 2011; **93**: 1440-1448 [PMID: 22058292 DOI: 10.1302/0301-620X.93B11.27632]
73 **Engebretsen L**, Lew WD, Lewis JL, Hunter RE, Benum P. Anterolateral rotatory instability of the knee. Cadaver study of extraarticular patellar-tendon transposition. *Acta Orthop Scand* 1990; **61**: 225-230 [PMID: 2371815 DOI: 10.3109/17453679008993505]
74 **Marom N**, Ouanezar H, Jahandar H, Zayyad ZA, Fraychineaud T, Hurwit D, Imhauser CW, Wickiewicz TL, Pearle AD, Nawabi DH. Lateral Extra-articular Tenodesis Reduces Anterior Cruciate Ligament Graft Force and Anterior Tibial

Translation in Response to Applied Pivoting and Anterior Drawer Loads. *Am J Sports Med* 2020; **48**: 3183-3193 [PMID: 33017168 DOI: 10.1177/0363546520959322]

75 **Ferretti A**, Monaco E, Gaj E, Andreozzi V, Annibaldi A, Carrozzo A, Vieira TD, Sonnery-Cottet B, Saithna A. Risk Factors for Grade 3 Pivot Shift in Knees With Acute Anterior Cruciate Ligament Injuries: A Comprehensive Evaluation of the Importance of Osseous and Soft Tissue Parameters From the SANTI Study Group. *Am J Sports Med* 2020; **48**: 2408-2417 [PMID: 32631068 DOI: 10.1177/0363546520935866]

76 **Saithna A**, Daggett M, Helito CP, Monaco E, Franck F, Vieira TD, Pioger C, Kim JG, Sonnery-Cottet B. Clinical Results of Combined ACL and Anterolateral Ligament Reconstruction: A Narrative Review from the SANTI Study Group. *J Knee Surg* 2021; **34**: 962-970 [PMID: 32023631 DOI: 10.1055/s-0040-1701220]

77 **Engebretsen L**, Lew WD, Lewis JL, Hunter RE. The effect of an iliotibial tenodesis on intraarticular graft forces and knee joint motion. *Am J Sports Med* 1990; **18**: 169-176 [PMID: 2343985 DOI: 10.1177/036354659001800210]

78 **Duthon VB**, Magnussen RA, Servien E, Neyret P. ACL reconstruction and extra-articular tenodesis. *Clin Sports Med* 2013; **32**: 141-153 [PMID: 23177468 DOI: 10.1016/j.csm.2012.08.013]

79 **Kelly SR**, Cutter BM, Huish EG Jr. Biomechanical Effects of Combined Anterior Cruciate Ligament Reconstruction and Anterolateral Ligament Reconstruction: A Systematic Review and Meta-analysis. *Orthop J Sports Med* 2021; **9**: 23259671211009879 [PMID: 34250171 DOI: 10.1177/23259671211009879]

80 **Sonnery-Cottet B**, Saithna A, Cavalier M, Kajetanek C, Temponi EF, Daggett M, Helito CP, Thaunat M. Anterolateral Ligament Reconstruction Is Associated With Significantly Reduced ACL Graft Rupture Rates at a Minimum Follow-up of 2 Years: A Prospective Comparative Study of 502 Patients From the SANTI Study Group. *Am J Sports Med* 2017; **45**: 1547-1557 [PMID: 28151693 DOI: 10.1177/0363546516686057]

81 **Sonnery-Cottet B**, Haidar I, Rayes J, Fradin T, Ngbilo C, Vieira TD, Freychet B, Ouanezar H, Saithna A. Long-term Graft Rupture Rates After Combined ACL and Anterolateral Ligament Reconstruction Versus Isolated ACL Reconstruction: A Matched-Pair Analysis From the SANTI Study Group. *Am J Sports Med* 2021; **49**: 2889-2897 [PMID: 34351825 DOI: 10.1177/03635465211028990]

82 **Ferretti A**, Monaco E, Giannetti S, Caperna L, Luzon D, Conteduca F. A medium to long-term follow-up of ACL reconstruction using double gracilis and semitendinosus grafts. *Knee Surg Sports Traumatol Arthrosc* 2011; **19**: 473-478 [PMID: 20602086 DOI: 10.1007/s00167-010-1206-1]

83 **Cantin O**, Lustig S, Rongieras F, Saragaglia D, Lefèvre N, Graveleau N, Hulet C; Société Française de Chirurgie Orthopédique et Traumatologique. Outcome of cartilage at 12years of follow-up after anterior cruciate ligament reconstruction. *Orthop Traumatol Surg Res* 2016; **102**: 857-861 [PMID: 27544885 DOI: 10.1016/j.otsr.2016.06.011]

84 **Hewison CE**, Tran MN, Kaniki N, Remtulla A, Bryant D, Getgood AM. Lateral Extra-articular Tenodesis Reduces Rotational Laxity When Combined With Anterior Cruciate Ligament Reconstruction: A Systematic Review of the Literature. *Arthroscopy* 2015; **31**: 2022-2034 [PMID: 26116497 DOI: 10.1016/j.arthro.2015.04.089]

85 **Song GY**, Hong L, Zhang H, Zhang J, Li Y, Feng H. Clinical Outcomes of Combined Lateral Extra-articular Tenodesis and Intra-articular Anterior Cruciate Ligament Reconstruction in Addressing High-Grade Pivot-Shift Phenomenon. *Arthroscopy* 2016; **32**: 898-905 [PMID: 26524939 DOI: 10.1016/j.arthro.2015.08.038]

86 **Helito CP**, Camargo DB, Sobrado MF, Bonadio MB, Giglio PN, Pécora JR, Camanho GL, Demange MK. Combined reconstruction of the anterolateral ligament in chronic ACL injuries leads to better clinical outcomes than isolated ACL reconstruction. *Knee Surg Sports Traumatol Arthrosc* 2018; **26**: 3652-3659 [PMID: 29610972 DOI: 10.1007/s00167-018-4934-2]

87 **Lemaire M**. Ruptures anciennes du ligament croisé antérieur. *Fréquence-Clinique-Traitement. J Chir* 1967; **93**: 311-320 [DOI: 10.1016/b978-2-294-72966-9.00009-2]

88 **Jesani S**, Getgood A. Modified Lemaire Lateral Extra-Articular Tenodesis Augmentation of Anterior Cruciate Ligament Reconstruction. *JBJS Essent Surg Tech* 2019; **9** [PMID: 32051777 DOI: 10.2106/JBJS.ST.19.00017]

89 **Muller B**, Willinge GJA, Zijl JAC. Minimally Invasive Modified Lemaire Tenodesis. *Arthrosc Tech* 2021; **10**: e29-e36 [PMID: 33532204 DOI: 10.1016/j.eats.2020.09.006]

90 **MacIntosh DL**, Darby TA. Lateral substitution reconstruction. *J Bone Joint Surg* 1976; **58B**: 142

91 **Losee RE**, Johnson TR, Southwick WO. Anterior subluxation of the lateral tibial plateau. A diagnostic test and operative repair. *J Bone Joint Surg Am* 1978; **60**: 1015-1030 [PMID: 721850 DOI: 10.2106/00004623-197860080-00001]

92 **Ellison AE**. Distal iliotibial-band transfer for anterolateral rotatory instability of the knee. *J Bone Joint Surg Am* 1979; **61**: 330-337 [PMID: 429400 DOI: 10.2106/00004623-197961030-00002]

93 **Benum P**. Anterolateral rotary instability of the knee joint. Results after stabilization by extraarticular transposition of the lateral part of the patellar ligament. A preliminary report. *Acta Orthop Scand* 1982; **53**: 613-617 [PMID: 7102280 DOI: 10.3109/17453678208992267]

94 **Andrews JR**, Sanders R. A "mini-reconstruction" technique in treating anterolateral rotatory instability (ALRI). *Clin Orthop Relat Res* 1983; 93-96 [PMID: 6822011 DOI: 10.1097/00003086-198301000-00018]

95 **Zarins B**, Rowe CR. Combined anterior cruciate-ligament reconstruction using semitendinosus tendon and iliotibial tract. *J Bone Joint Surg Am* 1986; **68**: 160-177 [PMID: 3944155 DOI: 10.2106/00004623-198668020-00001]

96 **Wilson WJ**, Scranton PE Jr. Combined reconstruction of the anterior cruciate ligament in competitive athletes. *J Bone Joint Surg Am* 1990; **72**: 742-748 [PMID: 2355037 DOI: 10.2106/00004623-199072050-00015]

97 **Marcacci M**, Zaffagnini S, Iacono F, Neri MP, Loreti I, Petitto A. Arthroscopic intra- and extra-articular anterior cruciate ligament reconstruction with gracilis and semitendinosus tendons. *Knee Surg Sports Traumatol Arthrosc* 1998; **6**: 68-75 [PMID: 9604189 DOI: 10.1007/s001670050075]

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ORIGINAL ARTICLE

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Social media growth of orthopaedic surgery residency programs in response to the COVID-19 pandemic

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Abstract

BACKGROUND

In the Spring of 2020, residency programs across the country experienced rapid and drastic changes to their application process as a result of the coronavirus disease 2019 (COVID-19) pandemic. In response, residency programs shifted to virtual events and began harnessing social media to communicate with applicants.

AIM

To analyze the changes in social media usage by orthopaedic surgery programs in response to the COVID-19 pandemic.

METHODS

Based on the 2019 residency and fellowship electronic database, accredited US orthopaedic surgery programs were reviewed for social media presence on Instagram and Twitter. Approximately 47000 tweets from 2011-2021 were extracted through the Twitter application programming interface. We extracted: Total number of followers, accounts following, tweets, likes, date of account creation, hashtags, and mentions. Natural language processing was utilized for

tweet sentiment analysis and classified as positive, neutral, or negative. Instagram data was collected and deemed current as of August 11, 2021. The account foundation date analysis was based on the date recognized as the start of the COVID-19 outbreak in the United States, before or after March 1, 2020.

RESULTS

A total of 85 (42.3%) orthopaedic surgery residency program Twitter handles were identified. Thirty-five (41.2%) programs joined Twitter in the nine months after the 2020 covid outbreak. In 2020, there was a 126.6% increase in volume of tweets by orthopaedic surgery residency accounts as compared to 2019. The median number of followers was 474.5 (interquartile range 205.0-796.5). The account with the highest number of tweets was Hospital for Special Surgery (@HSpecialSurgery) with 13776 tweets followed by University of Virginia (@UVA_Ortho) with 5063 and Yale (@OrthoAtYale) with 899. Sentiment analysis before 2020 revealed 30.4% positive, 60.8% neutral, and 8.8% negative sentiments across tweets. Interestingly, the positive sentiment percentage increased in 2020 from 30.4% to 34.5%. Of the 201 ACGME-accredited orthopaedic residency programs on Fellowship and Residency Electronic Interactive Database, 115 (57.2%) participate on Instagram, with 101 (87.8%) identified as "resident"-managed *vs* 14 (12.2%) identified as "department"-managed. Over three quarters (77.4%) of Instagram accounts were created after March 1, 2020. The average number of followers per account was 1089.5 with an average of 58.9 total posts.

CONCLUSION

Our study demonstrates a substantial growth of Instagram and Twitter presence by orthopaedic surgery residency programs during the COVID-19 pandemic. These data suggest that orthopaedic residency programs have utilized social media as a new way to communicate with applicants and showcase their programs in light of the challenges presented by the pandemic.

Key Words: Social media; COVID-19; Orthopaedic surgery; Residency

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Core Tip: In response to the challenges of the coronavirus disease 2019 (COVID-19) pandemic, orthopaedic surgery residency programs drastically increased their presence on social media. Our paper investigates the use of social media by orthopaedic surgery residency programs in response to the COVID-19 pandemic. We analyzed how ACGME-accredited programs have substantially increased their social media presence to address the gaps created by changes in the application and recruitment processes. With continued uncertainty regarding the pandemic, we demonstrate why programs currently not employing social media as a resource should consider it as a legitimate opportunity for outreach and recruitment.

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INTRODUCTION

Social media has proven to be a valuable tool for education and collaboration. There are almost 4 billion social media users around the globe, equating to over 50% of the global population[1]. As the use of social media continues to grow in the general population, it has also become an increasingly popular platform for healthcare and global outreach. Other social media platforms, such as Instagram and Twitter, are used for public health outreach, professional networking, and the dissemination of research findings[2]. In the past, orthopaedic surgery social medial presence has been primarily limited to practice management and patient outreach[3].

In the Spring of 2020, residency programs across the country experienced rapid and drastic changes to their application process due to the coronavirus disease 2019 (COVID-19) pandemic. Applicants and programs alike faced novel challenges including the elimination of visiting rotations, in-person interviews, open houses, and social exchanges. For very competitive specialties, such as orthopaedic surgery, applicants lost critical opportunities to display their abilities, earn letters of recommendation,

and build relationships at institutions of interest[4]. Similarly, residency training programs did not have the opportunity to showcase their programs and evaluate applicants in person. In response to these changes, residency programs adopted virtual events and began harnessing social media to communicate with applicants. Prior literature reported 85% of interviewees utilized at least one social media platform to learn more about individual programs[5]. Another study showed up to 77.8% of applicants feel that residency programs should be utilizing social media as a means of communication, and the majority of applicants (54.3%) in the 2021 application cycle were influenced by social media with regards to interest in specific residency programs[6]. Considering the new challenges that emerged, social media has allowed programs and applicants with a platform to engage with one another in meaningful ways.

Several studies have looked at social media use in other surgical subspecialties including plastic surgery, urology, general surgery, and otolaryngology[4,7-10]. However, there is limited literature about the changes and trends of social media implementation by orthopaedic surgery residency programs during the COVID-19 pandemic. In the present study, we investigate the use of social media by orthopaedic surgery residency programs in response to the COVID-19 pandemic. We hypothesize that programs have substantially increased their social media presence to address the gaps created by changes in the application and recruitment processes because of the pandemic.

MATERIALS AND METHODS

A list of ACGME-accredited orthopaedic surgery residency programs was compiled from the Fellowship and Residency Electronic Interactive Database (FREIDA) in August 2021. A total of 201 programs were identified. Prior studies have suggested that residency programs more often utilize Instagram and Twitter as platforms for delivery of information as opposed to other similar social media alternatives such as Facebook[11,12]. Therefore, all programs were reviewed for ownership of Instagram and Twitter accounts. Programs were determined to have social media accounts through a Google search and extensive search within each social media platform. On the Google search engine, residency programs were searched using the corresponding program name followed by "orthopaedic surgery residency" and the social media platform of interest. If no evidence of the account of interest, social media specific searches were conducted on Instagram and Twitter using the text "(Program name) orthopaedic surgery residency." Private or personal social media accounts were excluded. All social media accounts were identified as residency only or department only. A residency account was defined as one that specifically denoted its affiliation with the institution's residency program. Instagram data was collected and deemed current as of August 11, 2021. Twitter data was collected and deemed current as of July 5, 2021. This study did not require Institutional Review Board approval as all information is publicly available and did not directly involve patient care.

Approximately 47000 tweets from 2011-2021 were extracted through the Twitter application programming interface on July 5, 2021. The following information was extracted: total number of followers, accounts following, tweets, likes, date of account creation, hashtags, and mentions. Natural language processing was utilized for tweet sentiment analysis and classified as positive, neutral, or negative. Statistical analysis was performed using Python 3.8.9 with the libraries NumPy 1.21 and NLTK 3.6.2. Figures were generated using Python, Matplotlib 3.4.2, and Seaborn 0.11.1.

For identified Instagram accounts, the date of first post was used as a proxy for account foundation date. The foundation date was assessed for establishment before or after March 1, 2020 – the date recognized as the start of the COVID-19 outbreak in the United States. Accounts were classified as either a residency or department account and the total number of posts and followers were recorded. Additionally, accounts were noted for having their program website in the biography section as well as specific highlights on their Instagram "story."

RESULTS

Twitter

We identified Twitter handles for 85 (42.3%) orthopaedic surgery residency programs, 35 (41.2%) of which joined Twitter in 2020 (Figure 1). From 2011 to 2021, 46807 tweets were extracted. In 2011, there were a total of 127 tweets compared to 8195 in 2019, 10377 in 2020, and 5,270 in 2021 (through July 5, 2021) (Table 1). From 2019 to 2020 alone, there was a 126.6% increase in volume of tweets by orthopaedic surgery residency accounts (Figure 2).

The median number of tweets for all orthopaedic surgery residency programs was 103.5 [interquartile range (IQR) 32.5-563.0], the median number of followers was 474.5 (IQR 205.0-796.5), and the median number of accounts following was 152.5 (IQR 54.5-431.75) (Table 2).

The account with the highest number of tweets was @HSpecialSurgery with 13776 tweets followed by @UVA_Ortho with 5063 and @OrthoAtYale with 899. Before 2020, the most commonly used hashtag (#) by orthopaedic surgery twitter accounts was #hughston, followed by #RothmanOrtho (Figure 3A).

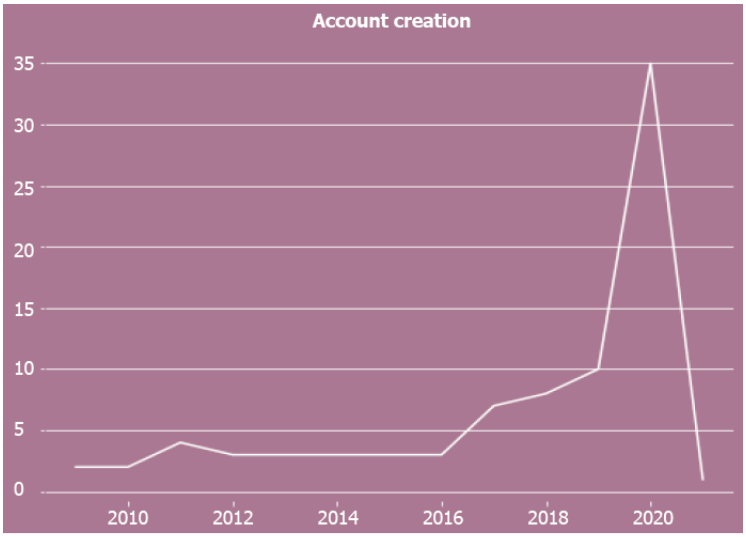
Table 1 Total number of tweets per year

Year	Tweets by orthopaedic surgery programs
2011	127
2019	8195
2020	10377
2021	5270

Table 2 Orthopaedic surgery residency program twitter accounts

	Median	IQR
Number of tweets	103.5	[32.5-563.0]
Number of followers	474.5	[205.0-796.5]
Number following	152.5	[54.5-431.75]
Number of likes	84.5	[22.25-525.75]

IQR: Interquartile range.



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Figure 1 Orthopaedic surgery residency twitter accounts created. This figure demonstrates the number of new orthopaedic surgery residency Twitter accounts that were created from 2009-2021.

After 2020, the most used hashtag by orthopaedic surgery twitter accounts was #COVID-19, followed by #orthotwitter and #OrthoMatch2021 (Figure 3B). Before 2020, the account with the highest number of mentions was @BrianColeMD, followed by @MOR_Docs and @AAOS1 (Figure 4A). After 2020, the account with the highest number of mentions was @HSpecialSurgery, followed by @AAOS1 and @BillLevineMD (Figure 4B).

Sentiment analysis before 2020 revealed 30.4% positive, 60.8% neutral, and 8.8% negative sentiments across tweets (Figure 5A). Interestingly, the positive sentiment percentage increased in 2020 from 30.4% to 34.5% (Figure 5B). Word cloud analysis, a visual representation of word frequency, revealed an emergence of "resident," "covid," and "virtual" after 2020 (Figure 6A) compared to before 2020 (Figure 6B).

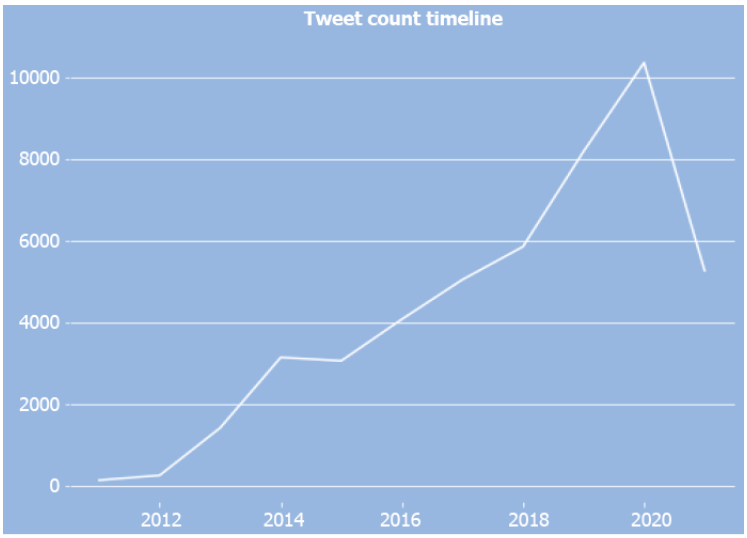
Instagram

Of the 201 ACGME-accredited orthopaedic surgery residency programs on FREIDA, 115 (57.2%) participate on Instagram, with 101 (87.8%) identified as residency-run *vs* department-run. Over three quarters (77.4%) of accounts were created after March 1, 2020. Additionally, 90 (78.3%) of the identified accounts had a link to the program website in their Instagram (Table 3). To quantify the level of activity

Table 3 Instagram accounts

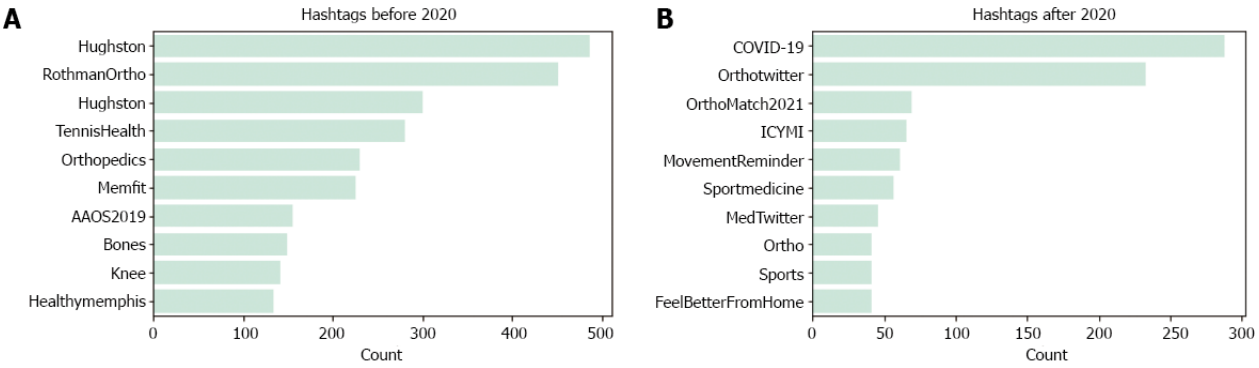
	Number of accounts (%)	Created after March 1, 2020 (%)	Residency run accounts (%)	Website link in bio
Instagram accounts	115 (57.2)	89 (77.4)	101 (87.8)	90 (78.3)

Out of 201 identified orthopaedic surgery residency programs.



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Figure 2 Tweet count timeline. This figure demonstrates the number of 'tweets' generated by orthopaedic surgery residency Twitter accounts from 2011-2021.



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Figure 3 Top 10 most common twitter hashtags. A: This figure illustrates the ten most common hashtags used by orthopaedic surgery residency Twitter accounts prior to the year 2020; B: This figure illustrates the ten most common hashtags used by orthopaedic surgery residency Twitter accounts after the year 2020. A hashtag is defined as using the "#" symbol and associating it with a word or phrase.

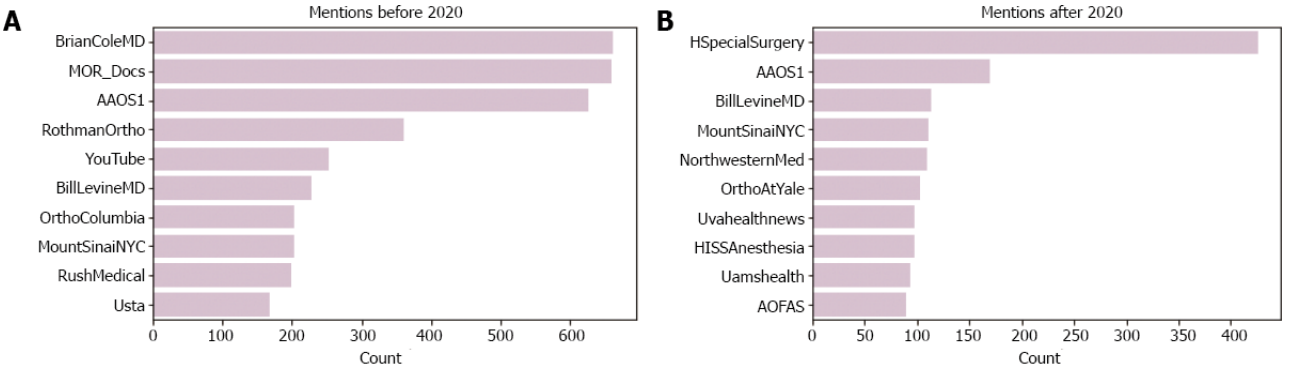
and engagement *via* Instagram, we examined the number of followers and posts by programs. The average number of followers per account was 1089.5 (SD = 606.4) with an average of 58.9 (SD = 56.5) total posts (Table 4). The most common post type included advertisements for virtual sessions, resident spotlights, and photos illustrating resident life.

DISCUSSION

The complex nature of COVID-19 has made the residency application process challenging for programs and applicants alike. As a result, orthopaedic surgery residency programs have turned to online platforms such as Instagram and Twitter to showcase their institutions and interact with applicants. Social media has helped fill the void left by limited away rotations, virtual interviews, and an uncertain application process. With the proliferation orthopaedic surgery programs social media use, it is

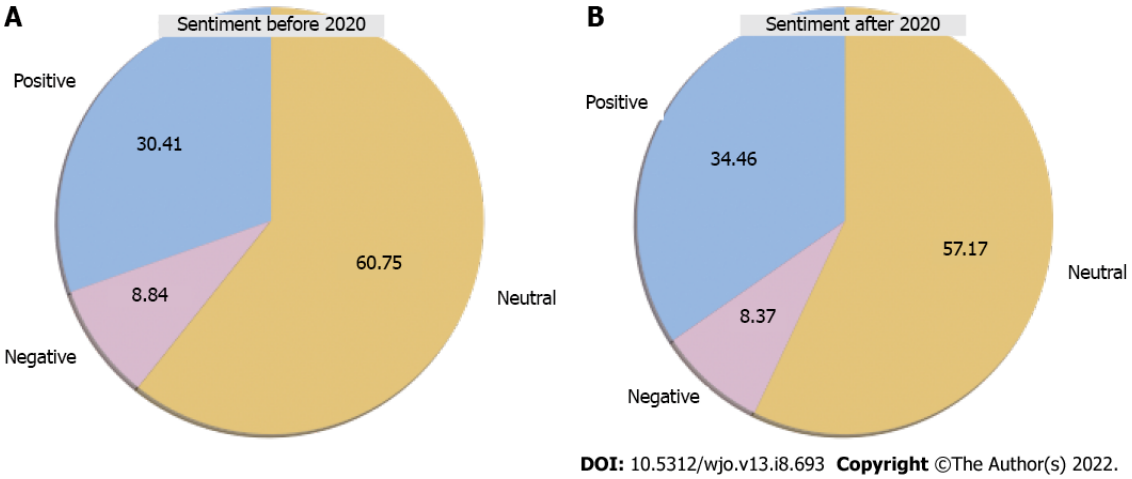
Table 4 Instagram data

	Mean
Number of followers	1089.5
Number of posts	58.9



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Figure 4 Top 10 most common twitter mentions. A: This figure illustrates the ten most common Twitter mentions used by orthopaedic surgery residency Twitter accounts prior to the year 2020; B: This figure illustrates the ten most common Twitter mentions used by orthopaedic surgery residency Twitter accounts after the year 2020. A Twitter "mention" is defined as tagging or mentioning another account using the @ symbol.



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Figure 5 Tweet sentiment analysis. A: This figure illustrates the percentage of positive, negative, and neutral tweets sent out by orthopaedic surgery residency accounts prior to the year 2020; B: This figure illustrates the percentage of positive, negative, and neutral tweets sent out by orthopaedic surgery residency accounts after the year 2020.

increasingly important to understand the uses and trends associated with each platform.

After March 1, 2020, Instagram account creation amongst orthopaedic surgery residency programs grew 342%. Instagram's platform, which allows users to post captioned images with no character limit, offers opportunities for posts about resident life and culture. For example, Instagram "stories" offer real-time snapshots documenting the day-to-day life of a resident. Accounts have also posted resident spotlights filled with information about residents' backgrounds, interests, and personal lives, ultimately providing a glimpse into the personalities and diversity of a programs' residents[11]. Twitter, on the other hand, is a more text-centered platform and is commonly used in an academic or informative manner[12]. It has provided applicants with the opportunity to directly converse with program directors, residents, and educators in the absence of in-person events. It has also been used as a source of reliable information regarding virtual events and program specific details[13].

To our knowledge, there is just one prior study evaluating the effects of the COVID-19 pandemic on social media among orthopaedic surgery residency programs. Yong *et al*[3] evaluated Facebook, Twitter, and Instagram use by orthopaedic surgery residency programs in May 2019, July 2020, and November 2020. In their cross-sectional study, the authors found a 300% increase in social media account



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Figure 6 Word cloud analysis. A: This figure illustrates a word cloud of the most common words used in tweets sent out by orthopaedic surgery residency Twitter accounts prior to the year 2020. Larger words indicate words that were detected more often; B: This figure illustrates a word cloud of the most common words used in tweets sent out by orthopaedic surgery residency Twitter accounts after the year 2020. Larger words indicate words that were detected more often.

prevalence amongst orthopaedic surgery residency programs from May 2019 to November 2020, with Instagram experiencing the largest account growth and creation. The authors conclude that the proliferation in social media use by residency programs was directly related to the effects of the COVID-19 pandemic.

Based on the results of Yong *et al*[3], we attempted to further evaluate the trends in social media use among orthopaedic surgery residency programs. There are several important differences between the current study and Yong's results. Our complex algorithm extracted important data from twitter to evaluate a significant number of variables over a ten-year period. Yong examined trends at three points in time over 18-mo. In addition to the variables evaluated by Yong (account creation and number of followers), the present study provides data on total number of tweets per year and median number of tweets per account, allowing for a more in-depth understanding of twitter use amongst orthopaedic surgery programs. Furthermore, we provide specific information on the most active twitter accounts before and after the pandemic, as well as the accounts with the most mentions, which may be important information for applicants looking to network or for programs hoping to increase their twitter presence. Finally, a unique strength of the present study is our use of word cloud analysis, which provides a visual representation of the most tweeted words and phrases by orthopaedic surgery programs, unsurprisingly showing an increased use of the words "covid" and "virtual" after the start of the pandemic.

Several studies have shown similar increases in social media usage within other specialties, including neurology, pediatrics, and otolaryngology. Following the start of the pandemic, Gaini *et al*[14] reported almost half of the neurology residency programs on social media announced at least one online virtual event *via* their website or social media. This suggests that social media has not only been used to connect with applicants, but also to announce virtual opportunities. Pruett *et al*[15] found that pediatric residency programs utilize social media to highlight resident wellness, program culture, and resident lifestyle. The authors also suggest that residency programs should increase the number of virtual opportunities applicants have to engage in live conversation with residents and faculty. Ahmadmehrabi *et al*[16] found that 61% of otolaryngology programs have at least 1 social media account, with Twitter being used to facilitate dialogue between applicants, programs, and various institutions. In short, many residency programs across numerous medical specialties have found unique ways to harness social media in the post-pandemic application process.

For most applicants, the transition to a virtual application process has provided increased schedule flexibility, virtual access to information, and a decreased financial burden that comes with interviewing and traveling[7]. Excluding away rotations, the average orthopaedic surgery applicant spends about $7000 on the interview process and submits 85.7 applications[17]. While the virtual application process provides some obvious benefits to applicants, it also creates disadvantages for both programs and applicants. A lack of in-person interviews may prevent programs and applicants from being able to candidly evaluate one another. Furthermore, an inability to experience a program's culture and city in person may make it difficult for an applicant to picture him or herself moving to that location for five or more years. These challenges are magnified by the fact that most away rotators are limited to one externship, whereas prior to the pandemic, applicants would routinely complete two or more away rotations. This is especially difficult for applicants, as many view their sub-internships as an opportunity to make an impression, obtain letters of recommendation, show interest at specific programs, and evaluate their comfort and lifestyle in a new city. Based on the aforementioned information, orthopaedic surgery programs should continue to utilize virtual platforms to supplement the traditional interview process, as they have been shown to influence interest in certain programs for the majority of orthopedic surgery applicants[6]. However, virtual interactions should not be seen as a replacement to externships and in-person interviews.

The proliferation of social media use amongst orthopaedic surgery residency programs may pose unforeseen risks to applicants. While following the social media account of a prospective residency program may signal an applicant's interest, it can also draw attention to the applicant. A 2015 study found that 18% of general surgery residency program directors reported visiting applicants' social media accounts and 11% admitted to lowering an applicants' rank as a result of their online activities [18]. The authors of the present study believe programs will increasingly visit the social media accounts of applicants, especially as applicants provide their usernames when they choose to follow the program's social media account. Applicants must be cognizant of their online etiquette and must consider how their posts may be viewed by future colleagues, employers, and patients[19].

The rise of social media usage amongst orthopedic surgery residency programs has been clearly identified as a factor in the application process for medical students. Social media usage within orthopedic surgery has also been reported in the context of patient education and clinical implications. Specifically, studies have shown that social media is a growing platform for surgeons to communicate with and educate patients in order to improve patient outcomes, but long-term efficacy and practicality of social media in patient communication is still unclear[20]. Within the scope of orthopedic surgery residency programs, the clinical implications of social media are unclear and have not yet been thoroughly studied. It is clear, however, that social media is quickly becoming a critical component of education and training with one study revealing 77% of internal medicine residents utilizing social media for medical education purposes[21]. Several programs have included resident education and training, as well as patient outcomes, as a component of their social media content, but the implications of this with regard to clinical outcomes have not yet been reported in the literature.

There are several limitations to our study. Because social media use can only be reported as a snapshot in time, the reported number of posts, followers, and content at the time of data collection may no longer be up to date. Furthermore, while we were thorough in our efforts to identify social media accounts, it is possible that we may not have identified all social media accounts or may have misidentified some. Additionally, we included all social media accounts of orthopaedic surgery programs that have residency programs, whether the account itself was specifically geared towards applicants. While our data shows a decrease in activity from 2020 to 2021, it must be noted that only about half of the year 2021 was included, as data collection was performed on July 5, 2021. It remains to be seen whether twitter and Instagram use will continue to increase as the delta variant surges. Despite these limitations, the authors' multi-faceted evaluation of social media use amongst orthopaedic surgery residencies is the most comprehensive of its kind in the orthopaedic literature to date.

CONCLUSION

In response to the challenges of the COVID-19 pandemic, orthopaedic surgery residency programs drastically increased their presence on social media. It is likely that the utilization of social media will continue to persist into the future as platforms such as Instagram and Twitter have illuminated new ways for programs to interact with applicants. With continued uncertainty regarding the pandemic, programs currently not employing social media as a resource should consider it as a legitimate opportunity for outreach and recruitment. Orthopaedic surgery programs should continue to utilize virtual platforms to supplement the traditional interview process; however, virtual interactions should not be seen as a replacement to externships and in-person interviews. Further studies are needed to evaluate the true impact that increased social media use by orthopaedic surgery residency programs has on the application process, as well as the training and education of resident surgeons.

ARTICLE HIGHLIGHTS

Research background

As a result of the coronavirus disease 2019 (COVID-19) pandemic, orthopaedic surgery residency programs across the country experienced rapid and drastic changes to their application process. In response, residency programs shifted to virtual events and began harnessing social media to communicate with applicants.

Research motivation

Social media has become an integral part of business, education, and networking. However, there is scarce literature that explores the use of social media amongst orthopaedic surgery residency programs, specifically in response to the ongoing COVID-19 pandemic.

Research objectives

The aim of the study analyze and discuss the various changes in social media usage by orthopaedic surgery residency programs before and during the COVID-19 pandemic.

Research methods

Orthopaedic surgery programs were reviewed for social media presence on Instagram and Twitter. Instagram accounts were tallied for followers, number of posts, and date of creation. Twitter posts were characterized *via* type of post and sentiment using natural language processing.

Research results

In response to the pandemic, orthopaedic surgery residency programs greatly increased their presences on Instagram and Twitter. Both platforms were used in a similar manner to engage with applicants, however, it remains unknown what the impact this had on prospective applicants.

Research conclusions

Our study demonstrates a substantial growth of Instagram and Twitter presence by orthopaedic surgery residency programs associated with the COVID pandemic. This data suggest that orthopaedic surgery residency programs have utilized social media as a new way to communicate with applicants and showcase their programs in light of the challenges presented by the pandemic. The authors anticipate the current trend in social media will plateau as the visiting student precautions are returned to normal before stabilizing as a present but less pervasive means of communication.

Research perspectives

Further studies are needed to evaluate the true impact that increased social media use by orthopaedic surgery residency programs has on the application process.

FOOTNOTES

Author contributions: Geller JS, Massel DH, Rizzo MG, Schwartz EC, Milner JE, and Donnally CJ contributed to the design and implementation of the research, to the analysis of the results, and to the writing of the manuscript; all authors have read and approve the final manuscript.

Institutional review board statement: As the data utilized to conduct this study is publicly available, this study was exempt from the need for institutional review board approval.

Informed consent statement: As the data utilized to conduct this study is publicly available, this study was exempt from the need for informed consent.

Conflict-of-interest statement: All authors report no relevant conflict of interest for this article.

Data sharing statement: No additional data are available.

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REFERENCES

1 **Ramesh Masthi NR**, Pruthvi S, Phaneendra MS. A Comparative Study on Social Media Usage and Health Status among Students Studying in Pre-University Colleges of Urban Bengaluru. *Indian J Community Med* 2018; **43**: 180-184 [PMID: 30294084 DOI: 10.4103/ijcm.IJCM_285_17]
2 **Bludevich BM**, Fryer M, Scott EM, Buettner H, Davids JS, LaFemina J. Patterns of General Surgery Residency Social Media Use in the Age of COVID-19. *J Surg Educ* 2021; **78**: e218-e225 [PMID: 34016568 DOI: 10.1016/j.jsurg.2021.04.017]
3 **Yong TM**, Pappas MA, Ray GS, McManus TG, Coe MP. Analyzing the Proliferation of Social Media Use Among Orthopaedic Surgery Residency Programs. *JB JS Open Access* 2021; **6** [PMID: 34291181 DOI: 10.2106/JBJS.OA.21.00017]
4 **DeAtkine AB**, Grayson JW, Singh NP, Nocera AP, Rais-Bahrami S, Greene BJ. #ENT: Otolaryngology Residency Programs Create Social Media Platforms to Connect With Applicants During COVID-19 Pandemic. *Ear Nose Throat J* 2020; 145561320983205 [PMID: 33355006 DOI: 10.1177/0145561320983205]
5 **Economides JM**, Choi YK, Fan KL, Kanuri AP, Song DH. Are We Witnessing a Paradigm Shift? *Plast Reconstr Surg Glob Open* 2019; **7**: e2288 [PMID: 31592016 DOI: 10.1097/GOX.0000000000002288]
6 **Checketts JX**, Hunt T, Checketts BR, Scott JT, Johnson M, Boose M, Schwartz M, Chalkin B. Analysis of Social Media Perceptions Among Orthopaedic Surgery Residency Applicants and Social Media Use by Residency Programs During the 2020 to 2021 Cycle. *JB JS Open Access* 2021; **6** [PMID: 34957367 DOI: 10.2106/JBJS.OA.21.00083]
7 **Fang HA**, Boudreau H BS, Khan S, Singh NP, Rais-Bahrami S, King TW, Corey B, Chen H. An evaluation of social media utilization by general surgery programs in the COVID-19 era. *Am J Surg* 2021; **222**: 937-943 [PMID: 33906728]
8 **Azoury SC**, Mazzaferro DM, Piwnica-Worms W, Messa CA 4th, Othman S, Stranix JT, Serletti JM, Kovach SJ, Fosnot J. An Update on Social Media in Academic Plastic Surgery Training Programs: The Rising Trend of Likes, Shares, and Retweets. *Ann Plast Surg* 2020; **85**: 100-104 [PMID: 32079812 DOI: 10.1097/SAP.0000000000002289]
9 **Manning E**, Calaway A, Dubin JM, Loeb S, Sindhani M, Kutikov A, Ponsky L, Mishra K, Bukavina L. Growth of the Twitter Presence of Academic Urology Training Programs and Its Catalysis by the COVID-19 Pandemic. *Eur Urol* 2021; **80**: 261-263 [PMID: 34006446 DOI: 10.1016/j.eururo.2021.05.002]
10 **Ho P**, Margolin E, Sebesta E, Small A, Badalato GM. #AUAMatch: The Impact of COVID-19 on Social Media Use in the Urology Residency Match. *Urology* 2021; **154**: 50-56 [PMID: 34033828 DOI: 10.1016/j.urology.2021.05.019]
11 **Harp T**, Szeto MD, Presley CL, Meckley AL, Geist R, Anderson J, Laughter MR, Rundle CW, Husayn SS, Dellavalle RP. Usage and engagement with Instagram by dermatology residency programs during the COVID-19 pandemic compared with Twitter and Facebook. *J Am Acad Dermatol* 2021; **85**: e313-e315 [PMID: 34418516 DOI: 10.1016/j.jaad.2021.05.071]
12 **Kim YH**, Ali NS, Vidal NY. Social media use in residency recruitment during the COVID-19 pandemic. *Dermatol Online J* 2021; **27** [PMID: 34387054 DOI: 10.5070/D327654053]
13 **Daggubati LC**, Ryan CA, Brandon C, Madden DB, Farou N, Mansouri A, Zacharia BE. #Neurosurgery: A Temporal and Content Analysis of Academic Neurosurgery on Twitter. *World Neurosurg* 2021; **153**: e481-e487 [PMID: 34242826 DOI: 10.1016/j.wneu.2021.06.150]
14 **Gaini RR**, Patel KM, Khan SA, Singh NP, Love MN. A rise in social media utilization by U.S. neurology residency programs in the era of COVID-19. *Clin Neurol Neurosurg* 2021; **207**: 106717 [PMID: 34091422 DOI: 10.1016/j.clineuro.2021.106717]
15 **Clay Pruett J**, Deneen K, Turner H, Kozar T, Singh NP, King TW, Nichols MH. Social Media Changes in Pediatric Residency Programs During COVID-19 Pandemic. *Acad Pediatr* 2021; **21**: 1104-1107 [PMID: 34126258 DOI: 10.1016/j.acap.2021.06.004]
16 **Ahmadmehrabi S**, Xie DX, Ward BK, Bryson PC, Byrne P. OHNS Residency Program and Applicant Social Media Presence During the COVID-19 Pandemic. *Ann Otol Rhinol Laryngol* 2021; **130**: 961-965 [PMID: 33455439 DOI: 10.1177/0003489420987977]
17 **Aiyer AA**, Granger CJ, McCormick KL, Cipriano CA, Kaplan JR, Varacallo MA, Dodds SD, Levine WN. The Impact of COVID-19 on the Orthopaedic Surgery Residency Application Process. *J Am Acad Orthop Surg* 2020; **28**: e633-e641 [PMID: 32732651 DOI: 10.5435/JAAOS-D-20-00557]
18 **Rohde SC**, White EM, Yoo PS. Residency Program Use of Social Media in the COVID-19 Era: An Applicant's Perspective. *J Surg Educ* 2021; **78**: 1066-1068 [PMID: 33358933 DOI: 10.1016/j.jsurg.2020.12.011]
19 **Ashiofu E**, Thomas L. The Role of Social Media in Psychiatry Recruitment: a Survey of Program Directors. *Acad Psychiatry* 2021; **45**: 742-745 [PMID: 34268678 DOI: 10.1007/s40596-021-01500-4]
20 **Duymuş TM**, Karadeniz H, Şükür E, Atiç R, Zehir S, Azboy İ. Social media and Internet usage of orthopaedic surgeons. *J Clin Orthop Trauma* 2017; **8**: 25-30 [PMID: 28360492 DOI: 10.1016/j.jcot.2016.10.007]
21 **Galiatsatos P**, Porto-Carreiro F, Hayashi J, Zakaria S, Christmas C. The use of social media to supplement resident medical education - the SMART-ME initiative. *Med Educ Online* 2016; **21**: 29332 [PMID: 26750511 DOI: 10.3402/meo.v21.29332]

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ORIGINAL ARTICLE

Retrospective Cohort Study

Fluctuation of visual analog scale pain scores and opioid consumption before and after total hip arthroplasty

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Abstract

BACKGROUND

Patients who undergo orthopedic procedures are often given excess opioid medication. Understanding the relationship between pain and opioid consumption following total hip arthroplasty (THA) is key to creating safe and effective opioid prescribing guidelines.

AIM

To evaluate the association between the quantity of opioid consumption in relation to pain scores both pre-and postoperatively in patients undergoing primary THA.

METHODS

We retrospectively reviewed patients who underwent primary THA from November 2018-May 2019 and answered both the visual analog scale (VAS) pain and opioid medication questionnaires pre-and postoperatively. Both surveys were delivered daily for 7-days before surgery through the first 30 postoperative days. Survey results were divided into preoperative, postoperative days 1-7, postoperative days 8-14, and postoperative days 15-30 for analysis. Mean opioid pill consumption and VAS pain scores in each time period were determined and compared to patients' preoperative status using hierarchical Poisson and linear regressions, respectively.

RESULTS

There were 105 patients included. Mean VAS pain scores were the highest preoperatively 7.41 ± 1.72. However, VAS pain scores significantly declined in each successive postoperative category compared to preoperative scores: postoperative day 1-7 (5.07 ± 1.79; $P < 0.001$), postoperative day 8-14 (3.60 ± 1.64; P

< 0.001), and postoperative day 15-30 (3.15 ± 1.63; P < 0.001). Mean opioid pill consumption preoperatively was 0.68 ± 1.29 pills. Compared to preoperative opioid consumption, opioid use was significantly greater between postoperative days 1-7 (1.51 ± 1.58; P = 0.001) and postoperative days 8-14 (1.00 ± 1.27; P = 0.043). Opioid consumption declined below preoperative levels between postoperative days 15-30 (0.35 ± 0.72; P = 0.160) which correlates with a VAS pain score of 3.15.

CONCLUSION

All patients experienced significant benefit and pain relief from having undergone THA. Average postoperative opioid consumption decreased below preoperative consumption between postoperative days 15-30, which was associated with a VAS pain score of 3.15. These results can be used to appropriately guide opioid prescribing practices and set patient expectations regarding pain management following THA.

Key Words: Opioids; Narcotics; Pain; Visual analog scale; Total hip arthroplasty

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Core Tip: Our results should be used to appropriately guide opioid prescribing patterns and set patient expectations regarding expected pain management following total hip arthroplasty (THA). This will not only give patients a baseline to reference during their recovery but also limit redundant billing expenses related to unnecessary prescription of medication and avoidable outpatient visits due to post-operative pain. However, without further research that considers other patient factors that influence pain severity, our understanding of the independent impact of pain on opioid consumption after THA remains uncertain.

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INTRODUCTION

Total hip arthroplasty (THA) is one of the most common and successful orthopedic procedures[1]. Arguably one of the greatest improvements in THA peri-operative management over the last decade has been the continuous advancements in pain management regimens that have greatly improved the rate of recovery following the procedure[2-4]. However, due to the highly invasive nature of the procedure, postoperative pain becomes difficult to avoid entirely despite advancements in surgical techniques and perioperative protocols[5]. While joint-related pain is expected to steadily subside after surgical rehabilitation, numerous patients report persistent pain leading to the development of chronic pain postoperatively[6]. Furthermore, the amount of pain that patients experience may perhaps be the most important determinant of satisfaction after THA[7]. Some previous studies suggest that patients who consume more opioids report less satisfaction with pain relief and greater pain intensity[8,9].

Opioids have long been established as a primary analgesic modality for patients undergoing THA and are prescribed routinely for acute pain management following surgery[10]. However, opioid misuse remains a rapidly growing public health crisis which has led to a heightened focus on conservative prescribing patterns in orthopedic surgery[11]. Recent data suggests that the United States ranks number one among all other countries worldwide in daily narcotic consumption[12]. Specifically, orthopedic surgeons are the third-highest group of opioid prescribers among physicians, accounting for almost 8% of all opioid prescriptions in the United States[13]. Limiting access to unused medications while ensuring adequate pain management has been a proposed strategy for improving current prescription practices[14-16]. Although recent studies have highlighted a pattern of patients receiving excess opioid medication after undergoing various orthopedic procedures, there has been minimal evidence to suggest an optimal supply of pain medication postoperatively[16-23]. Therefore, in order to create a safe and effective prescribing guideline that minimizes the over-prescription of opioids and to effectively advise patients pre- and postoperatively, it is imperative to discern the relationship between pain severity and opioid consumption.

The visual analog scale (VAS) is a simple and frequently used method to quantify variations in pain intensity for both clinical and investigational purposes[24-26]. The assessment of pain is generally difficult due to its multifaceted subjective nature, which can vary among individuals. Despite this diversity, the VAS pain questionnaire is widely used in the literature and clinical practice. It is a simple

patient-reported outcome tool and requires relatively little patient training to measure pain scores. To our knowledge, no previous study has analyzed the relationship between VAS pain scores and perioperative opioid consumption in patients undergoing THA.

The purpose of this study is to evaluate the association between the quantity of opioid consumption in relation to VAS pain scores both pre- and postoperatively in patients undergoing primary THA. We hypothesize that both opioid consumption and VAS pain scores will decrease for all patients following surgery when compared to their preoperative status.

MATERIALS AND METHODS

Study design

A retrospective review of prospectively collected data was performed at a tertiary, urban, academic medical center to identify consecutive patients who underwent primary, elective THA from November 2018 to May 2019. The inclusion criteria comprised patients who answered both the VAS pain and opioid medication questionnaires pre- and postoperatively. Results from both surveys were separated into four time points for analysis (preoperative, postoperative days 1-7, postoperative days 8-14, and postoperative days 15-30). Patients under the age of 18, those undergoing THA for non-elective or oncologic reasons, revision THA, those who did not have a recorded response for both questionnaires, and any patient receiving opioid pain medications for conditions not related to their operative hip were excluded from this study. A total of 1142 primary THAs were performed at our institution within the period of interest, of which, 270 (24%) were performed by the senior author (Davidovitch RI). All cases included in this study were performed by the senior author (Davidovitch RI) utilizing a direct anterior approach with the assistance of fluoroscopy.

All patients participated in our institutional-wide comprehensive total joint pathway program, which encompasses standardized protocols for all aspects of perioperative care and postoperative rehabilitation. The records and existing data are de-identified and are part of our institutional quality improvement program; therefore, the present study was exempt from human-subjects review by our institutional review board.

Outcome measures

The primary outcomes measures included VAS pain scores and opioid consumption over time. VAS pain scores were calculated based on a 0 to 10 scale, with 0 representing no pain and 10 being the worst pain imaginable[24,25]. The VAS pain score was selected as an outcome measure based on its ability to detect immediate changes with a minimal clinically important difference (MCID) ranging from 1.86 to 2.36 for THA[25]. Opioid consumption was defined as the number of narcotic pills taken per day. The various opioids reported by patients included tramadol, hydromorphone, hydrocodone, oxycodone, and morphine sulfate[27]. Mean VAS pain scores and opioid pills consumed preoperatively were compared to the means on postoperative days 1-7, days 8-14, and days 15-30 to determine the time point at which postoperative opioid consumption decreases below preoperative consumption and its relation to VAS pain scores. Postoperative time points and the calculation of their means were chosen to provide a comparison to the baseline seven-day interval measured preoperatively.

Opioid-sparing pain protocol

Our institution implemented a novel opioid-sparing protocol for all patients undergoing THA beginning in October 2018 (Supplementary material). The previously established World Health Organization (WHO) analgesic ladder was used as a framework for the development of this novel protocol[28]. With the addition of this protocol, our healthcare providers and patients adhere to standardized order sets for the administration of multimodal analgesia medications throughout the perioperative period[4,29]. Within one month of planned THA, patients are evaluated at our institution's preadmission test center. Thorough medication reconciliation is performed and patients who are actively consuming opiates are advised and instructed to taper or discontinue its usage prior to undergoing surgery.

In the operating room, patients are given initial propofol infusions for sedation. Subsequently, patients receive a single dose of spinal anesthetic containing 0.5% ropivacaine or 0.5% bupivacaine. Prior to wound closure, patients are administered two separate homogenously diluted 60-cc injections by the operating surgeon. The first injection was a cocktail containing 20 cc of liposomal bupivacaine (one vial) mixed with 40 cc of 0.9% normal saline solution while the second injection was a cocktail containing 40 cc of non-liposomal bupivacaine (0.25% weight/volume) and 15 mg of ketorolac with 20 cc of 0.9% normal saline solution. All patients receive a total of two grams of intravenous (IV) tranexamic acid (TXA). One gram before surgical incision and another gram during surgical wound closure. Patients who could not receive IV TXA [contraindication for TXA administration: (1) Subarachnoid hemorrhage (2) Intravascular clotting; and (3) Known tranexamic acid hypersensitivity] received 3 g topically in the wound mixed in 100cc saline solution.

All patients receive similar postoperative multimodal analgesia medications during the immediate post-anesthesia care unit period, on the surgical floor, and discharge. Postoperative pain management was accomplished using mostly non-narcotic medications. Patient-controlled analgesia, as well intravenous opioid administration, was strongly discouraged, except in rare situations of breakthrough pain when alternatives had been exhausted. Additionally, patients receive a prescription of aspirin 81 mg twice daily as the primary deep venous thrombosis prophylaxis, which also has analgesic effects as part of our multimodal approach. Following discharge, patients are assessed for adequate pain control (and severity) at multiple time points *via* telephone and during scheduled follow-up visits.

Data collection

As part of our institutional standard of care, patients were preoperatively registered for an electronic patient engagement application (EPEA; Force Therapeutics, New York, NY) by clinical care coordinators at the time of surgical scheduling. The EPEA is a mobile and web-based technology that wirelessly delivers digital patient reported outcome questionnaires to patients at pre-defined time intervals. This application was used to collect VAS pain scores and quantity of opioid consumption daily for seven days before surgery through the first 30 postoperative days.

The collected baseline patient demographic data included gender, age, body mass index (BMI; kg/m^2), American Society of Anesthesiologists (ASA) classification, race, smoking status, length of stay (LOS; days), and surgical time (minutes). LOS was determined by calculating the difference between the time of admission and discharge following surgery. Surgical time was derived from calculating the time difference between the initial skin incision and the completion of skin closure. All demographic data were extracted from our institution's electronic data warehouse (Epic Caboodle. version 15; Verona, WI) using Microsoft SQL Server Management Studio 2017 (Redmond, WA).

Statistical analysis

All statistical analyses were performed using SPSS v25 (IBM Corporation, Armonk, New York). The data were organized using Microsoft Excel software. Baseline demographic characteristics of the study participants were tallied for each variable collected. Descriptive data are represented as means ± SD or counts (%). Hierarchical Poisson regression was used to compare mean opioid pill consumption preoperatively to postoperative days 1-7, days 8-14, and days 15-30. Hierarchical linear regression was used to compare VAS pain scores preoperatively to postoperative days 1-7, days 8-14, and days 15-30. The incidence rate ratio and exponentiated beta coefficients are also reported along with an associated 95% confidence interval (CI). A P value of less than 0.05 was considered to be statistically significant.

RESULTS

A total of 105 patients were identified who underwent primary THA *via* a direct anterior approach with the assistance of fluoroscopy. The majority of the study participants were female (63%), between the age 65-74 years old (38%), had a BMI < 30 kg/m^2 (62%), ASA class II (74%), Caucasian (90%), and non-smokers (68%). Additionally, the majority of the patients in this study had a surgical time spanning between 60-120 min (78%) and an in-hospital LOS of 1 day or less following surgery (75%). Full demographic details are highlighted in Table 1.

Opioid consumption and VAS pain scores

The average number of opioid pills consumed preoperatively was 0.68 ± 1.29. The number of opioids consumed between postoperative days 1-7 (1.51 ± 1.58; P = 0.001) and postoperative days 8-14 (1.00 ± 1.27; P = 0.043) was significantly greater when compared to patients' preoperative opioid consumption. However, opioid consumption between postoperative days 15-30 did not significantly differ from their preoperative status (0.35 ± 0.72; P = 0.160). This suggests that despite an initial rise in opioid requirements postoperatively, patients experience a decreased need for pain relief 15-30 postoperatively and in fact have a similar if not less opioid consumption in comparison to their preoperative opioid consumption level (Figure 1). These findings are summarized in Table 2.

The mean VAS pain score for the study participants preoperatively was 7.41 ± 1.72. This significantly differed from the VAS pain scores between postoperative days 1-7 (5.07 ± 1.79; P < 0.001), days 8-14 (3.60 ± 1.64; P < 0.001), and days 15-30 (3.15 ± 1.63; P < 0.001) (Table 3). The differences exceeded the proposed MCID for the VAS pain score, making these findings clinically significant. Furthermore, the mean VAS pain score between postoperative days 15-30 correlated with a decline in opioid consumption below patients' preoperative opioid consumption status. The average postoperative VAS pain score of patients who did not take opioids was approximately 3.50, which suggests that a general decline in pain occurs at roughly days 8-14 postoperatively and becomes much lower between postoperative days 15-30 (Figure 2). Additionally, there was a significant linear relationship between VAS pain scores and the number of opioid capsules consumed, which may indicate that as patients' perception of their pain intensified, their reliance on opioid pain medication increased accordingly (P < 0.001; Table 4).

Table 1 Patient demographics (*N* = 105)

Patient demographics (*N* = 105), *n* (%)	
Gender	
Male	39 (37)
Female	66 (63)
Age (yr)	
< 55	17 (16)
55-64	30 (29)
65-74	40 (38)
≥ 75	18 (17)
BMI (kg/m)^2	
Underweight (< 18.5)	2 (2)
Normal (18.5-24.9)	30 (29)
Overweight (25.0-29.9)	33 (31)
Obese (> 30)	40 (38)
ASA Classification	
I	9 (9)
II	78 (74)
III or IV	18 (17)
Race	
Caucasian	94 (90)
Non-caucasian	11 (10)
Smoking Status	
Current smoker	2 (2)
Former smoker	31 (30)
Never smoker	71 (68)
LOS (d)	
0	34 (32)
1	45 (43)
> 1	26 (25)
Surgical Time (min)	
< 60	20 (19)
60-120	82 (78)
> 120	3 (3)

DISCUSSION

Over the past few decades, the number of opioids prescribed to manage patients with chronic non-cancer related pain such as osteoarthritis has dramatically increased[16,18,30-33]. This reported rise carries substantial implications for orthopedic surgeons, as patients who undergo orthopedic procedures are prescribed more opioid medications on average than patients of most other specialties [13]. The impact of opioids has gained significant clinical and research interest given their potential to prognosticate postoperative outcomes and patient satisfaction. Recent evidence now suggests that opioids provide no additional benefits compared to non-opioid medications such as ibuprofen and acetaminophen to manage pain associated with osteoarthritis and have higher rates of adverse events [34-38]. Additionally, previous studies have also reported that patients who used more opioids postoperatively experienced less satisfaction and greater pain intensity irrespective of the procedure type[8,9]. Therefore, gaining a better understanding of the relationship between opioid use and pain is

Table 2 Number of opioid pills consumed per day (*N* = 105, 564 observations)

Time	Average daily opioid use (SD)	Incidence rate ratio (95%CI)	*P* value
Preop	0.68 (1.29)	---	---
Postop days 1-7	1.51 (1.58)	2.43 (1.44, 4.10)	**0.001**
Postop days 8-14	1.00 (1.27)	1.76 (1.02, 3.03)	**0.043**
Postop days 15-30	0.35 (0.72)	0.66 (0.36, 1.18)	0.160

SD: Standard deviation; CI: Confidence interval.

Table 3 Visual analog scale pain score (*N* = 105, 504 observations)

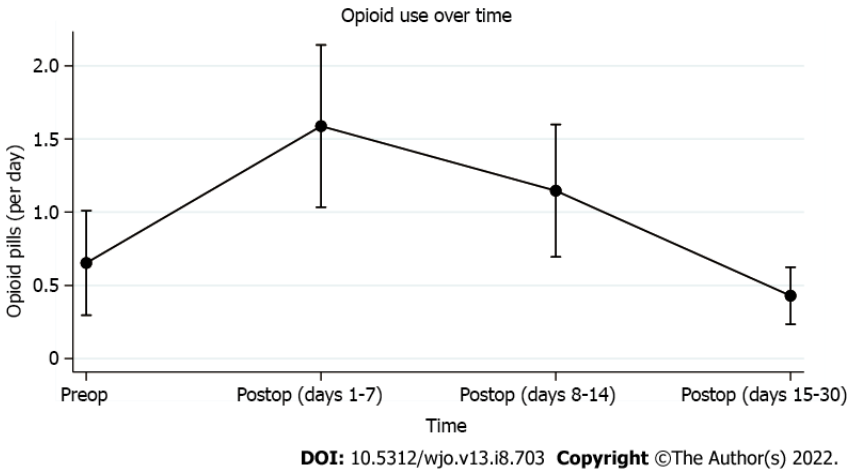
Time	Average VAS pain score (SD)	Beta coefficient (95%CI)	*P* value
Preop	7.41 (1.72)	---	---
Postop days 1-7	5.07 (1.79)	-3.00 (-3.34, -2.65)	**< 0.001**
Postop days 8-14	3.60 (1.64)	-4.43 (-4.79, -4.07)	**< 0.001**
Postop days 15-30	3.15 (1.63)	-5.21 (-5.57, -4.86)	**< 0.001**

VAS: Visual analog scale; SD: Standard deviation; CI: Confidence interval.

Table 4 Comparison of mean postop visual analog scale pain score and opioid use (*N* = 105)

	No opioid use (50.2%)	1 Opioid pill (22.3%)	2+ Opioid pills (27.5%)	*P* values
VAS pain score (SD)	3.48 (1.81)	4.30 (1.63)	5.32 (1.76)	**< 0.001**

SD: Standard deviation.

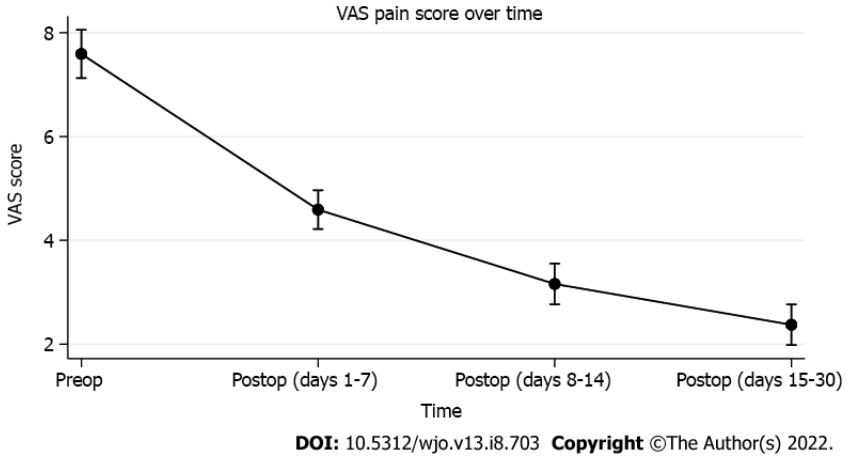


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Figure 1 Mean opioid consumption over time.

essential given the shifting emphasis placed upon health safety and quality. The findings of the present study not only demonstrate that all patients achieve significant pain relief following THA, but that average postoperative opioid consumption decreased below preoperative consumption by days 15-30 postoperatively.

Bot *et al*[9] found that opioid use preoperatively along with lower patient self-efficacy were the best predictors of decreased satisfaction, and the administration of more opioids does not improve satisfaction with pain relief. This is consistent with our findings as patients reported higher VAS pain scores as their opioid intake increased. However, there have been few studies that have documented a correlation between greater opioid use and higher satisfaction with pain relief[39,40]. Carragee *et al*[41]



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Figure 2 Mean visual analog scale pain score over time.

compared morphine use following a femur fracture in both the American and Vietnamese populations and found that although American patients used much more morphine in comparison to Vietnamese patients (30 mg/kg *vs* 0.9 mg/kg), they were less satisfied with their pain relief. Perhaps, drug dependence or addiction may be a confounding factor in achieving satisfaction with pain relief. Vranceanu *et al*[42] previously cited effective coping strategies (higher self-efficacy) as the most effective pain reliever. It may be that significant preoperative opioid intake reflects greater psychologic distress that translates to higher reported subjective pain scores postoperatively.

In our study, both opioid consumption and VAS pain scores decreased successively at each of the timeframes evaluated. This implies that patients needed fewer opioid pills as time progressed but were still able to achieve significant pain relief. Implementing standardized, evidence-based opioid prescribing protocols may optimize the number of opioid prescriptions provided to patients and are particularly paramount for patients at risk of transitioning from short-term to long-term opioid therapy postoperatively[4,16,43-45]. Interestingly, the VAS pain score between postoperative days 1-7 was less than patients' preoperative status; however, the number of opioid pills consumed was higher during postoperative days 1-7. We postulate this may be due to the increased perceived pain burden experienced by patients after undergoing such an invasive procedure.

The amount of opioids prescribed after orthopedic procedures vary widely in the literature, and only a few established guidelines exist that have standardized acceptable duration and magnitude of opioid use[17,46]. Our findings showed that patients ceased to depend on opioids between postoperative days 15-30 compared to their preoperative consumption status, which correlated to a mean VAS pain score of 3.15. This information can be used to set patient expectations and allows surgeons to tailor their prescribing habits based on pain intensity reported by their patients. However, other risk factors in addition to pain also need to be considered. Patients with mental health conditions, such as depression and anxiety are more likely to be prescribed opioids at both higher doses and for longer durations[47, 48]. Not only have previous studies reported that prolonged opioid use may induce depression, but also that depressed patients seek medical attention for pain more frequently, and are three times more likely to be prescribed chronic opioid therapy[49,50]. Rhon *et al*[51] found that the use of pain medication prior to surgery, younger age, female, lower socioeconomic status (education and household income), high health-seeking behavior, and presence of substance abuse, insomnia, or mental health disorders prior to surgery were all significant in predicting chronic opioid use after surgery. However, it is likely that a combination of these variables may provide a greater predictive value for determining the likelihood of chronic opioids following surgery.

A recent study by Cook *et al*[52] showed that nearly 40% of THA patients do not fill their opioid prescriptions after surgery and proposed that strong consideration should be given to alternative pain control methods. It has been previously documented that many patients who fill an opioid prescription do not use any pills[16], thus the true number of patients who require opioids following surgery is likely lower than the number of patients who fill a prescription. Ideally, opioid prescriptions after surgery should balance adequate pain management against the duration of treatment. Although their analysis did not include THA, Scully *et al*[46] proposed that the optimal length of opioid prescriptions for common orthopedic procedures is around 6 to 15 d. This is corroborated by the findings of our study as opioid consumption quantity reached below the preoperative levels between days 15-30 postoperatively.

This study is not without limitations. The retrospective nature of this study has the potential to introduce inherent bias. The study population was majority female and age 65 years or older which causes inherent selection bias. Both the opioid and pain surveys that were administered relied on self-reporting by the patients. Due to the nature of the self-reported survey, opioid dependence could be

undetected in our study cohort. All patients in this study underwent THA *via* the direct anterior approach by a single surgeon, thus our results may not be generalizable to patients who undergo THA *via* other surgical approaches. Additionally, we excluded any patients who underwent revision of their primary implant or were hospitalized due to any postoperative complications. These patients may be the heaviest postoperative users of opioids due to a difficult and prolonged recovery resulting in higher pain intensity. Indeed, most patients included in the present study had a LOS of less than two days, and further analyses may benefit from addressing how lengthened in-patient stays affect VAS and the subsequent prescription of opioids postoperatively. In addition, the pain threshold of each patient is different making the generalizability of our results relatively difficult. Although we accounted for all non-THA related pain indications, we could not quantify all possible pain events after surgery that could necessitate prescription opioid therapy. Theoretically, a patient could have obtained an opioid prescription after undergoing THA for an issue unrelated to their orthopedic procedure. Patients who have pre-existing psychiatric conditions, anxiety, and/or fear of pain may confound the data, as they are unlikely to show improvement in pain, regardless of pain score. We did not quantify both opioid and non-opioid oral analgesic use such as meloxicam and aspirin according to oral morphine equivalent or collect the duration of preoperative opioid use. In addition, our analysis of PO opioid medication did not take into account IV opioids received perioperatively. This study only considered opioid intake; therefore, analgesics consumed by patients that may reduce the need for opioid intake could have possibly skewed the results. Furthermore, while VAS scores may be generalizable, an individual's immediate post-operative opioid consumption is dictated by subjective measures such as anesthesia type could introduce confounding variables that are difficult to quantify[53]. Lastly, we did not account for patients who may have had unreported adverse effects (constipation, nausea, vomiting, hypotension, *etc.*) due to opioid consumption and stopped their intake during the postoperative periods evaluated in this study. Future investigations comparing multiple surgical approaches for THA and including patients from different regions of the country and various parts of the world would help further elucidate our findings. Despite these limitations, the results presented can aid surgeons' opioid prescribing patterns based on their patients' reported pain levels following THA.

CONCLUSION

All patients experienced significant pain relief from having undergone THA. The average postoperative opioid consumption decreased below preoperative opioid consumption status between days 15-30 postoperatively. This decline in opioid consumption was associated with a relative VAS pain score of 3.15. Our results should be used to appropriately guide opioid prescribing patterns and set patient expectations regarding expected pain management following THA. This will not only give patients a baseline to reference during their recovery but also limit redundant billing expenses related to unnecessary prescription of medication and avoidable outpatient visits due to post-operative pain. However, without further research that considers other patient factors that influence pain severity, our understanding of the independent impact of pain on opioid consumption after THA remains uncertain.

ARTICLE HIGHLIGHTS

Research background

The purpose of this study is to evaluate the association between the quantity of opioid consumption in relation to visual analog scale (VAS) pain scores both pre- and postoperatively in patients undergoing primary total hip arthroplasty (THA). The amount of opioids prescribed after orthopaedic procedures vary widely in the literature, and only a few established guidelines exist that have standardized acceptable duration and magnitude of opioid use. Our findings showed that patients ceased to depend on opioids between postoperative days 15-30 compared to their preoperative consumption status, which correlated to a mean VAS pain score of 3.15. This information can be used to set patient expectations and allows surgeons to tailor their prescribing habits based on pain intensity reported by their patients.

Research motivation

The impact of opioids has gained significant clinical and research interest given their potential to prognosticate postoperative outcomes and patient satisfaction. Therefore, gaining a better understanding of the relationship between opioid use and pain is essential given the shifting emphasis placed upon health safety and quality.

Research objectives

The purpose of this study is to evaluate the association between the quantity of opioid consumption in relation to VAS pain scores both pre- and postoperatively in patients undergoing primary THA. We hypothesize that both opioid consumption and VAS pain scores will decrease for all patients following

surgery when compared to their preoperative status.

Research methods

Administer surverys to aassociate VAS pain scores with opioiid pill consumption.

Research results

Our findings showed that patients ceased to depend on opioids between postoperative days 15-30 compared to their preoperative consumption status, which correlated to a mean VAS pain score of 3.15.

Research conclusions

This information can be used to set patient expectations and allows surgeons to tailor their prescribing habits based on pain intensity reported by their patients.

Research perspectives

Future research should aim to consider other patient factors that influence pain severity. Our current understanding of the independent impact of pain on opioid consumption after THA remains inconclusive.

FOOTNOTES

Author contributions: Singh V, Tang A, and Bieganowski T write the manuscript; Singh V collected the data; Singh V and Anil U did the analysis; Macaulay W did the edits. Schwarzkopf R and Davidovitch RI are responsible for conceptualization and manuscript editing.

Institutional review board statement: The present study retrospectively analysed de-identified data for institutional quality improvement initiative and was therefore exempted from human-subjects review by our Institutional Review Board.

Informed consent statement: Informed consent was not needed for this study. This was a quality improvement initiative at our institution.

Conflict-of-interest statement: Singh V, Tang A, Bieganowski T and Anil U have nothing to disclose. Macaulay W holds stock options in OrthoAlign. Schwarzkopf R is a paid consultant for Smith & Nephew and Intellijoint. He also has stock options in Gauss Surgical outside the submitted work. Davidovitch RI is a paid consultant for Radlink, Schaerer Medical, Exactech, and Medtronics.

Data sharing statement: The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

STROBE statement: The authors have read the STROBE Statement—checklist of items, and the manuscript was prepared and revised according to the STROBE Statement—checklist of items.

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REFERENCES

1 **Learmonth ID**, Young C, Rorabeck C (2007) The operation of the century: total hip replacement. Lancet 370: 1508-1519 [DOI: 10.1016/S0140-6736(07)60457-7]
2 **Liu W**, Cong R, Li X, Wu Y, Wu H. Reduced opioid consumption and improved early rehabilitation with local and

intraarticular cocktail analgesic injection in total hip arthroplasty: a randomized controlled clinical trial. *Pain Med* 2011; **12**: 387-393 [PMID: 21266004 DOI: 10.1111/j.1526-4637.2010.01043.x]

3 **Yu SW**, Szulc AL, Walton SL, Davidovitch RI, Bosco JA, Iorio R. Liposomal Bupivacaine as an Adjunct to Postoperative Pain Control in Total Hip Arthroplasty. *J Arthroplasty* 2016; **31**: 1510-1515 [PMID: 26872584 DOI: 10.1016/j.arth.2016.01.004]

4 **Padilla JA**, Gabor JA, Schwarzkopf R, Davidovitch RI. A Novel Opioid-Sparing Pain Management Protocol Following Total Hip Arthroplasty: Effects on Opioid Consumption, Pain Severity, and Patient-Reported Outcomes. *J Arthroplasty* 2019; **34**: 2669-2675 [PMID: 31311667 DOI: 10.1016/j.arth.2019.06.038]

5 **Højer Karlsen AP**, Geisler A, Petersen PL, Mathiesen O, Dahl JB. Postoperative pain treatment after total hip arthroplasty: a systematic review. *Pain* 2015; **156**: 8-30 [PMID: 25599296 DOI: 10.1016/j.pain.0000000000000003]

6 **Beswick AD**, Wylde V, Gooberman-Hill R, Blom A, Dieppe P. What proportion of patients report long-term pain after total hip or knee replacement for osteoarthritis? *BMJ Open* 2012; **2**: e000435 [PMID: 22357571 DOI: 10.1136/bmjopen-2011-000435]

7 **Brokelman RBG**, van Loon CJM, Rijnberg WJ. Patient vs surgeon satisfaction after total hip arthroplasty. *J Bone Jt Surg - Ser B* 2003 [DOI: 10.1302/0301-620X.85B4.13411]

8 **Nota SP**, Spit SA, Voskuyl T, Bot AG, Hageman MG, Ring D. Opioid Use, Satisfaction, and Pain Intensity After Orthopedic Surgery. *Psychosomatics* 2015; **56**: 479-485 [PMID: 25624183 DOI: 10.1016/j.psym.2014.09.003]

9 **Bot AG**, Bekkers S, Arnstein PM, Smith RM, Ring D. Opioid use after fracture surgery correlates with pain intensity and satisfaction with pain relief. *Clin Orthop Relat Res* 2014; **472**: 2542-2549 [PMID: 24777731 DOI: 10.1007/s11999-014-3660-4]

10 **Chou R**, Fanciullo GJ, Fine PG. Clinical Guidelines for the Use of Chronic Opioid Therapy in Chronic Noncancer Pain. *J Pain* 2009; **10** [DOI: 10.1016/j.spinee.2010.01.027]

11 **Trasolini NA**, McKnight BM, Dorr LD. The Opioid Crisis and the Orthopedic Surgeon. *J Arthroplasty* 2018; **33**: 3379-3382.e1 [PMID: 30075877 DOI: 10.1016/j.arth.2018.07.002]

12 International Narcotics Control Board/ United Nations (2018) International Narcotics Control Board: Narcotic drugs estimated world requirements for 2018—statistics for 2017 [DOI: 10.18356/34f1db17-en-fr-es]

13 **Volkow ND**, McLellan TA, Cotto JH, Karithanom M, Weiss SR. Characteristics of opioid prescriptions in 2009. *JAMA* 2011; **305**: 1299-1301 [PMID: 21467282 DOI: 10.1001/jama.2011.401]

14 **Volkow ND**, McLellan TA. Curtailing diversion and abuse of opioid analgesics without jeopardizing pain treatment. *JAMA* 2011; **305**: 1346-1347 [PMID: 21467287 DOI: 10.1001/jama.2011.369]

15 **Bartels K**, Mayes LM, Dingmann C, Bullard KJ, Hopfer CJ, Binswanger IA. Opioid Use and Storage Patterns by Patients after Hospital Discharge following Surgery. *PLoS One* 2016; **11**: e0147972 [PMID: 26824844 DOI: 10.1371/journal.pone.0147972]

16 **Sabatino MJ**, Kunkel ST, Ramkumar DB, Keeney BJ, Jevsevar DS. Excess Opioid Medication and Variation in Prescribing Patterns Following Common Orthopaedic Procedures. *J Bone Joint Surg Am* 2018; **100**: 180-188 [PMID: 29406338 DOI: 10.2106/JBJS.17.00672]

17 **Bedard NA**, Sierra RJ, Mabry T. Opioids After Orthopaedic Surgery: There Is a Need for Universal Prescribing Recommendations: Commentary on an article by Matthew J. Sabatino, MD, MS, *et al*.: "Excess Opioid Medication and Variation in Prescribing Patterns Following Common Orthopaedic Procedures". *J Bone Joint Surg Am* 2018; **100**: e17 [PMID: 29406353 DOI: 10.2106/JBJS.17.01480]

18 **Bedard NA**, Sierra RJ, Mabry T. Opioids After Orthopaedic Surgery: There Is a Need for Universal Prescribing Recommendations: Commentary on an article by Matthew J. Sabatino, MD, MS, *et al*.: "Excess Opioid Medication and Variation in Prescribing Patterns Following Common Orthopaedic Procedures". *J Bone Joint Surg Am* 2018; **100**: e17 [PMID: 29406353 DOI: 10.2106/JBJS.17.01480]

19 **Traven SA**, Brinton DL, Woolf SK, Leddy LR, Gottschalk MB, Slone HS. Notable Variability in Opioid-prescribing Practices After Common Orthopaedic Procedures. *J Am Acad Orthop Surg* 2021; **29**: 219-226 [PMID: 32568996 DOI: 10.5435/JAAOS-D-19-00798]

20 **Kim N**, Matzon JL, Abboudi J, Jones C, Kirkpatrick W, Leinberry CF, Liss FE, Lutsky KF, Wang ML, Maltenfort M, Ilyas AM. A Prospective Evaluation of Opioid Utilization After Upper-Extremity Surgical Procedures: Identifying Consumption Patterns and Determining Prescribing Guidelines. *J Bone Joint Surg Am* 2016; **98**: e89 [PMID: 27869630 DOI: 10.2106/jbjs.15.00614]

21 **Adalbert JR**, Ilyas AM. Implementing Prescribing Guidelines for Upper Extremity Orthopedic Procedures: A Prospective Analysis of Postoperative Opioid Consumption and Satisfaction. *Hand (N Y)* 2021; **16**: 491-497 [PMID: 31441326 DOI: 10.1177/1558944719867122]

22 **O'Neil JT**, Wang ML, Kim N, Maltenfort M, Ilyas AM. Prospective Evaluation of Opioid Consumption After Distal Radius Fracture Repair Surgery. *Am J Orthop (Belle Mead NJ)* 2017; **46**: E35-E40 [PMID: 28235120]

23 **Chatha K**, Borroto W, Goss L, Ghisa C, Gilot G, Sabesan VJ. How orthopedic surgeons can impact opioid use and dependence in shoulder arthroplasty. *JSES Int* 2020; **4**: 105-108 [PMID: 32195471 DOI: 10.1016/j.jses.2019.10.113]

24 **Brokelman RB**, Haverkamp D, van Loon C, Hol A, van Kampen A, Veth R. The validation of the visual analogue scale for patient satisfaction after total hip arthroplasty. *Eur Orthop Traumatol* 2012; **3**: 101-105 [PMID: 22798966 DOI: 10.1007/s12570-012-0100-3]

25 **Danoff JR**, Goel R, Sutton R, Maltenfort MG, Austin MS. How Much Pain Is Significant? *J Arthroplasty* 2018; **33**: S71-S75.e2 [PMID: 29567002 DOI: 10.1016/j.arth.2018.02.029]

26 **Chapman CR**, Casey KL, Dubner R. Pain measurement: an overview. *Pain* 1985; **22**: 1-31 [DOI: 10.1016/0304-3959(85)90145-9]

27 **da Costa BR**, Nüesch E, Kasteler R, Husni E, Welch V, Rutjes AW, Jüni P. Oral or transdermal opioids for osteoarthritis of the knee or hip. *Cochrane Database Syst Rev* 2014; CD003115 [PMID: 25229835 DOI: 10.1002/14651858.CD003115.pub4]

28 **Anekar AA**, Cascella M. WHO Analgesic Ladder. 2022 May 15. In: StatPearls [Internet]. Treasure Island (FL): StatPearls

Publishing; 2022 Jan- [PMID: 32119322]
29 **Feng JE**, Mahure SA, Waren DP, Lajam CM, Slover JD, Long WJ, Schwarzkopf RM, Macaulay WB, Davidovitch RI. Utilization of a Novel Opioid-Sparing Protocol in Primary Total Hip Arthroplasty Results in Reduced Opiate Consumption and Improved Functional Status. *J Arthroplasty* 2020; **35**: S231-S236 [PMID: 32139187 DOI: 10.1016/j.arth.2020.02.009]
30 **Kaye AD**, Jones MR, Kaye AM, Ripoll JG, Galan V, Beakley BD, Calixto F, Bolden JL, Urman RD, Manchikanti L. Prescription Opioid Abuse in Chronic Pain: An Updated Review of Opioid Abuse Predictors and Strategies to Curb Opioid Abuse: Part 1. *Pain Physician* 2017; **20**: S93-S109 [PMID: 28226333 DOI: 10.36076/ppj.2017.s109]
31 **Kaye AD**, Jones MR, Kaye AM, et al (2017) Prescription opioid abuse in chronic pain: An updated review of opioid abuse predictors and strategies to curb opioid abuse (Part 2). Pain Physician [DOI: 10.36076/ppj.2017.s109]
32 **Manchikanti L**, Helm S 2nd, Fellows B, Janata JW, Pampati V, Grider JS, Boswell MV. Opioid epidemic in the United States. *Pain Physician* 2012; **15**: ES9-E38 [PMID: 22786464 DOI: 10.36076/ppj.2012/15/ES9]
33 **Weber KL**. The AAOS clinical practice guidelines. *J Am Acad Orthop Surg* 2009; **17**: 335-336 [PMID: 19474442 DOI: 10.5435/00124635-200906000-00001]
34 **Rozell JC**, Courtney PM, Dattilo JR, Wu CH, Lee GC. Preoperative Opiate Use Independently Predicts Narcotic Consumption and Complications After Total Joint Arthroplasty. *J Arthroplasty* 2017; **32**: 2658-2662 [PMID: 28478186 DOI: 10.1016/j.arth.2017.04.002]
35 **Zarling BJ**, Sikora-Klak J, Bergum C, Markel DC. How Do Preoperative Medications Influence Outcomes After Total Joint Arthroplasty? *J Arthroplasty* 2017; **32**: S259-S262 [PMID: 28578845 DOI: 10.1016/j.arth.2017.04.031]
36 **Kim K**, Chen KK, Roof M, Anoushiravani AA, Vigdorchik J, Schwarzkopf R. The effects of preoperative chronic opioid use in total hip arthroplasty. *J Clin Orthop Trauma* 2020; **11**: 73-78 [PMID: 32001989 DOI: 10.1016/j.jcot.2019.04.027]
37 **Busse JW**, Douglas J, Chauhan TS, Kobeissi B, Blackmer J. Perceptions and Impact of the 2017 Canadian Guideline for Opioid Therapy and Chronic Noncancer Pain: A Cross-Sectional Study of Canadian Physicians. *Pain Res Manag* 2020; **2020**: 8380171 [PMID: 32148601 DOI: 10.1155/2020/8380171]
38 **Busse JW**, Wang L, Guyatt GH. Meta-analysis of Opioids for Chronic Pain-Reply. *JAMA* 2019; **321**: 1936 [PMID: 31112257 DOI: 10.1001/jama.2019.2185]
39 **Decosterd I**, Hugli O, Tamchès E, Blanc C, Mouhsine E, Givel JC, Yersin B, Buclin T. Oligoanalgesia in the emergency department: short-term beneficial effects of an education program on acute pain. *Ann Emerg Med* 2007; **50**: 462-471 [PMID: 17445949 DOI: 10.1016/j.annemergmed.2007.01.019]
40 **Shill J**, Taylor DM, Ngui B, Taylor SE, Ugoni AM, Yeoh M, Richardson J. Factors associated with high levels of patient satisfaction with pain management. *Acad Emerg Med* 2012; **19**: 1212-1215 [PMID: 23035970 DOI: 10.1111/j.1553-2712.2012.01451.x]
41 **Carragee EJ**, Vittum D, Truong TP, Burton D. Pain control and cultural norms and expectations after closed femoral shaft fractures. *Am J Orthop (Belle Mead NJ)* 1999; **28**: 97-102 [PMID: 10067712]
42 **Vranceanu AM**, Ring D. Factors associated with patient satisfaction. *J Hand Surg Am* 2011; **36**: 1504-1508 [PMID: 21794990 DOI: 10.1016/j.jhsa.2011.06.001]
43 **Inacio MC**, Hansen C, Pratt NL, Graves SE, Roughead EE. Risk factors for persistent and new chronic opioid use in patients undergoing total hip arthroplasty: a retrospective cohort study. *BMJ Open* 2016; **6**: e010664 [PMID: 27130165 DOI: 10.1136/bmjopen-2015-010664]
44 **Earp BE**, Silver JA, Mora AN, Blazar PE. Implementing a Postoperative Opioid-Prescribing Protocol Significantly Reduces the Total Morphine Milligram Equivalents Prescribed. *J Bone Joint Surg Am* 2018; **100**: 1698-1703 [PMID: 30278000 DOI: 10.2106/JBJS.17.01307]
45 **Sabesan VJ**, Echeverry N, Dalton C, Grunhut J, Lavin A, Chatha K. The impact of state-mandated opioid prescribing restrictions on prescribing patterns surrounding reverse total shoulder arthroplasty. *JSES Int* 2021; **5**: 663-666 [PMID: 34223412 DOI: 10.1016/j.jseint.2021.04.009]
46 **Scully RE**, Schoenfeld AJ, Jiang W, Lipsitz S, Chaudhary MA, Learn PA, Koehlmoos T, Haider AH, Nguyen LL. Defining Optimal Length of Opioid Pain Medication Prescription After Common Surgical Procedures. *JAMA Surg* 2018; **153**: 37-43 [PMID: 28973092 DOI: 10.1001/jamasurg.2017.3132]
47 **Goplen CM**, Verbeek W, Kang SH, Jones CA, Voaklander DC, Churchill TA, Beaupre LA. Preoperative opioid use is associated with worse patient outcomes after Total joint arthroplasty: a systematic review and meta-analysis. *BMC Musculoskelet Disord* 2019; **20**: 234 [PMID: 31103029 DOI: 10.1186/s12891-019-2619-8]
48 **Braden JB**, Sullivan MD, Ray GT, Saunders K, Merrill J, Silverberg MJ, Rutter CM, Weisner C, Banta-Green C, Campbell C, Von Korff M. Trends in long-term opioid therapy for noncancer pain among persons with a history of depression. *Gen Hosp Psychiatry* 2009; **31**: 564-570 [PMID: 19892215 DOI: 10.1016/j.genhosppsych.2009.07.003]
49 **Sullivan MD**. Depression Effects on Long-term Prescription Opioid Use, Abuse, and Addiction. *Clin J Pain* 2018; **34**: 878-884 [PMID: 29505419 DOI: 10.1097/AJP.0000000000000603]
50 **Scherrer JF**, Salas J, Lustman PJ, Burge S, Schneider FD. Change in opioid dose and change in depression in a longitudinal primary care patient cohort. *Pain* 2015; **156**: 348-355 [PMID: 25599457 DOI: 10.1097/01.j.pain.0000460316.58110.a0]
51 **Rhon DI**, Snodgrass SJ, Cleland JA, Sissel CD, Cook CE. Predictors of chronic prescription opioid use after orthopedic surgery: derivation of a clinical prediction rule. *Perioper Med (Lond)* 2018; **7**: 25 [PMID: 30479746 DOI: 10.1186/s13741-018-0105-8]
52 **Cook DJ**, Kaskovich SW, Pirkle SC, Mica MAC, Shi LL, Lee MJ. Benchmarks of Duration and Magnitude of Opioid Consumption After Total Hip and Knee Arthroplasty: A Database Analysis of 69,368 Patients. *J Arthroplasty* 2019; **34**: 638-644.e1 [PMID: 30642706 DOI: 10.1016/j.arth.2018.12.023]
53 **Risitano S**, Indelli PF. Is "symmetric" gap balancing still the gold standard in primary total knee arthroplasty? *Ann Transl Med* 2017; **5**: 325 [PMID: 28861422 DOI: 10.21037/atm.2017.06.18]

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ORIGINAL ARTICLE

Retrospective Cohort Study

Functional and clinical outcome with modified lateral approach total hip arthroplasty in stiff hips with ankylosing spondylitis

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Abstract

BACKGROUND

Ankylosing spondylitis at total hip arthroplasty (THA) has significant hip stiffness with flexion deformity, restricted mobility, and function. Range of movement (ROM) improvement with good functional outcome is seen following THA in these hips. The modified Hardinge approach without abductor compromise is helpful in these stiff hips with associated flexion deformity.

AIM

To assess improvement in ROM and functional outcomes with a modified lateral approach THA in ankylosing spondylitis with stiff hips.

METHODS

A total of 69 hips that underwent THA with a modified Hardinge approach in 40 patients were evaluated at a mean follow-up of 38.33 mo. All individuals ambulated with weight-bearing as tolerated and ROM exercises from the 1st postoperative day. Modified Harris hip score and ROM were assessed during follow-up. Quality of life assessments using the 36-item and 12-item short form health surveys were done along with clinical and functional outcomes at follow-up. SPSS 22.0 was used for statistical analysis. The correlation of ROM and functional score change was performed using Pearson's correlation coefficient.

RESULTS

Sixty-nine hips with a significant decrease in ROM preoperatively with 32 clinically fused hips showed significant improvement in flexion range. The mean flexion in 69 hips improved from 29.35 ± 31.38 degrees to 102.17 ± 10.48 degrees. The mean difference of 72.82 with a P value < 0.0001 was significant. In total, 45 out of 69 hips had flexion deformity, with 13 hips having a deformity above 30

degrees. The flexion during the follow-up was below 90 degrees in 3 hips. Eleven hips had flexion of 90 degrees at follow-up, while the remaining 55 hips had flexion above 100 degrees. Modified Harris hip score improved from 17.03 ± 6.02 to 90.66 ± 7.23 (P value < 0.0001). The 36-item short form health survey at the follow-up indicated health status in 40 patients as excellent in 11, very good in 20, good in 5, fair in 3, and poor in 1. The mean mental health score was 84.10 ± 11.58. Pain relief was good in all 69 hips. Altogether, 28/40 patients (70%) had no pain, 9 patients (22%) had occasional pain, and 3 patients (8%) had mild to moderate pain with unusual activity. Heterotopic ossification was seen in 21 hips with Brooker class 1 in 14 hips.

CONCLUSION

Modified Hardinge approach THA in ankylosing spondylitis with stiff hips with flexion deformity significantly improved ROM, Harris hip score, and quality of life indicated by the 36-item and 12-item short form health surveys.

Key Words: Ankylosing Spondylitis; Stiff; flexion deformity; Harris hip score; Hip range of movement; 36-item short form health survey score; Total hip arthroplasty modified Hardinge approach

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Core Tip: Ankylosing spondylitis is characterized by significant hip stiffness with mobility restriction and decreased quality of life. Range of movement is reduced with coexistent flexion deformity. Total hip arthroplasty improves mobility by enhancing the quality of life. The modified Hardinge approach leaves the posterior two-thirds of the abductors intact. This approach is helpful in these hips with flexion deformity with good clinical and functional outcomes. Range of movement, Harris hip score, and quality of life indicated by the 36-item short form health survey score have shown promising results.

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INTRODUCTION

Ankylosing spondylitis (AS) belongs to the spondyloarthropathy group of disorders affecting the young with progressive stiffness of the spine and hip joints. The hip joint is involved in 25%-50% of patients [1], with bilateral hip disease seen in 50%-90% of AS[2-5]. Disability in these individuals is predominantly due to decreased movement resulting in stiffness restricting their activities. The hip involvement presents varying degrees of stiffness with bony ankylosis seen in about 40% at total hip arthroplasty (THA)[6]. The majority of these young patients have fixed deformities with loss of spinal mobility. THA improves the functional outcome in these patients with significant activity limitations and progressive stiffness in their spine and hips.

THA in these hips significantly improves the range of movement (ROM) and pain relief with marked improvement in function and mobility[4]. However, the associated risks are ectopic bone formation, reduced ROM, and re-ankylosis after THA in AS[6].

We aimed to assess the functional and clinical outcome in AS with stiff hips after THA with the modified lateral approach. ROM and functional outcomes using the modified Harris hip score (HHS), 36-item short-form health survey score (SF-36), and 12-item short form health survey (SF-12) scores were calculated for assessment.

MATERIALS AND METHODS

A retrospective analysis of clinically stiff hips with AS who underwent THA in our unit between 2012 to 2018 were included. The criteria for inclusion were individuals over 18 years of age diagnosed with AS with decreased ROM with THA in our unit and had come for follow-up more than 6 mo after the procedure. Based on these criteria, 168 patients fulfilled the criteria for this study. In total, 69 hips in 40 patients who could be assessed clinically during the study period were included in this study. Sixty-two patients with AS were reviewed, and 22 patients had to be excluded due to insufficient data. The

remaining were not available for a clinical evaluation during the study period. Data for the 40 patients were collected for clinical review. Information was also obtained from the medical records. Preoperative details regarding ROM, pain, and other data regarding the hip joint involvement were collected and compared with the data obtained at clinical follow-up. SPSS 22.0 was used for statistical analysis. The correlation of ROM and functional score change was done using Pearson's correlation coefficient.

Data regarding medical management by the rheumatology department was also collected. Informed consent was obtained from all patients. Institutional Review Board approval was obtained for this study.

Surgical technique

Sixty-nine hips were stiff, and 32 were clinically fused. Bilateral hip arthritis in 24 individuals had simultaneous THA in the same sitting. Five patients had staged THA for bilateral hip arthritis. Eleven individuals underwent unilateral THA. Two of the senior authors carried out all the THAs. The modified Hardinge approach was used for all the hips[7,8]. The Mallory modification with preservation of the posterior two-thirds of the abductors is the approach routinely utilized in our unit for all THAs except hips with a requirement for posterior or posterosuperior augmentation and reconstruction. The Mallory modification essentially preserves the posterior two-thirds of the gluteus medius rather than detaching the entire abductor in the classical Hardinge approach. The anterior one-third was cut at the musculotendinous junction to enable effective repair at the end of the procedure.

Templating was done preoperatively for all cases to assess the size of the acetabulum and femur. Lateral positioning for THA was challenging in the fused and stiff hips. Circumferential capsular release was done to enable mobilization of the proximal femur and provide complete exposure to the acetabulum. The capsule in these stiff hips was opened anterolateral and released from the entire bony acetabular margin. The capsular tissue was elevated, and the thickened fibrotic tissue interfering with the acetabular preparation was excised.

A femoral neck osteotomy was done in situ for 26 fused hips that could not be dislocated after defining the acetabular margins and the proximal femur with soft tissue release. Care was taken to support the limb on completion of the osteotomy to prevent additional propagation to the calcar region and the acetabular margins. Additional bony resection was done on the neck cut to leave enough calcar for stable femoral component implantation. Acetabulum reaming was done only after defining the margins. Sequential reaming onto the resected neck and head was done after ensuring to avoid eccentric reaming and maintaining the anterior and posterior wall thickness. The residual pulvinar identified the medial wall, and reaming continued gradually to obtain the best fit of the acetabular component.

The acetabulum was cementless in all our cases. Acetabular components in this series were Pinnacle (Depuy, United States) in 34 hips, R3 (Smith and Nephew, United States) in 29 hips, Trident (Stryker, United States) in 2 hips, and Latitud (Meril, India) in 4 hips. Screw fixation was used in 42 hips to augment fixation. The femur was prepared with the limb adducted and externally rotated to accommodate a cementless component in 61 hips, while 8 hips required a cemented fixation for Dorr type C femur. Cementless femur components were Corail (Depuy, United States) in 30 hips, Synergy (Smith and Nephew, United States) in 12 hips, Polarstem (Smith and Nephew, United States) in 13 hips, Latitud (Meril, India) in 4 hips, and Accolade (Stryker, United States) in 2 hips. The 8 cemented femoral implants were C stem (Depuy, United States) in 2 hips, CPCS (Smith and Nephew, United States) in 4 hips, and CPT (Zimmer, Warsaw, United States) in 2 hips. The head size depended on the acetabular component, with a mean head size of 32.92 mm (28 mm in 9 hips, 32 mm in 35 hips, 36 mm in 25 hips).

No constrained or dual mobility liners were used. Copious lavage with saline to remove all the bone debris was done before closure to reduce the chances of heterotopic ossification. A stable calcar cortical split was seen in the proximal femur in 2 hips at THA with the last broach size used, which required wiring for additional stability. Fracture of the greater trochanter was seen at the final reduction in 1 hip, which required stabilization with stainless steel wires.

All patients were given parenteral antibiotics for 48 h and ambulated with weight-bearing as tolerated by the next day after surgery. Deep vein thrombosis prophylaxis with aspirin was given for 6 wk. The patients with stiff hips were initially encouraged prolonged sitting as soon as tolerated to ensure spinal posture and muscle balance and then mobilized actively as mobility restriction was significant before surgery. The patients were ambulated as soon as tolerated with support, which was gradually weaned after 6 wk.

The preoperative and follow-up flexion and total ROM for each hip were compared. The ROM measurement was done with a goniometer. The total ROM for each hip was compared with the total ROM possible at the last follow-up. The improvement in flexion was compared for each hip. The SF-36 and SF-12 scores were calculated to assess the overall quality of life (QOL). Neuromuscular studies or magnetic resonance imaging were not used to assess hip abductors. The modified HHS, ROM, SF-36, and SF-12 scores were used to assess the overall outcome in these patients. The X-rays were evaluated for heterotopic ossification (HO), the presence of any radiolucent lines, lysis in the Charnley acetabular zones, and the Gruen femur zones with the implants.

The mean ± SD was analyzed based on the distribution of HHS and SF-12 and SF-36 scores. The distribution of the HHS, SF-12, and SF-36 were tabulated for all patients. SPSS 22.0 was used for statistical analysis. P value < 0.05 was considered as statistical significance.

RESULTS

There were 69 hips in 40 patients diagnosed as AS with stiff hips that underwent THA at our unit between January 2012 and December 2018 were included in this study. There were 36 males and 4 females with a mean age of 36.6 years (24 to 58). Sixty-nine hips were studied as 24/40 patients (60%) underwent simultaneous bilateral THA.

ROM

Forty-three hips were found to have preoperative flexion less than 30 degrees (Figure 1). In total, 45/69 hips had flexion deformity, with 13 hips having a deformity above 30 degrees. Three hips had preoperative flexion of 90 degrees, and two hips had preoperative flexion of 100 degrees. Five hips had external rotation deformity of 30 degrees. Significant internal and external rotation restriction was seen in the remaining 64 hips. All hips included had considerable restriction of daily activity with arthritis. The mean preoperative total ROM in 69 hips improved from 45.29 ± 47.20 to a mean of 223.59 ± 27.41. The mean flexion in 69 hips improved from 29.35 ± 31.38 degrees to 102.17 ± 10.48 degrees. The mean difference was 72.97, with a P value < 0.0001 being statistically significant. The total ROM in 32 clinically fused hips improved from a mean of 5.47 ± 9.22 to 223.59 ± 23.33 degrees at the last follow-up.

The flexion at follow-up was below 90 degrees in 3 hips. Eleven hips had flexion of 90 degrees at follow-up, while the remaining 55 hips had flexion above 100 degrees.

The modified HHS improved from 17.03 ± 6.02 to 90.66 ± 7.23 at follow-up. This improvement was found to be statistically significant (P < 0.001). At the follow-up, 30/40 patients had a modified HHS > 90 (Table 1).

Pain score

Pain scoring was done as part of the HHS assessment. All 40 patients had pain with restriction of movement for 31.08 ± 36 mo before THA. Pain relief was good in all 69 hips. Altogether, 28/40 patients (70%) had no pain, while 9 patients (22%) had occasional pain without any compromise in activity. Three patients (8%) had mild to moderate pain with unusual activity.

QOL SF-36 score and general health

SF-36 is to date the most commonly used health-related QOL measure in research and has been used to assess the health status of AS patients and compared with normal individuals[9-11]. SF-36 focuses on eight domains with physical and mental components with outcome measures indicating the health-related QOL[12]. The responses are assessed in all domains, and the score is generated with higher scores indicating better health. This assessment has been used in the evaluation of patients after THA and total knee arthroplasty[12,13].

The SF-36 measures eight scales that include physical functioning, role limitations due to physical health, bodily pain, general health, vitality, social functioning, role limitations due to emotional problems, and mental health. This used extensively assessment tool is a reliable, detailed measure of overall physical and mental health. The mental health score of 84.10 ± 11.58, along with all other subscores, favored the assessment as an excellent overall outcome (Table 2). The SF-36 questionnaire scores calculated at the follow-up in 40 patients indicated general health as excellent or very good in 31 out of 40 patients (Table 3).

SF-12

This short form survey instrument used in outcome assessment is quicker with fewer details and two components. The mean physical score of the physical component summary in 40 patients was 45.22 ± 8.94, and the mean score of the mental component summary was 57.63 ± 5.18.

Radiology

Preoperative assessment included spine as well as hip anteroposterior and lateral views. The anteroposterior view was done in all hips for immediate postoperative assessment. All 69 hips at follow-up showed implants with stable acetabular and femoral components. No radiolucent lines, lysis, or implant loosening was seen in all the Charnley and Gruen zones. HO was seen in 21 hips with Brooker class 1 in 14 hips, class 2 in 5 hips, and class 3 in 2 hips (Figure 2).

Complications

There were no dislocations or early infections in our series. One bilateral THA presented 73 mo postoperatively with symptoms suggestive of low-grade infection. He had been on irregular medical treatment and was also diagnosed with chronic venous insufficiency secondary to perforator incompetence in his lower limbs. He underwent a staged revision for his coagulase-negative *Staphylococcus* infection. There were no other early or delayed complications detected through the last follow-up.

Table 1 Comparison of preoperative and follow-up flexion, range of movement, and Harris hip score

Movement	Preoperative	Follow-up	Mean difference (95%CI)	*P* value
Flexion	29.35	102.17	65.76 ± 71.37	< 0.0001
ROM total	45.29	220.65	132.97 ± 171.86	< 0.0001
ROM score	1.71	4.95	3.33 ± 3.18	< 0.0001
MHHS	17.03	90.66	53.84 ± 72.16	< 0.0001

ROM: Range of movement; MHHS: Modified Harris hip score.

Table 2 Distribution of general health status and the 36-item short form health survey in 40 patients

SF-36 scores		
Mental health	(*n* = 40)	84.10 ±11.58
Role limitations due to emotional problems	(*n* = 40)	94.17 ± 19.81
Social functioning	(*n* = 40)	86.25 ± 16.70
Energy fatigue/vitality	(*n* = 40)	71.87 ± 16.63
General health	(*n* = 40)	63.12 ± 24.22
Bodily pain	(*n* = 40)	80.00 ± 19.23
Physical functioning	(*n* = 40)	69.63 ± 18.58
Role limitations due to physical health	(*n* = 40)	85.00 ± 33.87

SF-36: 36-item short form health survey.

Table 3 The 36-item short form health survey scores compared to other series

SF-36 scores	Our series	Bahardoust *et al*[10], 2012	Dagfinrud *et al*[9], 2004	van Tubergen *et al*[19], 2002
Mental health	84.10 (11.58)	39.9 (28.2)	70 (19)	65.5 (18.1)
Role limitations due to emotional problems	94.17 (19.81)	79.1 (19.2)	66 (42)	68.5 (41.3)
Social functioning	86.25 (16.70)	28.5 (29.2)	70 (27)	64.6 (24.6)
Energy fatigue/vitality	71.87 (16.63)	56.2 (21.4)	43 (23)	42.6 (16.5)
General health	63.12 (24.22)	42.1 (26.3)	51 (24)	42.8 (20.2)
Bodily pain	80.00 (19.23)	48.2 (28.4)	44 (22)	48.3 (19.2)
Physical functioning	69.63 (18.58)	28.3 (11.1)	71 (23)	55.8 (23.4)
Role limitations due to physical health	85.00 (33.87)	31.2 (12.6)	44 (41)	35.6 (38.1)

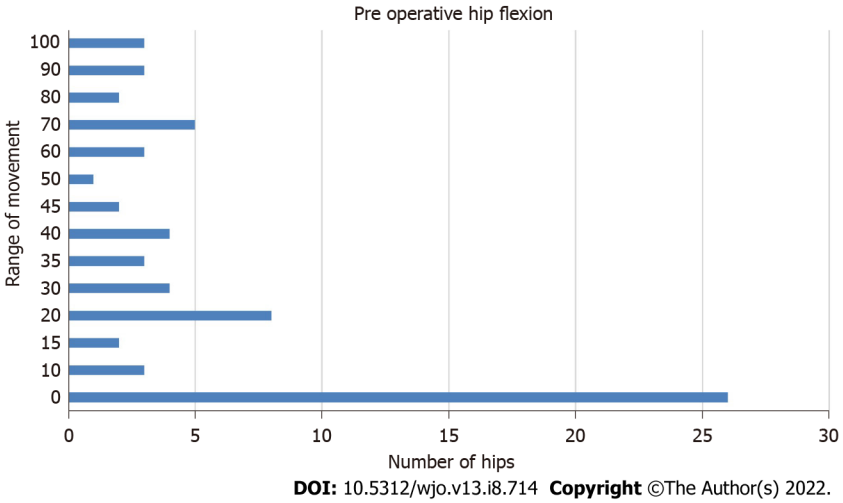
SF-36: 36-item short form health survey.

DISCUSSION

THA effectively relieves pain and improves ROM and function in AS. Five percent of AS patients have been reported to need hip replacement surgery, and the overall rate of joint replacement surgery in AS has increased by 40%[14]. Previous studies have shown and established that AS has a higher male-to-female ratio of about 2:1 to 3:1, and it was evident in this series as 90% of patients were males.

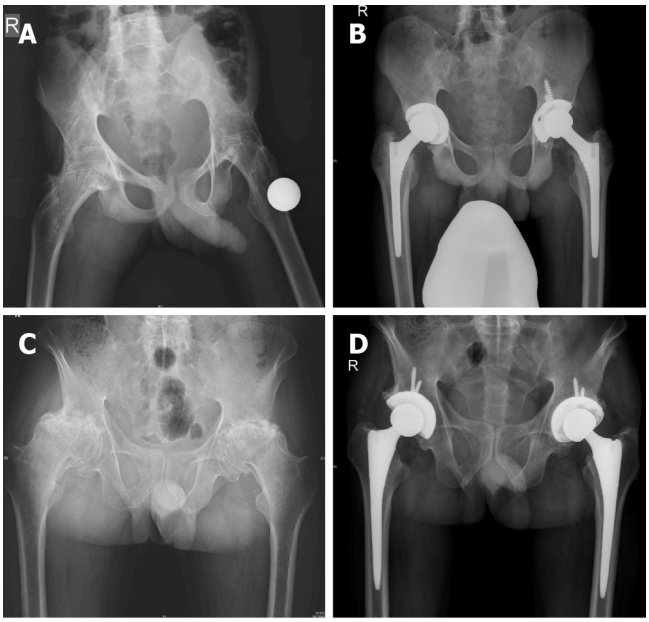
Patients with stiff hips or bony ankylosis have significant functional disabilities. THA brings about dramatic changes in function and QOL in these young patients. The increased hip ROM and subsequent functional improvement in these individuals support THA in this condition.

The Mallory modification of the Hardinge approach is used routinely for THA in our unit. A lateral approach with trochanteric osteotomy has been described[3]. There is a lack of data regarding functional outcomes following THA in AS with fused hips with this approach. There has been a concern with the



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Figure 1 Distribution of preoperative flexion range in 69 hips.



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Figure 2 Preoperative assessment and immediate postoperative assessment of hips. A: Eighteen-year-old male with 4 year history of progressive stiffness presented with bony ankylosis and flexion deformity of 25 degrees in the right hip; B: Four years postoperative bilateral simultaneous total hip arthroplasty. Brooker grade 2 heterotopic ossification left hip, flexion 90 degrees bilateral, Harris hip score 88, flexion 90 degrees, 12-item short form health survey physical component summary 39.83, and mental component summary 58.36; C: Forty-six-year-old male bilateral hip progressive stiffness for more than 10 years, flexion deformity 30 degrees bilateral with 20 degrees further range of movement in flexion; D: Two-year-postoperative bilateral simultaneous total hip arthroplasty, flexion 100 degrees right, 90 degrees left, Harris hip score 95, 12-item short form health survey physical component summary 52.88, and mental component summary 56.12.

approach in AS fused hips related to abductor compromise. Hence the posterior approach has been advocated[4]. The modified lateral approach preserves the posterior two-thirds of the abductor and is helpful, especially in stiff hips with flexion deformity, as the approach facilitates the anterior capsular release.

Flexion deformity in the 45 hips was successfully corrected with this modified lateral approach's extensive soft tissue release. The in situ neck resection in 26 fused hips was performed to prevent damage to the posterior acetabular wall during osteotomy[4]. Limb positioning with external rotation of the femur helps in posterior capsular release between the gluteus medius and the iliopsoas insertions. Femoral broaching and optimal sizing without damage to the residual abductor insertion is facilitated by external rotation of the limb with the modified lateral approach. Femoral anteversion assessment is enabled with proximal femur access provided through this approach. The posterior approach could be challenging for femoral neck osteotomy, especially in fused hips with external rotation deformity. Early mobilization after flexion deformity correction with extensive anterior release in these hips improves

ROM and prevents stiffness.

The choice of implant for the acetabulum was based on the bone quality at the time of preparation. Gradual sequential reaming with information obtained from preoperative templating aided in cementless fixation with optimum fit and bone stock utilization in all 69 hips with additional screws when necessary. A cemented femur was used in 8 Dorr C femurs, and cementless components achieved stable fixation in the remaining 61 hips. Increased risk of intraoperative femur fracture would be high if uncemented fixation is attempted with larger sizes to achieve stable fixation in the larger canal with thin cortices. The proximal femur required wiring in 2 hips for medial femur calcar split seen at preparation. Cementless implants in AS have found favor with long-term survivorship in recent series[4] instead of cemented fixation, which was advocated earlier[5].

The average follow-up of patients in our series was 38.33 mo with no evidence of clinical or radiological signs of implant loosening. There were 21 hips with HO seen at follow-up with no functional limitations. Our protocol with copious lavage before closure to remove bone debris and active postoperative mobilization was to reduce the risk of HO. With rheumatology input, the patients were restarted on their disease-modifying antirheumatic drugs 1 wk after THA.

The mean flexion in 69 hips changed from 29.35 ± 31.38 to 102.17 ± 10.48 degrees, indicating a mean improvement of 72.82 degrees. The ROM in 43 hips with flexion less than 30 degrees and 23 fused hips also recorded significant improvement in their flexion at follow-up compared to patients who had preoperative ROM of more than 90 degrees. This significant improvement in ROM in the 69 hips resulted in considerable improvement in the hip function at follow-up.

Modified HHS improved from 17.03 ± 6.02 to 90.66 ± 7.23, which was statistically significant ($P < 0.001$) as 30/40 patients had a modified HHS > 90 at follow-up. This improvement in HHS is due to the significant increase in the activity levels achieved in these stiff hips. In this study, 92% of our patients had no pain or ignorable pain that did not compromise any activity, and 8% had moderate pain with unusual activity that required occasional analgesics for pain relief.

Thirty-one out of 40 patients showed excellent or good scores in SF-36 and SF-12 physical and mental component analysis, which was comparable with other QOL analyses done in spondyloarthropathy [15]. Improvement in ROM with HHS and SF-36 indicates an overall improvement in the hip joint function and the QOL. Data regarding the functional outcome and health-related QOL after THA in AS has been limited[4,15].

The functional scores and the QOL assessment have been reported in patients with AS[10]. The mental component did not significantly change, and the mean physical component score was significantly lower in the study group[10,16]. The SF-36 scores in this series did not have a preoperative value for comparison. AS patients have significantly impaired QOL, with most domains affected in the SF-36 assessment.

SF-36 at follow-up indicated significant improvement in the QOL after THA in this group of patients with AS. The overall QOL was good in all the domains assessed. The number of cases may have been too small (69 THAs) for analyzing the short-and mid-term effects of THA in AS. However, good scores were obtained in the physical and emotional quotient[17] (Table 3).

The SF-36 scores, which evaluate eight domains used as a functional outcome measure, have added value when used with the modified HHS and the ROM improvement in these stiff hips. SF-12 has a physical and mental component assessment and has fewer elements when compared to SF-36. The SF-36 used to assess functional outcomes in THA and total knee arthroplasty was found to significantly improve following THA[12]. Our series considered the improvement in ROM and the modified HHS. The modified HHS allows evaluation of the hip joints studied, as the HHS allows evaluation of the whole patient. The evaluation of the individual joint deformity and ROM, especially in the bilateral THAs, is possible with the modified HHS. These scores and the SF-36 showed a significant overall improvement in these patients with stiff hips in AS (Table 4).

The limitations of this study include a relatively short duration of follow-up and a small number of patients that could be included in this series. The retrospective nature of this study is another limitation. A 5-year follow-up with radiological and clinical outcomes would have been ideal for studying the various outcomes, while our study's average follow-up was 38.33 mo (range 6-83 mo). We will continue to follow up on these patients to study the clinical, radiological, and overall outcomes. The risk of complications in THA with AS is associated with stiffness of the spine. The possibility of fractures and component loosening are a few complications that could be seen at longer follow-up times[18].

CONCLUSION

THA with a modified lateral approach in AS with stiff hips has significant improvement in the ROM, HHS, overall function, and QOL as indicated by functional outcome measures with SF-12 and SF-36 scores.

Table 4 Comparison of parameters with other series

Ref.	Patients (hips)	Follow-up in mo	Pain relief, %	Final MHHS	ROM score/mean flexion	Approach	Complications, %
Bisla *et al*[20], 1976	23 (34)	42.5	91	NS	ROM-3	NS	5.88
Resnick *et al*[21], 1976	11 (21)	36	NS	NS	NS	NS	0
Williams *et al*[22], 1977	56 (99)	36	NS	NS	NS	NS	10
Baldursson *et al*[23], 1977	10 (18)	45.6	94	NS	Flexion-90	NS	0
Shanahan *et al*[24], 1982	12 (16)	89	94	NS	NS	NS	6.25
Finsterbush *et al*[25], 1988	23 (35)	90	NS	NS	Flexion-86	NS	14.28
Walker *et al*[26], 1991	19 (29)	58	97	NS	ROM-4	NS	0
Gualtieri *et al*[27], 1992	39 (73)	90	89	NS	NS	NS	0
Brinker *et al*[28], 1996	12 (20)	75	90	89.1	ROM-4	Posterior, lateral	0
Sochart *et al*[29], 1997	24 (43)	276	100	NS	ROM-4	NS	27.9
Lehtimäki *et al*[30], 2001	54 (76)	240	NS	NS	NS	NS	3.94
Joshi *et al*[31], 2002	103 (181)	120	96	NS	NS	Lateral, Hardinge	10.5
Kim *et al*[32], 2007	12 (24)	132	NS	82.3	NS	Lateral	12.5
Bhan *et al*[6], 2008	54 (92)	102	62	82.6	ROM-4	Posterior	14
Li *et al*[33], 2009	24 (39)	36	NS	91	ROM-4	Posterolateral	2.5
Tang *et al*[2], 2000	58 (95)	135.4	94	88.8	ROM-4.2	Posterior	20
Bangjian *et al*[34], 2012	12 (24)	50.4	100	86.25	Flexion-84	Posterolateral	0
Malhotra *et al*[35], 2012	23 (32)	42	NS	87.1	ROM-4	Posterior	4.7
Siavashi *et al*[36], 2014	77 (NA)	12	NS	88.22	ROM-5	Posterior, lateral	20.8
Xu *et al*[37], 2017	54 (81)	42	NS	86.1	Flexion-82.5	Posterolateral	0
Our series	40 (69)	38.33	92	90.67	Flexion-102.1739, ROM-4.9514	Modified Hardinge	1.4

ROM: Range of movement; MHHS: Modified Harris hip score; NS: Not specified; NA: Not available.

ARTICLE HIGHLIGHTS

Research background

Total hip arthroplasty (THA) with modified lateral approach has been used routinely in our unit for arthritic hips not requiring posterior wall reconstruction. A good exposure of the acetabulum with preservation of the posterior abductors is optimal for hips with flexion deformities.

Research motivation

THA with modified lateral approach is not associated with abductor compromise and results in good functional outcome as seen in individuals coming back for follow-up.

Research objectives

The objective was to have a functional and overall assessment of hips with ankylosing spondylitis at follow-up after THA. Assessment of functional outcome with described tools such as the 36-item and 12-item short form health surveys with the hip scores would provide adequate information.

Research methods
Patients with ankylosing spondylitis were assessed at follow-up after THA. Functional, clinical, and radiological assessment was done at the follow-up.

Research results
The results showed significant improvement in the functional scores in all domains with improvement in range of movement and quality of life.

Research conclusions
Modified lateral approach THA in ankylosing spondylitis improves range of movement, function, and quality of life.

Research perspectives
Long-term follow-up of 5 years to 10 years with comparison to other approaches would provide a better comparison of the efficacy of the lateral approach.

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FOOTNOTES

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REFERENCES

1 **Burki V**, Gossec L, Payet J, Durnez A, Elhai M, Fabreguet I, Koumakis E, Meyer M, Paternotte S, Roure F, Dougados M. Prevalence and characteristics of hip involvement in spondyloarthritis: a single-centre observational study of 275 patients. *Clin Exp Rheumatol* 2012; **30**: 481-486 [PMID: 22513241]
2 **Tang WM**, Chiu KY. Primary total hip arthroplasty in patients with ankylosing spondylitis. *J Arthroplasty* 2000; **15**: 52-58 [PMID: 10654462 DOI: 10.1016/s0883-5403(00)91155-0]
3 **Hamadouche M**, Kerboull L, Meunier A, Courpied JP, Kerboull M. Total hip arthroplasty for the treatment of ankylosed hips: a five to twenty-one-year follow-up study. *J Bone Joint Surg Am* 2001; **83**: 992-998 [PMID: 11451967 DOI: 10.2106/00004623-200107000-00003]

4 **Lin D**, Charalambous A, Hanna SA. Bilateral total hip arthroplasty in ankylosing spondylitis: a systematic review. *EFORT Open Rev* 2019; **4**: 476-481 [PMID: 31423331 DOI: 10.1302/2058-5241.4.180047]

5 **Kubiak EN**, Moskovich R, Errico TJ, Di Cesare PE. Orthopaedic management of ankylosing spondylitis. *J Am Acad Orthop Surg* 2005; **13**: 267-278 [PMID: 16112983 DOI: 10.5435/00124635-200507000-00006]

6 **Bhan S**, Eachempati KK, Malhotra R. Primary cementless total hip arthroplasty for bony ankylosis in patients with ankylosing spondylitis. *J Arthroplasty* 2008; **23**: 859-866 [PMID: 18722294 DOI: 10.1016/j.arth.2007.07.014]

7 **Frndak PA**, Mallory TH, Lombardi AV Jr. Translateral surgical approach to the hip. The abductor muscle "split". *Clin Orthop Relat Res* 1993; 135-141 [PMID: 8403638]

8 **Mulliken BD**, Rorabeck CH, Bourne RB, Nayak N. A modified direct lateral approach in total hip arthroplasty: a comprehensive review. *J Arthroplasty* 1998; **13**: 737-747 [PMID: 9802658 DOI: 10.1016/s0883-5403(98)90024-9]

9 **Dagfinrud H**, Mengshoel AM, Hagen KB, Loge JH, Kvien TK. Health status of patients with ankylosing spondylitis: a comparison with the general population. *Ann Rheum Dis* 2004; **63**: 1605-1610 [PMID: 15547084 DOI: 10.1136/ard.2003.019224]

10 **Bahardoust M**, Hajializade M, Amiri R, Mousazadeh F, Pisoudeh K. Evaluation of health-related quality of life after total hip arthroplasty: a case-control study in the Iranian population. *BMC Musculoskelet Disord* 2019; **20**: 46 [PMID: 30704434 DOI: 10.1186/s12891-019-2428-0]

11 **Yang X**, Fan D, Xia Q, Wang M, Zhang X, Li X, Cai G, Wang L, Xin L, Xu S, Pan F. The health-related quality of life of ankylosing spondylitis patients assessed by SF-36: a systematic review and meta-analysis. *Qual Life Res* 2016; **25**: 2711-2723 [PMID: 27324038 DOI: 10.1007/s11136-016-1345-z]

12 **Lindner M**, Nosseir O, Keller-Pliessnig A, Teigelack P, Teufel M, Tagay S. Psychosocial predictors for outcome after total joint arthroplasty: a prospective comparison of hip and knee arthroplasty. *BMC Musculoskelet Disord* 2018; **19**: 159 [PMID: 29788969 DOI: 10.1186/s12891-018-2058-y]

13 **Mariconda M**, Galasso O, Costa GG, Recano P, Cerbasi S. Quality of life and functionality after total hip arthroplasty: a long-term follow-up study. *BMC Musculoskelet Disord* 2011; **12**: 222 [PMID: 21978244 DOI: 10.1186/1471-2474-12-222]

14 **Vander Cruyssen B**, Muñoz-Gomariz E, Font P, Mulero J, de Vlam K, Boonen A, Vazquez-Mellado J, Flores D, Vastesaeger N, Collantes E; ASPECT-REGISPONSER-RESPONDIA working group. Hip involvement in ankylosing spondylitis: epidemiology and risk factors associated with hip replacement surgery. *Rheumatology (Oxford)* 2010; **49**: 73-81 [PMID: 19605374 DOI: 10.1093/rheumatology/kep174]

15 **Rohde G**, Berg KH, Pripp AH, Prøven A, Haugeberg G. No deterioration in health-related quality of life in patients with axial spondyloarthritis followed for 5 years in ordinary outpatient clinics in the biological treatment era. *Qual Life Res* 2020; **29**: 99-107 [PMID: 31559519 DOI: 10.1007/s11136-019-02308-4]

16 **Rojanasopondist P**, Galea VP, Connelly JW, Matuszak SJ, Rolfson O, Bragdon CR, Malchau H. What Preoperative Factors are Associated With Not Achieving a Minimum Clinically Important Difference After THA? *Clin Orthop Relat Res* 2019; **477**: 1301-1312 [PMID: 31136425 DOI: 10.1097/CORR.0000000000000667]

17 **Neuprez A**, Neuprez AH, Kaux JF, Kurth W, Daniel C, Thirion T, Huskin JP, Gillet P, Bruyère O, Reginster JY. Total joint replacement improves pain, functional quality of life, and health utilities in patients with late-stage knee and hip osteoarthritis for up to 5 years. *Clin Rheumatol* 2020; **39**: 861-871 [PMID: 31720892 DOI: 10.1007/s10067-019-04811-y]

18 **Blizzard DJ**, Penrose CT, Sheets CZ, Seyler TM, Bolognesi MP, Brown CR. Ankylosing Spondylitis Increases Perioperative and Postoperative Complications After Total Hip Arthroplasty. *J Arthroplasty* 2017; **32**: 2474-2479 [PMID: 28438449 DOI: 10.1016/j.arth.2017.03.041]

19 **van Tubergen A**, Coenen J, Landewé R, Spoorenberg A, Chorus A, Boonen A, van der Linden S, van der Heijde D. Assessment of fatigue in patients with ankylosing spondylitis: a psychometric analysis. *Arthritis Rheum* 2002; **47**: 8-16 [PMID: 11932872 DOI: 10.1002/art1.10179]

20 **Bisla RS**, Ranawat CS, Inglis AE. Total hip replacement in patients with ankylosing spondylitis with involvement of the hip. *J Bone Joint Surg Am* 1976; **58**: 233-238 [PMID: 1254628]

21 **Resnick D**, Dwosh IL, Goergen TG, Shapiro RF, D'Ambrosia R. Clinical and radiographic "reankylosis" following hip surgery in ankylosing spondylitis. *AJR Am J Roentgenol* 1976; **126**: 1181-1188 [PMID: 179378 DOI: 10.2214/ajr.126.6.1181]

22 **Williams E**, Taylor AR, Arden GP, Edwards DH. Arthroplasty of the hip in ankylosing spondylitis. *J Bone Joint Surg Br* 1977; **59-B**: 393-397 [PMID: 925047 DOI: 10.1302/0301-620X.59B4.925047]

23 **Baldursson H**, Brattström H, Olsson T. Total hip replacement in ankylosing spondylitis. *Acta Orthop Scand* 1977; **48**: 499-507 [PMID: 596146 DOI: 10.3109/17453677708989738]

24 **Shanahan WR**, Kaprove RE, Major PA, Hunter T, Baragar FD. Assessment of longterm benefit of total hip replacement in patients with ankylosing spondylitis. *J Rheumatol* 1982; **9**: 101-104 [PMID: 7086768]

25 **Finsterbush A**, Amir D, Vatashki E, Husseini N. Joint surgery in severe ankylosing spondylitis. *Acta Orthop Scand* 1988; **59**: 491-496 [PMID: 3188851 DOI: 10.3109/17453678809148770]

26 **Walker LG**, Sledge CB. Total hip arthroplasty in ankylosing spondylitis. *Clin Orthop Relat Res* 1991; 198-204 [PMID: 1984917]

27 **Gualtieri G**, Gualtieri I, Hendriks M, Gagliardi S. Comparison of cemented ceramic and metal-polyethylene coupling hip prostheses in ankylosing spondylitis. *Clin Orthop Relat Res* 1992; 81-85 [PMID: 1516332]

28 **Brinker MR**, Rosenberg AG, Kull L, Cox DD. Primary noncemented total hip arthroplasty in patients with ankylosing spondylitis. Clinical and radiographic results at an average follow-up period of 6 years. *J Arthroplasty* 1996; **11**: 802-812 [PMID: 8934320 DOI: 10.1016/s0883-5403(96)80180-x]

29 **Sochart DH**, Porter ML. Long-term results of total hip replacement in young patients who had ankylosing spondylitis. Eighteen to thirty-year results with survivorship analysis. *J Bone Joint Surg Am* 1997; **79**: 1181-1189 [PMID: 9278078 DOI: 10.2106/00004623-199708000-00010]

30 **Lehtimäki MY**, Lehto MU, Kautiainen H, Lehtinen K, Hämäläinen MM. Charnley total hip arthroplasty in ankylosing spondylitis: survivorship analysis of 76 patients followed for 8-28 years. *Acta Orthop Scand* 2001; **72**: 233-236 [PMID:

11480596 DOI: 10.1080/00016470152846538]
31 **Joshi AB**, Markovic L, Hardinge K, Murphy JC. Total hip arthroplasty in ankylosing spondylitis: an analysis of 181 hips. *J Arthroplasty* 2002; **17**: 427-433 [PMID: 12066271 DOI: 10.1054/arth.2002.32170]
32 **Kim YL**, Shin SI, Nam KW, Yoo JJ, Kim YM, Kim HJ. Total hip arthroplasty for bilaterally ankylosed hips. *J Arthroplasty* 2007; **22**: 1037-1041 [PMID: 17920478 DOI: 10.1016/j.arth.2007.03.027]
33 **Li J**, Xu W, Xu L, Liang Z. Hip resurfacing arthroplasty for ankylosing spondylitis. *J Arthroplasty* 2009; **24**: 1285-1291 [PMID: 19682837 DOI: 10.1016/j.arth.2009.07.003]
34 **Bangjian H**, Peijian T, Ju L. Bilateral synchronous total hip arthroplasty for ankylosed hips. *Int Orthop* 2012; **36**: 697-701 [PMID: 21751023 DOI: 10.1007/s00264-011-1313-8]
35 **Malhotra R**, Kannan A, Kumar V, Nagaraj C, Marimuthu K, Khatri D. Hip resurfacing arthroplasty in inflammatory arthritis a 3- to 5-year follow-up study. *J Arthroplasty* 2012; **27**: 15-20 [PMID: 21414743 DOI: 10.1016/j.arth.2011.02.016]
36 **Siavashi B**, Mohseni N, Zehtab MJ, Ramim T. Clinical outcomes of total hip arthroplasty in patients with ankylosed hip. *Arch Bone Jt Surg* 2014; **2**: 25-30 [PMID: 25207309]
37 **Xu J**, Zeng M, Xie J, Wen T, Hu Y. Cementless total hip arthroplasty in patients with ankylosing spondylitis: A retrospective observational study. *Medicine (Baltimore)* 2017; **96**: e5813 [PMID: 28121928 DOI: 10.1097/MD.0000000000005813]

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ORIGINAL ARTICLE

Retrospective Cohort Study

Higher cost of arthroplasty for hip fractures in patients transferred from outside hospitals *vs* primary emergency department presentation

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Abstract

BACKGROUND

In 2016 Centers for Medicare and Medicaid Services proposed bundled payments for hip fractures to improve the quality and decrease costs of care. Patients transferred from other facilities may be imposing a financial risk on the hospitals that accept these patients.

AIM

To determine the costs associated with patients that either presented to the emergency department or were transferred from another hospital or skilled nursing facility (SNF) with the diagnosis of a hip fracture requiring operative intervention.

METHODS

A retrospective single institution review was conducted for all arthroplasty patients from 2010 to 2015. Inclusion criteria included a total or partial hip replacement for a hip fracture. Exclusion criteria included pathologic, periprosthetic, and fracture non-union. Data was collected to compare total observed costs for patients from the emergency department, patients from skilled nursing facilities, and patients from an outside hospital.

RESULTS

A total of 223 patients met the inclusion criteria. 135 (60.54%) of these patients presented primarily to the emergency department, 58 patients (26.01%) were transferred from an outside hospital, and 30 patients (13.43%) were transferred from a SNF. Cost data analysis showed that outside hospital patients demonstrated significantly greater total cost for their hospitalization ($43302) compared to emergency department patients ($28875, P = 0.000) and SNF patients ($28282, P = 0.000).

CONCLUSION

Patients transferred from an outside hospital incurred greater costs for their hospitalization than patients presenting from an emergency department or SNF. This is a strong argument for risk-adjustment models when bundling payments for the care of hip fracture patients.

Key Words: Total hip arthroplasty; Cost; Transfer; Outside hospital; Hip fracture

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Core Tip: Transfers to regional tertiary care centers of critically ill and severely injured patients have been shown to decrease morbidity and mortality. Many of these patients have increased morbidity, length of stay, blood transfusion requirements, and intensive care utilization has been previously documented in transferred patients. To our knowledge, this study is the first to document this phenomenon in patients with femoral neck fractures being treated with arthroplasty. With the nationwide implementation of bundled payments looming, determining the additional risks and costs associated with providing referral services for community and regional hospitals is essential. It is clear from our data that patients transferred from an outside hospital more significantly strain the resources of the receiving tertiary care hospital compared to those patients who present primarily to the emergency department. This is a strong argument for robust risk-adjustment models that potentially even include patient point of origin.

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INTRODUCTION

The Centers for Medicare and Medicaid Services (CMS) began the Comprehensive Care for Joint Replacement (CJR) model in 2016, which aims to hold hospitals accountable for the quality of care delivered from surgery until 90 d after discharge. As has already been reported, episode-of-care payments for elective Total Joint Arthroplasty (TJA) can vary widely and depend on a number of factors. These factors may include the type of procedure, patient comorbidities, discharge disposition, and readmission rates[1,2]. In July 2016, the CMS proposed implementing bundled payments for hip fracture care in order to control costs and improve quality[3]. This has led to concern that patients with multiple comorbidities or surgically complex patients may either be denied necessary care or transferred to other facilities to prevent financial loss at the initial institution. Transfer to a tertiary care facility is necessary in medically complex or critically ill patients and is protected by the Emergency Medical Treatment and Active Labor Act of 1986 (EMTALA). Furthermore, while EMTALA requires hospitals with special capabilities to accept transfers from less specialized facilities, there are no guidelines defining appropriateness of transfers. The implementation of this bundled care model may result in an increase in unnecessary transfers of high-risk patients to tertiary care centers and safety-net hospitals[4,5]. As a result, it is important to understand not only the greater financial risk associated with accepting these patients, but also, the potential for increased morbidity and mortality of patients who are transferred.

Transfers to tertiary care centers, in general, can reduce mortality associated with critically ill and complex patients[6,7]. However, several studies in the orthopaedic literature demonstrate that transfers can be influenced by factors such as insurance status and time of the week with inappropriate transfers rates ranging between 16%-52%[8-13]. Other studies have shown that the transfer of medically and surgically complex patients can negatively impact the receiving hospitals' outcome measures and mortality rates[4,14]. These hospital quality metrics are available to the public. If these metrics are negatively influenced by inappropriate transfers, this may deter a patient from undergoing an elective procedure at these institutions. However, this has not been demonstrated in the literature as of yet.

The goal of this study was to examine financial and clinical outcomes in hospitalizations for unplanned arthroplasty in hip fractures between patients transferred from outside hospitals, patients presenting to the emergency department, and patients transferred from skilled nursing facilities. This study will help to further characterize the differences in cost and outcomes between these subsets of unplanned arthroplasty patients, which has not been previously documented to the best of our knowledge. This information is useful to physicians, hospital administrators, and payers as it may identify patient groups that utilize increased resources and suffer increased morbidity and/or mortality.

MATERIALS AND METHODS

Between 2010 and 2015, demographic, financial, and outcomes data were collected on all arthroplasty patients at our institution, a tertiary care center, as part of an Institutional Review Board-approved patient safety initiative. All patients underwent either total hip arthroplasty or proximal femoral hemiarthroplasty by one of three fellowship trained arthroplasty surgeons at this institution. In all cases, the procedural billing code for the arthroplasty procedure was the primary code submitted to the patient's insurance or medicare. For the purposes of this study, we included all patients with a diagnosis of basicervical, midcervical, or transcervical femoral neck fractures. Exclusion criteria included pathologic fractures, periprosthetic fractures, and fracture non-unions.

The data collected for the patient safety initiative included age, sex, race, diagnosis, facility of origin, secondary diagnoses, American Society of Anaesthesiologists (ASA) score, length of stay, length of intensive care unit stay, total observed cost, charges, mortality, discharge disposition, and procedure codes. Total observed cost include all costs related to the arthroplasty procedure and subsequent inpatient care of the patient. The patient's point of origin was determined to be our own institution's emergency department (ED), outside skilled nursing facility (SNF) or intermediate care facility, and outside hospital (OSH). These locations were verified by reviewing the patient's individual medical record. Patients who were transferred from an outside hospital or nursing facility to the emergency department were considered as transfers from an outside hospital or SNF, respectively. Patients who were transported to the emergency department from a physician's office or urgent care were considered emergency department patients. Finally, two patients that were directly admitted from clinic with a diagnosis of femoral neck fracture were not included in the study as they were previously known to and followed by the treating team and could be a potential source of bias in the analysis.

Statistical analysis

The data was utilized to examine differences in morbidity, mortality, cost, length of stay, and discharge disposition between hip fracture patients based on the individual point of origin prior to presenting to our institution. Each diagnosis, ASA score, Charlson comorbidity index, and surgical procedure performed were confirmed with individual chart review. For categorical variables, a Pearson chi-square analysis was performed.

RESULTS

A total of 223 patients met the inclusion criteria and were included in the study. The number of patients that presented primary to the ED at our institution, typically by EMS or medical transport, was 135 (60.54%). The number of patients that were transferred from an outside hospital to an inpatient unit or to the emergency department was 58 (26.01%). Lastly, the number of patients transferred from a SNF or intermediate care facility was 30 patients (13.43%). Patient cohorts and demographics are presented in Table 1.

ED patients and SNF patients were significantly older than OSH patients (P = 0.001). ED and SNF patients were not significantly different from each other in age.

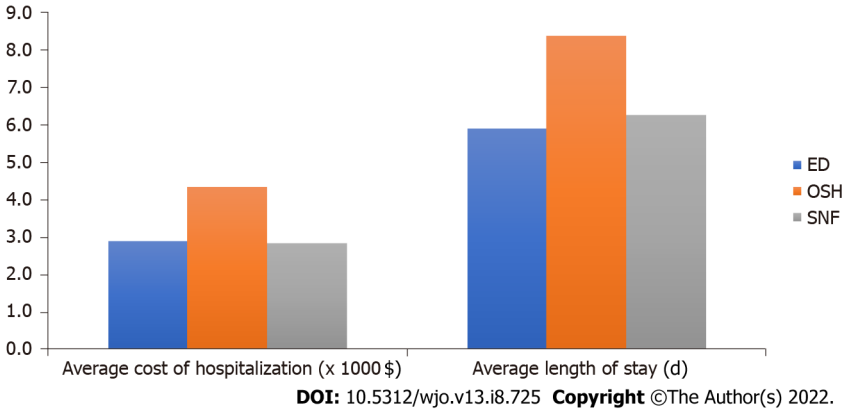
There was a larger percentage of ASA 4 patients amongst OSH and SNF patients and significantly lower percentage of ASA 1 and ASA 2 patients compared to the ED patients (P = 0.001). There was no significant difference in average age-adjusted Charlson comorbidity index across all three groups. There was a significantly higher number of female patients (80.00%) who presented to the ED compared to transfers from OSHs (53.45%) and SNFs (53.33%) (P = 0.000). There was a trend toward increased utilization of hemiarthroplasty in SNF patients compared to ED and OSH patients that did not reach statistical significance (P = 0.070). Finally, there was no significant difference in race (white *vs* non-white) between the three groups (P = 0.583).

Cost data analysis showed that OSH patients demonstrated significantly greater total cost for their hospitalization ($43302) compared to ED patients ($28875, P = 0.000) and SNF patients ($28282, P = 0.000). OSH patients' costs per hospitalization average 149% and 153% of the cost per hospitalization of ED patients and SNF patients, respectively. There was no significant difference in total cost between ED patient and SNF patients (P = 0.805). This data is summarized in Figure 1. For reference purposes, the average total inpatient cost for the 1540 elective total hip arthroplasties performed at our institution

Table 1 Patient demographics by cohort

Variable	Emergency department patients (*n* = 135)	Outside hospital transfer patients (*n* = 58)	Skilled nursing facility and intermediate care facility patients
Average age	79.53	72.25 (*P* = 0.001)	83.25
Sex	80.00% female (*P* = 0.0000)	53.45% female	53.33% female
ASA score			
ASA 1 or 2	25.92% (*P* = 0.0007)	17.24%	3.33%
ASA 3	62.22%	56.90%	70.00%
ASA 4	11.85%	25.86% (*P* = 0.0007)	26.67% (*P* = 0.0007)
Average Charlson comorbidity index	5.17	5.51	6.07
Percentage hemiarthroplasty (*vs* THA)	71.11%	68.97%	90.00%
Race	88.14% white	93.10% white	90.00% white

ASA: American Society of Anaesthesiologists; THA: Total hip arthroplasty.



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Figure 1 Average cost of hospitalization and average length of stay of patients from different points of origin. ED: Emergency department; OSH: Outside hospital; SNF: Skilled nursing facility.

during the same time period as our study population is $22,182. Therefore, the non-elective hip arthroplasty patients' costs per hospitalization average 193%, 130%, and 127% of the cost per hospitalization of elective total hip patients for OSH, ED, and SNF patients, respectively.

Average LOS was significantly greater in the OSH patients (8.38 d) compared to ED patients (5.89 d, *P* = 0.003) and SNF patients (6.27 d, *P* = 0.027). No significant difference was found between ED patients and SNF patients in average LOS (*P* = 0.599). This data is also summarized in Figure 1.

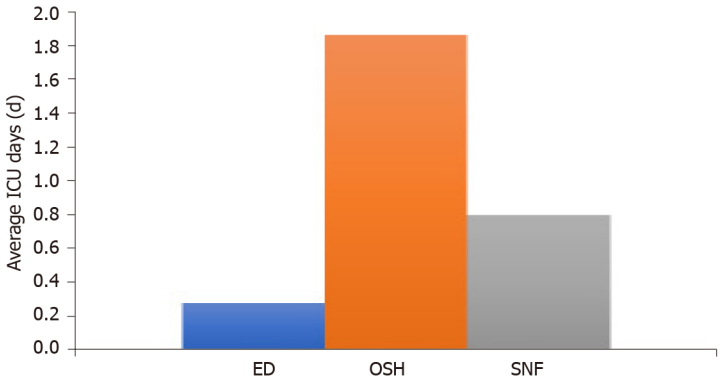
Of the 135 ED patients, there were 3 in-hospital deaths (2.22%). There were 2 in-hospital deaths among the 58 patients transferred from outside hospitals (3.45%) and 3 in-hospital deaths among the 30 patients transferred from SNFs or intermediate care facilities (10.00%). Owing to the low number of mortalities, these differences did not reach statistical significance.

Average intensive care unit (ICU) days per hospitalization was significantly greater in the OSH patients (1.86 d) compared to ED patients (0.28 d, *P* = 0.001) and SNF patients (0.80 d, *P* = 0.002). There was no significant difference in ICU days per hospitalization between SNF and ED patients. This data is summarized in Figure 2.

Analysis of patient discharge destination showed that ED patients were more likely to be discharged home than OSH and SNF patients. There were no other statistically significant differences in discharge destination based on point of origin. This data is summarized in Figure 3.

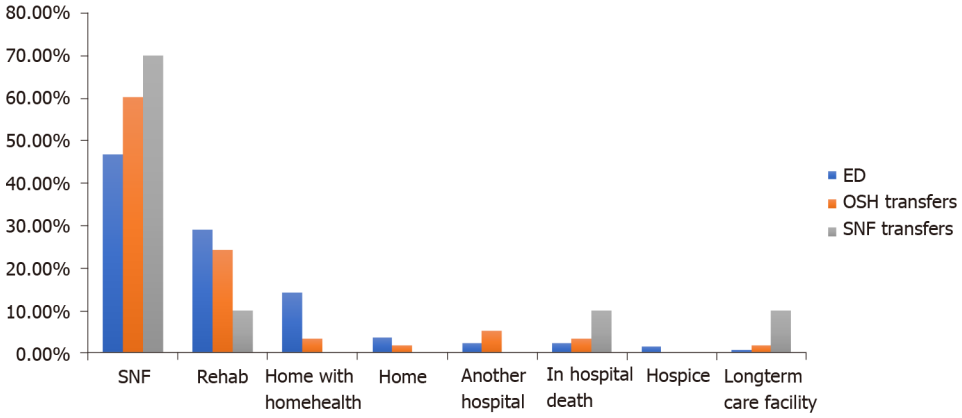
DISCUSSION

Transfers to regional trauma centers and tertiary care centers of critically ill and severely injured



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Figure 2 Average intensive care unit days per hospitalization (days) from patient point of origin. ICU: Intensive care unit; ED: Emergency department; OSH: Outside hospital; SNF: Skilled nursing facility.



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Figure 3 Discharge destination based on patient point of origin. ED: Emergency department; OSH: Outside hospital; SNF: Skilled nursing facility.

patients have been shown to decrease morbidity and mortality[15,16]. As one might expect given the illness severity seen in many of these transferred patients, increased morbidity, length of stay, blood transfusion requirements, and intensive care utilization has been previously documented in transferred patients[8,11,17]. To our knowledge, this study is the first to document this phenomenon in patients with femoral neck fractures being treated with arthroplasty.

The aim of this study was to compare demographic information, procedure utilization, cost differences, morbidity, and mortality in non-elective hip arthroplasty performed for fracture at an academic medical center based upon patient point of origin. With the nationwide implementation of bundled payments looming, determining the additional risks and costs associated with providing referral services for community and regional hospitals is essential. It is not surprising that patients transferred from an OSH incurred greater costs for their hospitalization than ED and SNF patients. Medically complex patients with significant comorbidities, associated injuries, or critical illness are often difficult for community hospitals to manage and are frequently transferred to tertiary care centers. Previous studies have also found increased cost with non-elective hip arthroplasty compared to elective total hip replacement[4,5].

Our study showed increased length of stay and increased number of average ICU stays per hospitalization for transfered patients from an OSH compared to those patients presenting to our ED. These results are not surprising but demonstrate the greater burden OSH patients place on facilities, staffing, and healthcare providers. It may also reflect that a delay in getting the patient to the operating room can lead to medical complications and morbidity. Our study also found that ED patients were more likely to have ASA 1 or ASA 2 scores compared to SNF and OSH patients. Patients transferred from an OSH also incurred greater costs than those who presented primarily to our ED.

It is clear from our data that patients transferred from an OSH more significantly strain the resources of the receiving tertiary care hospital compared to those patients who present primarily to the ED. This is an important finding in light of proposed bundled care programs. Bundled care programs, which can disincentive hospitals and providers from taking care of sick and costly patients, may increase the number of hip fracture patients being transferred to tertiary care centers especially with clear

appropriate transfer guidelines lacking. This would further strain the resources of the receiving hospital and could potentially penalize those centers that are willing to provide care for these vulnerable patients. This is a strong argument for robust risk-adjustment models that potentially even include patient point of origin.

One obvious strength of our study is that it is the first to specifically look at cost and morbidity of hip fracture patients undergoing arthroplasty based on their point of origin. We were able to include a large number of patients over nearly a five year period. All total hip arthroplasty and hemiarthroplasty procedures were performed by three fellowship trained arthroplasty surgeons and therefore, variation in surgeon skill and experience is minimal. The data from our initial database was able to be corroborated through our electronic medical records and any disparities or omissions corrected. Finally, our study was able to determine differences in cost for hospitalizations, not charges, a more accurate representation of reimbursement from Medicare, Medicaid, or private insurance.

This study is not without its limitations. We did not examine the reason for transfer to our facility. This analysis may have allowed us to subcategorize patients based on the indication for the transfer and further determine which specific patient groups or which comorbidities are most likely to lead to increased cost, prolonged hospitalization, increased morbidity, or mortality. Additionally, we did not examine surgical complications, readmissions, or transfusion requirements which are further indicators of morbidity. Another limitation is that this is a retrospective analysis of prospectively collected data. Finally, our entire study was limited to a single institution and is subject to institution specific policies and biases that may limit the generalizability of our conclusions. However, we feel that any tertiary medical center with a large referral basis is likely to find similar results.

CONCLUSION

Patients transferred from an outside hospital incurred greater costs for their hospitalization than patients presenting from an emergency department or SNF. This is a strong argument for risk-adjustment models when bundling payments for the care of hip fracture patients.

ARTICLE HIGHLIGHTS

Research background

Rising healthcare expenditure, especially with the projected rise in total joint arthroplasty has lead the Center for Medicare Services to propose bundled payments.

Research motivation

Possible effects of bundle payments on tertiary hospital systems have not been evaluated.

Research objectives

This study aims to evaluate potential effects of bundled payment systems on a large tertiary hospital system.

Research methods

This is a retrospective study of a single hospital system evaluating the observed cost of care for patients presenting with hip fractures from the emergency department, skilled nursing facilities and outside hospital transfers.

Research results

Cost data analysis showed that patient transferred from an outside hospital demonstrate significantly higher costs compared to patients from a skilled nursing facility or the emergency department.

Research conclusions

Given the increased costs associated with patients transferred from outside hospitals this may call for a risk adjustment models when bundling for the care of hip fracture patients.

Research perspectives

Future research will have to further evaluate cost originators to adjust payment models appropriately.

FOOTNOTES

Author contributions: Haug EC wrote and revised the manuscript and collected data; Pehlivan H and Macdonell JR contributed equally and helped design the study and collect data; Novicoff W did the statistical portion; Browne J, Brown T and Cui Q are the senior surgeons; and All authors contributed to this study equally.

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STROBE statement: The authors have read the STROBE Statement, and the manuscript was prepared and revised according to the STROBE Statement.

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REFERENCES

1 **Altman SH**. The lessons of Medicare's prospective payment system show that the bundled payment program faces challenges. *Health Aff (Millwood)* 2012; **31**: 1923-1930 [PMID: 22949439 DOI: 10.1377/hlthaff.2012.0323]
2 **Bozic KJ**, Ward L, Vail TP, Maze M. Bundled payments in total joint arthroplasty: targeting opportunities for quality improvement and cost reduction. *Clin Orthop Relat Res* 2014; **472**: 188-193 [PMID: 23649225 DOI: 10.1007/s11999-013-3034-3]
3 **US Centers for Medicare and Medicaid Services**. Notice of proposed rulemaking for bundled payments for high-quality coordinated cardiac and hip fracture care. July 25, 2016. Available from: https://www.cms.gov/Newsroom/MediaReleaseDatabase/Fact-sheets/2016-Fact-sheets-items/2016-07-25.html
4 **Kamath AF**, Austin DC, Derman PB, Israelite CL. Unplanned hip arthroplasty imposes clinical and cost burdens on treating institutions. *Clin Orthop Relat Res* 2013; **471**: 4012-4019 [PMID: 23928711 DOI: 10.1007/s11999-013-3226-x]
5 **Sams JD**, Milbrandt JC, Froelich JM, Rainville AD, Allan DG. Hospital outcome after emergent vs elective revision total hip arthroplasty. *J Arthroplasty* 2010; **25**: 826-828 [PMID: 20378305 DOI: 10.1016/j.arth.2010.01.097]
6 **Celso B**, Tepas J, Langland-Orban B, Pracht E, Papa L, Lottenberg L, Flint L. A systematic review and meta-analysis comparing outcome of severely injured patients treated in trauma centers following the establishment of trauma systems. *J Trauma* 2006; **60**: 371-8; discussion 378 [PMID: 16508498 DOI: 10.1097/01.ta.0000197916.99629.eb]
7 **MacKenzie EJ**, Rivara FP, Jurkovich GJ, Nathens AB, Frey KP, Egleston BL, Salkever DS, Scharfstein DO. A national evaluation of the effect of trauma-center care on mortality. *N Engl J Med* 2006; **354**: 366-378 [PMID: 16436768 DOI: 10.1056/NEJMsa052049]
8 **Archdeacon MT**, Simon PM, Wyrick JD. The influence of insurance status on the transfer of femoral fracture patients to a level-I trauma center. *J Bone Joint Surg Am* 2007; **89**: 2625-2631 [PMID: 18056494 DOI: 10.2106/JBJS.F.01499]
9 **Thakur NA**, Plante MJ, Kayiaros S, Reinert SE, Ehrlich MG. Inappropriate transfer of patients with orthopaedic injuries to a Level I trauma center: a prospective study. *J Orthop Trauma* 2010; **24**: 336-339 [PMID: 20502210 DOI: 10.1097/BOT.0b013e3181b18b89]
10 **Crichlow RJ**, Zeni A, Reveal G, Kuhl M, Heisler J, Kaehr D, Vijay P, Musapatika DL. Appropriateness of patient transfer with associated orthopaedic injuries to a Level I trauma center. *J Orthop Trauma* 2010; **24**: 331-335 [PMID: 20502209 DOI: 10.1097/BOT.0b013e3181ddfde9]
11 **Nathens AB**, Maier RV, Copass MK, Jurkovich GJ. Payer status: the unspoken triage criterion. *J Trauma* 2001; **50**: 776-783 [PMID: 11371832 DOI: 10.1097/00005373-200105000-00002]
12 **Koval KJ**, Tingey CW, Spratt KF. Are patients being transferred to level-I trauma centers for reasons other than medical necessity? *J Bone Joint Surg Am* 2006; **88**: 2124-2132 [PMID: 17015587 DOI: 10.2106/JBJS.F.00245]
13 **O'Connell RS**, Haug EC, Malasitt P, Mallu S, Satpathy J, Isaacs J, Mounasamy V. Appropriateness of patients transferred with orthopedic injuries: experience of a level I trauma center. *Eur J Orthop Surg Traumatol* 2018; **28**: 551-554 [PMID: 29374803 DOI: 10.1007/s00590-018-2134-x]

14 **Rosenberg AL**, Hofer TP, Strachan C, Watts CM, Hayward RA. Accepting critically ill transfer patients: adverse effect on a referral center's outcome and benchmark measures. *Ann Intern Med* 2003; **138**: 882-890 [PMID: 12779298 DOI: 10.7326/0003-4819-138-11-200306030-00009]

15 **Brauer CA**, Coca-Perraillon M, Cutler DM, Rosen AB. Incidence and mortality of hip fractures in the United States. *JAMA* 2009; **302**: 1573-1579 [PMID: 19826027 DOI: 10.1001/jama.2009.1462]

16 **Sampalis JS**, Denis R, Lavoie A, Fréchette P, Boukas S, Nikolis A, Benoit D, Fleiszer D, Brown R, Churchill-Smith M, Mulder D. Trauma care regionalization: a process-outcome evaluation. *J Trauma* 1999; **46**: 565-79; discussion 579 [PMID: 10217218 DOI: 10.1097/00005373-199904000-00004]

17 **Spain DA**, Bellino M, Kopelman A, Chang J, Park J, Gregg DL, Brundage SI. Requests for 692 transfers to an academic level I trauma center: implications of the emergency medical treatment and active labor act. *J Trauma* 2007; **62**: 63-7; discussion 67 [PMID: 17215734 DOI: 10.1097/TA.0b013e31802d9716]

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ORIGINAL ARTICLE

Retrospective Study

Risk modeling of femoral neck fracture based on geometric parameters of the proximal epiphysis

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Abstract

BACKGROUND

Fractures of the proximal femur epiphysis are problematic for state health care because they are associated with severe medical and social problems and high morbidity and mortality rates.

AIM

To model the potential risk of hip fracture *via* femur geometric parameters.

METHODS

Seventy educational cadaveric femurs from people aged 14 to 80 years, 10 X-ray images from the records of the Human Anatomy Department and 10 X-ray images from the Department of Traumatology, Orthopedics and Disaster Surgery of Sechenov University, were evaluated. The parameters of the fractured bone were measured using images captured with a Canon d60 camera. The projection values of the proximal epiphysis of the cadaveric femurs and geometric parameters of the bones shown in the X-ray images were measured with Autodesk software

(AutoCAD 2018). Analysis of the video frames showing bone rotation reveal that the greater trochanter can be inscribed in a parallelepiped, where one of the faces is parallel to the plane of view in the frontal standard projection and is rectangular. The angle of bone rotation obtained by turning the cube corresponded to the angle measured with the second technique. This reliable method of calculating the rotation of the bone relative to the anterior projection was employed in subsequent calculations. The geometric parameters of the femur were measured using X-ray images according to the proposed method.

RESULTS

The geometric parameters of 70 femurs were analyzed, and correlation coefficients were calculated. Our measurement results were compared with those reported by other authors. The potential influence of femur geometry on force distribution in the proximal epiphysis of the femur was described, and a 2-dimensional model of the femur epiphysis associated with minimal neck fracture risk was provided. The assessment of the geometric parameters of the femoral epiphysis indicated the greatest risk of a varus fracture of the neck if the angle of the minimal resistance zone (AMRZ) index > 24° and the neck-shaft angle (NSA) < 127.5°. In contrast, the minimum risk was observed at AMRZ < 14° and NSA > 128.87°.

CONCLUSION

The proposed method provides the potential femur neck fracture risk based on geometric parameters.

Key Words: Fracture; Proximal epiphysis of femur; Risk; Traumatology; Hip neck; Risk assessment scale

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Core Tip: The neck-shaft angle (NSA) and angle of the minimal resistance zone [the area located in Ward's triangle (AMRZ)] were most associated with femoral neck fracture risk, and a method for calculating the true value of these parameters and risk stratification was developed. Assessment of the geometric parameters of the femoral epiphysis revealed the greatest risk of a varus fracture of the neck if the AMRZ index > 24° and NSA < 127.5°. In contrast, the minimum risk was observed at AMRZ < 14° and NSA > 128.87°.

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INTRODUCTION

Fractures of the proximal epiphysis of the femur are problematic for state health care because they are associated with severe medical and social problems[1], high morbidity rates[2], disability[3,4], and high mortality rates[5]. Bone strength depends on the mineral density, architectonics and remodeling ability of bones[6], which change over time due to various factors. Characteristics such as bone mineral density, bone geometry and the properties of bone materials are factors that constitute bone quality[6]. The process by which bone strength decreases due to chemical composition changes and by which it decreases in trabecular density is referred to as osteoporosis[7].

The results of multiple studies on the causes and risk factors of bone deterioration, such as osteoporosis, have been introduced in clinical practice. The Fracture Risk Assessment Tool (FRAX)[8] scale was developed by individuals at the University of Sheffield to evaluate fracture risk; the scale assesses the influence of factors that cause a decrease in bone strength. The FRAX scale allows us to predict the ten-year probability of fracture, to identify patients who require more detailed examinations, including X-ray densitometry, and to prevent excessive radiation exposure[9].

In recent years, numerous studies have investigated the distribution of strain in bone under an applied load, identified areas that are highly influenced by stress and fracture risk and determined the influence of bone cytoarchitectonics and geometry on stress apportionment. High-resolution computed tomography and magnetic resonance tomography are employed in this field to analyze bone morphometric parameters[10]. Finite element analysis is a technique that is widely employed for bone model

construction[11]. MATLAB is frequently utilized to calculate stress distributions in bone models[1]. The authors assessed changes in bone sample flexibility *via* a microhardness tester[12]. Other authors have detected structures in loaded femurs *via* a tension detector fixed to the bone[13]. The results of these investigations have been implemented in osteosynthesis operations[14] and endoprosthesis engineering applications[15].

This study aimed to determine the geometric parameters of the proximal femur that contribute most to femoral neck fracture. A method for measuring bone geometric parameters *via* X-ray images is provided since X-ray images are widely employed by general practitioners, and thus, may be preferable for use in screening studies. According to this finding, in this study, we will mostly rely on X-ray imaging, as a widely utilized diagnostic method.

MATERIALS AND METHODS

Seventy femurs from the records of the Department of Human Anatomy at Sechenov University from people aged 14 to 80 years were selected to measure geometric parameters of the proximal epiphysis.

A video of femur rotation around the anatomic axis (for the estimation of the bone projection changes during the turning process) and stills from the video and X-ray images of the femur of 10 adult patients (18-24 years) were provided by the Department of Human Anatomy at Sechenov University (18-24 years), and 10 images of adult patients (18-63 years) were provided by the Department of Traumatology, Orthopedics and Disaster Surgery of Sechenov University (18-63 years). These X-ray images contained images of both femurs: one femur was fractured, and the other femur was intact and considered equal. The parameters of the fractured bone were measured using images captured with a Canon d60 camera.

The projection values of the proximal epiphysis of the femurs from the Department of Human Anatomy and geometric parameters of the bones shown in the X-ray images were measured with Autodesk software (AutoCAD 2018).

Method of measuring bone geometry parameters

To ensure accurate measurements, centimeter rulers were attached to the bones, which helped to correctly scale the images. The projection that defines the femoral neck base and accuracy of the neck-shaft angle (NSA) measurements, *i.e.*, the frontal standard projection (FSP), was selected to plot the segments signifying the main geometric parameters of the proximal epiphysis of the femur.

In this study, a method for assessing the morphometric parameters of the proximal femur based on the projection values and angle of rotation around the anatomical axis relative to the FSP was developed. In this study, the rotation angle was determined by the rotation of the cube installed on the tripod turning the bone. The rotation of the cube thus indicated the rotation of the bone at every point in time. The anatomical axis was drawn through the midpoint of the diaphyseal diameter. The mechanical axis passed through the center of the femoral head and the midpoint of the distal epiphysis of the thigh bone (half of the distance between the condyles). The femoral neck axis was determined by the segment passing through the center of the femoral head and the plane perpendicular to the midpoint of the upper base of the femoral neck.

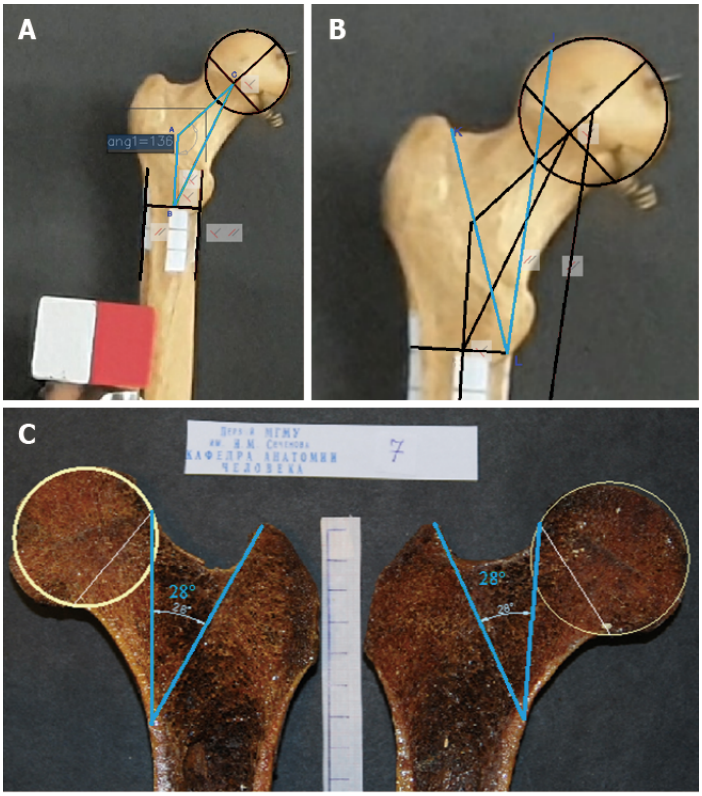
The triangle ABC designations, which are employed in formulas, comprising NSA (angle CAB); AC, the neck axis; and AB, the diaphyseal axis segment (connecting the diameter of the diaphysis to the neck axis), were plotted (Figure 1A) as a major component of the epiphysis of the proximal femur.

The angle between the principal compressive trabecular pattern and the secondary compressive group [angle of the minimal resistance zone (AMRZ)] was applied to assess the value of Ward's triangle. The principal compressive trabecular pattern and secondary compressive group are indicated by segments KL and LJ, respectively. Segment KL was defined as the segment from the upper projection point of the distal base of the neck (point K) to the lower projection point of the lesser trochanter (point L). The segment LJ was defined as the segment parallel to the mechanical axis, which connects the center of the femoral head to the point between the femoral condyles and passes through point L (Figure 1B).

The minimal resistance zone was demonstrated using photos of gross sections of the proximal epiphysis of the femur from the Department of Human Anatomy at Sechenov University. Trabecular patterns, following the course of the main forces acting on the femoral epiphysis under physiological vertical loading, were clearly visualized on the gross sections. The direction of the chosen segments corresponded to the physiological stress lines and comprised a zone containing fewer trabeculae than were present in adjacent areas (Figure 1C).

The projection values of the proximal femoral geometry parameters are equal to their actual values if the bone is positioned such that the planes of the CAB and KLJ triangles are parallel to the plane of the screen onto which the bone is projected. If the bone is somehow rotated, its parameter cannot be measured directly. Therefore, the bone elements that can assist in determining the presence of bone rotation relative to the standard projection and in measuring its angle were selected.

When analyzing the video frames that show bone rotation, we determined that the greater trochanter can be inscribed in a parallelepiped, one of the faces of which is a rectangle when the bone is in FSP.



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Figure 1 In this study, a method for assessing the morphometric parameters of the proximal femur based on the projection values and angle of rotation around the anatomical axis relative to the FSP was developed. A: Bone No. 9. Triangle ABC comprised the NSA (angle CAB); AC, neck axis; and AB, diaphyseal axis segment (connecting the diameter of the diaphysis to the neck axis); B: Bone No. 9. Angle KLJ was a part of Ward's triangle, designating the angle of the minimal resistance zone (AMRZ); C: Bone No. 7. The angle, indicating the borders of the AMRZ, was plotted on photos of gross bone sections.

Consequently, this geometric parameter was chosen to evaluate the rotation of triangle ABC relative to the anatomical axis, to which segment AB is parallel. Thus, on an X-ray, the angle of rotation of the bone relative to the FSP can be determined by calculating the angle of rotation of the parallelepiped that contains the greater trochanter using spatial construction (Figure 2).

To assess the reliability of determining the angle of rotation on the basis of the greater trochanter, this angle was calculated by measuring the angle of rotation of the cube fixed to a tripod using the following formula:

QCN =135°- arcos (a1/a), where a is the edge of the cube (whose length is 50 mm) and a1 is the length of the cube verge in a projection other than the FSP.

The angle of bone rotation obtained by turning the cube corresponded to the angle measured with the second technique, which uses the previously described feature of the large spit. Thus, this method of calculating the rotation of the bone relative to the anterior projection was deemed reliable and utilized in subsequent calculations. During the rotation of the bone around axis AB to a random angle, triangle ABC was projected onto ABC1.

The change in the projection value of the NSA as a function of the angle of the rotation is represented by the following equation:

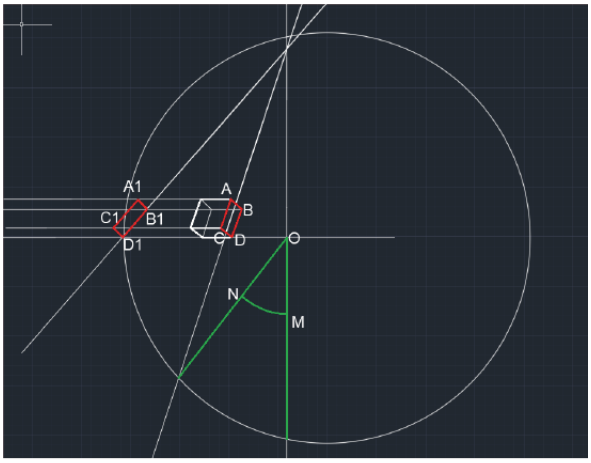
CAB = 180°-arctg (SA/(SC1/cosHSC)), where HSC is the angle of rotation, SA is the segment of the diaphyseal axis, and SC1 is the perpendicular segment, which passes through the center of the head of the femur to the diaphyseal axis (Figure 3A).

Based on the abovementioned findings, the formula for calculating the true value of the AMRZ takes into account the rotation of the bone:

$K_1L_1J_1$ = acrtg (KO/(cos (KOH) × OL)) + arctg (OJ/(cos (JOH) × OL)), where KLJ is the projection AMRZ, $K_1L_1J_1$ is the true AMRZ, KO and OJ are segments of the perpendicular line toward the diaphyseal axis passing through point J (Figure 3A), and KOH and JO indicate the angle of rotation.

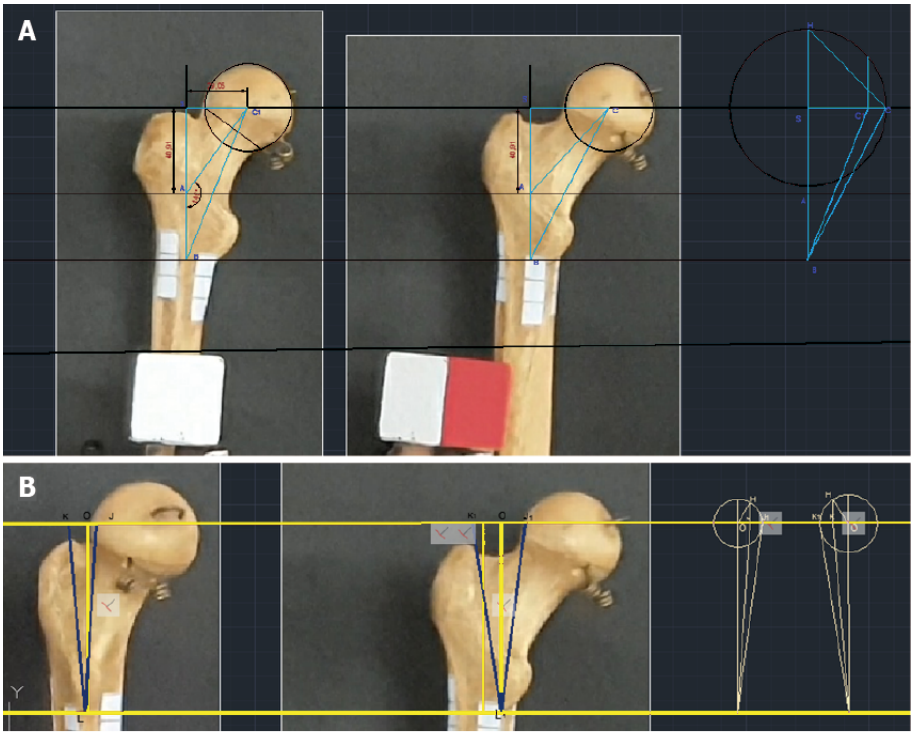
Determination of the true parameters of the proximal epiphysis of the femur from an X-ray

A technique is proposed for determining the angle of rotation of the bone relative to the plane of the X-ray image based on the estimated rotation of the greater trochanter. In this technique, a box is created around the greater trochanter. Geometric constructions (Figure 2) are performed to estimate the angle of rotation similar to the technique previously mentioned for native bones and their videos.



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Figure 2 Scheme of the constructions used to determine the angle of rotation of the bone (NOM).



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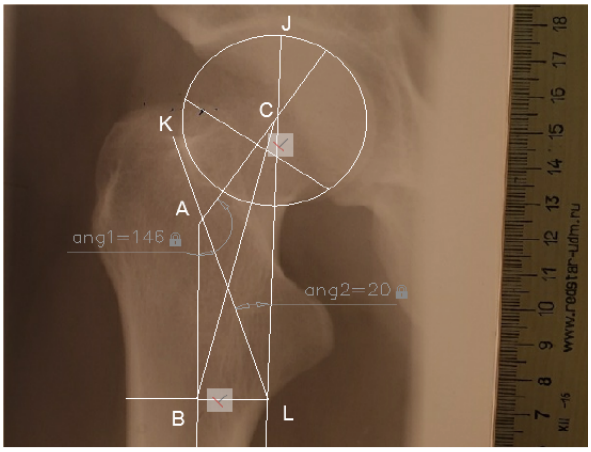
Figure 3 The angle of bone rotation obtained by turning the cube corresponded to the angle measured with the second technique, which uses the previously described feature of the large spit. A: Bone No. 9. Photo of the NSA and calculation of its true value based on the projection value and the rotation angle; B: Estimation of the true AMRZ based on its projection value and the rotation angle.

Subsequently, this value is used to determine the true AMRZ. The change in the projection magnitude of the NSA as a function of the angle of rotation can be represented by the following equation:

CAB = 180o-arctg (SA/(SC1/cosHSC)), where HSC is the angle of rotation, SA is the segment of the axis of the diaphysis, and SC1 is the segment of the perpendicular line connecting the center of the femoral head to the axis of the diaphysis (Figure 3B).

The true value of the AMRZ was calculated as follows:

$K_1L_1J_1$ = acrctg (KO/(cos (KOH) × OL)) + arctg (OJ/(cos (JOH) × OL)), where KLJ is the AMRZ projection, $K_1L_1J_1$ is the true AMRZ, KO and OJ are segments of the perpendicular line toward the axis of the diaphysis drawn through point J (Figure 2), and KOH and JOH are the angles of rotation (Figure 3B). When the plane including the axes of the neck and diaphysis is parallel to the plane of the X-ray, it is possible to directly measure the AMRZ (Figure 4).



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Figure 4 X-ray image from the Department of Human Anatomy showing triangle ABC and the AMRZ.

This study does not take into account any parameters other than geometric parameters. Sex, age, concomitant diseases and other conditions can affect these parameters, but this study evaluates the results of these effects.

RESULTS

Interrelations among proximal femoral morphometric parameters

The results of a statistical analysis of the geometric parameters of the proximal epiphysis of the femur are presented in Table 1.

The correlation coefficient for the correlation between the NSA and the AMRZ, for the correlation between segment BC and the zone of minimum resistance, and for the correlation between the length of segment BC and the upper-to-lower neck length ratio was -0.155, 0.0617, and -0.119, respectively, which indicates weak negative correlations among these parameters. These findings suggest that the NSA and AMRZ vary independently of each other, and regarding the influence of these changes on the risk of fracture of the femoral neck, they must be evaluated as independent values. The correlation coefficient between the NSA and the upper-to-lower neck length ratio was -0.396, that is, there was a moderate negative correlation between these parameters.

The strongest correlation was found between the AMRZ and the upper-to-lower neck length ratio, with a correlation coefficient of 0.872 (Figure 5). Based on this finding, we use the upper-to-lower neck length ratio to determine the size of the AMRZ.

Model of the proximal epiphysis that provides a minimal risk of femoral neck base fracture

The model of the proximal epiphysis, which provides a minimal risk of femoral neck base fracture, consists of an NSA of 134° (which is 1° smaller than the mean of the maximal and mean values of this parameter shown in our study (144°+125.9°)/2 = 134.99°)) and an AMRZ of 14° (minimal value of the parameter in our study) (Figure 6).

The femoral proximal epiphysis, which has parameters included in this model, is the most resistant to femoral neck base fracture when a patient falls on his or her side, according to our study.

Evaluation of the risk of femoral neck fracture using X-ray images

The scale was developed to evaluate the risk of femoral neck base fracture (Table 2). Scores were assigned to bone parameters within certain intervals, as specified in the table. According to the sum of the points, the degree of fracture risk for a given bone was determined: 2 points indicated low risk, 3-4 points indicated average risk, and 5-6 points indicated high risk. The analysis of 10 X-ray images stored in the Department of Human Anatomy and 10 X-ray images of patients from the Department of Traumatology, Orthopedics and Disaster Surgery of Sechenov University showed that the value of the NSA and AMRZ differed from the optimal value for all bones.

DISCUSSION

We aimed to determine the bone parameters that are risk factors for a fracture of the base of the femoral

Table 1 Values of the geometric parameters of the proximal epiphysis of the femur

	Range	Mean value	Standard deviation	Standard error	Coefficient of variation
Neck-shaft angle (degrees)	103-144	125.99	9.09	1.08	0.07
Angle of the minimal resistance zone (degrees)	14-36	23.90	5.67	0.67	0.24
AC	32.3-61.48	48.60	7.10	0.84	0.15
AB	17.94-57.3	38.61	10.05	1.19	0.26
BC	55.51-94.42	78.00	8.66	1.03	0.11
Upper neck length	14.19-33.79	21.44	5.09	0.60	0.24
Lower neck length	21.72-45.94	33.67	5.19	0.62	0.15

Table 2 Scale for determining the risk of femoral neck base fractures according to the morphometric parameters

	Neck-shaft angle	Angle of minimal resistance zone	The ratio of the top and bottom neck lengths
1 point	130.24 and more	14 and less	0.56 and less
2 points	127.5-130.24	18.95-29.95	0.57-0.74
3 points	Less than 127.5	More than 29.95	0.75 and more



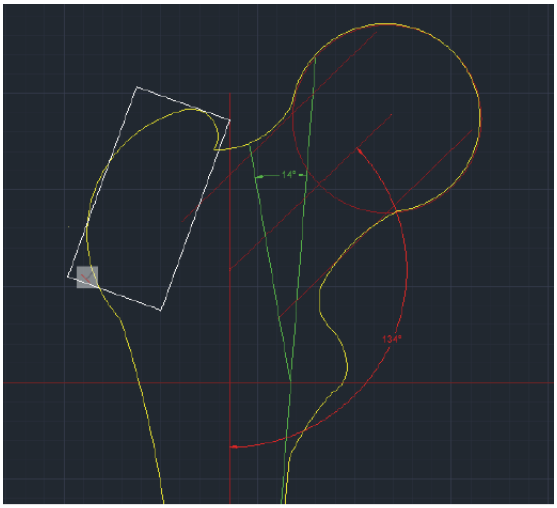
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Figure 5 Scatter plot showing the correlation between these parameters and the corresponding regression line.

neck when the patient falls on his or her side and did not take into account other types and mechanisms of fracture. However, the selected optimal values still remain within the reference values, even if they increase the risk of other mechanisms of femoral fracture.

In our study, we agree with the finding of several authors[16-20] that some bone parameters, such as NSA, have optimal values, and their deviations can cause a higher risk of fracture. In another study, the NSA value had a weak correlation with the size of the minimum resistance zone of the proximal femur (AMRZ), indicating that these parameters can independently influence fracture risk.

According to previous studies, neither a decrease in the NSA nor an increase in the NSA can be considered a reliable risk factor for femoral neck fracture since there are data that both confirm and disprove the influence of these factors on the probability of fracture[21-23]. Nevertheless, it has been confirmed that the strength of the proximal epiphysis decreases when the NSA decreases, and the stress that occurs in the proximal epiphysis under stress conditions shifts to its distal part. The femoral neck can be considered a lever, to the ends of which forces are applied. In this case, the value of the moment of forces that characterize the rotational action of forces acting on the proximal and distal part of the neck relative to the middle of the lever will increase as the NSA decreases. Based on measurements and a fracture risk assessment in another study, we assume that reducing the NSA causes an increase in the



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Figure 6 A two-dimensional model of the proximal femoral epiphysis on the frontal standard projection that provides a minimal risk of femoral neck base fracture after a simple mechanical fall (falling from a patient's own height).

risk of femoral neck base fracture.

In the field of orthopedics, proximal femur modeling is utilized to plan interventions and assess their results[24]. When planning corrective osteotomy, to calculate the true value of the NSA using X-ray images, the researchers employed X-ray images of the hip joints projected directly in the middle position, with internal rotation of the thigh, and in a position proposed by Lauenstein, with the mathematical tables proposed by Strzyzewski or Shartlain[19]. However, these measurements allow only approximate planning of the surgical intervention, so the results of the treatment depend heavily on the personal skills of the surgeon. 3-D modeling is considered a more accurate method; therefore, algorithms for calculating surgical interventions on 3D models have been introduced and are highly distributed[24-27].

Furthermore, modeling of the proximal femoral epiphysis is conducted to create mathematical models to assess the risk of fractures under the influence of external factors. In recent years, special attention has been given to the variability of the shape of the proximal femur and the influence of its geometry on its strength[28]. For this purpose, statistical shape models are employed to simultaneously assess the impact of risk factors and pathological changes in a variety of bone geometric phenotypes [29]. The analysis of the geometric and strength characteristics of cadaveric proximal femurs continues to be applied for more accurate construction of mathematical models[30,31].

However, in most cases, statistical shape models require three-dimensional images using tomographic methods. Since the 3D model is associated with a high computational burden, Jazinizadeh *et al*[32] compared the ability of 2D and 3D femur models to predict hip fracture risk and showed that their productiveness does not differ significantly.

We propose a method for calculating the true parameters of the proximal epiphysis based on one projection obtained using an X-ray image. Our technique is assumed to prevent the occurrence of femoral fracture in primary health care practice, unlike other techniques designed to correct the consequences of a fracture. We assume that our method can be used in combination with existing methods for assessing the risk of fractures, since it does not contradict but can complement other methods.

Our study has a retrospective design, which is its first limitation. In the course of this work, a small number of X-ray images were selected; other types and mechanisms of fracture were not taken into account; and any parameters of bone tissue, other than geometric characteristics, were not taken into account. With regard to the selection of cadaveric bones, the age, gender and other parameters of the owners of the bones were not taken into account. In addition, the impact of other risk factors for hip fractures has not been evaluated, and densitometry studies have not been performed.

The scale needs to be evaluated further in future studies and is not ready for use in clinical practice. However, the measurement of these parameters during screening studies can reduce the risk of severe injuries.

The suggested method for measuring the true parameters of the proximal femur does not require special equipment but is quite difficult to implement. This method can be used when special software is not available and in combination with other screening tools that use X-ray scans of the femur. Further improvements to this method are needed. Nevertheless, performing such measurements with modern X-ray diagnostic systems is not difficult. This method is assumed to be combined with other screening techniques and to be employed when other less complicated measurement methods are not available.

CONCLUSION

Disease prophylaxis *via* the assessment of risk factors and prevention is essential in modern medicine. Therefore, methods for assessing and diminishing risk should be developed. The method described in this article is assumed to be a tool for first-level health care to predict severe disabling damage. Early detection of the anatomic predisposition to fracture as well as the identification of osteoporosis shall allow general practitioners to identify patients who are in the femur fracture risk group because of proximal femur geometry pathological changes and to take opportune actions for bone strengthening. This screening approach will decrease morbidity, mortality and the costs required for treatment and rehabilitation. Simultaneously, with a decline in incidence, mortality is also expected to decrease. The plotting methods proposed in this study could also be applied to design mathematical models for preoperative preparations. However, in this way, these methods should be further developed.

ARTICLE HIGHLIGHTS

Research background

Currently, a fracture of the femoral neck is a serious health problem, as it very often leads to long-term hospitalization, disability and death of patients. Modern medicine implies the prevention of such serious injuries and their consequences. At the moment, there are methods for assessing bone mineral density, but its geometry remains beyond attention.

Research motivation

This study was created for the reasons that existing methods often do not take into account the geometric parameters of the bone, and is aimed at filling this gap and creating techniques that complement existing ones.

Research objectives

The purpose of this work was to study the influence of bone geometry on its strength, as well as to find ways to apply these data in practice. The results of the study were conceived as an addition to the existing methods of assessing the risk of fracture.

Research methods

In our study, we measured 70 cadaveric bones and 20 X-rays by creating digital copies of them and processing them in the AutoCAD environment. The cuts of the proximal epiphyses of bones were studied. An analysis was also carried out aimed at identifying parameters correlating with a high risk of fracture. A scale was created as a possible risk assessment tool.

Research results

In our research, we studied the course of bone beams, the distribution of bone tissue in the proximal epiphysis and found the zone that is most vulnerable to mechanical stress. The parameters of the proximal epiphysis were investigated and those that may indicate a higher risk of fracture were identified. A scale was proposed and tested to assess this risk.

Research conclusions

The geometric parameters of the bone reflect the features of the structure of the bone beams and the distribution of bone matter. There are parameters of the proximal epiphysis, the measurement of which with the help of modern imaging methods can help determine the increased risk of fracture of the proximal epiphysis of the femur. Modern methods of risk stratification often ignore the geometric parameters of the bone and our study suggests a way to take them into account to determine the risks of fracture.

Research perspectives

In order to develop the idea, it is possible to conduct a larger-scale study with a large number of participants. Further refinement of the scale is needed in order to clarify it and possibly expand it. With satisfactory results of refinement, it is possible to introduce the proposed methodology into practice for its clinical trial.

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FOOTNOTES

Author contributions: Shitova AD, Zubkov DD, Gadzhimuradova IA and Kniazev MO are responsible for measurement of bone parameters; Shitova AD, Olsufieva AV, Zubkov DD, Gadzhimuradova IA and Kniazev MO are responsible for data collection and analysis; Shitova AD, Olsufieva AV, Zubkov DD, Gadzhimuradova IA and Zharikova TS did the literature review; Shitova AD and Zubkov DD graphing in AutoCad2018; Zharikova TS created the figures; Kovaleva ON and Zharikov YO: project manager and scientific advisor.

Institutional review board statement: This study was reviewed and approved by the Ethics Committee of the I.M. Sechenov First Moscow State Medical University (Sechenov University).

Informed consent statement: Patients were not required to give informed consent to the study because the analysis of the X-ray images and anonymous clinical data that were obtained after each patient agreed to treatment by written consent. Cadaver material (70 femurs) was bequeathed to the Department of Human Anatomy by people and their relatives from 20 to 35 years ago, when these objects were designated for educational purposes for morphological departments.

Conflict-of-interest statement: All authors report no relevant conflict of interest for this article.

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REFERENCES

1 **Raaymakers EL**. Fractures of the femoral neck: a review and personal statement. *Acta Chir Orthop Traumatol Cech* 2006; **73**: 45-59 [PMID: 16613748]
2 **Gnudi S**, Ripamonti C, Gualtieri G, Malavolta N. Geometry of proximal femur in the prediction of hip fracture in osteoporotic women. *Br J Radiol* 1999; **72**: 729-733 [PMID: 10624337 DOI: 10.1259/bjr.72.860.10624337]
3 **Slobogean GP**, Sprague SA, Scott T, Bhandari M. Complications following young femoral neck fractures. *Injury* 2015; **46**: 484-491 [PMID: 25480307 DOI: 10.1016/j.injury.2014.10.010]
4 **Bartels S**, Gjertsen JE, Frihagen F, Rogmark C, Utvåg SE. Low bone density and high morbidity in patients between 55 and 70 years with displaced femoral neck fractures: a case-control study of 50 patients *vs* 150 normal controls. *BMC Musculoskelet Disord* 2019; **20**: 371 [PMID: 31409337 DOI: 10.1186/s12891-019-2732-8]
5 **Major LJ**, North JB. Predictors of mortality in patients with femoral neck fracture. *J Orthop Surg (Hong Kong)* 2016; **24**: 150-152 [PMID: 27574252 DOI: 10.1177/1602400205]
6 **Armas LA**, Lappe JM, Heaney RP. Calcium bone strength and fractures. In: Orwoll ES, Bilezikian JP, Vanderschueren D. Osteoporosis in men. USA: Academic Press, 2010: 235-241 [DOI: 10.1016/B978-0-12-374602-3.00019-5]
7 **International osteoporosis foundation**. 9, rue Juste-Olivier CH-1260 Nyon - Switzerland; [cited 27 Mar 2021]. Available from: http://www.iofbonehealth.org/what-is-osteoporosis
8 **FRAX ®Fracture Risk Assessment Tool**. Centre for Metabolic Bone Diseases, University of Sheffield, UK [cited 27 Mar 2021]. Available from: https://www.sheffield.ac.uk/FRAX/tool.aspx?country=9
9 **Tortora R**, Imperatore N, Capone P, Gerbino N, Rea M, Affinito G, Caporaso N, Rispo A. FRAX Score Can Be Used to Avoid Superfluous DXA Scans in Detecting Osteoporosis in Celiac Disease: Accuracy of the FRAX Score in Celiac Patients. *J Clin Densitom* 2018; **21**: 315-321 [PMID: 28625602 DOI: 10.1016/j.jocd.2017.05.010]
10 **Donnelly E**. Methods for assessing bone quality: a review. *Clin Orthop Relat Res* 2011; **469**: 2128-2138 [PMID: 21116752 DOI: 10.1007/s11999-010-1702-0]
11 **Barkaoui A**, Ben Kahla R, Merzouki T, Hambli R. Age and gender effects on bone mass density variation: finite elements

simulation. *Biomech Model Mechanobiol* 2017; **16**: 521-535 [PMID: 27659482 DOI: 10.1007/s10237-016-0834-x]
12 **Makuch AM**, Skalski KR, Pawlikowski M. The influence of the cumulated deformation energy in the measurement by the DSI method on the selected mechanical properties of bone tissues. *Acta Bioeng Biomech* 2017; **19**: 79-91 [PMID: 28869620]
13 **Park G**, Kim T, Forman J, Panzer MB, Crandall JR. Prediction of the structural response of the femoral shaft under dynamic loading using subject-specific finite element models. *Comput Methods Biomech Biomed Engin* 2017; **20**: 1151-1166 [PMID: 28632407 DOI: 10.1080/10255842.2017.1340459]
14 **Wieding J**, Souffrant R, Fritsche A, Mittelmeier W, Bader R. Finite element analysis of osteosynthesis screw fixation in the bone stock: an appropriate method for automatic screw modelling. *PLoS One* 2012; **7**: e33776 [PMID: 22470474 DOI: 10.1371/journal.pone.0033776]
15 **Ding HW**, Yu GW, Tu Q, Liu B, Shen JJ, Wang H, Wang YJ. Computer-aided resection and endoprosthesis design for the management of malignant bone tumors around the knee: outcomes of 12 cases. *BMC Musculoskelet Disord* 2013; **14**: 331 [PMID: 24267157 DOI: 10.1186/1471-2474-14-331]
16 **Grapharov KZ**. Clinical meaning of angle dimensions of femur in proximal region. *Med Almanah* 2012; **2**: 253-255
17 **Avdeev AI**, Poteryaykin ES, Kottsova YM. The role of size and shape of proximal femur in determination of the biological age of adults. *Bull Forensic Med* 2016; **3**: 17-19
18 **Nikolenko VN**, Fomicheva OA, Zhmurko RS, Yakovlev NM, Bessonova OS, Pavlov SV. Individual and typological morphometric features of the proximal femoral bone. *Saratov J Med Sci Res* 2010; **6**: 36-39
19 **Alekseev VP**. Osteomeriya: metodika antropometricheskih issledovanij. Moscow: Nauka, 1966
20 **Bergot C**, Bousson V, Meunier A, Laval-Jeantet M, Laredo JD. Hip fracture risk and proximal femur geometry from DXA scans. *Osteoporos Int* 2002; **13**: 542-550 [PMID: 12111014 DOI: 10.1007/s001980200071]
21 **Villette CC**, Zhang J, Phillips ATM. Influence of femoral external shape on internal architecture and fracture risk. *Biomech Model Mechanobiol* 2020; **19**: 1251-1261 [PMID: 31705336 DOI: 10.1007/s10237-019-01233-2]
22 **Kim DK**, Kim TH. Femoral neck shaft angle in relation to the location of femoral stress fracture in young military recruits: femoral head *vs* femoral neck stress fracture. *Skeletal Radiol* 2021; **50**: 1163-1168 [PMID: 33145605 DOI: 10.1007/s00256-020-03661-z]
23 **Numis AL**, Fox CH, Lowenstein DJ, Norris PJ, Di Germanio C. Comparison of multiplex cytokine assays in a pediatric cohort with epilepsy. *Heliyon* 2021; **7**: e06445 [PMID: 33748497 DOI: 10.1016/j.heliyon.2021.e06445]
24 **Oba M**, Kobayashi N, Inaba Y, Choe H, Ike H, Kubota S, Saito T. Mechanical Strength of the Proximal Femur After Arthroscopic Osteochondroplasty for Femoroacetabular Impingement: Finite Element Analysis and 3-Dimensional Image Analysis. *Arthroscopy* 2018; **34**: 2377-2386 [PMID: 29937343 DOI: 10.1016/j.arthro.2018.03.036]
25 **Yang P**, Lin TY, Xu JL, Zeng HY, Chen D, Xiong BL, Pang FX, Chen ZQ, He W, Wei QS, Zhang QW. Finite element modeling of proximal femur with quantifiable weight-bearing area in standing position. *J Orthop Surg Res* 2020; **15**: 384 [PMID: 32887611 DOI: 10.1186/s13018-020-01927-9]
26 **Dolatowski FC**, Temmesfeld MJ, Pierre-Jerome C, Borthne A, Hoelsbrekken SE. Bilateral symmetrical comparison of the proximal femur using 3D-CT models. *Surg Radiol Anat* 2018; **40**: 507-513 [PMID: 29322292 DOI: 10.1007/s00276-018-1968-6]
27 **Shetty V**, Wagh Y, Karade V, Maurya A, Parihar M, Shekhar S, Tandel J. CT-Based 3D Reconstruction of Lower Limb Versus X-Ray-Based 3D Reconstruction: A Comparative Analysis and Application for a Safe and Cost-Effective Modality in TKA. *Indian J Orthop* 2021; **55**: 1150-1157 [PMID: 34824715 DOI: 10.1007/s43465-021-00456-9]
28 **Hsu YH**, Estrada K, Evangelou E, Ackert-Bicknell C, Akesson K, Beck T, Brown SJ, Capellini T, Carbone L, Cauley J, Cheung CL, Cummings SR, Czerwinski S, Demissie S, Econs M, Evans D, Farber C, Gautvik K, Harris T, Kammerer C, Kemp J, Koller DL, Kung A, Lawlor D, Lee M, Lorentzon M, McGuigan F, Medina-Gomez C, Mitchell B, Newman A, Nielson C, Ohlsson C, Peacock M, Reppe S, Richards JB, Robbins J, Sigurdsson G, Spector TD, Stefansson K, Streeten E, Styrkarsdottir U, Tobias J, Trajanoska K, Uitterlinden A, Vandenput L, Wilson SG, Yerges-Armstrong L, Young M, Zillikens MC, Rivadeneira F, Kiel DP, Karasik D. Meta-Analysis of Genomewide Association Studies Reveals Genetic Variants for Hip Bone Geometry. *J Bone Miner Res* 2019; **34**: 1284-1296 [PMID: 30888730 DOI: 10.1002/jbmr.3698]
29 **Asvadi A**, Dardenne G, Troccaz J, Burdin V. Bone surface reconstruction and clinical features estimation from sparse landmarks and Statistical Shape Models: a feasibility study on the femur. *Med Eng Phys* 2021; **95**: 30-38 [PMID: 34479690 DOI: 10.1016/j.medengphy.2021.07.005]
30 **Rezaei A**, Carlson KD, Giambini H, Javid S, Dragomir-Daescu D. Optimizing Accuracy of Proximal Femur Elastic Modulus Equations. *Ann Biomed Eng* 2019; **47**: 1391-1399 [PMID: 30887275 DOI: 10.1007/s10439-019-02238-9]
31 **Miura M**, Nakamura J, Matsuura Y, Wako Y, Suzuki T, Hagiwara S, Orita S, Inage K, Kawarai Y, Sugano M, Nawata K, Ohtori S. Prediction of fracture load and stiffness of the proximal femur by CT-based specimen specific finite element analysis: cadaveric validation study. *BMC Musculoskelet Disord* 2017; **18**: 536 [PMID: 29246133 DOI: 10.1186/s12891-017-1898-1]
32 **Jazinizadeh F**, Quenneville CE. 3D Analysis of the Proximal Femur Compared to 2D Analysis for Hip Fracture Risk Prediction in a Clinical Population. *Ann Biomed Eng* 2021; **49**: 1222-1232 [PMID: 33123827 DOI: 10.1007/s10439-020-02670-2]

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Retrospective Study

Epidemiology of pelvic and acetabular fractures across 12-mo at a level-1 trauma centre

Rory Cuthbert, Samuel Walters, David Ferguson, Edward Karam, Jonathan Ward, Homa Arshad, Paul Culpan, Peter Bates

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Abstract

BACKGROUND

Despite motor-vehicle safety advancements and increasingly rigorous workplace safety regulations, trauma/suicide remains the leading cause of death under the age of 45 in the United Kingdom. To promote centralisation of care and optimisation of major trauma outcomes, in 2012 the National Health Service introduced the Trauma Network System. To our knowledge, this is the first study to analyse the epidemiology of pelvic and acetabular trauma over a one-year period at a level-1 trauma centre in the United Kingdom, since nationwide introduction of the Trauma Network System.

AIM

To characterize the epidemiology of high-energy pelvic and acetabular fractures over a one-year period at a level-1 trauma centre, and explore both resources required to care for these patients and opportunities for future research and injury prevention initiatives.

METHODS

227 consecutive patients at a level-1 trauma centre with pelvic and acetabular fractures were analysed between December 2017-December 2018. Paediatric patients (< 18 years) and fragility fractures were excluded, leaving 175 patients for inclusion in the study. Statistical analysis was performed using Fisher's exact test for categorical variables.

RESULTS

72% of pelvic and acetabular fractures occurred in male patients at a median age of 45 years. 15% were the result of a suicide attempt. 48% of patients required pelvic or acetabular surgery, with 38% undergoing further surgery for additional

orthopaedic injuries. 43% of patients were admitted to intensive care. The median inpatient stay was 13 days, and the 30- day mortality was 5%. Pelvic ring trauma was more commonly associated with abdominal injury ($P = 0.01$) and spine fractures ($P < 0.001$) than acetabular fractures. Vertical shear pelvic ring fractures were associated with falls ($P = 0.03$) while lateral compression fractures were associated with road traffic accidents ($P = 0.01$).

CONCLUSION

High energy pelvic and acetabular fractures are associated with concomitant orthopaedic fractures (most commonly spine and lower limb), intensive care admission and prolonged inpatient stays. Most pelvic ring injuries secondary to road traffic accidents are lateral compression type, demonstrating the need for future research to drive advancements in lateral impact vehicle safety along with mental health surveillance for those deemed to be potential suicide risks.

Key Words: Pelvis; Acetabulum; Orthopedics; Multiple trauma; Trauma centers

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Core Tip: To our knowledge, this is the first study to analyze the epidemiology of pelvic and acetabular trauma over a one-year period at a level-1 trauma centre in the United Kingdom since introduction of the Trauma Network System. This study demonstrates pelvic and acetabular fractures are associated with concomitant orthopaedic fractures (commonly spine and lower limb), intensive care admission and lengthy inpatient stays. Future injury prevention research should focus on advancements in lateral impact vehicle safety alongside mental health surveillance for patients deemed to be potential suicide risks.

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INTRODUCTION

Major trauma/suicide remains the leading cause of death under the age of 45 in the United Kingdom (UK)[1]. In an effort to centralise trauma care and optimise outcomes, the National Health Service (NHS) introduced the Trauma Network System in 2012[2]. This designated 27 hospitals in England as Major Trauma Centres (MTCs) responsible for the specialist management of severely injured patients. 22 MTCs are responsible for the management of adult pelvic and acetabular trauma[3].

To our knowledge, this is the first study to analyze the epidemiology of high-energy (non-fragility) pelvic and acetabular trauma over a one-year period at a major trauma centre in the United Kingdom since introduction of the Trauma Network System. Given evolving safety measures and public travel preferences, the primary objectives were to characterise the epidemiology of current pelvic and acetabular fractures and their associated injuries, to demonstrate the wide-ranging resources required to care for these patients and explore opportunities for future injury prevention research.

MATERIALS AND METHODS

Study design

This retrospective observational study analyzed consecutive patients presenting to a level-1 trauma centre in the UK between December 2017 and December 2018. Research and audit approval was obtained from the Clinical Effectiveness Unit, and the NHS Research Ethics Committee decision tool excluded need for ethical review.

227 patients with pelvic and acetabular fractures were identified using Abbreviated Injury Scale (AIS) codes on the institution's prospectively maintained Trauma Audit and Research Network database. All adult patients (≥ 18 years) with pelvic or acetabular fractures confirmed on computed tomography were included. Paediatric patients (< 18 years), fragility fractures (in accordance with the World Health Organisation definition as falls from standing height or less)[4] and patients who did not undergo computed tomography of the pelvis were excluded. This left a total of 175 patients for inclusion in the study.

Data collection

Orthopaedic multidisciplinary team documentation, consultant radiology reports and electronic patient records were analyzed by orthopaedic registrars (residents) to populate a standardised collection proforma. The following study outcomes were recorded: age, gender, pelvic or acetabular fracture (pelvic ring fracture only, pelvic ring and acetabulum fracture, acetabulum fracture only, iliac wing fracture, sacral body fracture, spinopelvic dissociation, other), Young-Burgess classification for pelvic ring fractures – lateral compression (LC) 1/2/3, anteroposterior compression (APC) 1/2/3, vertical shear (VS) or combined[5], open pelvic or acetabular injury, mechanism (fall, crush injury, other and road traffic accident which was further subdivided into pedestrian *vs* vehicle, vehicle *vs* vehicle and cyclist *vs* vehicle), suicide attempt, intensive care admission, head injury (AIS ≥ 1), abdominal injury (AIS ≥ 1), spine fracture, upper limb fracture / dislocation, lower limb fracture / dislocation, pelvic or acetabular surgery, number of further orthopaedic surgeries during admission, length of stay (days) and 30-d mortality.

Statistical analysis

Statistical analysis to compare groups within the study was performed using Fisher's exact test for categorical variables. This was preferred to the Chi-square test due to small numbers in some categories. The *P*-value for statistical significance was set at < 0.05. Statistical analysis was performed using Stata version 15.1 (Stata Corp LLC, College Station, Texas).

RESULTS

Epidemiological characteristics

72% of all pelvic and acetabular fractures occurred in male patients at a median age of 45 years. 48% of patients required pelvic or acetabular surgery, with 38% undergoing additional surgery for other orthopaedic injuries. 43% of patients were admitted to intensive care with a median total hospital stay of 13 d. The 30-d mortality for all high-energy pelvic and acetabular fractures was 5% with only 1.7% of patients dying within the first 24 h of injury (Table 1).

Spinopelvic dissociation was associated with the greatest likelihood of additional surgery for other orthopaedic injuries (43%), and the highest 30-d mortality rate (14%). 37% of pelvic ring fractures required surgical intervention comparative to 66% of acetabular fractures. Combined pelvic ring and acetabular fractures were associated with the longest median total hospital stay of 28 d (Table 1).

Mechanism of injury

51% of pelvic ring fractures occurred following road traffic accidents, 43% were the result of falls from height and 7% were secondary to crush injuries. Road traffic accidents were responsible for 59% of acetabulum fractures with 39% due to falls. The most common subcategory of road traffic accident in pelvic ring fractures was pedestrian *vs* vehicle (27%). The most common subcategory of road traffic accident in acetabular fractures was cyclist *vs* vehicle (23%).

71% of spinopelvic dissociations and 100% of sacrum body fractures were secondary to falls from height. 15% of all high energy pelvic and acetabular fractures were the result of a suicide attempt (Table 2).

Associated injuries

43% of all pelvic and acetabular fractures had an associated spine fracture. This was followed by lower limb fractures (31%), head injury (27%) and upper limb fractures (22%). 5% of all pelvic and acetabular fractures were open injuries (Table 3).

Comparison of pelvic ring and acetabulum fractures demonstrated a statistically significant association between pelvic ring fractures and both abdominal injury ($P = 0.01$) and spine fractures ($P < 0.001$) (Table 4).

Epidemiological characteristics based on the Young-Burgess classification

The breakdown of pelvic ring fractures based on the Young-Burgess classification is illustrated in Figure 1. There was a statistically significant difference between classification-types when the mechanism of injury was a fall ($P = 0.03$) or road traffic accident ($P = 0.01$). Falls were responsible for 86% of VS fractures, and 96% of all pelvic ring injuries secondary to road traffic accidents were LC-type. Crush injuries occurred more frequently in APC-type injuries (50%) but this did not reach statistical significance ($P = 0.05$) (Table 5).

Table 1 Epidemiological characteristics of pelvic and acetabular fractures

Variable	Pelvic ring fracture only, *n* (%)	Pelvic ring & acetabulum fracture, *n* (%)	Acetabulum fracture only, *n* (%)	Iliac wing fracture, *n* (%)	Sacrum body fracture, *n* (%)	Spinopelvic dissociation, *n* (%)	All pelvic & acetabular fractures, *n* (%)
Age, median [inter-quartile range]	44 [32, 59]	54 [48, 61]	46 [37, 65]	27 [23, 34]	53 [38, 69]	59 [39, 72]	45 [33, 61]
Gender							
Male	60 (64)	9 (82)	39 (89)	11 (92)	2 (29)	5 (71)	126 (72)
Female	34 (36)	2 (18)	5 (11)	1 (8)	5 (71)	2 (29)	49 (28)
ITU admission							
Yes	40 (43)	6 (55)	15 (34)	4 (33)	3 (43)	7 (100)	75 (43)
No	54 (57)	5 (45)	29 (66)	8 (67)	4 (57)	0 (0)	100 (57)
P&A surgery							
Yes	35 (37)	10 (91)	29 (66)	1 (8)	2 (29)	7 (100)	84 (48)
No	59 (63)	1 (9)	15 (34)	11 (92)	5 (71)	0 (0)	91 (52)
Orthopaedic surgeries							
2+	12 (13)	3 (27)	10 (23)	1 (8)	0 (0)	3 (43)	29 (17)
1	25 (27)	0 (0)	7 (16)	3 (25)	2 (29)	0 (0)	37 (21)
None	57 (60)	8 (73)	27 (61)	8 (67)	5 (71)	4 (57)	109 (62)
Length of stay, median [inter-quartile range]	14 [6, 28]	28 [20, 43]	10 [5, 26]	3 [1, 6]	14 [8, 26]	23 [16, 65]	13 [6, 28]
30-d mortality							
Alive	87 (93)	11 (100)	44 (100)	11 (92)	7 (100)	6 (86)	166 (95)
Dead	7 (7)	0 (0)	0 (0)	1 (8)	0 (0)	1 (14)	9 (5)

Table 2 Mechanism of pelvic and acetabular fractures

Mechanism	Pelvic ring fracture only, *n* (%)	Pelvic ring & acetabulum fracture, *n* (%)	Acetabulum fracture only, *n* (%)	Iliac wing fracture, *n* (%)	Sacrum body fracture, *n* (%)	Spinopelvic dissociation, *n* (%)	All pelvic & acetabular fractures, *n* (%)
Fall	40 (43)	4 (36)	17 (39)	7 (58)	7 (100)	5 (71)	80 (46)
Pedestrian *vs* Vehicle	25 (27)	3 (27)	8 (18)	2 (17)	0 (0)	0 (0)	38 (22)
Vehicle *vs* Vehicle	12 (13)	3 (27)	8 (18)	1 (8)	0 (0)	1 (14)	25 (14)
Cyclist *vs* Vehicle	10 (11)	1 (9)	10 (23)	1 (8)	0 (0)	1 (14)	23 (13)
Crush injury	7 (7)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	8 (5)
Gunshot	0 (0)	0 (0)	0 (0)	1 (8)	0 (0)	0 (0)	1 (1)
Suicide attempt	17 (18)	1 (9)	2 (5)	2 (17)	2 (29)	3 (43)	27 (15)

DISCUSSION

Non-fragility pelvic and acetabular fractures are the result of high-energy trauma. In our study, 47% of pelvic ring injuries were secondary to road traffic accidents and 40% followed falls from height. The incidence of road traffic accidents in pelvic ring fractures is lower than the incidence observed globally (road traffic accidents are reported as being responsible for 77% of pelvic ring fractures in India, for

Table 3 Associated injuries with pelvic and acetabular fractures

Injury	Pelvic ring fracture only, *n* (%)	Combined pelvic ring + acetabulum fracture, *n* (%)	Acetabulum fracture only, *n* (%)	Iliac wing fracture, *n* (%)	Sacrum body fracture, *n* (%)	Spinopelvic dissociation, *n* (%)	All pelvic & acetabular fractures, *n* (%)
Head injury	33 (35)	2 (18)	9 (20)	1 (8)	2 (29)	1 (14)	48 (27)
Spine fracture	48 (51)	6 (55)	5 (11)	5 (42)	6 (86)	6 (86)	76 (43)
Abdomen injury	24 (26)	2 (18)	3 (7)	5 (42)	1 (14)	3 (43)	38 (22)
Upper limb fracture	24 (26)	2 (18)	6 (14)	4 (33)	1 (14)	1 (14)	38 (22)
Lower limb fracture	30 (32)	3 (25)	16 (36)	2 (17)	1 (14)	3 (43)	55 (31)
Open P&A injury	5 (5)	0 (0)	0 (0)	3 (25)	0 (0)	0 (0)	8 (5)

Table 4 Comparison of associated injuries between pelvic ring and acetabular fractures

Injury	Pelvic ring fracture only, *n* (%)	Acetabulum fracture only, *n* (%)	*P* value
Head injury	33 (35)	9 (20)	0.11
Spine fracture	48 (51)	5 (11)	**< 0.001**
Abdomen injury	24 (26)	3 (7)	**0.01**
Upper limb fracture	24 (26)	6 (14)	0.13
Lower limb fracture	30 (32)	16 (36)	0.7
Open P&A injury	5 (5)	0 (0)	0.18

Table 5 Association between Young-Burgess fracture classification and mechanism of injury

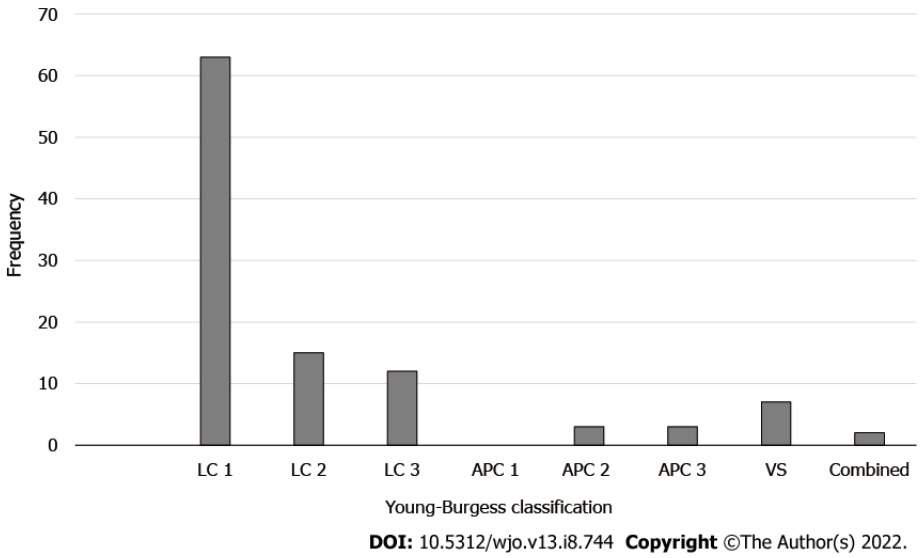
Mechanism	LC, *n* (%)	APC, *n* (%)	VS, *n* (%)	*P* value
Fall	34 (38)	3 (50)	6 (86)	**0.03**
Road traffic accident	52 (58)	1 (17)	1 (14)	**0.01**
Crush injury	4 (4)	2 (33)	0 (0)	0.05

Combined-type (n = 2) omitted from analysis due to insufficient dataset. LC: Lateral compression; APC: Anteroposterior compression; VS: Vertical shear.

example)[6]. Data in the UK from 1989-2001 demonstrated 63% of pelvic ring fractures were attributable to road traffic accidents[7]. The reduced incidence in our study can be explained by the progressive improvement in UK road and vehicle safety, which is illustrated by government figures demonstrating the decline in road traffic accidents causing serious injuries and fatalities[8]. This skew away from road injuries may also represent the local inner-city population, many of whom are socially deprived, with unusually high incidences of interpersonal violence and mental illness. Accordingly, it is notable that attempted suicide contributes to 15% of the high-energy injuries in our study.

59% of acetabular fractures occurred following road traffic accidents and 39% were secondary to falls from height. Again, this is lower than the incidence of acetabular fractures in road traffic accidents observed globally: 66% of acetabular fractures in Qatar were attributable to road traffic accidents and 28% were the results of falls from height[9].

Cyclist *vs* vehicle collisions were the commonest cause of acetabular fractures in road traffic accidents, and were responsible for 11% of pelvic ring fractures. Self-service cycle-hire schemes, cycle-to-work tax incentives and large-scale investment in cycling infrastructure has triggered a surge in cycling popularity in the UK. In Ireland, a 90% increase in cycling-related acetabular and pelvic fracture referrals was observed between 2016 and 2017[10]. There is a paucity of literature analysing pelvic and acetabular fractures in cyclists. Bass hypothesises that cyclists attached to their pedals by straps or clips are likely to fall directly onto the hip which could promote acetabular fractures[11]. Similarly, Cerynik reports a case of a professional cyclist falling on the right side and sustaining a hyperextension injury to



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Figure 1 Distribution of pelvic ring fractures according to Young-Burgess classification.

the left hip which remained clipped in the pedal[12]. Future research should seek to develop understanding of the mechanism of pelvic and acetabular fractures in cyclists and drive cycle safety advancements similar to those witnessed in motor vehicles.

15% of all pelvic and acetabular fractures occurred after a suicide attempt. Analysis of injury patterns demonstrates accidental falls are associated with upper limb injuries secondary to self-protection, whereas suicide attempts are associated with pelvic and acetabular fractures following direct impact or transmitted axial forces *via* the hip joint[13]. De Moore illustrated 54% of patients who attempted suicide by jumping from height were psychotic at the time of the incident – contrasting with 4% of patients who attempted suicide using a firearm[14]. This highlights the importance of dual orthopaedic and psychiatric care in the acute management and rehabilitation of these vulnerable patients. The success of this approach is evident in the literature: in a Swedish study of 12 patients who had attempted suicide by jumping from height, all patients were alive at 4 years with 75% reporting satisfactory quality of life outcomes[15]. We do not have outcome data on those who attempted suicide in our study.

Due to the high-energy mechanisms involved, pelvic and acetabular fractures are often associated with further injuries. In our study, lower limb fractures were observed in 32% of pelvic ring fractures and 36% of acetabular fractures. This is comparable with epidemiological analysis in India demonstrating lower limb fractures in 29% of pelvic ring fractures and 26% of acetabular fractures[6,16]. When comparing pelvic ring and acetabular fractures, there was a significant association between pelvic ring fractures and both spine fractures ($P < 0.001$) and abdominal injury ($P = 0.01$). 5% of our patients after high energy trauma had open injuries. This underlines the importance of the presence of multidisciplinary surgical teams at trauma calls; and supports British Orthopaedic Association Standards for Trauma guidance that all patients suffering high-energy trauma should have an examination of the perineum and rectum documented on arrival[17].

Despite our study solely analysing high-energy pelvic and acetabular fractures, the mortality rate was only 5% with just 1.7% of patients dying within the first 24 h of injury. In Giannoudis' largescale study of UK pelvic ring fractures published in 2007, the 3-mo mortality was 14.2% with a median time to death of 6.2 h[7]. This is likely a reflection of the vast multidisciplinary advancements in acute haemorrhage control – both in a pre- hospital setting and operatively *via* pelvic packing and interventional radiological techniques[18,19].

The Young-Burgess classification is the most widely used classification system for pelvic ring fractures and has been incorporated into Advanced Trauma Life Support guidelines[20]. This characterises pelvic ring injuries mechanistically, correlating with the direction and location of applied force [5]. In our study, there was a statistically significant association between falls and VS fractures ($P = 0.03$), and road traffic accidents and LC fractures ($P = 0.01$). The association between road traffic accidents and LC fractures may partly be explained by analysis demonstrating an increased risk of pelvic fracture following high magnitude side door or door panel intrusion in lateral impact crashes [21]. The need for improved lateral impact vehicle safety is evident, and in 2020 the European New Car Assessment Programme upgraded side mobile barrier testing to promote strengthening around the B-pillar (between the side doors of a car), fitment of side airbags and development of energy absorbing structures in seats and door panels[22].

The management of pelvic and acetabular fractures consumes considerable hospital resource. The literature has demonstrated pelvic fracture patients have more intensive care admissions (24.5% *vs* 11.7%) and longer inpatient stays (15 *vs* 8 d) than any other high-energy trauma patients[7]. In our

study, intensive care admission was necessary in 43% of patients, with a median total hospital length of stay of 13 d. Furthermore, 48% of patients required pelvic or acetabular surgery, with 38% undergoing additional surgery for other orthopaedic injuries. British Orthopaedic Association Guidelines advise reconstruction of the pelvic ring should occur within 72 h of stabilisation of the patient's physiological state[17], with Willett demonstrating time to surgery is a significant predictor of radiological and functional outcome for both elementary and associated displaced fractures of the acetabulum[23]. Therefore, it is crucial that major trauma centres allocate sufficient bed space and theatre capacity for the dedicated management of pelvic and acetabular fractures.

A principle of NHS funding is that insurance industries have a legal obligation to pay healthcare costs for patients who have been injured in an accident and have successfully claimed personal injury compensation. The tariff for the Injury Cost Recovery Scheme is currently capped at £915 per day with a maximum charge of £54682. Outpatient appointments are not funded by the scheme once the patient has received inpatient treatment[24]. Given the estimated cost of an intensive care bed alone is £1932 per night (which 43% of patients in our cohort required)[25], future research should analyse the direct cost of pelvic and acetabular fractures to help determine whether the current compensation arrangements adequately reimburse major trauma care.

This study has limitations which must be considered when interpreting findings. Patients could only be included if they had undergone computed tomography of the pelvis to allow fracture classification. This meant patients who died in a pre-hospital or very early ED setting, prior to undergoing computed tomography of the pelvis, were excluded from analysis. We acknowledge the inevitable effect of geographical and national variation in terms of making comparisons with other centres around the world. The single centre studied is an inner-city level-1 facility with high rates of interpersonal violence, mental illness and low socioeconomic status, compared with the rest of the UK. Therefore, the distribution of injuries will inevitably reflect this diversity. Comparison between nations is also difficult to control due to cultural, legal and behavioural differences within the population which will also affect injury types and mechanisms - examples include the use of roundabouts in the UK and Europe *vs* stop junctions in the United States. Suicide by gunshot is rare in the UK and Europe but much more common in United States and countries where firearm accessibility is relatively high, which may account for the high proportion of suicide falls from height in our series. Similarly, we recorded no pelvic or acetabular injuries resulting from gunshots, which would be much more common in other centres around the world. Moreover, the authors acknowledge the lack of clinical or radiological follow-up in this study. Ideally, an epidemiological study would be complemented by outcomes data, but this was not available for the cohort studied. Finally, analysis of the distribution of acetabular fractures in accordance with the Letournel and Judet classification system was not included in this study.

CONCLUSION

Pelvic and acetabular fractures most commonly occur in young male patients following high-energy trauma and are associated with concomitant orthopaedic injuries (most commonly spine and lower limb fractures), intensive care admission and long inpatient stays. The vast majority of pelvic ring injuries secondary to road traffic accidents are lateral compression type. Injury prevention research should seek to drive advancements in lateral impact cycle and motor vehicle safety, along with mental health surveillance for those deemed to be potential suicide risks.

ARTICLE HIGHLIGHTS

Research background

To optimise trauma outcomes, the National Health Service introduced the Trauma Network System in 2012 which designated 27 hospitals in England responsible for the specialist management of severely injured patients. To our knowledge, this is the first study to analyse the epidemiology of high-energy pelvic and acetabular trauma over a one-year period at a major trauma centre since introduction of the Trauma Network System.

Research motivation

Non-fragility pelvic and acetabular fractures are the result of high-energy trauma. Despite evolving safety measures, high-energy trauma/suicide remains the leading cause of death under the age of 45 in the United Kingdom. Therefore, it is critical that research explores opportunities for future injury prevention in these high-risk patients.

Research objectives

This study sought to characterise the epidemiology of high-energy pelvic and acetabular trauma, to demonstrate the wide-ranging resources required to care for these patients and explore opportunities

for future injury prevention research.

Research methods

227 consecutive patients at a level-1 trauma centre with pelvic and acetabular fractures were analyzed over a one-year period. Paediatric patients, fragility fractures and patients without computed tomography of the pelvis were excluded leaving 175 patients for inclusion in the study. Statistical analysis was performed using Fisher's exact test for categorical variables.

Research results

72% of pelvic and acetabular fractures occurred in male patients at a median age of 45 years. 15% were the result of a suicide attempt. 48% of patients required pelvic or acetabular surgery, with 38% undergoing further surgery for additional orthopaedic injuries. Vertical shear pelvic ring fractures were associated with falls (P = 0.03) while lateral compression fractures were associated with road traffic accidents (P = 0.01).

Research conclusions

High-energy pelvic and acetabular fractures are associated with concomitant orthopaedic fractures (most commonly spine and lower limb). Most pelvic ring injuries secondary to road traffic accidents are lateral compression type illustrating the need for future research to drive advancements in lateral impact vehicle safety.

Research perspectives

Future research should drive advancements in lateral impact vehicle safety given the statistically significant association between lateral compression fractures and road traffic accidents. Additionally, research should focus on mental health surveillance strategies for patients deemed to be potential suicide risks.

FOOTNOTES

Author contributions: Cuthbert R designed the research study, performed data acquisition, and wrote the manuscript; Walters S, Ferguson D and Karam E designed the research study and performed data acquisition; Ward J, Arshad A, Culpan P and Bates P contributed towards conception of the study and final editing; all authors revised the article critically for important intellectual content, and provided final approval for the paper to be published.

Institutional review board statement: The NHS Research Ethics Committee decision tool excluded need for ethical review as this was a retrospective observational study.

Informed consent statement: Informed consent was not required for the above study as data was collected retrospectively and anonymized.

Conflict-of-interest statement: All authors report no relevant conflict of interest for this article.

Data sharing statement: No additional data are available.

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REFERENCES

1 **Office for National Statistics**. Leading causes of death, UK: 2001 to 2018. Available from: https://www.ons.gov.uk/peoplepopulationandcommunity/healthandsocialcare/causesofdeath/articles/Leadingcausesofdeathuk/2001to2018 [DOI: 10.2307/977553]

2 **Major Trauma: Service Delivery**. London: National Institute for Health and Care Excellence (NICE); 2016 Feb- [PMID: 26913313]

3 **Moran CG**, Lecky F, Bouamra O, Lawrence T, Edwards A, Woodford M, Willett K, Coats TJ. Changing the System - Major Trauma Patients and Their Outcomes in the NHS (England) 2008-17. *EClinicalMedicine* 2018; **2-3**: 13-21 [PMID: 31193723 DOI: 10.1016/j.eclinm.2018.07.001]

4 **Osteoporosis: assessing the risk of fragility fracture**. London: National Institute for Health and Care Excellence (NICE); 2017 Feb- [PMID: 32186835]

5 **Young JW**, Burgess AR, Brumback RJ, Poka A. Pelvic fractures: value of plain radiography in early assessment and management. *Radiology* 1986; **160**: 445-451 [PMID: 3726125 DOI: 10.1148/radiology.160.2.3726125]

6 **Ghosh S**, Aggarwal S, Kumar V, Patel S, Kumar P. Epidemiology of pelvic fractures in adults: Our experience at a tertiary hospital. *Chin J Traumatol* 2019; **22**: 138-141 [PMID: 31056468 DOI: 10.1016/j.cjtee.2019.03.003]

7 **Giannoudis PV**, Grotz MR, Tzioupis C, Dinopoulos H, Wells GE, Bouamra O, Lecky F. Prevalence of pelvic fractures, associated injuries, and mortality: the United Kingdom perspective. *J Trauma* 2007; **63**: 875-883 [PMID: 18090020 DOI: 10.1097/01.ta.0000242259.67486.15]

8 **Gov UK**. Reported road casualties Great Britain, provisional results: 2019. Available from: https://www.gov.uk/government/statistics/reported-road-casualties-great-britain-provisional-results-2019 [DOI: 10.1016/0001-4575(91)90056-b]

9 **Ahmed M**, Abuodeh Y, Alhammoud A, Salameh M, Hasan K, Ahmed G. Epidemiology of acetabular fractures in Qatar. *Int Orthop* 2018; **42**: 2211-2217 [PMID: 29430606 DOI: 10.1007/s00264-018-3824-z]

10 **Fenelon C**, Murphy EP, Downey C, O'Daly BJ, Leonard M. A growing problem: cycling referrals to the National Centre for Pelvic and Acetabular Fracture Management in Ireland. *Ir J Med Sci* 2019; **188**: 855-859 [PMID: 30417243 DOI: 10.1007/s11845-018-1926-7]

11 **Bass A**, Lovell ME. Two cases of acetabular fractures sustained during competitive cycling. *Br J Sports Med* 1995; **29**: 205-206 [PMID: 8800858 DOI: 10.1136/bjsm.29.3.205]

12 **Cerynik DL**, Roshon M, Abzug JM, Harding SP, Tom JA. Pelvic fractures in professional cyclists: a report of 3 cases. *Sports Health* 2009; **1**: 265-270 [PMID: 23015883 DOI: 10.1177/1941738108326704]

13 **Papadakis SA**, Pallis D, Galanakos S, Georgiou DF, Kateros K, Macheras G, Sapkas G. Falls from height due to accident and suicide attempt in Greece. A comparison of the injury patterns. *Injury* 2020; **51**: 230-234 [PMID: 31902573 DOI: 10.1016/j.injury.2019.12.029]

14 **de Moore GM**, Robertson AR. Suicide attempts by firearms and by leaping from heights: a comparative study of survivors. *Am J Psychiatry* 1999; **156**: 1425-1431 [PMID: 10484956 DOI: 10.1176/ajp.156.9.1425]

15 **Borg T**, Holstad M, Larsson S. Quality of life in patients operated for pelvic fractures caused by suicide attempt by jumping. *Scand J Surg* 2010; **99**: 180-186 [PMID: 21044937 DOI: 10.1177/145749691009900314]

16 **Trikha V**, V G, Cabrera D, Bansal H, Mittal S, Sharma V. Epidemiological assessment of acetabular fractures in a level one trauma centre: A 7-Year observational study. *J Clin Orthop Trauma* 2020; **11**: 1104-1109 [PMID: 33192015 DOI: 10.1016/j.jcot.2020.09.009]

17 **British Orthopaedic Association**. BOAST - The Management of Patients with Pelvic Fractures. Available from: https://www.boa.ac.uk/resources/boast-3-pdf.html

18 **Woods TN**, Scott KR, Quick JA. New Advances in the Care of the Hemorrhaging Patient. *Mo Med* 2018; **115**: 434-437 [PMID: 30385991]

19 **Franco DF**, Zangan SM. Interventional Radiology in Pelvic Trauma. *Semin Intervent Radiol* 2020; **37**: 44-54 [PMID: 32139970 DOI: 10.1055/s-0039-3401839]

20 **ATLS Subcommittee**. ; American College of Surgeons' Committee on Trauma; International ATLS working group. Advanced trauma life support (ATLS®): the ninth edition. *J Trauma Acute Care Surg* 2013; **74**: 1363-1366 [PMID: 23609291 DOI: 10.1097/TA.0b013e31828b82f5]

21 **Schiff MA**, Tencer AF, Mack CD. Risk factors for pelvic fractures in lateral impact motor vehicle crashes. *Accid Anal Prev* 2008; **40**: 387-391 [PMID: 18215572 DOI: 10.1016/j.aap.2007.07.005]

22 **Euro NCAP**. Side Mobile Barrier. Available from: https://www.euroncap.com/en/vehicle-safety/the-ratings-explained/adult-occupant-protection/Lateral-impact/side-mobile-barrier/ [DOI: 10.1109/icdma.2012.139]

23 **Madhu R**, Kotnis R, Al-Mousawi A, Barlow N, Deo S, Worlock P, Willett K. Outcome of surgery for reconstruction of fractures of the acetabulum. The time dependent effect of delay. *J Bone Joint Surg Br* 2006; **88**: 1197-1203 [PMID: 16943472 DOI: 10.1302/0301-620X.88B9.17588]

24 **Gov UK**. NHS injury cost recovery scheme. Available from: https://www.gov.uk/government/publications/nhs-injury-cost-recovery-scheme [DOI: 10.1016/0277-9390(92)90129-y]

25 **Llywodraeth Cymru Welsh Government**. Together for Health –A Delivery Plan for the Critically Ill- A Delivery Plan up to 2016 for NHS. Available from: https://www.wales.nhs.uk/documents/Delivery-Plan-for-the-critically-ill.pdf

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ORIGINAL ARTICLE

Retrospective Study

Effect of pelvic fixation on ambulation in children with neuromuscular scoliosis

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Abstract

BACKGROUND

The effect of posterior spinal fusion (PSF) incorporating the pelvis on an ambulatory patient's ability to mobilize after the fusion is not well understood.

AIM

To see whether a posterior spinal fusion with pelvic fixation using iliac or sacral alar iliac screws in ambulatory neuromuscular scoliosis (NMS) patients influences postoperative ambulatory ability.

METHODS

A retrospective review of all patients with NMS that underwent PSF with fixation incorporating the pelvis between January 1, 2012 and February 29, 2019. A total of 118 patients were eligible, including 11 ambulatory patients. The primary outcome was the maintenance of ambulatory status postoperatively. Secondary outcomes included postoperative curve magnitude, pelvic obliquity, and complications, comprising infections, instrumentation failure, and any unplanned returns to the operative room.

RESULTS

The ambulatory function was maintained in all 11 ambulatory NMS patients. One patient had an improvement in functional status with equipment-free ambulation postoperatively. An average postoperative follow-up was 19 mo. The overall complication rate was 19.4% (n = 23) with no significant differences between the groups in infection (P = 0.365), hardware failure (P = 0.505), and reoperation rate (P = 1.0). Ambulatory status did not affect complication rate (P = 0.967).

CONCLUSION

Spinal fusion to the pelvis in ambulatory patients with NMS provides effective deformity correction without the reduction in ambulatory capabilities.

Key Words: Pelvic fixation; Ambulation; Neuromuscular scoliosis; Pediatrics; Posterior spinal fusion; Pelvis

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Core Tip: Neuromuscular scoliosis (NMS) represents a medically and surgically complex disorder that can have a profound impact on the patient's quality of life and the ability of their caretakers to provide adequate care. The purpose of this study is to determine whether posterior spinal fusion with pelvic fixation using iliac or sacral-alar iliac screws in ambulatory NMS patients affects postoperative ambulatory ability.

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INTRODUCTION

Neuromuscular scoliosis (NMS) represents a medically and surgically complex disorder that can have a profound impact on the patient's quality of life and the ability of their caretakers to provide adequate care[1,2]. In patients with retained mobility, progression of the neuromuscular disease may result in a loss of their ability to ambulate. Conversely, in non-ambulatory and wheelchair-bound patients, it can lead to difficulty in sitting balance, resulting in hand-dependent sitting, development of decubitus ulcers, and hygiene-related issues[2-4]. The primary goal for patients with NMS is to prevent major curve progression while restoring coronal and sagittal alignment over a balanced pelvis[2,4,5]. To achieve this goal, spinal instrumentation must often be extended into the pelvis. Historically, the fusion of the spine to the pelvis has been taboo, recommended only when pelvic obliquity was > 15 degrees or in low lumbar curves in which the sacrum is affected by the curve[3,6-8]. In 2002, Tsirikos *et al*[4] published their study on cerebral palsy patients who underwent a posterior spinal fusion (PSF) with extension to the pelvis using a unit rod. In their 24 ambulatory patients that underwent PSF to the pelvis, only one patient lost ambulatory function secondary to heterotopic ossification of her hips. This study showed, for the first time, that ambulatory patients who undergo fusion to the pelvis retained mobility after surgery. Recently, a study by Menger *et al*[9] has reported the effects of using PSF with pedicle screws and S2 sacral alar-iliac screws in ambulatory patients with any diagnosis of pediatric scoliosis. Of their 25 patients, only one patient had a decline in postoperative ambulation. However, no study to date has specifically evaluated outcomes in ambulatory children with NMS after a PSF using modern instrumentation. This study aimed to determine whether PSF with pelvic fixation using iliac or sacral-alar iliac (SAI) screws in ambulatory NMS patients influences postoperative ambulatory ability.

MATERIALS AND METHODS

An institutional review board approval was obtained for this study (IRB# 2018-0161). An informed consent exemption was also obtained through a waiver. A retrospective review of all patients with NMS who underwent PSF between January 1, 2012 and February 29, 2019 at a single academic children's hospital was performed, yielding 169 patients. Patients were excluded if their fusion did not extend to the pelvis using iliac or SAI screws, yielding a total of 118 patients for the study. The primary outcome was the maintenance of ambulatory status postoperatively. Secondary outcomes included postoperative curve magnitude, pelvic obliquity, and complications, comprising infections, instrumentation failure,

and any unplanned returns to the operative room (UPRORs). Statistical analysis was performed using IBM SPSS Statistics, Version 26.0 (Armonk, NY). Pearson's Chi-Square and Leven's test for equality were used as appropriate for all categorical data. Significance was set at an alpha level of 0.05.

RESULTS

A total of 118 patients, including 11 ambulatory patients, were enrolled in the study. Detailed demographic and diagnosis data of ambulatory and non-ambulatory patients with NMS are included in Table 1.

No ambulatory patient with NMS became non-ambulatory after PSF with pelvic fixation. In one case, a 19-year-old male that underwent PSF from T1 to the pelvis with SAI screws had an improvement with the ability to ambulate in the clinic free of mobility aids. Table 2 outlines the differences between major curve magnitude (MCM) and pelvic obliquity (PO) for both groups preoperatively and postoperatively and the average change for both parameters.

The major curve magnitude was similar between the groups. However, the preoperative PO was significantly larger in the non-ambulatory *vs* the ambulatory group (15.5 degrees *vs* 7.8 degrees, $P < 0.0001$). Furthermore, when comparing the total change of MCM and PO between the ambulatory and non-ambulatory groups, no significant difference was found (MCM $P = 0.181$; PO $P = 0.143$). SAI screws were used in 114 patients, iliac bolts were used in 2 patients, and iliac screws were used in 2 patients. The type of pelvic fixation used did not affect postoperative ambulatory status ($P = 0.965$), and all ambulatory patients had pelvic fixation consisting of SAI screws.

The total complication rate for all patients enrolled was 19.4% ($n = 23$). The complication profile for the entire patient population and ambulatory and non-ambulatory groups is summarized in Table 3. No statistically significant difference was found in reoperation, injection, or hardware failure rates between the two groups. All patients with hardware failure required revision of spinal fixation. Overall, the patient's ambulatory status did not affect the overall postoperative complication rate ($P = 0.967$).

A small subset of our patients had previous spinal correction surgery, including three ambulatory and ten non-ambulatory patients. Prior surgery performed included the use of vertical expandable prosthetic titanium rib (VEPTR) rods (6), an extension of previous posterior spinal fusion (4), previous staged anterior spinal fusion (2), and the use of growing rods (1). Within this small subgroup, previous surgery did not affect ambulation ($P = 0.209$), postoperative infections ($P = 0.180$), or hardware failure (0.538). Prior surgery significantly affected the need for reoperation ($P = 0.001$), despite no significant difference in infection or hardware failure rates. Prior surgical procedures also significantly affected curve magnitude ($P = 0.044$) and PO ($P = 0.015$).

DISCUSSION

The effect of PSF with pelvic fixation in children with the ability to ambulate has long been an unclarified question. This study focused on the outcomes of patients with NMS who underwent PSF with extension to the pelvis using either SAI or iliac screws. In our study, we found that all patients could ambulate at the same or higher function after PSF with extension to the pelvis. Additionally, we found no significant difference between ambulatory and non-ambulatory groups in complications, UPRORs, hardware failure, or postoperative infections.

To date, this is only the second investigation to report on ambulatory patients with NMS undergoing PSF with fixation to the pelvis using modern pelvic fixation constructs. When comparing our results with the current literature, our findings are consistent. Tsirikos *et al*[4] have evaluated the ambulatory status of 24 NMS patients that underwent PSF incorporating the pelvis using a unit-rod construct. Only one patient in their study lost the ability to ambulate after fusion to the pelvis, and this was secondary to heterotopic ossification of the hips and unrelated to the spinal fusion. Patient- and caregiver-reported outcome questionnaires were also used to assess the postoperative function. Improvements in sitting ability, head and trunk balance, physical appearance, and respiration were noted without any change in ambulatory ability. Furthermore, 12 patients in their study underwent preoperative and postoperative gait analysis. They did not find any significant difference in postoperative gait mechanics in any of these patients. However, patients in their study received a unit rod in contrast to our cohort, where the majority had SAI or iliac screws for pelvic fixation. Menger *et al*[9] have evaluated the effect of PSF with extension to the pelvis in 25 ambulatory children with scoliosis from various diagnoses. Their patients included idiopathic, syndromic, neuromuscular, and congenital scoliosis, of which neuromuscular scoliosis only comprised 28%. They found that all patients retained the ability to ambulate postoperatively, with only one patient noting a decreased ability after fusion. Patient-reported outcomes showed that 25% of the patients noted a change in ambulatory ability while PROMIS T scores completed by most patients fell within one standard deviation of normal, showing only mild ambulatory deficit compared to the normal population. Our study supports these findings, showing no change in ambulation in our patient population.

Table 1 Patient demographics

		Ambulatory	Non-ambulatory	Total	*P* value
Gender					0.405
	Female	4	53	57	
	Male	7	54	61	
Race					
	Black	2	70	72	
	White	8	32	40	
	Hispanic	0	2	2	
	Asian	0	1	1	
	Other	1	2	3	
Age at surgery		16.91 (4.93)	13.32 (3.32)	13.65 (3.63)	0.122
Average follow-up		18.43	18.43	19.14	
Diagnosis					
	Cerebral palsy	5	85	90	
	Post-traumatic spinal cord injury	0	10	10	
	Spina bifida	0	7	7	
	Myopathy	2	0	2	
	Muscular dystrophy	1	2	3	
	Spinal muscular atrophy	0	2	2	
	Alexander's disease	0	1	1	
	Charcot marie tooth	1	0	1	
	Pelizaeus merzbacher disease	0	1	1	
	Lennox gastaut syndrome	1	0	1	
	Geroderma osteodysplasia	1	0	1	

Table 2 Preoperative and postoperative deformity measurements

	Preoperative		Postoperative		Average correction	
	Major curve magnitude	Pelvic obliquity	Major curve magnitude	Pelvic obliquity	Major curve magnitude	Pelvic obliquity
Ambulatory	60.1 (28-110)	7.8 (2-14)	26.9 (12-61)	4.7 (0-15)	33.2	3.1
Non-ambulatory	70 (12-140)	15.5 (0-47)	26.4 (2-81)	8.3 (0-37)	43.6	7.2
P value	0.221	0.000	0.912	0.122		

Mean values with range within parentheses, all values in degrees.

Adult spinal deformity literature provides further insight into the effects of pelvic fixation with PSF. A study by Kondo *et al*[10] has investigated the pre- and postoperative physical function of 30 patients who underwent long spinal fusion from the thoracic spine to the ilium. They found that all patients had significantly improved pain, balance, and 6-minute walking test after PSF. Furthermore, they found that patients with significantly worse preoperative sagittal balance and pelvic tilt had greater improvements in gait speed, gait endurance, and dynamic balance compared to patients with less significant sagittal imbalance or pelvic tilt. Yagi *et al*[11] have investigated the difference between the effect of PSF to the pelvis with iliac screws and the upper instrumented vertebrae in 30 adult female patients. Gait analysis was obtained preoperatively and at 12-18 mo postoperatively, showing an improvement in gait pattern and gait ability. Additionally, Edwards *et al*[12] have investigated the difference in long PSF from the thoracic spine to either L5 or the pelvis in 95 adult patients. Their findings were consistent, showing improved Scoliosis Research Society 24 patient-reported outcomes for both groups and no significant

Table 3 Complication profile between ambulatory and non-ambulatory groups

	Reoperation rate	Infection rate	Hardware failure rate
Overall	18.6	12.7	5.9
Ambulatory	18.2	0	9.1
Non-ambulatory	18.7	14	5.6
P value	0.239	0.365	0.505

All values in percentages.

difference between them. Our findings, although in a vastly different patient population, are consistent with the results of these studies.

Our study had several limitations. First, ambulatory patients with NMS requiring PSF were rare at our institution and only comprised 9.3% of our total patient population. It is possible that a significant difference might be found between ambulators and non-ambulators with NMS with a larger number of patients. Second, gait lab analysis was not available for the included patients, making it difficult to compare the effects of pelvic fixation on postoperative ambulation more objectively. Finally, by not having long-term postoperative follow-up in all patients, it is possible that some patients had a change of ambulatory status unknown to our institution. Despite these limitations, our study is the first in the literature to evaluate the effect of pelvic fixation on postoperative ambulatory status in patients receiving PSF using modern pelvic fixation instrumentation, demonstrating that the postoperative complication profile remains unchanged compared to non-ambulatory controls.

CONCLUSION

In conclusion, we found that it is safe for ambulatory patients with NMS to undergo PSF incorporating the pelvis using modern constructs. Additionally, posterior spinal fusion with extension to the pelvis has no significant effect on complications, UPRORs, hardware failure, or postoperative infections.

ARTICLE HIGHLIGHTS

Research background

Ambulatory patients with neuromuscular scoliosis are a rare subset of patients in which treatment does not compromise their ability to ambulate.

Research motivation

Insufficient research has been done to support the effects of posterior spinal fusion incorporating the pelvis on the ability to ambulate in ambulatory patients with neuromuscular scoliosis.

Research objectives

To report the effect of posterior spinal fusion incorporating the pelvis on the ability to ambulate after fusion in patients with neuromuscular scoliosis.

Research methods

This is a retrospective analysis of patient function outcomes after undergoing posterior spinal fusion incorporating the pelvis over a seven-year period at our children's hospital.

Research results

Of the eleven patients fitting this criterion, no patient lost their ability to ambulate after undergoing posterior spinal fusion incorporating the pelvis.

Research conclusions

According to our findings, there is no effect on the ambulatory function of neuromuscular patients after posterior spinal fusion incorporating the pelvis.

Research perspectives

Although more evidence is needed, the experience at our institution would support that posterior spinal

fusion incorporating the pelvis does not affect the patients' ability to mobilize in ambulatory neuromuscular scoliosis patients.

FOOTNOTES

Author contributions: Drake LC performed study design, x-ray measurements, statistical analysis, and manuscript preparation; Sukkarieh H contributed to study design and manuscript preparation; McDonald TC contributed to study design and manuscript preparation; Bhanat E contributed to statistical analysis and manuscript preparation; Quince E contributed to x-ray measurements and statistical analysis; Atkins M contributed to x-ray measurements and statistical analysis; Wright P contributed to study design and manuscript preparation; Brooks JT contributed to study design, statistical analysis, and manuscript preparation

Institutional review board statement: The study was reviewed and approved by the University of Mississippi Medical Center Institutional Review Board [Approval No. 2018-01610].

Informed consent statement: Patients were not required to give informed consent to the study because the analysis used anonymous clinical data that were obtained after each patient agreed to treatment by written consent.

Conflict-of-interest statement: Brooks JT is a paid consultant of Depuy-Synthes, A Johnson & Johnson Company; paid consultant of OrthoPediatrics; and a paid presenter or speaker of Medtronic Spine. The remaining authors declare no conflicts of interest.

Data sharing statement: Statistical code and dataset are available from the corresponding author at jaysson.brooks@tsrh.org. Participants did not give informed consent for data sharing.

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REFERENCES

1 **Yoshida K**, Kajiura I, Suzuki T, Kawabata H. Natural history of scoliosis in cerebral palsy and risk factors for progression of scoliosis. *J Orthop Sci* 2018; **23**: 649-652 [PMID: 29705176 DOI: 10.1016/j.jos.2018.03.009]
2 **McCarthy JJ**, D'Andrea LP, Betz RR, Clements DH. Scoliosis in the child with cerebral palsy. *J Am Acad Orthop Surg* 2006; **14**: 367-375 [PMID: 16757676 DOI: 10.5435/00124635-200606000-00006]
3 **McCarthy RE**. Management of neuromuscular scoliosis. *Orthop Clin North Am* 1999; **30**: 435-449, viii [PMID: 10393765 DOI: 10.1016/s0030-5898(05)70096-1]
4 **Tsirikos AI**, Chang WN, Shah SA, Dabney KW, Miller F. Preserving ambulatory potential in pediatric patients with cerebral palsy who undergo spinal fusion using unit rod instrumentation. *Spine (Phila Pa 1976)* 2003; **28**: 480-483 [PMID: 12616161 DOI: 10.1097/01.BRS.0000048649.72919.6B]
5 **Benson ER**, Thomson JD, Smith BG, Banta JV. Results and morbidity in a consecutive series of patients undergoing spinal fusion for neuromuscular scoliosis. *Spine (Phila Pa 1976)* 1998; **23**: 2308-2318 [DOI: 10.1097/00007632-199811010-00012]
6 **Akesen B**, Atici T, Eken G, Ulusaloglu AC. The comparison of the results after spinal fusion with or without iliac screw insertion in the treatment of neuromuscular scoliosis. *Acta Orthop Traumatol Turc* 2018; **52**: 435-437 [PMID: 30266422 DOI: 10.1016/j.aott.2017.12.005]
7 **Modi HN**, Suh SW, Song HR, Fernandez HM, Yang JH. Treatment of neuromuscular scoliosis with posterior-only pedicle screw fixation. *J Orthop Surg Res* 2008; **3**: 23 [PMID: 18544164 DOI: 10.1186/1749-799X-3-23]
8 **Van Zundert J**, Vanelderen P, Kessels AG. Re: Chou R, Atlas SJ, Stanos SP, *et al*. Nonsurgical interventional therapies for low back pain: a review of the evidence for an American Pain Society clinical practice guideline. Spine (Phila Pa 1976) 2009;34: 1078-93. *Spine (Phila Pa 1976)* 2010; **35**: 841; author reply 841-841; author reply 842 [PMID: 20357643 DOI: 10.1097/BRS.0b013e3181d2ad36]
9 **Menger R**, Park P, Marciano G. Ambulatory capacity following fusion to the sacrum with pelvic fixations pediatric spinal deformity patients. *Spine Deform* 2020 [DOI: 10.1007/s43390-020-00238-7]
10 **Kondo R**, Yamato Y, Nagafusa T. Effect of corrective long spinal fusion to the ilium on physical function in patients with

adult spinal deformity. *Eur Spine J* 2017; **26**: 2138-2145 [DOI: 10.1007/s00586-017-4987-9]

11 **Yagi M**, Fujita N, Tsuji O, Nagoshi N, Yato Y, Asazuma T, Ishii K, Nakamura M, Matsumoto M, Watanabe K. Effect of the upper instrumented vertebral level (upper *vs* lower thoracic spine) on gait ability after corrective surgery for adult spinal deformity. *Spine J* 2018; **18**: 130-138 [PMID: 28669859 DOI: 10.1016/j.spinee.2017.06.026]

12 **Edwards CC 2nd**, Bridwell KH, Patel A, Rinella AS, Berra A, Lenke LG. Long adult deformity fusions to L5 and the sacrum. A matched cohort analysis. *Spine (Phila Pa 1976)* 2004; **29**: 1996-2005 [PMID: 15371700 DOI: 10.1097/01.brs.0000138272.54896.33]

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ORIGINAL ARTICLE

Prospective Study

Quantitative alpha-defensin testing: Is synovial fluid dilution important?

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Abstract

BACKGROUND

Alpha-defensin has been widely studied for the diagnosis of periprosthetic joint infection (PJI). However, there is a lack of detailed information regarding the proper laboratory technique of the enzyme-linked immunosorbent assay (ELISA) method, such as sample dilution.

AIM

To assess the influence of dilution in the synovial fluid during ELISA for the diagnosis of knee PJI; and determine which dilution presents a better performance.

METHODS

Forty samples of synovial fluid from arthroplasty knees were included, 17 in the infected group and 23 in the aseptic group, according to Musculoskeletal Infection Society criteria. Initially, five synovial fluid samples from each group were assessed for quantitative analysis of alpha-defensin using ELISA. Different dilution ratios (1:10, 1:100, 1:500, 1:1000 and 1:5000) were tested based on the predetermined cutoff value of 5.2 mg/L. The dilutions that performed better were used to compare the results of all samples.

RESULTS

For infected cases, a gradual increase in the dilution of synovial fluid samples led to an equivalent increase in alpha-defensin level. The same was not observed in the aseptic cases. Both 1:1000 and 1:5000 dilutions presented satisfactory results to differentiate infected and aseptic cases. Further analyses were performed using 1:1000 and 1:5000 for all 40 samples. The 1:1000 dilution resulted in a sensitivity of 88.2% (95%CI, 66%-98%) and specificity of 95.7% (95%CI, 79%-99%), whereas the 1:5000 dilution presented a sensitivity of 94.1% (95%CI, 73%-99%) and a specificity of 100% (95%CI, 86%-100%).

CONCLUSION

The synovial fluid dilution had an important influence on the alpha-defensin ELISA results. Dilutions of 1:5000 showed the best performance for the diagnosis of knee PJI. The results of this study set the basis for a more reliable and reproducible alpha-defensin ELISA during the investigation of PJI, contributing to the expansion of this technique in different treatment centers worldwide.

Key Words: Alpha-defensin; Enzyme-linked immunosorbent assay; Periprosthetic joint infection; Laboratory findings

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Core Tip: Alpha-defensin is an antimicrobial peptide widely studied in patients with periprosthetic joint infection. Indeed, the analysis of alpha-defensin concentration in the synovial fluid by enzyme-linked immunosorbent assay (ELISA) has been gaining ground. However, there is a lack of information regarding the detailed technique for synovial fluid ELISA, particularly in regard to its dilution. Therefore, this study analyzed the influence of dilution in synovial fluid samples for the alpha-defensin ELISA method. We presume that this novel information may be helpful to make ELISA more reproducible and widely accessible for different treatment centers worldwide.

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INTRODUCTION

Periprosthetic joint infection (PJI) is an increasingly common and devastating complication that can lead to significant morbidity and mortality[1,2]. Since neither clinical examination nor laboratory tests are always trustworthy, the diagnosis of PJI remains a challenge[3]. Indeed, there is no gold-standard method for its diagnosis[4]. Therefore, several groups around the world have attempted to refine the diagnostic criteria of PJI[2,5,6]. The criteria score proposed (and later updated) by the Musculoskeletal Infection Society (MSIS) is the one most used by orthopedic surgeons[2].

Regarding the different strategies to improve the diagnosis of PJI, the use of biomarkers has been extensively studied in recent years[1,7,8]. Alpha-defensin has gained attention as one of the most reliable markers[9,10]. Defensins are antimicrobial peptides that act as part of the host's innate immune response against pathogen invasion and are produced in increased numbers during septic inflammation [11,12]. Thus, synovial-fluid alpha-defensin has shown excellent results in diagnosing PJI[13,14]. Two different modalities are available to measure synovial alpha-defensin: The qualitative alpha-defensin lateral flow test and the quantitative enzyme-linked immunosorbent assay (ELISA)[15]. Particularly, the ELISA method has presented the best results, so it was included as a criterion in the new International Consensus on Orthopedic Infections 2018 consensus[6].

Despite the importance and the many studies about alpha-defensin in synovial fluid[15,16], there is a lack of detailed information regarding the ELISA technique[13]. In fact, some crucial information about the reproducibility of the test and the standardization of specific cutoff values are unclear. Dilution of the synovial fluid sample is necessary for the test, but the ideal ratios are not known.

Therefore, this study aimed to evaluate the potential influence of dilution on the quantitative alpha-defensin ELISA test for the diagnosis of PJI in the synovial fluid of patients undergoing total knee arthroplasty (TKA). We hypothesized that changes in the dilution of the joint fluid would influence the

test performance for the diagnosis of PJI.

MATERIALS AND METHODS

The study was approved by the local ethics committee (No. 71039317.3.0000.0068). All the included patients signed the consent form.

Between January 2017 and December 2018, this study enrolled patients with primary TKA and any suspicious signs or symptoms of chronic infection, as follows: more than three months of persistent knee pain, effusion or local heat, presence of a draining sinus, early failure of the prosthesis (less than 5 years), fever and malaise. Patients who had used antibiotic therapy for at least four weeks before the evaluation or had an insufficient volume of synovial fluid during knee aspiration were excluded. Forty-five patients were assessed for recruitment. Of these, five did not have enough synovial fluid and were excluded from the study. The other 40 patients were included. They were divided into two groups: infected and noninfected (aseptic painful). Seventeen (42.5%) patients were considered to have infection, and 23 (57.5%) patients were classified as having aseptic painful TKA. Positive infection was confirmed if the MSIS criteria for PJI were fulfilled[17], as follows: presence of a draining sinus communicating with the joint or at least two positive cultures of the same microorganism, or if three out of the following five criteria were present: elevated serum C-reactive protein and erythrocyte sedimentation rate, elevated synovial white blood cell count, elevated percentage of synovial polymorphonuclear leukocytes (PMNs), positive histological analysis of periprosthetic tissue and a single positive culture of synovial fluid or periprosthetic tissue. For chronic PJI, synovial cell count and differential cutoff values were 3.000 cells/μL, 80% PMN.

Synovial fluid was collected from each patient. Using a sterile technique, the lateral suprapatellar approach was performed, and a 20-mL syringe with a 21-gauge needle was used to aspirate the joint fluid. A minimum of 0.5 mL was aspirated and stored in a tube with ethylenediaminetetraacetic acid (EDTA). The tubes were transported to the laboratory within one hour after aspiration at room temperature. Previous studies have estimated the stability of alpha-defensin levels in synovial fluid for a minimum of 48 h at room temperature[13]. The fluid was centrifuged for ten minutes at 2000 rpm according to our laboratory standardization, and the supernatant was frozen at -80°C until use[13].

Determination of synovial alpha-defensin concentrations

Reagents from the commercially available ELISA test kit (Hycult Biotech®, Uden, The Netherlands) were used according to the manufacturer's instructions. However, as anticipated, there was no manufacturer recommendation for synovial fluid dilution. In this study, ten samples (five from each group) were randomly selected and diluted in the buffer included in the kit at 1:10, 1:100, 1:500, 1:1000 and 1:5000. All dilutions were tested in duplicate. The reactions were read at 450 nanometers in an ELISA SpectraMax 190 reader (Molecular Devices, San Jose, United States) in accordance with the package insert instructions. The results of spectrophotometry were obtained in optical density (OD) units. The OD values were plotted on the vertical axis, and the corresponding concentrations were plotted on the horizontal axis (logarithmic scale). The concentration was multiplied by the dilution factor to obtain the actual alpha-defensin value in mg/L. A cutoff value of 5.2 mg/L was used since the same value was used as the cutoff in previous studies[13,18].

Initially, ten out of 40 cases were selected to define which dilutions would provide the best performance. After detecting which dilutions performed better, we expanded the analysis to all other cases. All samples were tested with the selected dilution ratio, following the same procedures as described above except for the serial dilution.

Statistical analysis

Statistical analysis was performed using GraphPad Prism version 8 (GraphPad Software, La Jolla, CA). The results of the alpha-defensin synovial fluid are expressed as mean and range. Differences between the two groups were compared using the Mann–Whitney test. To assess the performance of the test using 1:1000 and 1:5000 dilutions, the sensitivity, specificity, positive predictive value and negative predictive value were evaluated through the Wilson-Brown method. The 95% confidence interval (95%CI) was also calculated. $P < 0.05$ was considered to be statistically significant.

RESULTS

Table 1 shows the demographic and laboratory results of the included patients. Regarding the initial assessment, five samples from each group were tested using different dilutions. In the infected group, a gradual increase in synovial fluid dilution resulted in an equivalent elevation of alpha-defensin levels. The same response was not observed in the aseptic group (Figure 1). In addition, the best diagnostic performance of the test was obtained at 1:1000 and 1:5000 dilutions. Table 2 summarizes these findings.

Table 1 Demographics and laboratory results of the included patients

	Total	Aseptic cases	Infected cases
Sex			
Male	9	4	5
Female	31	19	12
Age (range)	67.57 (47-85)	67.65 (47-85)	67.47 (51-84)
Laterality			
Right knee	21	13	8
Left knee	19	10	9
Inflammatory disease			
RA	8	5	3
Gout	2	0	2
Major Criteria			
Sinus Tract	4	0	4
2 positive cultures	2	0	2
Minor criteria			
CRP and ESR +	9	0	9
WBC count	15	1	14
PMN%	14	0	14
Hystological +	5	0	5
1 culture	12	1	11

RA: Rheumatoid arthritis; CRP: C-reactive protein; ESR: Erythrocyte sedimentation rate; WBC: White blood cells; PMN: Polymorphonuclear neutrophils.

Table 2 Mean and range in mg/L of the initial 10 cases (5 from infected and 5 from aseptic group) in several dilutions

	Dil. 1:10, mean (range)	Dil. 1:100, mean (range)	Dil. 1:500, mean (range)	Dil. 1:1000, mean (range)	Dil. 1:5000, mean (range)
Infected cases	0.04 (0.03-0.05)	0.52 (0.40-0.76)	2.92 (1.68-4.45)	6.68 (3.62-9.62)	32.67 (12.65-50.18)
Aseptic cases	0.01 (0-0.03)	0.09 (0.02-0.30)	0.21 (0.12-0.55)	0.3 (0.24-0.48)	1.43 (1.4-1.49)
P	0.016	0.008	0.008	0.008	0.008

Mann-Whitney test.

We next evaluated all of the remaining samples using these dilution ratios. The results of the alpha-defensin tests including all patients are displayed in Table 3 and Figure 2. At a dilution of 1:1000, statistical analysis indicated a sensitivity of 88.2% (95%CI, 66%-98%), a specificity of 95.7% (95%CI, 79%-99%), a positive predictive value of 93.8% (95%CI, 72%-99%) and a negative predictive value of 91.7% (95%CI, 74%-99%). In this situation, one false positive and two false negatives were found.

At the 1:5000 dilution, a sensitivity of 94.1% (95%CI, 73%-99%), a specificity of 100% (95%CI, 86%-100%), a positive predictive value of 100% (95%CI, 81%-100%) and a negative predictive value of 95.8% (95%CI, 80%-99%) were observed. Only one false-negative result was identified within the infected group. This misdiagnosed case presented with a draining sinus and had positive intraoperative cultures.

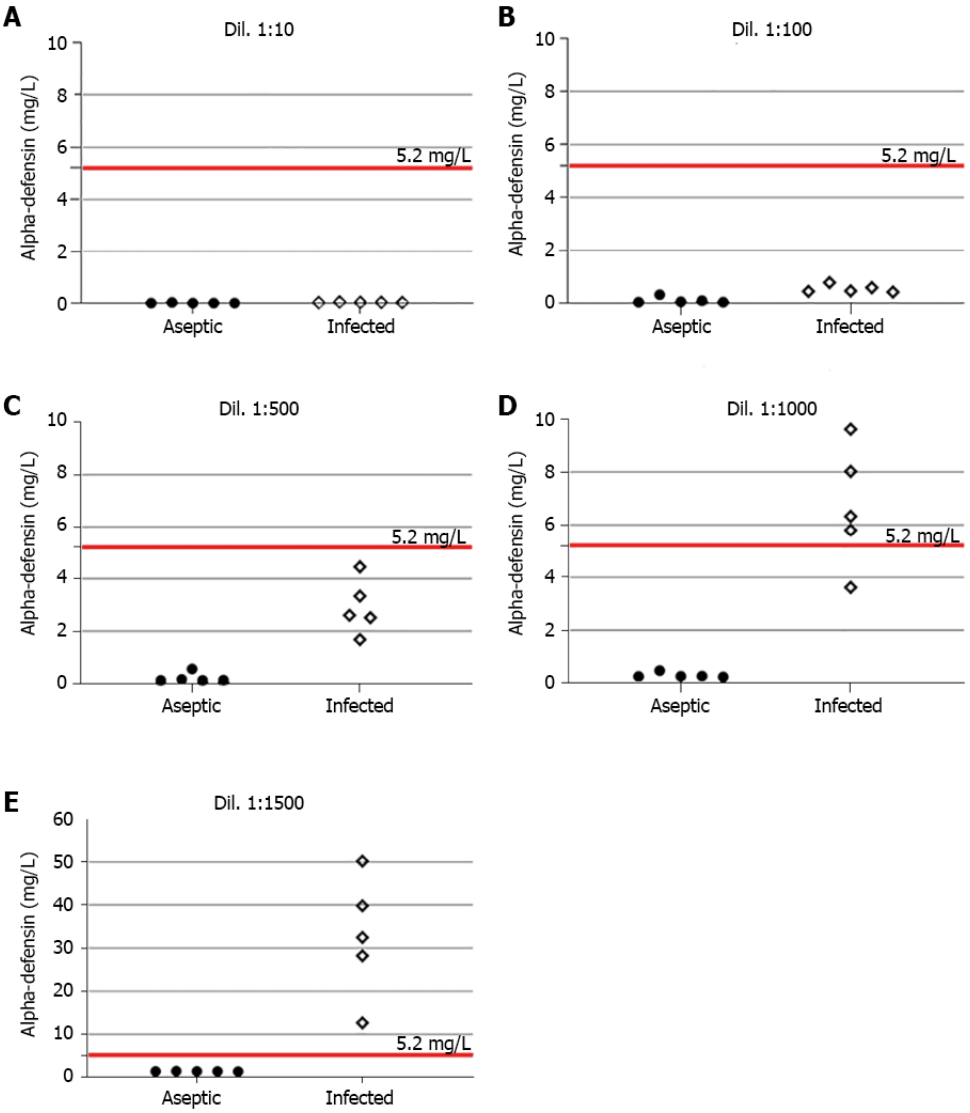
DISCUSSION

To the best of our knowledge, there is a lack of studies detailing and testing the influence of different

Table 3 Mean and range of synovial fluid alpha-defensin values (in mg/dL) of all patients

	Number of cases	Dilution of 1:1000	Dilution of 1:5000
Infected cases	17 (42.5%)	6.60 (0.26-9.62)	24.10 (5.72-50.18)
Aseptic cases	23 (57.5%)	0.74 (0.24-8.54)	1.50 (1.22-4.66)
P		< 0.001	< 0.001

Mann-Whitney test.

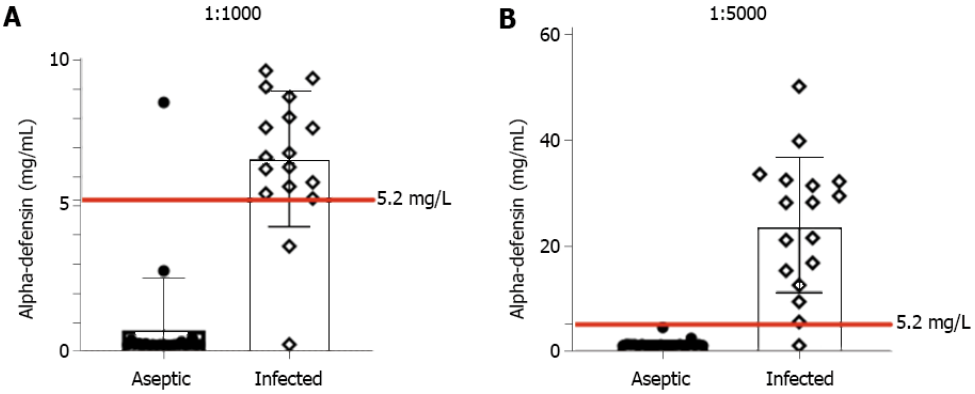


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Figure 1 Results of alpha-defensin concentration (mg/L) according to each dilution. A: 1:10; B: 1:100; C: 1:500; D: 1: 1000; and E: 1:5000. Noteworthy, for infected cases a gradual increase in the sample dilution resulted in an increasing level of alpha-defensin. The same was not observed in the aseptic cases. In addition, both 1:1000 and 1:5000 dilutions presented favorable results to differentiate infected and aseptic cases.

dilutions on the synovial fluid alpha-defensin ELISA test for the diagnosis of TKA infection. The novel results of this laboratory study support our hypothesis that the right synovial fluid dilution is crucial for a high diagnostic accuracy of the alpha-defensin ELISA test. Here, we found positive results using dilutions of 1:1000 and 1:5000, the best results occurring with a 1:5000 dilution ratio.

As mentioned above, in one of the first studies of synovial fluid alpha-defensin, a cutoff value of 5.2 mg/L of alpha-defensin was defined as the threshold for the diagnosis of PJI[19]. However, the dilutions applied to obtain this cutoff value were not described, making it hard to replicate the methods, even using the same alpha-defensin ELISA kit. In our study, using a 5.2 mg/L cutoff, the most effective dilution to distinguish between infection and noninfection was 1:5000. Using this dilution ratio, only



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Figure 2 Results of synovial fluid alpha-defensin values of all patients using 1:1000 and 1:5000 dilution. A: 1:1000 dilution; B: 1:5000 dilution. As observed, there was one case of false negative in the infected group.

one false-negative result was found. Similar to other patients[10,13], this patient presented with a drainage sinus, though our patient had positive intraoperative cultures, which was not seen in that other series. We also showed that although a dilution of 1:1000 had satisfactory results for detecting infected cases, it had lower sensitivity and specificity.

Another interesting consideration relates to the prozone phenomenon. The prozone phenomenon, also known as the hook effect, is a false-negative response that occurs in immunological tests as a consequence of an excess of either antigen or antibody[20]. In an alpha-defensin test, if the amount of antigen (*i.e.*, alpha-defensin) is greater than the amount of antibody, the secondary antibody (*i.e.*, peroxidase) will not bind properly, and the test will present a false result. This could be the reason for some false-negative values during the alpha-defensin assay. In this study, we did not directly assess the influence of dilution on the prozone phenomenon, but since lower dilutions are more likely to exhibit the prozone effect, the latest dilutions may be helpful to overcome this phenomenon[21], potentially allowing a more precise differentiation between TKA infection and asepsis.

Some limitations of our study must be considered. The small sample size may underpower the study. However, the consistent findings with different dilutions and the excellent results using a 1:5000 dilution reduced the need to increase the sample size. In addition, despite the exciting progressive improvement in the test performance with serial dilutions, we did not demonstrate the actual reason why it occurs. Further studies are necessary to answer this question. Even so, we describe in detail the analysis of synovial fluid alpha-defensin by ELISA, including the best dilutions for the most accurate diagnosis of knee PJI. Moreover, the information provided herein may ensure the reproducibility of the test across the laboratories, with more precise data.

CONCLUSION

Changes in synovial fluid dilution for ELISA had an important influence on the determination of alpha-defensin levels. Based on the cutoff value of 5.2 mg/L, dilutions of both 1:1000 and 1:5000 were adequate to support the diagnosis of TKA infection. The 1:5000 dilution showed the best performance in separating the infection and the aseptic cases, making it the most reliable dilution during knee PJI investigation. Therefore, the results of this study lay the foundation for a more reliable and reproducible alpha-defensin ELISA during the investigation of PJI, contributing to the expansion of this technique to different treatment centers worldwide.

ARTICLE HIGHLIGHTS

Research background

Periprosthetic joint infection (PJI) is a serious complication post-surgery that is associated with substantial morbidity and financial burden to the healthcare system. The alpha-defensin quantitative enzyme-linked immunosorbent assay (ELISA) is one of the most useful methods to investigate PJI.

Research motivation

Although the alpha-defensin ELISA is currently the most reliable test to diagnose PJI, there is a lack of detailed information regarding its proper laboratory technique, including the best sample dilution.

Research objectives

This study aimed to assess the influence of dilution in the synovial fluid during ELISA for the diagnosis of knee PJI and determine which dilution presents a better performance.

Research methods

In this prospective study, 40 cases of total knee arthroplasty were evaluated: 17 classified as PJI and 23 classified as aseptic knees. Initially, 5 synovial fluid samples from each group were assessed by ELISA using different dilution ratios (1:10, 1:100, 1:500, 1:1000 and 1:5000). The dilutions had better performance were used to compare the results of all samples.

Research results

For infected cases, a gradual increase in the synovial fluid dilution led to an equivalent increase in alpha-defensin level, which was not seem in the aseptic cases. Both 1:1000 and 1:5000 dilutions presented satisfactory results to differentiate infected and aseptic cases. Further analyses were performed using 1:1000 and 1:5000 for all 40 samples. The 1:1000 dilution resulted in a sensitivity of 88.2% (95%CI, 66%-98%) and specificity of 95.7% (95%CI, 79%-99%), whereas the 1:5000 dilution presented a sensitivity of 94.1% (95%CI, 73%-99%) and a specificity of 100% (95%CI, 86%-100%).

Research conclusions

Synovial fluid dilution appears to influence the alpha-defensin ELISA results. Dilutions of 1:5000 showed the best performance for the diagnosis of knee PJI.

Research perspectives

The results of this current study may set the basis for more reliable and reproducible alpha-defensin ELISA during PJI investigation, contributing to the expansion of this technique in different treatment centers worldwide.

FOOTNOTES

Author contributions: Abdo RCT collected the samples; Leite CBG wrote the article; Abdo RCT, Leite CBG, Lima ALLM and Bonfa E contributed to the data analysis; Abdo RCT, Gobbi RG, Lima ALLM, Bonfa E, Pécora JR and Demange MK contributed to the intellectual concept and design of the study; Pasoto SG performed the laboratory tests and contributed to the strategy for alpha-defensin analysis according to its dilution; Leon EP conducted the laboratory tests; Gobbi RG reviewed the article.

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Informed consent statement: All study participants, or their legal guardian, provided written consent prior to study enrollment.

Conflict-of-interest statement: All authors report no relevant conflict of interest for this article.

Data sharing statement: There is no additional data available.

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REFERENCES

1 **Chen Y**, Kang X, Tao J, Zhang Y, Ying C, Lin W. Reliability of synovial fluid alpha-defensin and leukocyte esterase in diagnosing periprosthetic joint infection (PJI): a systematic review and meta-analysis. *J Orthop Surg Res* 2019; **14**: 453 [PMID: 31856885 DOI: 10.1186/s13018-019-1395-3]

2 **Parvizi J**, Tan TL, Goswami K, Higuera C, Della Valle C, Chen AF, Shohat N. The 2018 Definition of Periprosthetic Hip and Knee Infection: An Evidence-Based and Validated Criteria. *J Arthroplasty* 2018; **33**: 1309-1314.e2 [PMID: 29551303 DOI: 10.1016/j.arth.2018.02.078]

3 **Tan TL**, Kheir MM, Shohat N, Tan DD, Kheir M, Chen C, Parvizi J. Culture-Negative Periprosthetic Joint Infection: An Update on What to Expect. *JB JS Open Access* 2018; **3**: e0060 [PMID: 30533595 DOI: 10.2106/JBJS.OA.17.00060]

4 **Goswami K**, Parvizi J, Maxwell Courtney P. Current Recommendations for the Diagnosis of Acute and Chronic PJI for Hip and Knee-Cell Counts, Alpha-Defensin, Leukocyte Esterase, Next-generation Sequencing. *Curr Rev Musculoskelet Med* 2018; **11**: 428-438 [PMID: 30062484 DOI: 10.1007/s12178-018-9513-0]

5 **Elkins JM**, Kates S, Lange J, Lichstein P, Otero J, Soriano A, Wagner C, Wouthuyzen-Bakker M. General Assembly, Diagnosis, Definitions: Proceedings of International Consensus on Orthopedic Infections. *J Arthroplasty* 2019; **34**: S181-S185 [PMID: 30348558 DOI: 10.1016/j.arth.2018.09.069]

6 **Shohat N**, Bauer T, Buttaro M, Budhiparama N, Cashman J, Della Valle CJ, Drago L, Gehrke T, Marcelino Gomes LS, Goswami K, Hailer NP, Han SB, Higuera CA, Inaba Y, Jenny JY, Kjaersgaard-Andersen P, Lee M, Llinás A, Malizos K, Mont MA, Jones RM, Parvizi J, Peel T, Rivero-Boschert S, Segreti J, Soriano A, Sousa R, Spangehl M, Tan TL, Tikhilov R, Tuncay I, Winkler H, Witso E, Wouthuyzen-Bakker M, Young S, Zhang X, Zhou Y, Zimmerli W. Hip and Knee Section, What is the Definition of a Periprosthetic Joint Infection (PJI) of the Knee and the Hip? *J Arthroplasty* 2019; **34**: S325-S327 [PMID: 30343971 DOI: 10.1016/j.arth.2018.09.045]

7 **Balato G**, de Matteo V, Ascione T, Di Donato SL, De Franco C, Smeraglia F, Baldini A, Mariconda M. Laboratory-based versus qualitative assessment of α-defensin in periprosthetic hip and knee infections: a systematic review and meta-analysis. *Arch Orthop Trauma Surg* 2020; **140**: 293-301 [PMID: 31300864 DOI: 10.1007/s00402-019-03232-5]

8 **Bonanzinga T**, Ferrari MC, Tanzi G, Vandenbulcke F, Zahar A, Marcacci M. The role of alpha defensin in prosthetic joint infection (PJI) diagnosis: a literature review. *EFORT Open Rev* 2019; **4**: 10-13 [PMID: 30800475 DOI: 10.1302/2058-5241.4.180029]

9 **Bingham J**, Clarke H, Spangehl M, Schwartz A, Beauchamp C, Goldberg B. The alpha defensin-1 biomarker assay can be used to evaluate the potentially infected total joint arthroplasty. *Clin Orthop Relat Res* 2014; **472**: 4006-4009 [PMID: 25256621 DOI: 10.1007/s11999-014-3900-7]

10 **Bonanzinga T**, Zahar A, Dütsch M, Lausmann C, Kendoff D, Gehrke T. How Reliable Is the Alpha-defensin Immunoassay Test for Diagnosing Periprosthetic Joint Infection? *Clin Orthop Relat Res* 2017; **475**: 408-415 [PMID: 27343056 DOI: 10.1007/s11999-016-4906-0]

11 **Chalifour A**, Jeannin P, Gauchat JF, Blaecke A, Malissard M, N'Guyen T, Thieblemont N, Delneste Y. Direct bacterial protein PAMP recognition by human NK cells involves TLRs and triggers alpha-defensin production. *Blood* 2004; **104**: 1778-1783 [PMID: 15166032 DOI: 10.1182/blood-2003-08-2820]

12 **Ganz T**, Selsted ME, Szklarek D, Harwig SS, Daher K, Bainton DF, Lehrer RI. Defensins. Natural peptide antibiotics of human neutrophils. *J Clin Invest* 1985; **76**: 1427-1435 [PMID: 2997278 DOI: 10.1172/JCI112120]

13 **Deirmengian C**, Kardos K, Kilmartin P, Cameron A, Schiller K, Parvizi J. Combined measurement of synovial fluid α-Defensin and C-reactive protein levels: highly accurate for diagnosing periprosthetic joint infection. *J Bone Joint Surg Am* 2014; **96**: 1439-1445 [PMID: 25187582 DOI: 10.2106/JBJS.M.01316]

14 **Frangiamore SJ**, Gajewski ND, Saleh A, Farias-Kovac M, Barsoum WK, Higuera CA. α-Defensin Accuracy to Diagnose Periprosthetic Joint Infection-Best Available Test? *J Arthroplasty* 2016; **31**: 456-460 [PMID: 26545577 DOI: 10.1016/j.arth.2015.09.035]

15 **Eriksson HK**, Nordström J, Gabrysch K, Hailer NP, Lazarinis S. Does the Alpha-defensin Immunoassay or the Lateral Flow Test Have Better Diagnostic Value for Periprosthetic Joint Infection? *Clin Orthop Relat Res* 2018; **476**: 1065-1072 [PMID: 29601381 DOI: 10.1007/s11999.0000000000000244]

16 **Marson BA**, Deshmukh SR, Grindlay DJC, Scammell BE. Alpha-defensin and the Synovasure lateral flow device for the diagnosis of prosthetic joint infection: a systematic review and meta-analysis. *Bone Joint J* 2018; **100-B**: 703-711 [PMID: 29855233 DOI: 10.1302/0301-620X.100B6.BJJ-2017-1563.R1]

17 **Parvizi J**, Gehrke T; International Consensus Group on Periprosthetic Joint Infection. Definition of periprosthetic joint infection. *J Arthroplasty* 2014; **29**: 1331 [PMID: 24768547 DOI: 10.1016/j.arth.2014.03.009]

18 **Deirmengian C**, Kardos K, Kilmartin P, Cameron A, Schiller K, Booth RE Jr, Parvizi J. The alpha-defensin test for periprosthetic joint infection outperforms the leukocyte esterase test strip. *Clin Orthop Relat Res* 2015; **473**: 198-203 [PMID: 24942960 DOI: 10.1007/s11999-014-3722-7]

19 **Deirmengian C**, Kardos K, Kilmartin P, Cameron A, Schiller K, Parvizi J. Diagnosing periprosthetic joint infection: has the era of the biomarker arrived? *Clin Orthop Relat Res* 2014; **472**: 3254-3262 [PMID: 24590839 DOI: 10.1007/s11999-014-3543-8]

20 **Hoofnagle AN**, Wener MH. The fundamental flaws of immunoassays and potential solutions using tandem mass spectrometry. *J Immunol Methods* 2009; **347**: 3-11 [PMID: 19538965 DOI: 10.1016/j.jim.2009.06.003]

21 **Kim HS**, Choi AR, Yang M, Oh EJ. EDTA Treatment for Overcoming the Prozone Effect and for Predicting C1q Binding in HLA Antibody Testing. *Ann Lab Med* 2019; **39**: 572-576 [PMID: 31240886 DOI: 10.3343/alm.2019.39.6.572]

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CASE REPORT

Bilateral hip heterotopic ossification with sciatic nerve compression on a paediatric patient–An individualized surgical approach: A case report

João Pedro Gouveia Nóbrega, Pedro Jordão, Joana Arcângelo

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Abstract

BACKGROUND

Neurogenic heterotopic ossification is an acquired serious complication described in patients with central nervous system disorders and defined by bone formation in non-osseous tissue.

CASE SUMMARY

We present an unusual case of a 13-yr-old boy presenting with hip pain and severe gait impairment 5 mo after the diagnosis of hemiplegia following a spontaneous intracerebral haemorrhage. Computed tomography revealed bilateral heterotopic ossification of both the paretic and the non-paretic limbs, with entrapment of the sciatic nerve. The choice of surgical or nonsurgical management of such patients depends on the timing of diagnosis, the symptoms, and the extent of maturation of the ossified lesions. Surgical resection remains the only treatment with proven, evidence-based effectiveness. The choice of surgical approach largely depends on the location of the ossified lesions.

CONCLUSION

We believe the plane of dissection presented is a satisfactory option for resection of a posteromedial mass and sciatic nerve release.

Key Words: Hip; Heterotopic ossification; Pediatrics; Orthopedics; Ressection surgery; Case report

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Core Tip: Rare case of a post-stroke bilateral neurogenic heterotopic ossification of the hip with sciatic nerve entrapment in a paediatric patient with an individualised surgical approach for resection and release of the sciatic nerve.

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INTRODUCTION

Neurogenic heterotopic ossification (NHO) is a process of ectopic bone deposition in non-skeletal tissue in the setting of an event involving the central nervous system, such as a stroke, cerebral anoxia, or cranial or medullary injury. Its severity and clinical presentation vary depending on the extension of the ossified lesion and the compromise of adjacent neurovascular structures. The etiopathogenesis of NHO is unclear, but existing evidence supports the involvement of neuronal control mechanisms[1] and conversion of mesenchymal progenitor cells to osteoblast lineages[2] with the participation of prostaglandin E2 and osteoblast stimulating factors[3]. In this report, we introduce a case of a paediatric patient who, following a haemorrhagic stroke, developed bilateral hip NHO with entrapment of the sciatic nerve and with the unusual involvement of both the paretic and nonparetic limbs. We describe our surgical approach and resection strategy.

CASE PRESENTATION

Chief complaints

A 13-yr-old boy with sickle cell trait presented with hip pain and limited range of motion.

History of present illness

The patient had a 5-mo history of painful bilateral hip stiffness that progressively impaired his gait. Extensive bilateral heterotopic ossification was seen on pelvic radiographs (Figure 1).

History of past illness

The patient had an history of right fronto-temporal haemorrhagic stroke because of an arteriovenous malformation, complicated with a right chronic subdural haemorrhage resulting in right facial nerve palsy with dyspraxia and left hemiplegia that has persisted since then.

Personal and family history

There is no personal and family history.

Physical examination

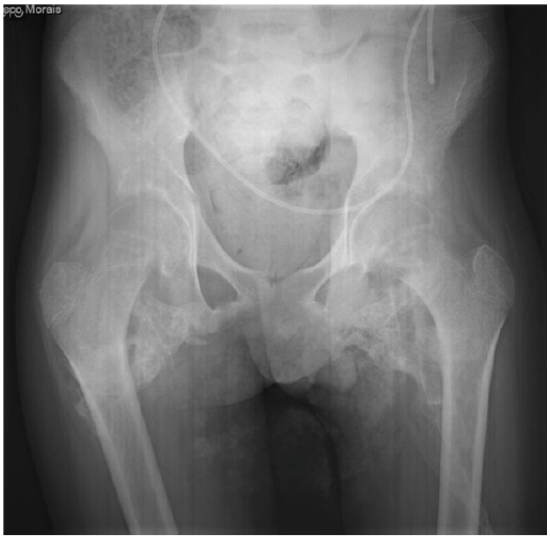
Motor examination revealed left spastic hemiparesis (0/5) with hyperreflexia and right side upper limb motor function of 4+/5 and 3/5 on the ipsilateral lower limb. The patient presented with painful, generalized and progressive limited passive range of motion of both hips, and soon was completely bedridden.

Laboratory examinations

There is no laboratory examinations.

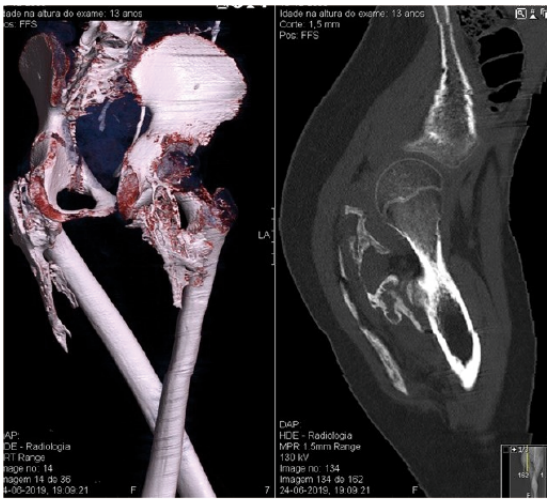
Imaging examinations

A computed tomography (CT) scan documented extensive calcification occupying the ischial-femoral space, with bilateral involvement of the posterior muscles of the thigh, mainly the external obturator, gemellus inferior and the proximal aspect of the biceps femoris. A 2.5 cm extension and oedema resulted in osseous incarceration of the proximal aspect of the sciatic nerve that was more evident on the right side (Figures 2 and 3).



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Figure 1 Antero-posterior pelvic radiograph showing extensive bilateral heterotopic ossification.



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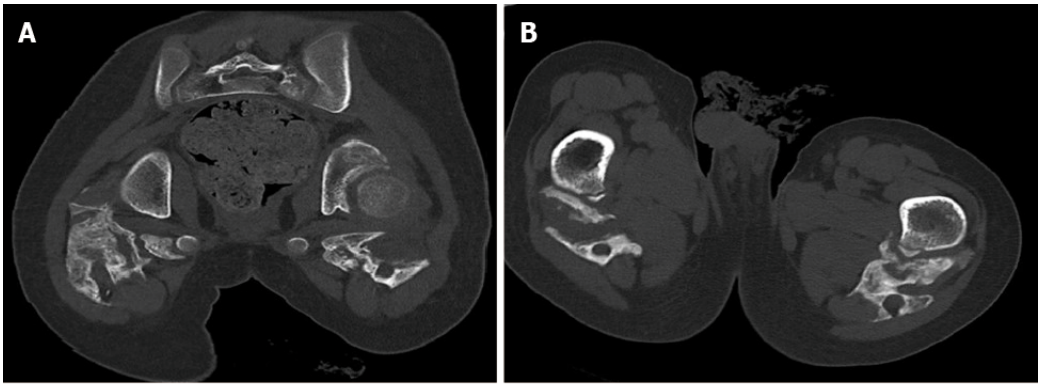
Figure 2 Computed tomography showing a bilateral bony bridge between the ischium and postero-medial proximal femur that limits hip range of motion.

FINAL DIAGNOSIS

The patient was diagnosed with posteromedial bilateral heterotopic ossification with entrapment of both proximal aspects of the sciatic nerve.

TREATMENT

Surgical resection of the ossified lesion and release of the sciatic nerve were performed, starting with the right hip. A modified posterior thigh approach that was developed by the senior author was used for both hips. The procedure was performed with the patient in a ventral position and began with a "lazy S" incision made in the centre of the gluteal region (Figure 4A). The gluteus maximus was detached from its distal insertion point on the proximal femur and retracted proximally, a manoeuvre intended to preserve gluteus vascularization from the superior gluteal artery. The sciatic nerve was then identified at both extremities of the ossification and subsequently released (Figure 4B and C). Note that a fibrous capsule that had formed between the nerve and the bone facilitated the dissection, which was performed with Kerrison forceps and meticulous haemostasis.



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Figure 3 Computed tomography and axial view. A: A proximal section showing ossification of the gluteal and posterior thigh musculature; B: A distal section showing ossification around the sciatic nerve.

OUTCOME AND FOLLOW-UP

Resection was performed on the left hip 6 wk later, and radiographic evaluation revealed a limited NHO relapse on the right hip (Figure 5A). Postoperatively, the patient began partial weight-bearing walking and participation in a rehabilitation program. After 1-yr of follow-up, there was no further development of the NHO lesions on radiographic evaluations and the patient had experienced a significant clinical improvement, being able to resume walking (Figure 5B).

DISCUSSION

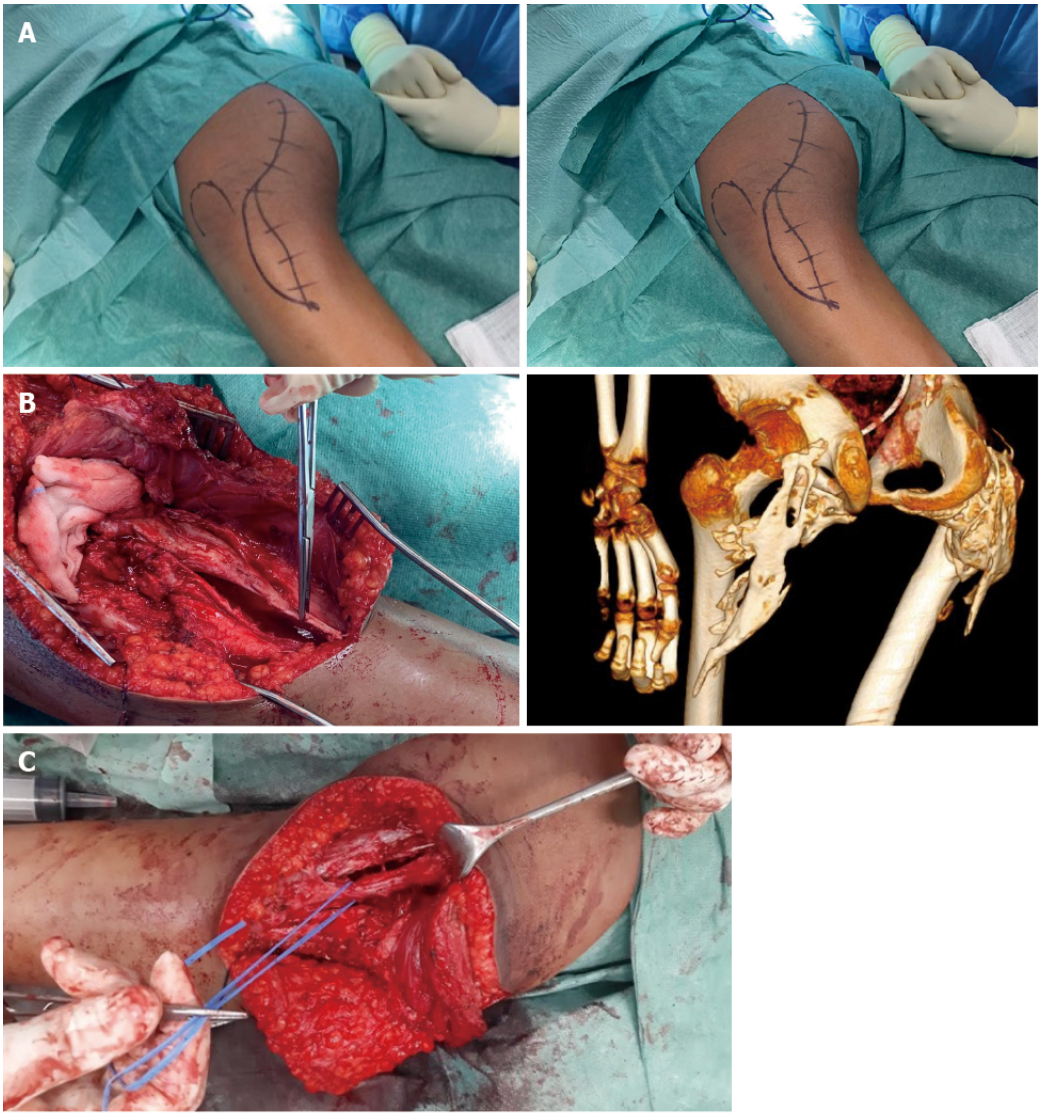
NHO is not often encountered in the paediatric population, and that has resulted in the use of diagnostic and treatment methods based on experience and evidence obtained in adults. To our knowledge, this is the first published case of a post-stroke bilateral NHO of the hip with sciatic nerve entrapment in a paediatric patient. Management of these patients is complex and requires multidisciplinary intervention. Even though there is a lack of evidence to support their effectiveness, and there are some conflicting viewpoints, conservative measures remain the first approach in the early stages of NHO. Pharmacological therapy with bisphosphonates and indomethacin has demonstrated efficacy in the early inflammatory phase of NHO, reducing disease progression. Non-steroidal anti-inflammatory drugs, particularly indomethacin, reduce the incidence of NHO in patients with spinal cord injury[4] but increase the risk of haemorrhagic complications that could be serious in patients with sickle cell trait, such as ours.

Furthermore, peri-articular radiation is considered another valid early-stage therapeutic modality that has been found to be more effective than non-steroidal anti-inflammatory drugs[5]. It is considered useful for inactivating the high mitotic rate of the pluripotent osteoprogenitor cells recruited by the inflammatory cascade and their differentiation into osteoblasts and chondrocytes[6]. Low-dose radiation therapy administered preoperatively or less than 72 h postoperatively represents an effective treatment [7], not only in reducing the size of NHO lesions[8] but also the risk of recurrence[9], with minimal side effects[10].

Another conservative treatment applied is physical therapy, but whether it plays a significant role in the mitigation of NHO lesions remains unclear. It has been suggested that forced manipulation of the extremity can induce HO formation by increasing inflammation[11], whereas lack of movement can cause HO formation and progression to ankylosis. Cautious use of a gentle range of motion is considered the best approach. In this case, we believe that recurrence of the HO on the right hip was promoted by the immobilization incurred while the patient waited for surgery of his left hip. It was only after both hips were operated and freed of ossification, and mobilization was resumed that the HO on the right side stopped progressing. Besides that, postoperative low-dose radiation therapy could have also contributed to minimization of the high risk for recurrence of HO lesions after resection on the right hip.

For this particular case, the patient presented with severe pain, gait impairment and the presence of signs of neurological compromise. It is generally agreed in the orthopaedic community[12] that fully matured hip HO limits the use and efficacy of conservative treatment modalities as curative options. Therefore, surgical intervention remains the mainstay for treatment of mature HO lesions.

First of all, surgical intervention should not aim for a complete resection, as this could incur an increased risk of haemorrhage and infection. A "functional" resection that increases mobility and alleviates pain is preferable. Furthermore, the location of the heterotopic ossification on the hip, which



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Figure 4 Intraoperative views. A: Lazy "S" incision in the gluteal region; B: Resection of ossified lesions; C: Release of the sciatic nerve path.

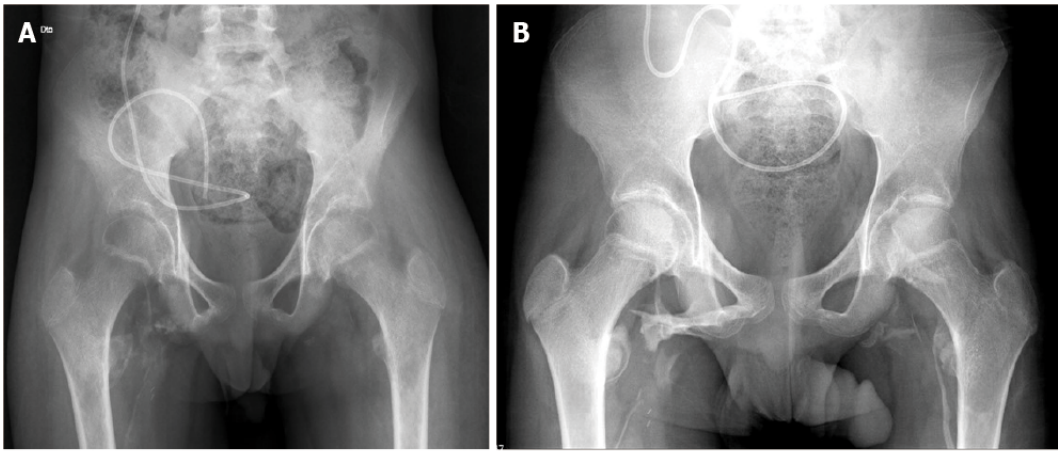
will guide the choice of surgical approach, is largely determined by certain aetiologies; for example, posterior lesions, like in our case, are typically associated with cerebral anoxia.

In our case, the heterotopic calcification had an extension below the plane of the greater gluteus muscle, from the trochanteric region to the ischiatic region. Traditional approaches (such as the postero-lateral Gibson approach) do not allow for a clear exposition of this space. The transgluteal approach has the disadvantage of muscle denervation, and proximal disinsertion of the greater gluteus muscle may jeopardize its vascularization (gluteal artery, branch of the internal iliac artery). Thus, through an S-shaped incision that allows a wide area of exposure, the distal tendinous release of the greater gluteus muscle and the progressive disinsertion of this muscle exposes the entire plane of the rotators and hamstrings (where the major HO lesion lies) without compromising innervation and vascularization.

Controversy persists in the timing of surgery. It is accepted that HO lesions should not be surgically treated until bone maturation is complete with presence of defined cortical margins, which often appear around 6 mo after the beginning of ossification. Some authors suggest waiting 18 mo[8,13]. A recent study suggests that the risk of recurrence is independent of the time to surgery. Early surgery was found to prevent the development of joint ankylosis, and subsequent induction of epiphyseal osteoporosis, progressive cartilage loss, loss of function, joint stiffness, and bone demineralization with increased risk of fracture.

CONCLUSION

A posterior approach of the gluteal region with gluteus maximus distal disinsertion from proximal



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Figure 5 Radiograph. A: Radiograph obtained immediately after left hip resection, note the regrowth of ossification on the right hip, which was treated first; B: Radiograph at 1 yr after surgery shows limited regrowth of heterotypic ossification on the right hip with signs of cortical maturation.

femur and proximal retraction with a meticulous sciatic nerve release are favorable therapeutic options for severe posterior heterotopic ossifications. This case illustrates the practical difficulties of managing such patients and reinforces the need for specific guidelines not only for treatment and timing but also for the use of adjuvant therapy in the paediatric population, for which the literature is sparse.

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REFERENCES

1 **O'Brien MM**, Murray T, Keeling F, Williams D. Intracerebral haemorrhage and hemiplegia with heterotopic ossification of the affected hip. *BMJ Case Rep* 2015; **2015** [PMID: 26243751 DOI: 10.1136/bcr-2015-211467]
2 **Urist MR**, Nakagawa M, Nakata N, Nogami H. Experimental myositis ossificans: cartilage and bone formation in muscle in response to a diffusible bone matrix-derived morphogen. *Arch Pathol Lab Med* 1978; **102**: 312-316 [PMID: 580725]
3 **Shehab D**, Elgazzar AH, Collier BD. Heterotopic ossification. *J Nucl Med* 2002; **43**: 346-353 [PMID: 11884494]
4 **Banovac K**, Williams JM, Patrick LD, Haniff YM. Prevention of heterotopic ossification after spinal cord injury with indomethacin. *Spinal Cord* 2001; **39**: 370-374 [PMID: 11464310 DOI: 10.1038/sj.sc.3101166]

5 **Cai L**, Wang Z, Luo X, She W, Zhang H. Optimal strategies for the prevention of heterotopic ossification after total hip arthroplasty: A network meta-analysis. *Int J Surg* 2019; **62**: 74-85 [PMID: 30615954 DOI: 10.1016/j.ijsu.2018.12.011]

6 **Meyers C**, Lisiecki J, Miller S, Levin A, Fayad L, Ding C, Sono T, McCarthy E, Levi B, James AW. Heterotopic Ossification: A Comprehensive Review. *JBMR Plus* 2019; **3**: e10172 [PMID: 31044187 DOI: 10.1002/jbm4.10172]

7 **Milakovic M**, Popovic M, Raman S, Tsao M, Lam H, Chow E. Radiotherapy for the prophylaxis of heterotopic ossification: A systematic review and meta-analysis of randomized controlled trials. *Radiother Oncol* 2015; **116**: 4-9 [PMID: 26163090 DOI: 10.1016/j.radonc.2015.05.022]

8 **Davis E**, Williams K, Matheney TH, Snyder B, Marcus KJ, Shore BJ. Radiation Prophylaxis for Hip Salvage Surgery in Cerebral Palsy: Can We Reduce the Incidence of Heterotopic Ossification? *J Pediatr Orthop* 2019; **39**: e386-e391 [PMID: 30543561 DOI: 10.1097/BPO.0000000000001314]

9 **Cipriano C**, Pill SG, Rosenstock J, Keenan MA. Radiation therapy for preventing recurrence of neurogenic heterotopic ossification. *Orthopedics* 2009; **32** [PMID: 19750999 DOI: 10.3928/01477447-20090728-33]

10 **Georhakopoulos I**, Kouloulias V, Kougiountzopoulou A, Platoni K, Antypas C, Liakouli Z, Nikoloudi S, Kelekis N, Moulopoulou LE, Zygogianni A. Radiation therapy for the prevention of heterotopic ossification: Efficacy and toxicity of single fraction radiotherapy. *Orthop Rev (Pavia)* 2020; **12**: 8577 [PMID: 32922703 DOI: 10.4081/or.2020.8577]

11 **Michelsson JE**, Rauschning W. Pathogenesis of experimental heterotopic bone formation following temporary forcible exercising of immobilized limbs. *Clin Orthop Relat Res* 1983; 265-272 [PMID: 6406124 DOI: 10.1097/00003086-198306000-00039]

12 **Winkler S**, Wagner F, Weber M, Matussek J, Craiovan B, Heers G, Springorum HR, Grifka J, Renkawitz T. Current therapeutic strategies of heterotopic ossification--a survey amongst orthopaedic and trauma departments in Germany. *BMC Musculoskelet Disord* 2015; **16**: 313 [PMID: 26494270 DOI: 10.1186/s12891-015-0764-2]

13 **Denormandie P**, de l'Escalopier N, Gatin L, Grelier A, Genêt F. Resection of neurogenic heterotopic ossification (NHO) of the hip. *Orthop Traumatol Surg Res* 2018; **104**: S121-S127 [PMID: 29174871 DOI: 10.1016/j.otsr.2017.04.015]

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LETTER TO THE EDITOR

Rates of readmission and reoperation after operative management of midshaft clavicle fractures in adolescents

Mohamed Kamal Mesregah

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Abstract

The present letter to the editor is a commentary on the study titled "Rates of readmission and reoperation after operative management of midshaft clavicle fractures in adolescents". There is a debate over whether surgical treatment of clavicle shaft fractures improves clinical outcomes in adolescents. The readmission and reoperation rates following surgery should be identified.

Key Words: Readmission; Reoperation; Clavicle fractures; Operative fixation; ORIF; Adolescents

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Core Tip: Most mid-shaft clavicular fractures in adolescents have been typically treated nonoperatively with satisfactory outcomes. There is a major controversy over whether surgical treatment of clavicle shaft fractures in adolescents improves clinical outcomes in the same way it does in adults. There is a need to conduct multiple prospective randomized studies or large comparative database studies to better assess the operative management.

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TO THE EDITOR

I read with great interest the retrospective study on the national rates of readmission

and reoperation after open reduction internal fixation (ORIF) of midshaft clavicle fractures in adolescents by Carrillo *et al*[1], published in your esteemed journal in December 2021 issue.

I agree with the authors that there is a need to identify the national readmission and reoperation rates following ORIF of midshaft clavicle fractures in adolescents. Most clavicular fractures in adolescents have been typically treated nonoperatively, especially those affecting the mid-shaft of the clavicle[2,3]. In adolescents, there remains a major controversy over whether surgical treatment of clavicle shaft fractures improves the clinical outcomes in the same way it does in adults[4].

For the purpose of Carrillo *et al*[1] study, the authors utilized the Healthcare Cost and Utilization Project State Inpatient Database (SID) for the years 2005-2012 in Florida and 2005-2009 in California. This database includes inpatient discharge records from community hospitals in those states.

For identification of patient cohort, the authors used two codes. The first code is CPT 23515 code, which by definition refers to (Open treatment of clavicular fracture, includes internal fixation when performed). However, the other code used by the authors is ICD-9 CM 79.39 code, which refers to (open reduction of fracture with internal fixation, other specified bone), which means that this code is not specific at all to the clavicular fractures. Therefore, I am afraid the authors included in the study adolescent patients with fractures in other body bones, other than clavicular fractures.

Moreover, the authors identified only 334 clavicle fractures in adolescents managed operatively. This number is considered low to determine readmission and reoperation rates in large database studies such as SID. The authors should at least have used SID for years up to 2020 in both states.

The authors also reported that 11 (3.3%) patients were readmitted within 90 d of surgery. However, this low rate is not clinically important as those 11 patients may have been admitted for other reasons unrelated to the index surgery.

Nonoperative care is the successful historical treatment and the current safest treatment for midshaft clavicular fractures in adolescents. Operative care is overused in adolescents for clavicle fractures. To better assess the operative management, there is a need to conduct multiple prospective randomized studies or large comparative database studies.

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REFERENCES

1 **Carrillo LA**, Wu HH, Chopra A, Callahan M, Katyal T, Swarup I. Rates of readmission and reoperation after operative management of midshaft clavicle fractures in adolescents. *World J Orthop* 2021; **12**: 1001-1007 [PMID: 35036342 DOI: 10.5312/wjo.v12.i12.1001]

2 **Gausden EB**, Fabricant PD. Management of Clavicle Fractures in Adolescents: A Critical Analysis Review. *JBJS Rev* 2018; **6**: e4 [PMID: 30204645 DOI: 10.2106/JBJS.RVW.17.00194]

3 **Lenza M**, Faloppa F. Conservative interventions for treating middle third clavicle fractures in adolescents and adults. *Cochrane Database Syst Rev* 2016; **12**: CD007121 [PMID: 27977849 DOI: 10.1002/14651858.CD007121.pub4]

4 **Yang S**, Andras L. Clavicle Shaft Fractures in Adolescents. *Orthop Clin North Am* 2017; **48**: 47-58 [PMID: 27886682 DOI: 10.1016/j.ocl.2016.08.007]



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Consensus Delphi study on guidelines for the assessment of anterior cruciate ligament injuries in children

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Abstract

Background: Knee examination guidelines in minors are intended to aid decision-making in the management of knee instability. Clinical question: A Delphi study was conducted with a formal consensus process using a validated methodology with sufficient scientific evidence. A group consensus meeting was held to develop recommendations and practical guidelines for use in the assessment of instability injuries in children. Key findings: there is a lack of evidence to analyse anterior cruciate ligament injuries in children and their subsequent surgical management if necessary. Diagnostic guidelines and clinical assessment of the patient based on a thorough examination of the knee are performed and a guide to anterior cruciate ligament exploration in children is developed. Clinical application: In the absence of a strong evidence base, these established guidelines are intended to assist in that decision-making process to help the clinician decide on the most optimal treatment with the aim of benefiting the patient as much as possible. Following this expert consensus, surgical treatment is advised when the

patient has a subjective sensation of instability accompanied by a pivot shift test ++, and may include an anterior drawer test + and a Lachman test +. If these conditions are not present, the conservative approach should be chosen, as the anatomical and functional development of children, together with a physiotherapy programme, may improve the evolution of the injury.

Key Words: Anterior cruciate ligament; Diagnoses and examinations; Sports injuries; Knee; Injury to minors

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Core Tip: A Delphi study was conducted with a formal consensus process using validated methodology with scientific evidence to develop recommendations and practical guidelines for the assessment of instability injuries in children. Following this expert consensus, surgical treatment is advised when the patient has a subjective sensation of instability accompanied by a pivot shift test ++, and may include an anterior drawer test + and a Lachman test +. If these conditions are not present, the conservative approach should be chosen, as the anatomical and functional development of children, together with a physiotherapy programme, may improve the evolution of the injury.

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INTRODUCTION

Physiopathology of the anterior cruciate ligament

The anterior cruciate ligament (ACL) has a viscoelastic capacity that provides the possibility of dissipating the energy received through adjustments in its length and in the internal distribution of loads[1,2], that is, it has the capacity to generate microscopic adjustments in relation to the internal stresses it has to withstand[3].

ACL injury occurs as a result of excessive force in the anterior translational direction of the tibia or rotation of the femur on the tibia[4].

The most common mechanism of ligament failure is the sequential rupture of bundles of collagen fibres distributed throughout the ligament and not located in a specific area. As it does not have the plastic capacity to deform, ruptures of the ligament are defined as total or partial. There is controversy regarding what is a partial rupture, and there are studies that define it as a hemorrhage in the femoral insertion while others define it as a rupture of the anteromedial and posterolateral fascicles. The American Medical Association establishes a classification in which partial tears correspond to second-degree ligament injuries. Another way of estimating the type of injury is in relation to the percentage of the ligament injured. Partial tears are considered to be between 25% and 75%[5-8]. Partial tears in turn can be classified as high grade when more than 50% of the fibres of the ligament are involved or low grade when the involvement is less than 50%[8].

In general, a partial ACL injury can be defined as a combination of the following factors[8]: (1) Asymmetrical Lachman test result; (2) Pivot Shift negative; (3) Measurement with KT-1000 less than or equal to 3 mm; and (4) Arthroscopic evidence of partial ACL injury.

Adults more frequently suffer ruptures in the medial substance while lesion settlement in children is more frequently observed between the layers of mineralized and non-mineralized fibrocartilage[9].

Once the histological rupture occurs, the ACL goes through four phases: inflammatory, epiligamentous regeneration, proliferative and remodeling. These states are similar to those occurring in other connective tissues but with peculiarities, probably related to two facts: Firstly, the ACL is immersed in the synovial fluid which, due to its characteristics, modifies cell metabolism and the inflammatory response, also preventing the formation of the fibrin clot necessary for the union of the ends of the rupture; furthermore, the vascularization of the ACL after rupture is compromised as the vascular branches that irrigate it also break[10-13]. The flow of synovial fluid is responsible for the fibrin clot not forming by dispersing the blood in the form of hemarthrosis[13]. As a consequence of this lack of fibrin clot there is a decrease in proteins of the extracellular matrix and cytosines such as fibrinogen and fibronectin and Willebrand factor within the ACL wound[14,15].

In injuries of tibial eminence fractures it has been observed that ACL fibres suffer plastic deformation with permanent elongation of the fibers. This fact may be responsible for residual clinical laxity even in cases where surgical reduction or healing has occurred[16].

Ethiopathogenesis of anterior cruciate ligament injuries

The mechanisms of injury are multifactorial and include both extrinsic and intrinsic causes[17-24].

The type of pattern of ACL injury depends on the degree of skeletal maturity, this fact may be related to differences in skeletal rigidity and conditions the type of injury in both groups. Tibial avulsion injuries and partial ACL ruptures are more frequent in patients with skeletal immaturity and complete ruptures are more frequent in mature or partially mature patients[25].

The ACL can be injured by two mechanisms, direct contact or non-contact. Approximately 70% of them are due to non-contact injury mechanisms[24-26]. Not all authors define ACL contact injuries in the same way; while some authors define them in relation to those that occur in the absence of contact between players, others define them as the absence of a direct blow to the knee. In fact, there are authors who define "non-contact injuries with disturbance" by referring to injuries resulting from body-body contact, but without direct trauma to the knee[25]. Contact injuries involve injurious mechanisms of hyperextension or excessive valgus stress while the mechanisms that occur in non-contact injuries occur during the development of rapid decelerations or rotations performed in gestures involving pivoting on a fixed foot[27]. In addition, non-contact injuries are often accompanied by an internal hip rotation. This body position in non-contact injuries leads to a collapse in knee valgus or "dynamic knee valgus"[28-30]. It has also been observed that in non-contact injuries the centre of body mass is delayed in relation to the supporting base[24]. Although, as indicated above, the type of injury may be influenced by the degree of skeletal maturity, the injury mechanisms are the same in children and adults[25].

Several studies have shown that non-contact injuries from team ball sports occur at a bending angle of less than 30°. Modifications of the knee valgus angle were observed: in basketball where there was an increase from 4° to 15° in 30 ms, in handball from 3° to 16° in 40 ms, and these periods coincide with the maximum vertical force[31-33]. From this it can be deduced that the valgus position in a relatively straight leg (15°-40°) may be a key factor in the risk of ACL injury. It has also been observed that female athletes with a higher risk of injury land in a position of higher dynamic valgus and high loads of separation. In alpine skiing, other situations are observed such as phantom foot mechanisms, boot-induced anterior drawer mechanisms or external valgus-rotation mechanism[34,35].

It is also important to know the injury mechanisms affecting the posterolateral complex (PCL) of the knee as they represent 16% of all ligament injuries of the knee; of the total PCL injuries only 28% occur in isolation, the rest being associated with ACL injury[36,37]. The common mechanisms of injury of this complex are related to forces in the posterolateral direction of the tibia, hyperextension of the knee and elevated external rotation of the tibia when the knee is in a position of partial flexion. The most frequent contexts in which these injuries occur are sports injuries, road accidents and falls[38].

Biochemical and structural changes following injuries to the ACL

After an injury at the level of the ACL, a significant increase in metalloproteinases and interleukins at the level of the matrix is observed. Due to the existence of poor vascularization of the articular cartilage and tendons of the knee, the possibility and capacity to eliminate these inflammatory cytokines is diminished. The effects of this difficulty in elimination, causes an increase in the activity of the same that can be translated with irreversible alterations at the level of the collagen and the anchorage points of the ACL[39].

Modifications have also been observed in terms of muscle mass and volume, with significant atrophy in the knee musculature of the injured extremity, mainly in the quadriceps, which may be related to the presence of edema in the knee joint[40]. Altered quadriceps activation and the appearance of asynchronous contractions of the medial and lateral ischiotibial muscles have been reported after these injuries[40]. The changes produced in the quadriceps muscle mass may be due to adaptations of the muscle fibres together with the formation of alternative substances at the level of the matrix[39]. Some of the adaptations that occur at the level of the muscle fibre are the transition from type I to type IIa or IIb muscle fibres. These adaptations are not suffered in the same way by the different muscles[39]. Together with this, the lack of use decreases the size of the myofibre and stimulation at the level of the motor neuron[39].

At the biochemical level, alterations have been found in alpha-2 macroglobulin, myostatin, protein-72, mechano GF-C24E, synovial fluid and histochemical alterations at the level of collagen and cartilage [39].

In relation to the alteration of collagen after ACL injury, studies by Li *et al*[41] reveal that the degradation of collagen after ACL injury is irreversible and is replaced by another type of less structured collagen, thus affecting the integrity of the structure as a whole. This alteration in the synthesis of the correct collagen may be related to a greater probability of developing post-traumatic osteoarthritis.

Most knees with ACL injury experience altered levels of anti-inflammatory chemotactic cytosines causing longer periods of inflammation. In addition, pro-inflammatory and proteoglycan chemicals have been identified with consequent deterioration of the knee joint in patients with ACL injury[41].

Variations in the levels of certain chondrocyte-degrading interleukins have also been observed[42]. In addition, these biochemical modifications can also influence the level of bone tunnels in ACL reconstructions[43]. Therefore, the synovial fluid will have a significant and important effect on knee recovery[41].

Risk factors for anterior cruciate ligament injury

Risk factors for injury are classified into extrinsic and intrinsic causes[17-24]. Intrinsic causes are related to factors specific to the individual such as genetic, hormonal, anatomical factors, gender, neuromuscular and cognitive function, as well as previous injury to the knee. Extrinsic causes are external to the individual and among these factors the most studied are the level and type of activity, the type and surface of play, environmental conditions and the material used for the development of the sport or activity[44].

It is interesting that trained athletes have a high risk of breakage[45]. This fact may be related to situations in which there is an increase in joint efficiency. This occurs in situations where the individual acquires a greater degree of skill after practicing joint movements, which causes a decrease in antagonistic coactivation, making the ACL the only joint stabilizer in these circumstances[46]. Other studies also show the synergy between the stabilizing function of the rotational laxity of the ACL and the antagonistic coactivation of the hamstrings[47].

Anatomical changes in the knee in relation to age and gender

The anatomical region with the highest number of injuries in children and adolescents is the knee, which suffers up to 60% of injuries in the sports environment[31]. Among knee injuries, ACL ruptures have a 10 times higher incidence than the rest of the injuries. The relationship between specific anatomical characteristics and the risk of ACL injury has been studied, as well as the relationship with changes in anatomical characteristics during the stages of growth and skeletal maturation. Kiapour Ata [48] in 2016 conducted a study in which he observed significant differences in both the size and orientation of the age-dependent ACL in both females and males in healthy knees. They presented preliminary results indicating that changes in ACL size in relation to length, cross-section and area are significantly different in boys than in girls. Although it was observed that the ACL became more vertical in both the sagittal and coronal planes with similar patterns in boys and girls, the area of the ACL (cross-section) increased more in boys during early school age and late adolescence while girls showed this modification only when they became adolescents[48]. The same author also studied modifications of femoral condyles in relation to age and sex: Both bicondylar width and intercondylar notch increased continuously in boys after becoming adolescents, remaining constant in young adolescents; girls showed a higher medial femoral condyle curvature in late adolescents compared to boys of the same age and a more curved lateral femoral condyle compared to boys. They also found age-related anatomical modifications of the tibial plateau in both girls and boys. There was a difference in size, more pronounced in boys; slope, greater in girls; and depth, greater in boys, of the tibial plateau between girls and boys in the stages following skeletal maturation[49-52].

Risk factors for ACL rupture in skeletally immature patients

Risk factors for ACL rupture in skeletally immature patients are divided into intrinsic and extrinsic factors.

The most studied, and therefore best known, intrinsic factors are those related to anatomy: increased pelvic tilt, increased femoral anteversion, increased Q-angle, increased tibial slope fall, increased foot pronation, scaphoid fall and decreased intercondylar notch[48,50]. Also very important as a risk factor is female gender where ACL ruptures are 6 times more frequent compared to men[50]. In relation to this data, it is known that female patients are usually accompanied by data on hypermobility-hyperlaxity together with genu valgus and genu recurvatum[51].

In relation to hormonal factors, the relationship between the phase of the menstrual cycle and rupture of the ACL has been observed to be greater in the follicular phase where the concentration of estrogen is higher[50].

In relation to extrinsic factors, the most important are climatic conditions, footwear and its interaction with the playing field and court.

During summer conditions of light rain followed by evaporation of the same, this causes the surface to harden increasing ACL injuries in these conditions. It has also been studied how certain characteristics of footwear such as size, height and position of the lateral margin of the sole may increase ACL injuries[48,50,52].

Risk factors for injury to the anterior cruciate ligament in relation to its size

As previously mentioned, anatomical conditions are important in ACL injuries. The size of the ACL may be a risk factor for injury in those cases where there is a decrease in the size of the ACL. Davis *et al* [53] and Dienst *et al*[54] have presented studies relating the size of the ACL to greater risk of injury in load situations.

Intercondylar notch is another factor to be taken into account. Narrow intercondylar notches are associated with risk of ACL injury. Narrow intercondylar notches cause increased loading on the ACL [55-59]. With the consequent risk of injury; the correlation between narrow intercondylar notches and small ACLs has also been observed, with the width of the intercondylar notch being connected to the area of the ACL cross-section in pediatric populations, and is responsible for 24%-26% of the variations in the ACL cross-section area[48]. Narrow intercondylar notches produce a mechanical impact on the ACL and may have a tearing effect on the ACL when subjected to repetitive and high-risk movements, reducing the structural properties of the ligament over time[48].

Female sex in young adolescents is a risk factor for ACL injury, giving them a different anatomical profile[38]. One of the causes that may explain this fact may be related to a decrease in the inter-conditional space in this population of young adolescents compared to boys of the same age. Young adolescents also present steeper lateral tibial slopes and deeper tibial columns with the consequent greater risk of ACL injury[60-67].

As mentioned above, increased load on the ACL is associated with increased risk of ACL injury. The steep slopes of the posterior tibial plateau are related to this fact[68-74]. In activities involving weight loading, the posterior tibial slope causes a component of anterior shear force due to axial compression force[70].

The increase in the posterior tibial slope is found to be increased in adolescent girls[48] and may cause an increase in anterior tibial shear force[71-73] due to an acceleration of anterior tibial translation [74] with consequent damage to the ACL. Smaller tibial columns will stabilize less the femoral external rotation and femoral translation and may also cause an increase in ACL load[75,76].

Tibial depth has also been associated with the risk of ACL injury in cases where there is less medial tibial depth by providing less resistance to anterior tibial translation[71,72].

Risk factors related to the muscular state

There is no unanimity among the various authors on the correlation between an alteration at the muscular level and ACL injuries. Authors such as Zaínos *et al*[26] present a direct relationship between imbalances in the agonist-antagonist muscles of the knee together with muscle fatigue as with ACL injury. This author states that high levels of fatigue can lead to altered motor control leading to muscle imbalances, although there are not many studies that prove these claims. In the same vein, Orchard *et al* [77] indicate that excessive extensor force of the quadriceps muscles together with a decrease in the flexor force of the posterior femoral muscles are related to ACL injury. For Malinzak *et al*[78], motor control may be related to postures that put the ACL at risk in fact when a rapid lower limb maneuver will cause an angular change and an imbalance of the knee and hip; these modifications cause muscle adjustments that increase the risk of ACL injury. However, Garrido[79] and Benell *et al*[80] state that there is no relationship between knee muscle imbalances and ACL injury.

Associated injuries in anterior cruciate ligament injury

ACL injury may occur in isolation or be associated with injuries to other structures. In general, the structures most commonly associated with ACL injuries are: Meniscal injuries: These may appear in conjunction with ACL injury in 30% to 60% of individuals. The external meniscus injury is the most frequent in acute ACL injuries and the internal meniscus injury in patients with chronic instabilities[80-82]. Chondral injuries: from bone edema to impacted fractures and even osteochondral fragments[83]. Capsuloligamentous lesions: Usually appear when there are combined injury mechanisms.

Different authors have identified the appearance of associated lesions in relation to sex and age. Posterolateral contusion of the tibial plate tends to appear more frequently in women, while involvement in the external femoral condyle and soft tissue is more prevalent in men. Similarly, a higher rate of patellar tendon rupture has been observed in the adolescent population[84-86].

MATERIALS AND METHODS

A national group of surgeons, physiotherapists, basic scientists, orthopaedic surgeons and paediatric orthopaedic surgeons with experience in ACL instability was convened. A formal consensus process was conducted using a validated methodology. We reviewed the existing literature, held a consensus group meeting to develop recommendations, followed by a broader consultation meeting with an open invitation for final ratification. We conducted an iterative consensus (Delphi) study involving national and international experts in anterior cruciate ligament diagnosis. Group members were recruited through expressions of interest and specific invitations from experts. The Delphi study consisted of four rounds of anonymous surveys. Rounds 1 and 2 involved the generation and ranking of an extensive list of possible characteristics. In rounds 3 and 4, participants were presented with the results of previous rounds and asked to agree on a set of preliminary criteria. Panel participants (n = 34, range by Round 28-30) were predominantly highly experienced clinicians, representing a variety of clinical experience and all inhabited continents. Based on the initial rounds, a set of preliminary criteria was developed, incorporating three levels of diagnostic certainty: healthy ligament, partial rupture and suspected

complete rupture. Consensus was reached in Round 4, with a very high level of agreement (> 89%) for all levels of criteria and subcategories. The adoption of the criteria was supported by 96% of the panel members and the guidelines were reviewed and authorised by the NEUMUSK research group, followed by the trauma and orthopaedic specialists of the CEMTRO clinic in Madrid before final publication.

RESULTS

Following the literature review and the multidisciplinary group meeting, an assessment including the following screening tests is proposed.

ACL evaluation

The assessment of ACL injury is mostly clinical[87-92]. Different exploration tests have been described to assess the integrity or insufficiency of the ACL throughout history.

Georges K Noulis in 1875 first described the Trillat-Lachman test to evaluate ACL integrity with the knee in extension. In 1938, Palmer first discussed the "drawer sign" indicating that the positivity of this sign is a pathognomonic sign of ACL rupture. In 1960, Ritchei described Trillat-Lachman's technique again and 1976 Torg *et al*[93] (Lachman's student) described the test and made it known. The test described by John Lachman and released by Torg demonstrated the biomechanical superiority of the test over the previous drawer test. In 1976, Hughston *et al*[49] presented a classification of knee ligament instabilities and indicated that the ACL increases in association with ACL tear and posterior oblique ligament injury. In 1968, Slocum *et al*[101] defined and described a technique for "rotational instability" of the knee in relation to injury of the medial and ACL components[94-102]. Also in this year, Galway and Macintosh described the phenomenon of pivot shift in relation to rupture of the external capsule with injury of the ACL[98].

The Lachman test has a sensitivity of 62% and a specificity of 82% and is a sign of laxity. It is more sensitive for fibres in the posterolateral beam. The anterior drawer test has a sensitivity of 56% and a specificity of 82% and is a sign of ACL rupture. It is more sensitive for fibres in the anteromedial beam [99,100]. There is a variety of the anterior drawer test that is externally rotated and specifically allows assessment of posterior-internal structures[102].

The pivot shift test, Jerk test, has a sensitivity of about 90%. The existence of concomitant lesions such as LLI rupture, iliotibial strap rupture or mechanical interposition may make this test difficult[99].

For a correct diagnosis it is necessary to establish the difference between laxity and instability[102]: Laxity: Objective and quantifiable exploratory sign in relation to capsuloligamentous insufficiency. Instability: Subjective symptom of discomfort experienced by the patient.

The loss of stability of the knee is objectified according to the existence of laxity in the knee. The AOSSM (American Orthopaedic Society for Sports Medicine) Committee on Research and Education classifies them as follows[103]: Non-rotating, single plane linear: There are several types (anterior, posterior, internal and external). It is graded from 0 to 3 through the anterior drawer tests: 0: Normal laxity; 1 +: Anterior translation less than 0.5 cm; 2 ++: Anterior translation between 0.5 cm and 1 cm; 3 +++: Anterior translation between 1 cm and 1.5 cm.

Rotary, single or two-plane: they can be: Anterointernal: Abduction, external rotation and tibial anterior translation. It causes the internal tibial plate to move or sublux anteriorly in relation to the femur. Posterointernal: This occurs when there is a posterior translation of the internal tibial plate in relation to the femur. Anteroexternal: Excessive anterior translation of the external tibial plate. Postero-external: posterior translation of the external tibial plate.

Combined: all types of combinations can be found, the most common being: Anterointernal/antero-external, anterointernal/posterointernal and anterointernal/posteroexternal. Considering the approach followed by Guillén García *et al*[104] and his team regarding the diagnosis of knee stability, different criteria should be followed: (1) Anatomical: The proximal and distal insertion of the ACL is behind the femoral axis. This is why when the lesion mechanism is produced by a knee rotation and the foot is fixed, the ACL and menisci are broken; (2) Biomechanical: It is impossible for the PCL to be the axis of the knee. The PCL changes its angular arrangement on the tibial platform between 20º and 85º in relation to the knee's flexo-extension angle; and (3) Clinical: Both the healing and the tolerance of the patient to the ACL rupture are bad in contrast to the PCL in which maintaining a state of rest produces its healing and the tolerance of isolated injuries of the same by the patient are good.

In relation to the above, the classification of knee instabilities is as follows: Anterior laxity: Anterior laxity: Isolated ACL tear (very rare); Anteromedial laxity: ACL rupture next to the medial system; Antero-posterolateral laxity: ACL rupture next to the posterolateral system. Posterior laxity: Posterior laxity: Isolated PCL tear; Posteromedial laxity: Rupture of the PCL next to the posteromedial system; Posterolateral laxity: LCP rupture together with the posterolateral system. Combined antero-posterior laxity: ACL, PCL rupture along with medial or lateral systems.

Description of ACL assessment test

Before performing the specific tests, the healthy knee should be explored as a control for guidance. The

tests that produce the least pain should be started first to prevent the muscle spasm from interfering with the rest of the tests.

Lachman test: This is the main test to be carried out on an acute injury[100]. It is performed with the knee in a 30° knee flexion position and a force is applied in an anterior direction. It is considered positive in cases where the anterior displacement of the tibia is increased compared to the contralateral knee. It is important to note the end point of tibial displacement. This end point is soft or weak when there is a break in the ACL[100-105].

Anterior drawer flex/rotate test: Combines Lachman's test and lateral pivot shift. Both hands are used to firmly grip the calf and move the knee in a 15° to 30° flexion arc. When the ACL is broken, at 15° of flexion there is an anterior subluxation of the tibia and an external rotation of the femur. Increasing the flexion to 30° produces a posterior reduction of the tibia and an internal rotation of the femur[106]. There are authors who claim that this test has less sensitivity than Lachman's test, although it has more sensitivity than the tibial shift tests[107].

Anterior drawer test: This test assesses the anteroposterior femorotibial displacement with a starting position of 90º knee flexion and 45º hip flexion and the foot fixed on the table. From this position, traction and pressure movements are performed in a neutral anterior and posterior position, respectively; to put the capsuloligamentous structures in tension, the test is performed in internal rotation and external rotation. An important detail is to check the initial tibial starting point; if there is an injury at the level of the PCL it could give a false anterior tibial displacement when performing the technique[108].

Hughston *et al*[109] in 1976 described this technique by performing a proximal measurement in the tibia between the thumb and other fingers; the hamstrings are palpated to see if they are relaxed. From this position, an anterior tibial traction is performed to evidence the existence of laxity. If an end point is seen at the limit of the displacement, it is indicative of the continuity of the ACL. If the consistency of the endpoint is spongy and lacking in firmness, it is indicative of rupture of the ACL.

Anterior Neutral Box: The starting position is with the tibia in neutral position. If the test is positive it may be due to injury in: ACL, ACL and internal complex, ACL and external complex or both complexes [110].

Anterior drawer-external rotation: The starting position is with the external rotation of the tibia. In this position the structures of the internal complex are tightened. A moderate positive test result indicates injury of the internal complex, while a strong positive test result indicates injury of the posterior internal angle[101].

Anterior drawer test-Internal Rotation: The starting position is with tibial internal rotation. In this position the structures of the external complex are tightened. A moderate positive result indicates injury to the structures of the external complex. If it is intense positive, we must also think of injury of the PCL together with the structures of the external compartment (LCE, external capsule and posterior-external angle). In this case a further assessment of the postero-external capsule can be made by testing the external rotation recurvatum[109].

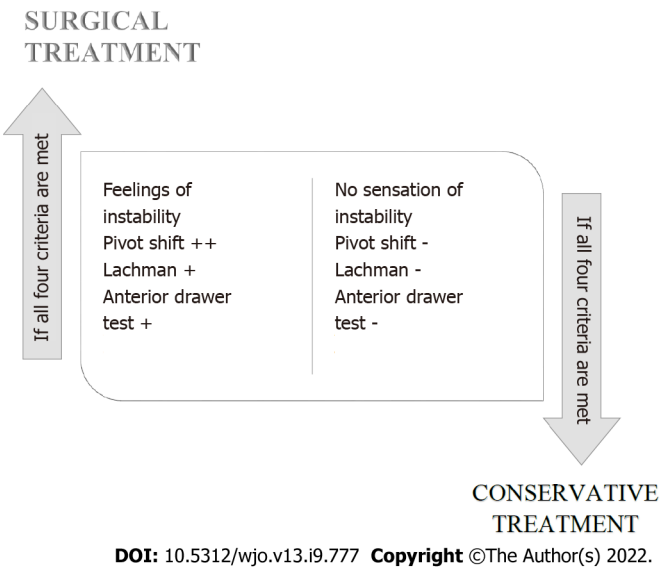
Pivot shift test: The starting position is in knee extension and valgus along with internal rotation of the tibia. A progressive flexion of the tibia is performed and towards 30° a posterior displacement of the tibia is felt on the femur. This displacement appears as a consequence of the reduction of the anterior subluxation of the tibia[110].

Hughston's jerk test: A 45° hip flexion is performed with the knee at 90°. A valgus force is applied and the knee is extended with the tibia in internal rotation. The test is positive when there is a transitory anterior subluxation of the tibia on the femur over the 30° of flexion, with a spontaneous reduction occurring as the knee is extended[109].

Test of internal rotation of the tibia: The starting position is with flexion of 45° or more of the knee and external rotation of the tibia. From this position, the leg is progressively extended, allowing internal rotation to occur while applying a valgus force with anterior pressure applied behind the head of the fibula. This produces anterior subluxation of the anterolateral tibia. As the knee approaches full extension, the tibia is reduced, producing an audible "snap"[111].

Slocum test: The patient is placed in the lateral position with the knee and hip of the healthy lower limb flexed. The pathological knee is placed in contact with the table in an extended position. Palpation of the fibula head is performed with the index finger of the left hand while the index finger of the right hand contacts the external femoral condyle. To perform the technique, a valgus force is applied to the knee in flexion. When the ACL is insufficient, the anterior subluxation of the tibia is reduced by reaching 30° of knee flexion. The reduction is felt with the fingers[112].

Figure 1 shows the summary diagram of the decision-making process regarding the assessment of the ACL and the decision to carry out conservative or surgical treatment.



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Figure 1 Diagram of the decision-making process regarding the assessment of the anterior cruciate ligament.

Capsuloligamentary complex and meniscus evaluation

In order to assess the existence of an associated lesion, together with the analysis of the stability of the knee, an exploration of the rest of the structures of the knee should be performed, paying special attention to the menisci and the internal and external collateral ligaments[100].

Evaluation of capsuloligamentous structures

When there is an ACL lesion, the study and assessment of the capsuloligamentary structures should include the assessment of both the external/internal collateral complex and the postero-internal and postero-external capsular complex. For this purpose, both the valgus and the forced varus must be evaluated both in full extension and in 30º flexion. It is important to increase strength progressively to the point of onset of pain to verify maximum laxity without the appearance of muscle spasm[112,113].

Valgus in extension: When the test is positive, the structures that may be damaged are: the superficial and deep portion of the LCM, posterior oblique ligament, PAPI, peripheral disinsertion of the medial meniscus and ACL. If it is very severe there could be injury of the PCL[85].

Valgus in 30° flexion: A slight positivity in the test will indicate a rupture of the superficial portion of the LLI. If the result is a severe yawn, other structures of the internal complex besides the ACL and PCL will also be affected[85].

Varus in extension: When the test is positive it will indicate injury of the LLL, middle capsule, arcuate ligament and Maissiat band, in addition to the ACL. If it is very severe, the PCL will also be injured[85].

Varus at 30° flexion: Mild external yawning indicates injury to the CLL. If the test result is very severe there will be injury to the medial capsule, the Maissiat band and the arcuate ligament[85].

Meniscal evaluation

It is essential to assess the presence or absence of meniscal pathology concomitant to ACL injuries. The diagnosis will obviously be clinical through evaluative tests that can be divided into[114]: (1) Tests that cause pain or clicks with palpation of the interline; (2) Tests that generate pain with rotation of the tibia on the femur.

With regard to the reliability of the meniscal tests, several studies have tried to prove the effectiveness of the different meniscal tests. There are differences in results between the researchers. Both types of evaluation tests have low diagnostic value when applied individually, increasing their usefulness when combined with the clinical history[114]. A cross-sectional study by Gobbo *et al*[115] in 2011, studied the sensitivity and specificity of the McMurray, Steinmann I, Steinmann II, Childress and Apley tests for both the medial and lateral meniscus. The analysis showed that the sensitivity for the medial meniscus was 89% and the specificity was 31% while for the lateral meniscus the sensitivity was 85% *vs* a specificity of 24%. This study corroborates the data presented previously that tests performed in isolation have a lower diagnostic value. In relation to the independent analysis of each test, the Apley test has the best specificity for both the medial and the lateral meniscus. In relation to the precision for detecting lesions, greater precision was obtained in the evaluation of lesions in the medial meniscus than in the lateral meniscus, except for the Apley test which showed the same predictive value for both

the lateral and medial meniscus lesions[115].

Genufonía

The knee has its own language with which it communicates what is happening to it. This language does so through sound. It is important to listen to the sounds that the knee shows us during its movement, which will help us to extract information about your injury[116].

DISCUSSION

ACL injuries are common in sports. Most ACL injuries are non-contact in nature and usually occur in certain athletic tasks. Complete ACL tears can lead to chronic knee problems, such as knee instability, damage to the meniscus and chondral surface, and osteoarthritis. Due to the increasing participation of children and adolescents in both organized sports and intense sports training at an early age, the number of ACL injuries in this age group has increased, accounting for 3.3% of ACL injuries[68-74].

Practice is not yet standardised and the literature to guide decision-making in children is very limited. This consensus process has been based on the expert experience of a diverse group of professionals treating and dealing with this injury, their thorough examination and subsequent decision-making focused on the prior assessment of the patient, and sometimes based on the experience of the healthcare professional conducting the patient study.

Although there is level 1 clinical evidence on screening for ACL rupture, this process is based on the practical and clinical experience of the examiner. However, there are few manuscripts that include screening for this injury in minors, so these guidelines have been developed in the healthcare setting. This consensus has been developed by a large group of experts in the field and has resulted in a solid and established method for the development of guidelines in the healthcare of the pathology in question. We believe that the knee has its own language with which it communicates what is happening to it. This language is expressed through sound, which is why the term genufonia is coined[116]. It is important to listen to the sounds that the knee shows us during its movement, which will help us to extract information about its injury.

It can be seen that the consensus statements cover the assessment and screening of ACL rupture in children. A decision is made in the evaluation of patients, depending on whether surgical treatment [117] or conservative treatment will be chosen.

CONCLUSION

ACL rupture is a complex pathology with multiple approaches that should be based primarily on patient assessment and evaluation. In the absence of a solid evidence base and the lack of consensus in the literature on the approach and exploration of this injury in minors, these established guidelines aim to contribute to that decision-making process to assist the clinician in performing the most optimal treatment with the goal of benefiting the patient as much as possible. Following this expert consensus, surgical treatment is advised when the patient has a subjective sensation of instability accompanied by a pivot Shift ++ test, and may include an anterior drawer + test and Lachman + test. If these conditions are not present, the conservative approach should be chosen, as the anatomical and functional development of the children, together with a physiotherapy programme, can improve the evolution of the injury.

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REFERENCES

1 **Woo SL**, Hollis JM, Adams DJ, Lyon RM, Takai S. Tensile properties of the human femur-anterior cruciate ligament-tibia complex. The effects of specimen age and orientation. *Am J Sports Med* 1991; **19**: 217-225 [PMID: 1867330 DOI: 10.1177/036354659101900303]
2 **Chu D**, LeBlanc R, D'Ambrosia P, D'Ambrosia R, Baratta RV, Solomonow M. Neuromuscular disorder in response to anterior cruciate ligament creep. *Clin Biomech (Bristol, Avon)* 2003; **18**: 222-230 [PMID: 12620785 DOI: 10.1016/s0268-0033(03)00002-0]
3 **Gabriel MT**, Wong EK, Woo SL, Yagi M, Debski RE. Distribution of in situ forces in the anterior cruciate ligament in response to rotatory loads. *J Orthop Res* 2004; **22**: 85-89 [PMID: 14656664 DOI: 10.1016/S0736-0266(03)00133-5]
4 **DeMorat G**, Weinhold P, Blackburn T, Chudik S, Garrett W. Aggressive quadriceps loading can induce noncontact anterior cruciate ligament injury. *Am J Sports Med* 2004; **32**: 477-483 [PMID: 14977677 DOI: 10.1177/0363546503258928]
5 **Noyes FR**, Mooar LA, Moorman CT 3rd, McGinniss GH. Partial tears of the anterior cruciate ligament. Progression to complete ligament deficiency. *J Bone Joint Surg Br* 1989; **71**: 825-833 [PMID: 2584255 DOI: 10.1302/0301-620X.71B5.2584255]
6 **Lamar DS**, Bartolozzi AR, Freedman KB, Nagda SH, Fawcett C. Thermal modification of partial tears of the anterior cruciate ligament. *Arthroscopy* 2005; **21**: 809-814 [PMID: 16012493 DOI: 10.1016/j.arthro.2005.03.003]
7 **Messner K**, Maletius W. Eighteen- to twenty-five-year follow-up after acute partial anterior cruciate ligament rupture. *Am J Sports Med* 1999; **27**: 455-459 [PMID: 10424214 DOI: 10.1177/03635465990270040801]
8 **DeFranco MJ**, Bach BR Jr. A comprehensive review of partial anterior cruciate ligament tears. *J Bone Joint Surg Am* 2009; **91**: 198-208 [PMID: 19122096 DOI: 10.2106/JBJS.H.00819]
9 **Souryal TO**, Freeman TR. Intercondylar notch size and anterior cruciate ligament injuries in athletes. A prospective study. *Am J Sports Med* 1993; **21**: 535-539 [PMID: 8368414 DOI: 10.1177/036354659302100410]
10 **Bolívar-Arroyo V**, Raya-Villarraso A, Garrido-Gómez J. Anterior cruciate ligament injury. New treatment options by tissue engineering. *Actual Medica* 2014; 99: 157-161 [DOI: 10.15568/am.2014.793.re02]
11 **Woo SL**, Vogrin TM, Abramowitch SD. Healing and repair of ligament injuries in the knee. *J Am Acad Orthop Surg* 2000; **8**: 364-372 [PMID: 11104400 DOI: 10.5435/00124635-200011000-00004]
12 **Murray MM**, Martin SD, Martin TL, Spector M. Histological changes in the human anterior cruciate ligament after rupture. *J Bone Joint Surg Am* 2000; **82**: 1387-1397 [PMID: 11057466 DOI: 10.2106/00004623-200010000-00004]
13 **Andersen RB**, Gormsen J. Fibrin dissolution in synovial fluid. *Acta Rheumatol Scand* 1970; **16**: 319-333 [PMID: 4099587 DOI: 10.3109/rhe1.1970.16.issue-1-4.37]
14 **Murray MM**, Spindler KP, Ballard P, Welch TP, Zurakowski D, Nanney LB. Enhanced histologic repair in a central wound in the anterior cruciate ligament with a collagen-platelet-rich plasma scaffold. *J Orthop Res* 2007; **25**: 1007-1017 [PMID: 17415785 DOI: 10.1002/jor.20367]
15 **Murray MM**, Spindler KP, Devin C, Snyder BS, Muller J, Takahashi M, Ballard P, Nanney LB, Zurakowski D. Use of a collagen-platelet rich plasma scaffold to stimulate healing of a central defect in the canine ACL. *J Orthop Res* 2006; **24**: 820-830 [PMID: 16555312 DOI: 10.1002/jor.20073]
16 **Trivedi V**, Mishra P, Verma D. Pediatric ACL Injuries: A Review of Current Concepts. *Open Orthop J* 2017; **11**: 378-388 [PMID: 28603569 DOI: 10.2174/1874325001711010378]
17 **Boden BP**, Dean GS, Feagin JA Jr, Garrett WE Jr. Mechanisms of anterior cruciate ligament injury. *Orthopedics* 2000; **23**: 573-578 [PMID: 10875418 DOI: 10.3928/0147-7447-20000601-15]
18 **McNair PJ**, Marshall RN, Matheson JA. Important features associated with acute anterior cruciate ligament injury. *N Z Med J* 1990; **103**: 537-539 [PMID: 2243642]
19 **Hewett TE**, Lindenfeld TN, Riccobene JV, Noyes FR. El efecto del entrenamiento neuromuscular sobre la incidencia de

lesiones de rodilla en atletas femeninas. Un estudio prospectivo. *Am J Sports Med* 1999; **27**: 699-706 [PMID: 10569353 DOI: 10.1177/03635465990270060301]

20 **Ireland ML**. Anterior cruciate ligament injury in female athletes: epidemiology. *J Athl Train* 1999; **34**: 150-154 [PMID: 16558558]

21 **Nichol Allison M**. Literature Review of Female Anterior Cruciate Ligament Injuries. *Senior Honors Theses* 2004; 88 [DOI: 10.1034/j.1600-0838.2002.120201.x]

22 **Romero D**. Analysis models for the prevention of sports injuries. Epidemiological study of injuries: The UEFA model in football. *Apunts Medicina de l'Esport* 2010; **45**: 95-102 [DOI: 10.1016/j.apunts.2010.02.007]

23 **Silvers HJ**, Mandelbaum BR. Prevention of anterior cruciate ligament injury in the female athlete. *Br J Sports Med* 2007; **41** Suppl 1: i52-i59 [PMID: 17609222 DOI: 10.1136/bjsm.2007.037200]

24 **LaBella CR**, Hennrikus W, Hewett TE; Council on Sports Medicine and Fitness, and Section on Orthopaedics. Anterior cruciate ligament injuries: diagnosis, treatment, and prevention. *Pediatrics* 2014; **133**: e1437-e1450 [PMID: 24777218 DOI: 10.1542/peds.2014-0623]

25 **McKay S**, Chen C, Rosenfeld S. Orthopedic perspective on selected pediatric and adolescent knee conditions. *Pediatr Radiol* 2013; **43** Suppl 1: S99-106 [PMID: 23478925 DOI: 10.1007/s00247-012-2587-8]

26 **Zahínos JI**, González C, Salinero J. Epidemiological study of the injuries, the processes of readaptation and prevention of the injury of anterior cruciate ligament in the professional football. *JSHR* 2010; **2**: 139-150 [DOI: 10.1016/0020-1383(87)90216-6]

27 **Dorizas JA**, Stanitski CL. Anterior cruciate ligament injury in the skeletally immature. *Orthop Clin North Am* 2003; **34**: 355-363 [PMID: 12974485 DOI: 10.1016/s0030-5898(02)00072-x]

28 **Hewett TE**, Myer GD, Ford KR. Lesiones del ligamento cruzado anterior en atletas femeninas: parte 1, mecanismos y factores de riesgo. *Am J Sports Med* 2006; **34**: 299-311 [DOI: 10.1177/0363546505284183]

29 **Hewett TE**, Torg JS, Boden BP. Video analysis of trunk and knee motion during non-contact anterior cruciate ligament injury in female athletes: lateral trunk and knee abduction motion are combined components of the injury mechanism. *Br J Sports Med* 2009; **43**: 417-422 [PMID: 19372088 DOI: 10.1136/bjsm.2009.059162]

30 **Boden BP**, Torg JS, Knowles SB, Hewett TE. Video analysis of anterior cruciate ligament injury: abnormalities in hip and ankle kinematics. *Am J Sports Med* 2009; **37**: 252-259 [PMID: 19182110 DOI: 10.1177/0363546508328107]

31 **Kirkendall DT**, Garrett WE Jr. The anterior cruciate ligament enigma. Injury mechanisms and prevention. *Clin Orthop Relat Res* 2000; 64-68 [PMID: 10738415 DOI: 10.1097/00003086-200003000-00008]

32 **Teitz CC**. Video analysis of ACL injuries. In: Griffin LY, ed. Prevention of noncontact ACL injuries. Rosemont, IL: American Association of Orthopaedic Surgeons. 2001; 87–92 [DOI: 10.5040/9781718209725.ch-016]

33 **Olsen OE**, Myklebust G, Engebretsen L, Bahr R. Injury mechanisms for anterior cruciate ligament injuries in team handball: a systematic video analysis. *Am J Sports Med* 2004; **32**: 1002-1012 [PMID: 15150050 DOI: 10.1177/0363546503261724]

34 **Krosshaug T**, Slauterbeck JR, Engebretsen L, Bahr R. Biomechanical analysis of anterior cruciate ligament injury mechanisms: three-dimensional motion reconstruction from video sequences. *Scand J Med Sci Sports* 2007; **17**: 508-519 [PMID: 17181770 DOI: 10.1111/j.1600-0838.2006.00558.x]

35 **Natri A**, Beynnon BD, Ettlinger CF, Johnson RJ, Shealy JE. Alpine ski bindings and injuries. Current findings. *Sports Med* 1999; **28**: 35-48 [PMID: 10461711 DOI: 10.2165/00007256-199928010-00004]

36 **LaPrade RF**, Terry GC. Injuries to the posterolateral aspect of the knee. Association of anatomic injury patterns with clinical instability. *Am J Sports Med* 1997; **25**: 433-438 [PMID: 9240974 DOI: 10.1177/036354659702500403]

37 **LaPrade RF**, Wentorf FA, Fritts H, Gundry C, Hightower CD. A prospective magnetic resonance imaging study of the incidence of posterolateral and multiple ligament injuries in acute knee injuries presenting with a hemarthrosis. *Arthroscopy* 2007; **23**: 1341-1347 [PMID: 18063179 DOI: 10.1016/j.arthro.2007.07.024]

38 **Dean RS**, LaPrade RF. ACL and Posterolateral Corner Injuries. *Curr Rev Musculoskelet Med* 2020; **13**: 123-132 [PMID: 31884674 DOI: 10.1007/s12178-019-09581-3]

39 **Reyes T**, Willoughby D. Biochemical and Structural Alterations in Skeletal Muscle Following ACL Injury: A Narrative Review. *IJKSS* 2020; **8**: 8-13 [DOI: 10.7575/aiac.ijkss.v.8n.1p.8]

40 **Yoh K**, Benjamin Infantolino W. Weekly Changes in Vastus Lateralis Volume Following ACL Injury. *IJATT* 2017; 22: 38-43 [DOI: 10.1123/ijatt.2015-0077]

41 **Li H**, Chen C, Chen S. Posttraumatic knee osteoarthritis following anterior cruciate ligament injury: Potential biochemical mediators of degenerative alteration and specific biochemical markers. *Biomed Rep* 2015; **3**: 147-151 [PMID: 25798238 DOI: 10.3892/br.2014.404]

42 **Larsson S**, Struglics A, Lohmander LS, Frobell R. Surgical reconstruction of ruptured anterior cruciate ligament prolongs trauma-induced increase of inflammatory cytokines in synovial fluid: an exploratory analysis in the KANON trial. *Osteoarthritis Cartilage* 2017; **25**: 1443-1451 [PMID: 28522220 DOI: 10.1016/j.joca.2017.05.009]

43 **Bigoni M**, Turati M, Gandolla M, Sacerdote P, Piatti M, Castelnuovo A, Franchi S, Gorla M, Munegato D, Gaddi D, Pedrocchi A, Omeljaniuk RJ, Locatelli V, Torsello A. Effects of ACL Reconstructive Surgery on Temporal Variations of Cytokine Levels in Synovial Fluid. *Mediators Inflamm* 2016; **2016**: 8243601 [PMID: 27313403 DOI: 10.1155/2016/8243601]

44 **Smith HC**, Vacek P, Johnson RJ, Slauterbeck JR, Hashemi J, Shultz S, Beynnon BD. Risk factors for anterior cruciate ligament injury: a review of the literature - part 1: neuromuscular and anatomic risk. *Sports Health* 2012; **4**: 69-78 [PMID: 23016072 DOI: 10.1177/1941738111428281]

45 **Renström P**, Arms SW, Stanwyck TS, Johnson RJ, Pope MH. Strain within the anterior cruciate ligament during hamstring and quadriceps activity. *Am J Sports Med* 1986; **14**: 83-87 [PMID: 3752352 DOI: 10.1177/036354658601400114]

46 **Person RS**. [Electromyographic investigations of coordination of the antagonistic muscles in development of motor habit]. *Zh Vyssh Nerv Deiat Im I P Pavlova* 1958; **8**: 17-27 [PMID: 13570554 DOI: 10.1136/bjo.38.10.605]

47 **Louie JK**, Mote CD Jr. Contribution of the musculature to rotatory laxity and torsional stiffness at the knee. *J Biomech*

1987; **20**: 281-300 [PMID: 3584153 DOI: 10.1016/0021-9290(87)90295-8]
48 **Kiapour Ata**. Age and Sex Dependent Variations in Knee Anatomy During Skeletal Maturation in Children and Adolescents. *Master's thesis, Harvard Medical School* 2016 [DOI: 10.1177/2325967121s00437]
49 **49 Hughston JC**, Whatley GS, Dodelin RA. The athlete and his knees. *South Med J* 1961; 54: 1372-1378 [PMID: 14449833 DOI: 10.1097/00007611-196112000-00008]
50 **Alentorn-Geli E**, Myer GD, Silvers HJ, Samitier G, Romero D, Lázaro-Haro C, Cugat R. Prevention of non-contact anterior cruciate ligament injuries in soccer players. Part 1: Mechanisms of injury and underlying risk factors. *Knee Surg Sports Traumatol Arthrosc* 2009; **17**: 705-729 [PMID: 19452139 DOI: 10.1007/s00167-009-0813-1]
51 **Hinton RY**, Rivera VR, Pautz MJ, Sponseller PD. Ligamentous laxity of the knee during childhood and adolescence. *J Pediatr Orthop* 2008; **28**: 184-187 [PMID: 18388713 DOI: 10.1097/BPO.0b013e3181652120]
52 **Gracia G**, Thévenin-Lemoine C, Laumonerie P, Sales de Gauzy J, Accadbled F; French Arthroscopy Society. Anterior cruciate ligament tears in children: Management and growth disturbances. A survey of French Arthroscopy Society members. *Orthop Traumatol Surg Res* 2019; **105**: 747-750 [PMID: 30982775 DOI: 10.1016/j.otsr.2019.02.017]
53 **Davis TJ**, Shelbourne KD, Klootwyk TE. Correlation of the intercondylar notch width of the femur to the width of the anterior and posterior cruciate ligaments. *Knee Surg Sports Traumatol Arthrosc* 1999; **7**: 209-214 [PMID: 10462209 DOI: 10.1007/s001670050150]
54 **Dienst M**, Schneider G, Altmeyer K, Voelkering K, Georg T, Kramann B, Kohn D. Correlation of intercondylar notch cross sections to the ACL size: a high resolution MR tomographic in vivo analysis. *Arch Orthop Trauma Surg* 2007; **127**: 253-260 [PMID: 16807752 DOI: 10.1007/s00402-006-0177-7]
55 **Anderson AF**, Dome DC, Gautam S, Awh MH, Rennirt GW. Correlation of anthropometric measurements, strength, anterior cruciate ligament size, and intercondylar notch characteristics to sex differences in anterior cruciate ligament tear rates. *Am J Sports Med* 2001; **29**: 58-66 [PMID: 11206258 DOI: 10.1177/03635465010290011501]
56 **LaPrade RF**, Burnett QM 2nd. Femoral intercondylar notch stenosis and correlation to anterior cruciate ligament injuries. A prospective study. *Am J Sports Med* 1994; **22**: 198-202; discussion 203 [PMID: 8198187 DOI: 10.1177/036354659402200208]
57 **Shelbourne KD**, Davis TJ, Klootwyk TE. The relationship between intercondylar notch width of the femur and the incidence of anterior cruciate ligament tears. A prospective study. *Am J Sports Med* 1998; **26**: 402-408 [PMID: 9617403 DOI: 10.1177/03635465980260031001]
58 **Simon RA**, Everhart JS, Nagaraja HN, Chaudhari AM. A case-control study of anterior cruciate ligament volume, tibial plateau slopes and intercondylar notch dimensions in ACL-injured knees. *J Biomech* 2010; **43**: 1702-1707 [PMID: 20385387 DOI: 10.1016/j.jbiomech.2010.02.033]
59 **Whitney DC**, Sturnick DR, Vacek PM, DeSarno MJ, Gardner-Morse M, Tourville TW, Smith HC, Slauterbeck JR, Johnson RJ, Shultz SJ, Hashemi J, Beynnon BD. Relationship Between the Risk of Suffering a First-Time Noncontact ACL Injury and Geometry of the Femoral Notch and ACL: A Prospective Cohort Study With a Nested Case-Control Analysis. *Am J Sports Med* 2014; **42**: 1796-1805 [PMID: 24866891 DOI: 10.1177/0363546514534182]
60 **Arendt E**, Dick R. Knee injury patterns among men and women in collegiate basketball and soccer. NCAA data and review of literature. *Am J Sports Med* 1995; **23**: 694-701 [PMID: 8600737 DOI: 10.1177/036354659502300611]
61 **Arendt EA**, Agel J, Dick R. Anterior cruciate ligament injury patterns among collegiate men and women. *J Athl Train* 1999; **34**: 86-92 [PMID: 16558564]
62 **Gwinn DE**, Wilckens JH, McDevitt ER, Ross G, Kao TC. La incidencia relativa de lesión del ligamento cruzado anterior en hombres y mujeres en la Academia Naval de los Estados Unidos. *Am J Sports Med* 2000; **28**: 98-102 [DOI: 10.1177/03635465000280012901]
63 **Lindenfeld TN**, Schmitt DJ, Hendy MP, Mangine RE, Noyes FR. Incidence of injury in indoor soccer. *Am J Sports Med* 1994; **22**: 364-371 [PMID: 8037278 DOI: 10.1177/036354659402200312]
64 **Messina DF**, Farney WC, DeLee JC. The incidence of injury in Texas high school basketball. A prospective study among male and female athletes. *Am J Sports Med* 1999; **27**: 294-299 [PMID: 10352762 DOI: 10.1177/03635465990270030401]
65 **Myklebust G**, Maehlum S, Holm I, Bahr R. A prospective cohort study of anterior cruciate ligament injuries in elite Norwegian team handball. *Scand J Med Sci Sports* 1998; **8**: 149-153 [PMID: 9659675 DOI: 10.1111/j.1600-0838.1998.tb00185.x]
66 **Renstrom P**, Ljungqvist A, Arendt E, Beynnon B, Fukubayashi T, Garrett W, Georgoulis T, Hewett TE, Johnson R, Krosshaug T, Mandelbaum B, Micheli L, Myklebust G, Roos E, Roos H, Schamasch P, Shultz S, Werner S, Wojtys E, Engebretsen L. Non-contact ACL injuries in female athletes: an International Olympic Committee current concepts statement. *Br J Sports Med* 2008; **42**: 394-412 [PMID: 18539658 DOI: 10.1136/bjsm.2008.048934]
67 **Stevenson H**, Webster J, Johnson R, Beynnon B. Gender differences in knee injury epidemiology among competitive alpine ski racers. *Iowa Orthop J* 1998; **18**: 64-66 [PMID: 9807709]
68 **Beynnon BD**, Hall JS, Sturnick DR, Desarno MJ, Gardner-Morse M, Tourville TW, Smith HC, Slauterbeck JR, Shultz SJ, Johnson RJ, Vacek PM. Increased slope of the lateral tibial plateau subchondral bone is associated with greater risk of noncontact ACL injury in females but not in males: a prospective cohort study with a nested, matched case-control analysis. *Am J Sports Med* 2014; **42**: 1039-1048 [PMID: 24590006 DOI: 10.1177/0363546514523721]
69 **Beynnon BD**, Vacek PM, Sturnick DR, Holterman LA, Gardner-Morse M, Tourville TW, Smith HC, Slauterbeck JR, Johnson RJ, Shultz SJ. Geometric profile of the tibial plateau cartilage surface is associated with the risk of non-contact anterior cruciate ligament injury. *J Orthop Res* 2014; **32**: 61-68 [PMID: 24123281 DOI: 10.1002/jor.22434]
70 **Giffin JR**, Vogrin TM, Zantop T, Woo SL, Harner CD. Efectos del aumento de la pendiente tibial en la biomecánica de la rodilla. *Am J Sports Med* 2004; **32**: 376-382 [DOI: 10.1177/0363546503258880]
71 **Hashemi J**, Chandrashekar N, Mansouri H, Slauterbeck JR, Hardy DM. The human anterior cruciate ligament: sex differences in ultrastructure and correlation with biomechanical properties. *J Orthop Res* 2008; **26**: 945-950 [PMID: 18302253 DOI: 10.1002/jor.20621]
72 **Hashemi J**, Chandrashekar N, Mansouri H, Gill B, Slauterbeck JR, Schutt RC Jr, Dabezies E, Beynnon BD. Shallow medial tibial plateau and steep medial and lateral tibial slopes: new risk factors for anterior cruciate ligament injuries. *Am*

J Sports Med 2010; **38**: 54-62 [PMID: 19846692 DOI: 10.1177/0363546509349055]

73 **Lipps DB**, Oh YK, Ashton-Miller JA, Wojtys EM. Morphologic characteristics help explain the gender difference in peak anterior cruciate ligament strain during a simulated pivot landing. *Am J Sports Med* 2012; **40**: 32-40 [PMID: 21917612 DOI: 10.1177/0363546511422325]

74 **McLean SG**, Oh YK, Palmer ML, Lucey SM, Lucarelli DG, Ashton-Miller JA, Wojtys EM. The relationship between anterior tibial acceleration, tibial slope, and ACL strain during a simulated jump landing task. *J Bone Joint Surg Am* 2011; **93**: 1310-1317 [PMID: 21792497 DOI: 10.2106/JBJS.J.00259]

75 **McLean SG**, Lucey SM, Rohrer S, Brandon C. Knee joint anatomy predicts high-risk in vivo dynamic landing knee biomechanics. *Clin Biomech (Bristol, Avon)* 2010; **25**: 781-788 [PMID: 20605063 DOI: 10.1016/j.clinbiomech.2010.06.002]

76 **Sturnick DR**, Argentieri EC, Vacek PM, DeSarno MJ, Gardner-Morse MG, Tourville TW, Slauterbeck JR, Johnson RJ, Shultz SJ, Beynnon BD. A decreased volume of the medial tibial spine is associated with an increased risk of suffering an anterior cruciate ligament injury for males but not females. *J Orthop Res* 2014; **32**: 1451-1457 [PMID: 24962098 DOI: 10.1002/jor.22670]

77 **Orchard J**, Seward H, Garlick D. Ground conditions and AFL injuries. In: Australian Conference of Science and Medicine in Sport. Canberra: Sports Medicine Australia 1997 [DOI: 10.3390/sports1030069]

78 **Malinzak RA**, Colby SM, Kirkendall DT, Yu B, Garrett WE. A comparison of knee joint motion patterns between men and women in selected athletic tasks. *Clin Biomech (Bristol, Avon)* 2001; **16**: 438-445 [PMID: 11390052 DOI: 10.1016/s0268-0033(01)00019-5]

79 **Garrido J**, Pineda Y, Piñeros A, Rodríguez M. Imbalancemuscular como factor de riesgo para lesiones deportivas de rodilla en futbolistas profesionales. Acta Colombiana de Medicina del Deporte. 2003. Available from: http://amedco.encolombia.com/deporte1091imbalance.htm

80 **Bennell K**, Wajswelner H, Lew P, Schall-Riaucour A, Leslie S, Plant D, Cirone J. Isokinetic strength testing does not predict hamstring injury in Australian Rules footballers. *Br J Sports Med* 1998; **32**: 309-314 [PMID: 9865403 DOI: 10.1136/bjsm.32.4.309]

81 **Dejour H**, Walch G, Neyret P, Adeleine P. [Results of surgically treated chronic anterior laxities. Apropos of 251 cases reviewed with a minimum follow-up of 3 years]. *Rev Chir Orthop Reparatrice Appar Mot* 1988; **74**: 622-636 [PMID: 3241893 DOI: 10.1016/j.knee.2004.02.001]

82 **Wexler G**, Hurwitz DE, Bush-Joseph CA, Andriacchi TP, Bach BR Jr. Functional gait adaptations in patients with anterior cruciate ligament deficiency over time. *Clin Orthop Relat Res* 1998; 166-175 [PMID: 9553549]

83 **Goldstein J**, Bosco JA. 3rd La rodilla deficiente en el LCA: historia natural y opciones de tratamiento. *Bull Hosp Jt Dis* 2001; **60**: 173-178 [DOI: 10.1007/s001670050043]

84 **Fayad LM**, Parellada JA, Parker L, Schweitzer ME. MR imaging of anterior cruciate ligament tears: is there a gender gap? *Skeletal Radiol* 2003; **32**: 639-646 [PMID: 14504836 DOI: 10.1007/s00256-003-0694-1]

85 **Millett PJ**, Willis AA, Warren RF. Associated injuries in pediatric and adolescent anterior cruciate ligament tears: does a delay in treatment increase the risk of meniscal tear? *Arthroscopy* 2002; **18**: 955-959 [PMID: 12426537 DOI: 10.1053/jars.2002.36114]

86 **Futch LA**, Garth WP, Folsom GJ, Ogard WK. Acute rupture of the anterior cruciate ligament and patellar tendon in a collegiate athlete. *Arthroscopy* 2007; **23**: 112.e1-112.e4 [PMID: 17210443 DOI: 10.1016/j.arthro.2005.07.030]

87 **Huang W**, Zhang Y, Yao Z, Ma L. Clinical examination of anterior cruciate ligament rupture: a systematic review and meta-analysis. *Acta Orthop Traumatol Turc* 2016; **50**: 22-31 [PMID: 26854045 DOI: 10.3944/AOTT.2016.14.0283]

88 **Abruscato K**, Browning K, Deleandro D, Menard Q, Wilhelm M, Hassen A. Diagnostic accuracy of the lever sign in detecting anterior cruciate ligament tears: A systematic review and meta-analysis. *Int J Sports Phys Ther* 2019; **14**: 2-13 [PMID: 30746288]

89 **Lelli A**, Di Turi RP, Spenciner DB, Dòmini M. The "Lever Sign": a new clinical test for the diagnosis of anterior cruciate ligament rupture. *Knee Surg Sports Traumatol Arthrosc* 2016; **24**: 2794-2797 [PMID: 25536951 DOI: 10.1007/s00167-014-3490-7]

90 **Leblanc MC**, Kowalczuk M, Andruszkiewicz N, Simunovic N, Farrokhyar F, Turnbull TL, Debski RE, Ayeni OR. Diagnostic accuracy of physical examination for anterior knee instability: a systematic review. *Knee Surg Sports Traumatol Arthrosc* 2015; **23**: 2805-2813 [PMID: 25763847 DOI: 10.1007/s00167-015-3563-2]

91 **Décary S**, Ouellet P, Vendittoli PA, Desmeules F. Reliability of physical examination tests for the diagnosis of knee disorders: Evidence from a systematic review. *Man Ther* 2016; **26**: 172-182 [PMID: 27697691 DOI: 10.1016/j.math.2016.09.007]

92 **Brady MP**, Weiss W. Clinical Diagnostic Tests Versus MRI Diagnosis of ACL Tears. *J Sport Rehabil* 2018; **27**: 596-600 [PMID: 29140170 DOI: 10.1123/jsr.2016-0188]

93 **Torg JS**, Conrad W, Kalen V. Clinical diagnosis of anterior cruciate ligament instability in the athlete. *Am J Sports Med* 1976; **4**: 84-93 [PMID: 961972 DOI: 10.1177/036354657600400206]

94 **Lichtenberg MC**, Koster CH, Teunissen LPJ, Oosterveld FGJ, Harmsen AMK, Haverkamp D, Hoornenborg D, Berg RP, Bloemers FW, Faber IR. Does the Lever Sign Test Have Added Value for Diagnosing Anterior Cruciate Ligament Ruptures? *Orthop J Sports Med* 2018; **6**: 2325967118759631 [PMID: 29568784 DOI: 10.1177/2325967118759631]

95 **Lange T**, Freiberg A, Dröge P, Lützner J, Schmitt J, Kopkow C. The reliability of physical examination tests for the diagnosis of anterior cruciate ligament rupture--A systematic review. *Man Ther* 2015; **20**: 402-411 [PMID: 25466498 DOI: 10.1016/j.math.2014.11.003]

96 **Décary S**, Ouellet P, Vendittoli PA, Roy JS, Desmeules F. Diagnostic validity of physical examination tests for common knee disorders: An overview of systematic reviews and meta-analysis. *Phys Ther Sport* 2017; **23**: 143-155 [PMID: 27693100 DOI: 10.1016/j.ptsp.2016.08.002]

97 **O'Shea KJ**, Murphy KP, Heekin RD, Herzwurm PJ. The diagnostic accuracy of history, physical examination, and radiographs in the evaluation of traumatic knee disorders. *Am J Sports Med* 1996; **24**: 164-167 [PMID: 8775114 DOI: 10.1177/036354659602400208]

98 **Leyes Vences M**, Forriol Campos F. Historia de la reparación del ligamento cruzado anterior History of anterior cruciate ligament repair. *Rev Esp Artrosc Cir* **24**: 38-58 [DOI: 10.24129/j.reaca.24e57.fs1703010]

99 **Boeree NR**, Ackroyd CE. Assessment of the menisci and cruciate ligaments: an audit of clinical practice. *Injury* 1991; **22**: 291-294 [PMID: 1937725 DOI: 10.1016/0020-1383(91)90008-3]

100 **Gürpınar T**, Polat B, Polat AE, Çarkçı E, Öztürkmen Y. Diagnostic Accuracy of Lever Sign Test in Acute, Chronic, and Postreconstructive ACL Injuries. *Biomed Res Int* 2019; **2019**: 3639693 [PMID: 31281835 DOI: 10.1155/2019/3639693]

101 **Slocum DB**, Larson RL. Rotatory instability of the knee. Its pathogenesis and a clinical test to demonstrate its presence. *J Bone Joint Surg Am* 1968; **50**: 211-225 [PMID: 5642814]

102 Noyes FR GE. Diagnosis of the knee ligaments injuries: technical concepts. Part II. New York: Churchill Livingstone 1988; 261-285 [DOI: 10.1002/hed.2890080511]

103 **Manzano-Serrano E**. Tesis Doctoral resultados de la cirugía del ACL plastias mixtas biológicas-sintéticas. Departamento de Cirugía. Facultad de Medicina. Universidad Complutense. Madrid, Mayo 1.995 [DOI: 10.32440/ar.2019.136.02.rev03]

104 **Guillén García PJC**, Madrigal J, Royo J, Concejero López V, Sobrado Pérez J. Traumatismos deportivos de la rodilla. *Revista de Ortopedia y Traumtología* 1985; 29 [DOI: 10.1016/s0482-5985(07)75579-7]

105 **Trillat A**, Dejour H, Bousquet G. Chirurgie du genou III Journées Lionaises 1978; 75-80 [DOI: 10.1016/b978-2-294-74053-4.00015-7]

106 **Noyes F**, Butíer D, Grood E. Clinical paradoxes of anterior cruciate inestability and a new test to detect its inestability. *Orthop Trans* **2**: 36-37 [DOI: 10.2519/jospt.1991.13.2.60]

107 **Tria AJ**, Mores TM. Diagnóstico de las lesiones de los ligamentos de la rodilla. En: Scott W.N. (ed). Lesiones del ligamento y el mecanismo extensor de la rodilla. Madrid. Mosby-Year Book de España: 1992; 87-99 [DOI: 10.24129/j.reaca.25e62.fs1805029]

108 **Cabot JR**. Lesiones ligamentosas de la rodilla. Ponencia oficial III. Congreso Hispano-Argentino de Cirugía ortopédica y traumatología, 1.973

109 **Hughston JC**, Andrews JR, Cross MJ, Moschi A. Classification of knee ligament instabilities. Part II. The lateral compartment. *J Bone Joint Surg Am* 1976; **58**: 173-179 [PMID: 1254620]

110 **Galway RD**, Beaupre A. , MacIntosh DL. Pivot shift: A clinical sign of symptomatic anterior cruciate insufficiency. *J Bone Joint Surg* 763-764 [DOI: 10.1097/00003086-198003000-00008]

111 **Losee RE**, Johnson TR, Southwick WO. Anterior subluxation of the lateral tibial plateau. A diagnostic test and operative repair. *J Bone Joint Surg Am* 1978; **60**: 1015-1030 [PMID: 721850]

112 **Slocum DB**, James SL, Larson RL, Singer KM. Clinical test for anterolateral rotary instability of the knee. *Clin Orthop Relat Res* 1976; 63-69 [PMID: 954292 DOI: 10.1097/00003086-197607000-00012]

113 Navarro Quilis A. Inestabilidad ligamentosa de la rodilla. Ponencia oficial XXI Congreso de la SECOT. *Garsi Madrid* 1983 [DOI: 10.1163/2210-7975_hrd-2433-0057]

114 **Gupta Y**, Mahara D, Lamichhane A. McMurray's Test and Joint Line Tenderness for Medial Meniscus Tear: Are They Accurate? *Ethiop J Health Sci* 2016; **26**: 567-572 [PMID: 28450773 DOI: 10.4314/ejhs.v26i6.10]

115 **Gobbo Rda R**, Rangel Vde O, Karam FC, Pires LA. Physical examinations for diagnosing meniscal injuries: Correlation with surgical findings. *Rev Bras Ortop* 2011; **46**: 726-729 [PMID: 27047833 DOI: 10.1016/S2255-4971(15)30332-3]

116 Guillén García P. Lenguaje de la rodilla. Medicina RANd editor. *Discurso de ingreso Madrid* 1997; 169-190 [DOI: 10.17711/sm.0185-3325.2015.001]

117 **Velázquez-Saornil J**, Ruíz-Ruíz B, Rodríguez-Sanz D, Romero-Morales C, López-López D, Calvo-Lobo C. Efficacy of quadriceps vastus medialis dry needling in a rehabilitation protocol after surgical reconstruction of complete anterior cruciate ligament rupture. *Medicine (Baltimore)* 2017; **96**: e6726 [PMID: 28445290 DOI: 10.1097/MD.0000000000006726]

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ORIGINAL ARTICLE

Case Control Study

Histological difference in ligament flavum between degenerative lumbar canal stenosis and non-stenotic group: A prospective, comparative study

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Abstract

BACKGROUND

Ligament flavum (LF) hypertropy is the main etiopathogenesis of lumbar canal stenosis (LCS). The purely elastic LF undergoes a morphological adaptation including a reduction in the elastic fibers and a consequent increase in the collagen content, fibrosis, cicatrization, and calcification. However, the morphometric analysis can delineate the LF in patients with LCS from those without LCS, which would help in better understanding LCS pathogenesis.

AIM

To compare the histopathological changes in LF between the degenerative LCS and non-stenotic (non-LCS) group.

METHODS

The present prospective study was conducted in 82 patients who were divided into two groups, namely LCS and non-LCS. Demographic details of the patients such as duration of symptoms, level of involvement, and number of segments were recorded. The LF obtained from both groups was histopathologically examined for the fibrosis score, elastic fiber degeneration, calcification, and

chondroid metaplasia. Morphometrical details included a change in elastin and collagen percentages, elastin/collagen ratio, elastic fiber fragmentation, and ligamentocyte numbers. All parameters were compared between the two groups by using the independent t test, Chi-square test, and Pearson's correlation test.

RESULTS

Out of 82 cases, 74 were analysed, 34 in LCS and 40 in non-LCS group. The mean ± SD age of presentation in LCS and non- LCS group was 49.2 ± 8.9 and 43.1 ± 14.3 respectively. The LCS group (n = 34) exhibited significant differences in fibrosis (P = 0.002), elastic fiber degeneration (P = 0.01), % elastic fragmentation (66.5 ± 16.3 *vs* 29.5 ± 16.9), % elastic, content (26.9 ± 6.7 *vs* 34.7 ± 8.4), % collagen content (63.6 ± 10.4 *vs* 54.9 ± 6.4), reduction of elastic/collagen (0.4 ± 0.1 *vs* 0.6 ± 0.1), and ligamentocyte number (39.1 ± 19.1 *vs* 53.5 ± 26.9) as compared to non-LCS group (n = 40). The calcification (P = 0.08) and Pearson's correlation between duration and loss of elastin was not significant. The difference in LF morphology is consistent in patient's ≥ 40 years of age among the groups as found in subgroup analysis. Similarly in the patents < 40 and > 40 in the non-LCS group.

CONCLUSION

LF is vital in the pathogenesis of LCS. The purely elastic LF undergoes a morphological adaptation that includes a reduction in the elastic fibers with a consequent increase in the collagen content, fibrosis, cicatrization, and calcification. The present study provides a detailed morphometric analysis to semiquantitatively delineate the LF changes in patients with LCS from those in patients without LCS.

Key Words: Spinal stenosis; Lumbar spine; Ligamentum flavum; histopathology; Morphometry

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Core Tip: The ligament flavum (LF) is vital in the pathogenesis of lumbar canal stenosis (LCS). The purely elastic LF undergoes a morphological adaptation that includes a reduction in the elastic fibers with a consequent increase in the collagen content, fibrosis, cicatrization, and calcification. The present study provides a detailed morphometric analysis to semiquantitatively delineate the LF changes in patients with LCS from those in patients without LCS.

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INTRODUCTION

Lumbar canal stenosis (LCS) is a common spinal disorder that affects elderly patients, leading to lower back pain, leg pain, and neurogenic claudication, which rarely ends in paresis[1,2]. Because the ligamentum flavum (LF) covers most of the posterior and lateral part of the lumbar spinal canal, the hypertrophied facets and LF hypertrophy (LFH) are responsible for LCS despite the disc complex, contributing to spinal canal narrowing[2,3]. Thus, morphological and histological changes in developing lumbar spinal canal encroachment must be studied[4,5]. With aging of the global population, a paradigm shift toward symptomatic LCS that requires surgical treatment is observed[6].

LF contains the purest form of elastic tissue among ligaments. These elastic fibers decrease with age and are replaced by collagen fibers[2]. The causes of LFH are multifactorial, including the activity levels, age, and mechanical stress[7,8]. Based on transmission electron microscopy findings, Postacchini *et al*[9] concluded that the reduced elasticity might cause bulging of the LF into the spinal canal even in the standing position.

Studies have exhibited a qualitative transformation in the dynamics of the LF components with degeneration[1,6,10-12]. The LFH exhibited loss of elastic fibers, increased content of collagen fibers, and chondrometaplasia, leading to calcification. A few studies have suggested this association of calcification[10], whereas two other studies have suggested a decrease in the elastin/collagen ratio[2,4]. Electron microscopy has revealed fragmentation and changes in the quality of elastic fibers.

Therefore, the present study attempted to explain the LF structure histologically in a semi-quantitative manner by using advanced imaging software.

MATERIALS AND METHODS

The present prospective study was conducted following the Helsinki Declaration principles and approved by the local institutional review board (T/IM/18-19/43 dated 04/01/2019). Valid written informed consent was obtained from all participants.

Study population

The present study was conducted in 74 adult patients undergoing lumbar spine surgery between January 2019 and March 2020 in the departments of orthopedics or neurosurgery in a tertiary care center. Patients with characteristic clinical and radiological findings of spinal stenosis were grouped as the LCS study group. Simultaneously, patients with lumbar disc herniation, infective etiology (tubercular or non-tubercular), trauma, and malignancy constituted the non-LCS study group. Patients with prior lumbar surgery were excluded from the study. Clinical details such as age, sex, duration of symptoms, and level of involvement were recorded.

LF samples were obtained from 82 patients who underwent decompressive laminectomy in piecemeal by using a Kerrison's rounger and sent for histopathological assay in neutral buffer formalin. Of these, eight samples were excluded due to sufficient tissue availability. Thus, the final analysis was conducted in 74 patients.

Histology

The harvested LF components were kept in a solution containing 10% neutral buffered formalin for 24 h. The tissues were processed overnight on an automatic tissue processor (Leica Biosystems Ltd.) and embedded in paraffin. Multiple 4-μm thick sections were cut. All sections were stained with haematoxylin and eosin (H & E), Verhoef-Van-Gieson stains (VVG), Masson trichrome stain (MTS), reticulin, and Von-krossa stains.

Light microscopy

The histological evaluation was performed by two experts who were blinded to the nature of the groups. Light microscopy was used to examine LF sections for elastic degeneration, fibrosis, metaplasia (chondroid or osteoid), hemorrhage, and calcification. Elastic degeneration was graded depending upon the percentage of elastic fibers exhibiting degenerative changes and elastin fiber fragmentation (1+: 0%–33%, 2+: 33%–66%, and 3+: > 67% of elastic fibers). Fibrosis was graded as per the criterion described previously[2].

Image acquisition and morphometric analysis

Digital images were obtained using a commercial imaging system (ZEN blue edition on ZEISS Scope A.1 microscope) at 200X magnification for H & E, VVG, and MTS stains in the tagged image file format. For each case, at least two areas from different LF regions were captured randomly. All images were imported in Image J software java windows-64 application (ImageJ bundled with 64-bit Java 1.8.0_172) for morphometric analysis.

The morphological analysis of the digital images of different stains was performed for elastin content (VVG), collagen content (MTS), and the number of ligamentocytes (H & E). The tool was used to estimate the percentage of collagen and elastic fibers, elastic to collagen fiber ratio, number of ligamentocytes, and elastic fiber width. Each parameter was estimated three times, and two independent observers recorded the average.

Statistical analysis

Continuous data are presented as mean ± standard deviation (SD). Differences in the mean between the groups were tested using the independent t test. The Chi-square test was used to compare the categorical variables between the two groups. Correlation between various morphological parameters and duration of symptoms was determined using the Pearson's correlation test for the stenotic group. Subgroup analysis was also performed for patients aged ≥ 40 years and for patients aged < 40 and ≥ 40 years in the non-LCS group. All differences associated with a chance probability of ≤ 0.05 were considered. Data were analyzed using the IBM Statistical Package for Social Sciences ver. 17 (SPSS Inc., Chicago, IL, United States).

RESULTS

Clinical features

Of the 74 cases, 34 cases constitute the LCS group and 40 cases constituted the non-LCS group (Figure 1). The mean ± SD age of presentation in the LCS and non-LCS groups was 49.2 ± 8.9 and 43.1 ± 14.3 years, respectively. The percentage of patients in the stenotic group aged > 40 years was 91%, whereas that in the non-stenotic group was 57.5%. This difference was statistically significant ($P = 0.001$) (Fischer exact test). Although the non-stenotic group included permanent lumbar disc herniation, other pathologies were also observed (Table 1). Single-level involvement was observed in majority of cases. L4-5 involvement was observed in 43.5% patients, followed by L3-4 and L5-S1 involvement (23% patients each). The remaining patients exhibited involvement in L1-2 and L2-3 levels.

Histological differences between LCS and non-LCS groups

The histological differences in elastin fibers, collagen content, and ligamentocytes were compared between the two groups. The LCS group exhibited higher elastic degeneration and fibrosis than the non-LCS group ($P = 0.01$ and 0.002, respectively) (Table 2; Figures 2-4). On the other hand, the extent of calcification, chondroid metaplasia, and hemorrhage was statistically nonsignificant between the groups.

LF exhibited a significant reduction in the elastin content in the LCS group ($P < 0.0001$, independent t test) and an increase in the collagen content ($P < 0.0001$, independent t test) compared with those in the non-LCS group. The elastin/collagen ratio, width of elastic fibers, and ligamentocyte number were also significantly lower in the LCS group than in the non-LCS group (Table 3).

Correlation of clinicopathological features between the LCS and non-LCS groups

The Pearson's correlation test indicated a moderate correlation between decrease in the number of ligamentocytes and age in both groups (non-LCS-R: −0.52, $P < 0.001$ and LCS-R: −0.578, $P < 0.001$). All other morphological changes were statistically nonsignificant. The duration of symptoms in the LCS group was not significantly correlated with morphological changes in both groups.

The ligamentocyte number was moderately correlated with the elastin content in the LCS group (R: −0.450, $P = 0.008$), (Figure 5). On the other hand, the collagen content was moderately correlated with the elastic content in the non-LCS group (R: −504, P: 0.001). The LCS group exhibited an inverse correlation between the elastin and collagen contents. However, this difference was statistically nonsignificant.

Subgroup analysis

Subgroup analysis exhibited a statistically nonsignificant difference between the patients aged < 40 years and those aged > 40 years in the LCS group. Additionally, the difference between the LCS and non-LCS groups in the percentage of patients aged > 40 years was statistically significant (Table 4).

DISCUSSION

The LF, which envelops the spinal canal, is a highly elastic structure that contains four times pure elastin than collagen[6]. If the LF surrounding the spinal canal becomes hypertrophic, it will compress the dural sac containing the cauda equina or the nerve root. Elsberg[13] first reported a case of LFH causing sciatica. Several clinical studies have reported that LFH is the primary pathology in LCS[1,2,4,6-10]. Although surgical excision is the only therapeutic management for patients with LFH in LCS, a deeper understanding of the pathophysiology can encourage future nonsurgical or prophylactic treatment modalities. Thus, the present study attempted to study the pathological changes in LF and compare the LCS and non-LCS study groups.

Etiology

Sairyo *et al*[1] had proposed that LFH occurs due to degenerative changes with aging process, and also due to increased mechanical stress occurring in instability. Wang *et al*[14] have experimentally demonstrated increased motion in lumbar spine induced LFH. Chuang *et al*[15] have found that age-related LFH occurred due to activation of the Akt and MAPK (apoptotic) pathways. The authors also postulated that hypertrophy is initiated in all subjects after the second decade of life. Zaki *et al*[16] also found that older individuals had some loss and rupture of elastic fibres with abnormal collagen, increase in vascularity and ossification particularly in the lumbar region as compared to the thoracic and cervical spine. Postacchini *et al*[9] observed that although older individuals with disc herniation exhibited some elastic fiber loss, the stenotic group of similar age exhibited more collagen and chondroid metaplasia and were strikingly different. However, the authors noted that there was no difference was observed in stenotic changes related to age and listhesis (degenerative), implying that instability does not accelerate hypertrophic changes[9]. The present study also exhibited no LCS-

Table 1 Demographic profile of the groups

Categories		LSS (*n* = 34)	Non-LSS (*n* = 40)	*P* value
Age in years, mean (SD)		49.2 (8.9)	43.1 (14.3)	
Sex in %		M:F – 59:41	M:F – 60:40	
Duration in weeks, mean (SD)		44.1 (11.6)	9.4 (8.1)	
Level	One	30 (88.2)	32 (80)	0.553
	Two	3 (8.8)	7 (17.5)	
	Three	1 (2.9)	1 (2.5)	
Diagnosis		Lumbar canal stenosis	PIVD – 18	
			Trauma – 8	
			Potts spine – 7	
			Tumour – 5	
			Epidural abscess (non-TB) – 2	

Table 2 Histological differences between the groups

Variable	Histological features	Stenotic (*n* = 34)	Non stenotic (*n* = 40)	*P* value (Chi square test)
Elastin degeneration	1+ and 2+	9 (26.5)	22 (55)	**0.010**
	3+	25 (73.5)	18 (45)	
Fibrosis	1+ and 2+	10	17	**0.002**
	3+	24	13	
Calcification	Absent	28	38	0.081
	Present	6	2	
Chondroid metaplasia	Absent	22	26	0.979
	Present	12	14	
Haemorrhage	Absent	17	23	0.519
	Present	17	17	

induced morphological changes in the non-LCS group of similar age. Similarly, no difference was observed in the non-LCS group with age < 40 years, whereas a statistically significant difference was observed from age > 40 years.

Levels and age

Sairyo *et al*[1] exhibited that LF thickness increased with age; however, the changes with age exhibited spinal level dependence. The increment at L4/5 and L3/4 levels was more extensive than that at L2/3 and L5/S1 levels. Similar changes in magnetic resonance imaging (MRI) were also reported by Kolte *et al*[7]. Okuda *et al*[10] exhibited that thickening was correlated to calcification, which was prime in LCS. A positive correlation was also observed by authors between calcification and clinical scoring (Japanese orthopedic association scores). The present study did not measure the thickness, either grossly, histologically, or radiologically. The present understanding of LCS has evolved from a pure 'static compression' (dependent on width) to a more "dynamic compression" that arises from the imbalance in LF components rather than actual width. Altun *et al*[2] hypothesized that the loss of elasticity is the contributing factor for LF infolding, leading to spinal canal narrowing[2].

Schräder *et al*[12] also studied 41 Ligaments in 21 patients and reported single-level stenosis in five patients, bi-segmental stenosis in 24 patients, and stenosis on three levels in 12 patients. Additionally, Hulmani *et al*[4] exhibited more double-level stenosis in their series. However, the present study exhibited more single-level involvement (n = 32) than double-level (n = 7) or multilevel (n = 1) involvement. This may be due to the higher age group cohort in the study by Hulmani *et al*[4] compared to that in the present study (72 *vs* 49) due to the preferential selection. The present study exhibited that L4-5 was the most common involvement, followed by L3-4. Sairyo *et al*[1] proposed that high mechanical stress might be responsible for the preferential increase in thickness at the L4-5 level.

Table 3 Morphometric differences between the groups

Factor		mean	SD	*t*	df	*P* value
% Elastin fragmentation	NS (40)	29.50	16.9	-9.51	71	**< 0.0001**
	S (34)	66.47	16.3			
Collagen content (area %)	NS (40)	54.94	6.41	-4.38	53.2	**< 0.0001**
	S (34)	63.59	10.36			
Elastic content (area %)	NS (40)	34.73	8.36	4.36	72	**< 0.0001**
	S (34)	26.94	6.71			
Elastin/Collagen ratio	NS (40)	0.63	0.14	6.01	71.27	**< 0.0001**
	S (34)	0.43	0.13			
Width of elastin fibers	NS (39)	4.37	1.07	5.44	71	**< 0.0001**
	S (34)	3.27	0.54			
Ligamentocyte numbers	NS (40)	53.45	26.85	2.6	72	**< 0.0001**
	S (34)	39.11	19.05			

Table 4 Subgroup analysis among groups > 40 years

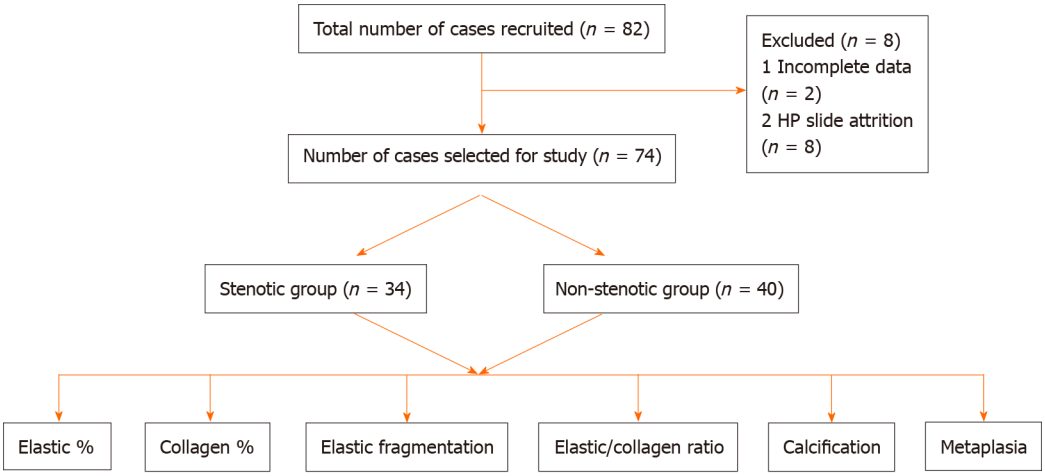
Factor		mean	SD	*t*	df	*P* value
% Elastin fragmentation	NS (25)	31.80	18.123	-7.4	43.93	**< 0.0001**
	S (31)	67.10	16.96			
Collagen content (area %)	NS (25)	55.12	7.62	-3.4	53.19	**0.001**
	S (31)	63.58	10.75			
Elastic content (area %)	NS (25)	34.898	7.92	4.20	46.6	**< 0.0001**
	S (31)	26.57	6.60			
Elastin/Collagen ratio	NS (25)	0.63	0.14	5.54	50.09	**< 0.0001**
	S (31)	0.43	0.13			
Width of elastin fibers	NS (25)	3.75	0.98	4.42	31.94	**< 0.0001**
	S (31)	2.77	0.49			
Ligamentocyte numbers	NS (25)	46.56	22.4.0	1.88	41.03	**0.66**
	S (31)	36.612	15.41			

Histology

Okuda *et al*[10] and Elsberg *et al*[13] observed that nearly all ligaments were calcified in LCS. Calcium deposition within the ligament significantly aggravated the symptoms, and this process increased with age. The increase in the formation of calcium crystals is a significant factor for LF thickening. Okuda *et al* [10] observed that the mean age of patients with calcification and those without calcification was 74 ± 2.0 and 68 ± 1.4 years, respectively. Therefore, patients with calcification were significantly older than those in the LCS group. No reactive granulomatous tissue formation was noticed in the calcification focus. Other researchers have reiterated a smooth transition between calcific zones and surroundings[10,17]. Okuda *et al*[10] reported focal and dispersion-type calcification in their patients with LCS and correlated calcification with a low clinical score.

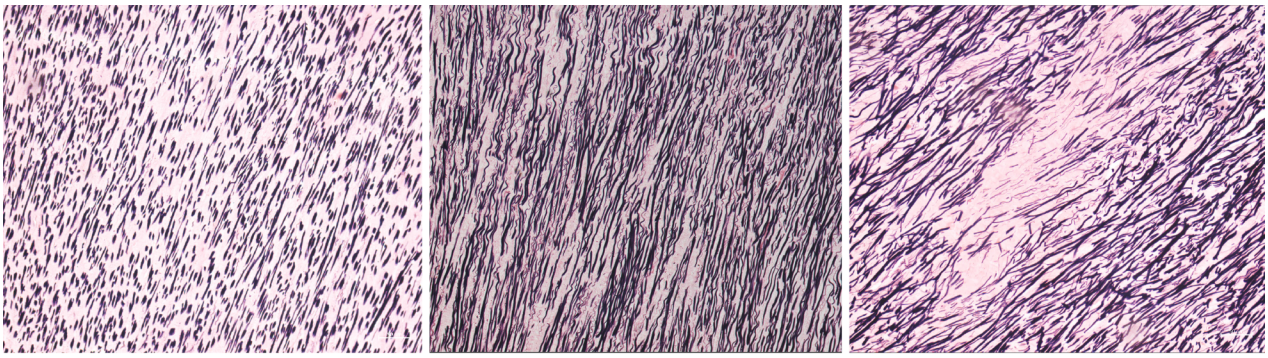
Altun *et al*[2], Hulmani *et al*[4], and Reyes-Sánchez *et al*[18] exhibited contrasting findings regarding calcification. No statistical difference was observed in calcification between the LCS group and the lumbar disc herniation (LDH) group in these studies.

Schräder *et al*[12] exhibited calcification of all the ligaments, and the patients also exhibited relevant fibrosis with decrease in the elastic/collagenous fiber ratio. Additionally, Sairyo *et al*[1] reported that the LCS group exhibited increased LF thickness and fibrosis with reduced elastic fibers. These transformations were more predominant along the dorsal side than those along the middle of the dural side. Sato tel. also found that dorsal side is affected 30 more than the dural side[19] Peng *et al*[20] revealed that the dorsal fibers of the LF were subjected to higher stress than the dural fibers that have a fluid-filled tube,



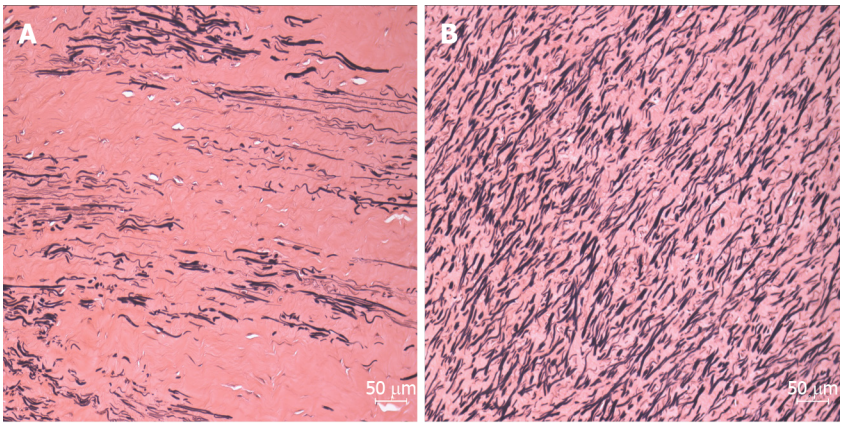
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Figure 1 Flow diagram of patients.



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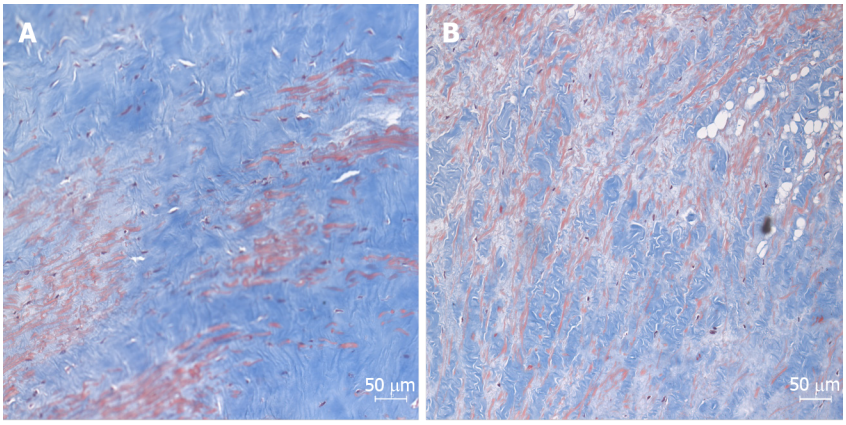
Figure 2 The three grades of elastic degeneration.



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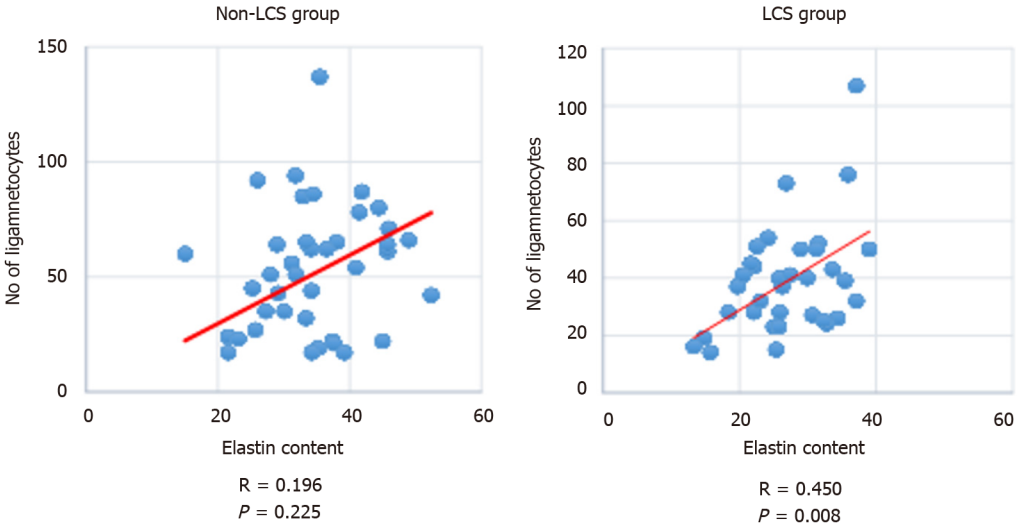
Figure 3 Von Geisson's stain showing the difference between lumbar canal stenosis & Non-lumbar canal stenosis in the number of elastic fibers. A: Lumbar canal stenosis; B: Non-lumbar canal stenosis.

which keeps it smooth. Hamdan *et al*[11] exhibited that the LCS changes were more in the central portion than in the attachments. Yabe *et al*[21] reported a severe reduction in elastic fibres on the dorsal hypertrophied LF. We did not differentiate among the sides as the stenotic effect was due to in-toto changes in LF. Moreover, the LF was removed piecemeal in most of our cases. Hence, such differences



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Figure 4 Masson's Trichrome stain showing the difference in the number of collagen fibers. A: Lumbar canal stenosis; B: Non-lumbar canal stenosis.



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Figure 5 Scatter plot showing the correlation between the elastic fibers and ligamentocyte numbers in the groups. LCS: Lumbar canal stenosis.

were not observed in the present study.

Fuertes *et al*[22] were first to comment on the anatomical and fiber arrangements on different layers. The authors realized that aging and repetitive stress altered the elastic fiber organization, causing disarray, derangement, and even complete transformation with no elastic fibers. In the present study, morphologic changes such as diameter irregularity, orientation turbulence, and extent of fragmentation were observed in elastic fibers. A similar finding was observed though electron microscopy in the study by Hulmani *et al*[4]. The image software was used to perform the morphometric study based on light microscopy. The present study did not exhibit significant ganglionic cystic changes or chondroid metaplasia despite substantial fibrosis. The present study noted a statistically significant reduction in the elastin percentage, increase in collagen, and reduction in the elastin/collagen ratio. This finding is in contrast to that of other studies. Additionally, a significant change was observed in the elastic fibers (4.37 ± 1.07 *vs* 3.27 ± 0.54; $P < 0.001$), fragmentation, and decrease in the number of ligamentocytes. Altun *et al*[2] reported that elastic fiber reduction or collagen increase was not significant, except for calcification. Okuda *et al*[10] first described elastic fiber degeneration, and it was accompanied by a proliferation of collagen fibers among elastic fibers. Additionally, Hulmani *et al*[4] reported findings such as ganglion-like cystic lesion, mucinous degeneration, and vascularization that were confirmed through electron microscopy. Reyes-Sánchez *et al*[18] exhibited more cystic degeneration, fibrillar appearance, and hypercellularity in the degenerative listhetic group than in the degenerative stenotic group. These results could be caused by instability rather than a degenerative disease in the spine. Schräder *et al*[12] noted that the parallel arrangement of LF elastic fibers was lost in degenerative LCS. This finding is concurrent with that of the present study and the study by Altun *et al*[2].

Significant fibrosis was observed in the LCS group in the present study[2,4]. This finding is in contrast to that of Hulmani *et al*[4] or Altun *et al*[2], and Cheung *et al*[23] exhibited a positive correlation between fibrosis and LFH in the LCS group. On the other hand, the developmental stenotic group exhibited paradoxically less fibrosis[23]. Okuda *et al*[10] also exhibited graded fibrosis in their LCS patients. However, the correlation with the clinical symptoms of patients was not significant. Additionally, the authors exhibited a large number of chondroid cells in patients with spondylolisthesis [10]. These findings are similar to those of Fukuyama *et al*[8], who postulated that unstable lumbar spine accelerates LF degeneration and chondrometaplasia.

LFH etiology is multifactorial. The morphological transformation that includes reduction in the elastin/collagen ratio, degeneration, fragmentation of the residual elastic fibers, fibrosis, cicatrization, and calcification leads to a loss in elasticity that can infold into the spinal canal, causing narrowing. Future studies can evaluate the correlation between symptom duration and progression of specific changes.

Several inflammatory cytokines have been studied which are responsible for the growth and reproduction and some of these plays' crucial role in inflammatory response and progressive LF fibrosis [24]. However, we have not studied any such markers.

Limitation

The present study exhibited that morphometric findings can be studied satisfactorily even in the absence of an electron microscope, which can be reproduced even in less sophisticated setups. However, it could not differentiate between the dorsal and dural aspects as we removed the LF piecemeal and not as a whole. The central and peripheral parts could not be segregated, which could allow more in-depth understanding, particularly of chondroid metaplasia. Clinical scoring, occupational activity, and MRI measurement were also ignored to keep the study simple. Additionally, gene expression was not studied in the present study.

CONCLUSION

The LCS and non-LCS groups differ in clinical parameters, mainly symptom duration. Histopathologically, the two groups exhibited significant differences in elastin degeneration, fragmentation, elastic/collagen ratio, fibrosis, and number of ligamentocytes. However, calcification was not significant between the groups.

ARTICLE HIGHLIGHTS

Research background

Ligament flavum (LF) hypertropy is the main etiopathogenesis of lumbar canal stenosis (LCS). The purely elastic LF undergoes a morphological adaptation including a reduction in the elastic fibers and a consequent increase in the collagen content, fibrosis, cicatrization, and calcification. However, the morphometric analysis can delineate the LF in patients with LCS from those without LCS, which would help in better understanding LCS pathogenesis.

Research motivation

The research is motivated due to high footfall of these patient on Orthopedic outpatient department. An interdepartmental meeting was made to analyze these patients and funds were provided by the institute.

Research objectives

To compare the histopathological changes in LF between the degenerative LCS and non-stenotic (non-LCS) group.

Research methods

The present prospective study was conducted in 82 patients who were divided into two groups, namely LCS and non-LCS. Demographic details of the patients such as duration of symptoms, level of involvement, and number of segments were recorded. The LF obtained from both groups was histopathologically examined for the fibrosis score, elastic fiber degeneration, calcification, and chondroid metaplasia. Morphometrical details included a change in elastin and collagen percentages, elastin/collagen ratio, elastic fiber fragmentation, and ligamentocyte numbers. All parameters were compared between the two groups by using the independent *t* test, Chi-square test, and Pearson's correlation test.

Research results

Of the total, we selected 74 patients. The number of patients in the LCS and non-LCS groups was 34 and 40, respectively. The mean ± standard deviation of age of presentation in the LCS and non-LCS groups was 49.2 ± 8.9 and 43.1 ± 14.3 years, respectively. The difference in fibrosis (P = 0.002), elastic fiber degeneration (P = 0.01), elastic fragmentation percentage (66.5% ± 16.3% *vs* 29.5% ± 16.9%), elastic content percentage (26.9% ± 6.7% *vs* 34.7% ± 8.4%), collagen content percentage (63.6% ± 10.4% *vs* 54.9% ± 6.4%), reduction of elastic/collagen ratio (0.4 ± 0.1 *vs* 0.6 ± 0.1), and ligamentocyte number (39.1 ± 19.1 *vs* 53.5 ± 26.9) between the LCS and non-LCS groups was statistically significant. The difference in calcification (P = 0.08) and Pearson's correlation between duration and loss of elastin was statistically nonsignificant. Subgroup analysis exhibited a consistent difference in LF morphology in patients aged ≥ 40 years between the two groups. A similar finding was observed in patients aged < 40 and > 40 years in the non-LCS group.

Research conclusions

The quality change in elastin fibers and an increase in the collagen content and fibrosis cause loss of elasticity in LF, contributing to LCS pathogenesis. However, calcification did not play a significant role in LCS pathogenesis.

Research perspectives

Tne study compare the histopathological changes in LF between the degenerative LCS and non-stenotic (non-LCS) group.

FOOTNOTES

Author contributions: Jain M, Sable B, Tirpude AP, and Sahu RN conceived the idea; Jain M got the ethical clearance and grant for the study; Jain M, Sahu RN, and Das G collected the sample; Sable M and Tirpude AP performed the histological analysis; The data were compiled by Jain M and Samanta SK; Sable M and Jain M performed the statistical analysis; Jain M, Samanta SK, and Das G wrote the manuscript, whereas the other authors provided critical inputs; All authors have read and agree to the content of the manuscript.

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Institutional review board statement: The study was reviewed and approved by the Institutional ethics committee of AIIMS Bhubaneswar (T/IM/18-19/43 dated 04/01/2019).

Informed consent statement: All patients gave informed consent.

Conflict-of-interest statement: There is no conflict of interest.

Data sharing statement: Participants gave informed consent for data sharing.

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REFERENCES

1 **Sairyo K**, Biyani A, Goel V, Leaman D, Booth R Jr, Thomas J, Gehling D, Vishnubhotla L, Long R, Ebraheim N. Pathomechanism of ligamentum flavum hypertrophy: a multidisciplinary investigation based on clinical, biomechanical, histologic, and biologic assessments. *Spine (Phila Pa 1976)* 2005; **30**: 2649-2656 [PMID: 16319751 DOI: 10.1097/01.brs.0000188117.77657.ee]

2 **Altun I**, Yüksel KZ. Histopathological Analysis of Ligamentum Flavum in Lumbar Spinal Stenosis and Disc Herniation.

Asian Spine J 2017; **11**: 71-74 [PMID: 28243372 DOI: 10.4184/asj.2017.11.1.71]

3 **Hansson T**, Suzuki N, Hebelka H, Gaulitz A. The narrowing of the lumbar spinal canal during loaded MRI: the effects of the disc and ligamentum flavum. *Eur Spine J* 2009; **18**: 679-686 [PMID: 19277726 DOI: 10.1007/s00586-009-0919-7]

4 **Hulmani D**, Garg B, Mehta N, Mridha AR, Nag TC, Farooque K. Morphological Changes in the Ligamentum Flavum in Degenerative Lumbar Canal Stenosis: A Prospective, Comparative Study. *Asian Spine J* 2020; **14**: 773-781 [PMID: 32429020 DOI: 10.31616/asj.2020.0041]

5 **Giles LG**, Kaveri MJ. Some osseous and soft tissue causes of human intervertebral canal (foramen) stenosis. *J Rheumatol* 1990; **17**: 1474-1481 [PMID: 2273488]

6 **Zhong ZM**, Zha DS, Xiao WD, Wu SH, Wu Q, Zhang Y, Liu FQ, Chen JT. Hypertrophy of ligamentum flavum in lumbar spine stenosis associated with the increased expression of connective tissue growth factor. *J Orthop Res* 2011; **29**: 1592-1597 [PMID: 21484860 DOI: 10.1002/jor.21431]

7 **Kolte VS**, Khambatta S, Ambiye MV. Thickness of the ligamentum flavum: correlation with age and its asymmetry-an magnetic resonance imaging study. *Asian Spine J* 2015; **9**: 245-253 [PMID: 25901237 DOI: 10.4184/asj.2015.9.2.245]

8 **Fukuyama S**, Nakamura T, Ikeda T, Takagi K. The effect of mechanical stress on hypertrophy of the lumbar ligamentum flavum. *J Spinal Disord* 1995; **8**: 126-130 [PMID: 7606119]

9 **Postacchini F**, Gumina S, Cinotti G, Perugia D, DeMartino C. Ligamenta flava in lumbar disc herniation and spinal stenosis. Light and electron microscopic morphology. *Spine (Phila Pa 1976)* 1994; **19**: 917-922 [PMID: 8009349 DOI: 10.1097/00007632-199404150-00009]

10 **Okuda T**, Baba I, Fujimoto Y, Tanaka N, Sumida T, Manabe H, Hayashi Y, Ochi M. The pathology of ligamentum flavum in degenerative lumbar disease. *Spine (Phila Pa 1976)* 2004; **29**: 1689-1697 [PMID: 15284518 DOI: 10.1097/01.brs.0000132510.25378.8c]

11 **Hamdan TA**, Jbara KK, Hatem HA. Histological Changes of Ligamenta Flava in Lumbar Disc Herniation and Spinal Canal Stenosis. *Basrah J Surg* 2005; **11**: 1-14 Available from: https://www.semanticscholar.org/paper/HISTOLOGICAL-CHANGES-OF-LIGAMENTA-FLAVA-IN-LUMBAR-Hatem-Jbara/9df6335c9351393e307b723bf70dea3a7980d2c2

12 **Schräder PK**, Grob D, Rahn BA, Cordey J, Dvorak J. Histology of the ligamentum flavum in patients with degenerative lumbar spinal stenosis. *Eur Spine J* 1999; **8**: 323-328 [PMID: 10483836 DOI: 10.1007/s005860050181]

13 **Elsberg C**. Experiences in spinal surgery: observations upon 60 Laminectomies for spinal disease. *Surg Gynecol Obs* 1913; **16**: 117-132

14 **Wang B**, Gao C, Zhang P, Sun W, Zhang J, Gao J. The increased motion of lumbar induces ligamentum flavum hypertrophy in a rat model. *BMC Musculoskelet Disord* 2021; **22**: 334 [PMID: 33823825 DOI: 10.1186/s12891-021-04203-x]

15 **Chuang HC**, Tsai KL, Tsai KJ, Tu TY, Shyong YJ, Jou IM, Hsu CC, Shih SS, Liu YF, Lin CL. Oxidative stress mediates age-related hypertrophy of ligamentum flavum by inducing inflammation, fibrosis, and apoptosis through activating Akt and MAPK pathways. *Aging (Albany NY)* 2020; **12**: 24168-24183 [PMID: 33223505 DOI: 10.18632/aging.104105]

16 **Zaki SM**. Study of the human ligamentum flavum in old age: a histological and morphometric study. *Folia Morphol (Warsz)* 2014; **73**: 492-499 [PMID: 25448909 DOI: 10.5603/FM.2014.0074]

17 **Baba H**, Maezawa Y, Furusawa N, Imura S, Tomita K. The role of calcium deposition in the ligamentum flavum causing a cauda equina syndrome and lumbar radiculopathy. *Paraplegia* 1995; **33**: 219-223 [PMID: 7609980 DOI: 10.1038/sc.1995.49]

18 **Reyes-Sánchez A**, García-Ramos CL, Deras-Barrientos CM, Alpizar-Aguirre A, Rosales-Olivarez LM, Pichardo-Bahena R. Ligamentum flavum in lumbar spinal stenosis, disc herniation and degenerative spondylolisthesis. An histopathological description. *Acta Ortop Mex* 2019; **33**: 308-313 [PMID: 32253853]

19 **Sato N**, Higashino K, Sakai T, Terai T, Goel VK, Biyani A, Ebraheim N, Takata Y, Hayashi F, Yamashita K, Morimoto M, Manabe H, Sairyo K. Role of Epiligament in Ligamentum Flavum Hypertrophy in Patients with Lumbar Spinal Canal Stenosis:a Pilot Study. *J Med Invest* 2018; **65**: 85-89 [PMID: 29593200 DOI: 10.2152/jmi.65.85]

20 **Peng YX**, Zheng ZY, Wang Md WG, Liu L, Chen Md F, Xu Md HT, Zhang ZM. Relationship between the location of ligamentum flavum hypertrophy and its stress in finite element analysis. *Orthop Surg* 2020; **12**: 974-982 [PMID: 32489000 DOI: 10.1111/os.12675]

21 **Yabe Y**, Hagiwara Y, Tsuchiya M, Honda M, Hatori K, Sonofuchi K, Kanazawa K, Koide M, Sekiguchi T, Itaya N, Itoi E. Decreased elastic fibers and increased proteoglycans in the ligamentum flavum of patients with lumbar spinal canal stenosis. *J Orthop Res* 2016; **34**: 1241-1247 [PMID: 26679090 DOI: 10.1002/jor.23130]

22 **Viejo-Fuertes D**, Liguoro D, Rivel J, Midy D, Guerin J. Morphologic and histologic study of the ligamentum flavum in the thoraco-lumbar region. *Surg Radiol Anat* 1998; **20**: 171-176 [PMID: 9706675 DOI: 10.1007/BF01628891]

23 **Cheung PWH**, Tam V, Leung VYL, Samartzis D, Cheung KM, Luk KD, Cheung JPY. The paradoxical relationship between ligamentum flavum hypertrophy and developmental lumbar spinal stenosis. *Scoliosis Spinal Disord* 2016; **11**: 26 [PMID: 27635416 DOI: 10.1186/s13013-016-0088-5]

24 **Sun C**, Zhang H, Wang X, Liu X. Ligamentum flavum fibrosis and hypertrophy: Molecular pathways, cellular mechanisms, and future directions. *FASEB J* 2020; **34**: 9854-9868 [PMID: 32608536 DOI: 10.1096/fj.202000635R]

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ORIGINAL ARTICLE

Clinical Trials Study

Short arm cast is as effective as long arm cast in maintaining distal radius fracture reduction: Results of the SLA-VER noninferiority trial

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Abstract

BACKGROUND

Distal radius fractures (DRFs) are a common challenge in orthopaedic trauma care, yet for those fractures that are treated nonoperatively, strong evidence to guide cast treatment is still lacking.

AIM

To compare the efficacy of below elbow cast (BEC) and above elbow cast (AEC) in maintaining reduction of manipulated DRFs.

METHODS

We conducted a prospective, monocentric, randomized, parallel-group, open label, blinded, noninferiority trial comparing the efficacy of BEC and AEC in the nonoperative treatment of DRFs. Two hundred and eighty patients > 18 years of age diagnosed with DRFs were successfully randomized and included for analysis over a 3-year period. Noninferiority thresholds were defined as a 2 mm difference for radial length (RL), a 3° difference for radial inclination (RI), and volar tilt (VT). The trial is registered at Clinicaltrials.gov (NCT03468023).

RESULTS

One hundred and forty-three patients were treated with BEC, and 137 were treated with AEC. The mean time of immobilization was 33 d. The mean loss of RL, RI, and VT was 1.59 mm, 2.83°, and 4.11° for BEC and 1.63 mm, 2.54°, and

3.52° for AEC, respectively. The end treatment differences between BEC and AEC in RL, RI, and VT loss were respectively 0.04 mm (95%CI: -0.36-0.44), -0.29° (95%CI: -1.03-0.45), and 0.59° (95%CI: -1.39-2.57), and they were all below the prefixed noninferiority thresholds. The rate of loss of reduction was similar.

CONCLUSION
BEC performs as well as AEC in maintaining the reduction of a manipulated DRF. Being more comfortable to patients, BEC may be preferable for nonoperative treatment of DRFs.

Key Words: Distal radius fracture; Immobilization; Below elbow cast; Above elbow cast; Short arm cast; Long arm cast

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Core Tip: Currently, there is no general agreement on how best to immobilize a distal radius fracture (DRF) although classic teaching was that immobilization of the elbow would ensure better control of fracture instability. This has been recently challenged by a number of new randomized controlled trials (RCTs) but no one was designed as a non-inferiority RCT, which is the most appropriate way to evaluate the hypothesis that blocking the elbow is unnecessary. We devised a large population noninferiority RCT to give statistical evidence that short arm cast is as effective as long arm cast to treat DRFs using predetermined noninferiority thresholds.

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INTRODUCTION

Distal radius fractures (DRFs) are a common clinical challenge in orthopaedic trauma care. Traditionally, it was thought that immobilization including the elbow would ensure better control of fracture instability, prevent loss of reduction, and result in better clinical outcomes. However, long arm casts are cumbersome and treatment with lighter short arm casts is generally considered a more comfortable option for patients. Currently, there is no general agreement on how best to immobilize a DRF. Various methods have been described, but no one approach has been identified as being more effective than another[1-4]. According to the latest clinical practice guidelines from the American Academy of Orthopaedic Surgeons, released in 2009, the evidence available for and against elbow immobilization in patients treated with a cast is "inconclusive" and the choice between them is down to the clinician's judgment[5]. The hypothesis that short arm casts might perform as well as long arm casts in maintaining the reduction of DRFs has been tested in a number of previous studies. These superiority randomized controlled trials (RCTs) have not found a significant difference in outcome and risk of loss of reduction between below elbow cast (BEC) and above elbow cast (AEC)[6-11]. However, the absence of any significant difference in these studies does not necessarily indicate equivalence[12]. To compare the efficacy and tolerability of these two treatment approaches, we designed a noninferiority randomized trial using predefined minimal clinically important difference thresholds.

In this paper, the terms short arm cast and BEC or long arm cast and AEC are used interchangeably.

MATERIALS AND METHODS

Design

The SLA-VER trial is a prospective, monocentric, randomized, parallel-group, open label, blinded, noninferiority trial (PROBE design), comparing the efficacy of BEC and AEC in maintaining reduction of manipulated DRFs. This study was approved by the local institutional review board (CE\1165CESC), conducted in accordance with the Declaration of Helsinki, and registered on ClinicalTrials.org (NCT03468023). All patients enrolled gave written informed consent.

Outcomes

The primary outcome was fracture reduction maintenance, measured as variation in radial length (RL), radial inclination (RI), and volar tilt (VT). The secondary outcomes included disability of arm, shoulder and hand (DASH) scores and short form 12 (SF-12) scores as measures of cast tolerability.

Population

All patients admitted to the emergency room with a diagnosis of DRF were enrolled according to the following inclusion criteria: Age ≥ 18 years; candidates for nonoperative treatment; displaced fracture requiring manipulation. The exclusion criteria were: Skeletally immature patients (less than 18); undisplaced fracture; fracture requiring surgical treatment; open fracture; hand/wrist/forehand skin lesion on fractured limb; vascular or neurological deficit; bilateral fracture; association with homolateral upper limb fracture. Patients with any medical comorbidity were included, but pregnant patients or patients requiring urgent or life-saving procedures were excluded. Patients were excluded from the study (*i.e.* dropouts) if reduction could not be achieved after two attempts (after which surgical treatment was offered), the cast was damaged or removed during treatment, or consent was withdrawn [13].

Procedures

Randomization was carried out by a statistician with no involvement in the clinical care of patients. Software random allocation in blocks of 4 resulted in 353 sequentially numbered opaque sealed envelopes. When a patient was eligible for enrollment, an envelope was opened to assign the participant to a treatment group. Closed manipulation was performed under hematoma block, and the forearm was immobilized in an opposite-to-dislocation position. The arm cast was a radial gutter made of plaster of Paris (POP) that was left open on the volar side to allow for swelling and then circumferentially closed 5-7 d later by applying an extra layer of POP (Figure 1). BEC patients were treated with a BEC extending from the metacarpal heads to 2-4 cm from the elbow crease. AEC patients were treated with an AEC extending from the metacarpal heads to the middle third of the arm. Posteroanterior (PA) and lateral view X-rays were taken pre and post manipulation and at 7 and 35 d. The radial gutter was closed at the first office visit and removed at the final visit. If closed manipulation failed to achieve satisfactory reduction, patients were offered surgical treatment and excluded from the study. If reduction was lost at 7 d, patients were offered surgical treatment. These patients were still considered for analysis as subjects who did not maintain satisfactory reduction at the final follow-up. Radiographic parameters were determined at each X-ray examination. RL was measured on the PA view as the distance between two lines drawn perpendicularly to the radial shaft long axis: one at the tip of the radial styloid and one at the ulnar border of the radius articular surface at the central reference point, which is a point midway between the volar and dorsal ulnar corners to eliminate variation caused by dorsal angulation as described by Slutsky[14]. RI was measured on the PA view by determining the angle between a line passing through the tip of the radial styloid and the medial corner of the articular surface of the radius and a line perpendicular to the shaft of the radius. VT was measured on the lateral view by the angle between the line of the distal articular surface (passing through the two most distal points of the dorsal and volar lips of the radius) and the longitudinal axis of the radius[14,15]. Fracture stability was assessed according to Lafontaine (dorsal angulation > 20°, dorsal comminution, articular involvement, associated ulnar fracture, and age > 60 years): If three or more of these criteria were present, the fracture was defined unstable[16]. The casting technique was assessed by means of cast index and three-point index[17,18]. Reduction was considered to be maintained when the following criteria, described by Graham, were met[13]: Loss of radial length < 5 mm, radial inclination ≥ 15°, and volar tilt between +15° and -20°. Given the variability of the criteria used to assess acceptability of reduction, we decided to further test the dataset against three other sets of criteria (combinations of different thresholds of RL, RI, and VT). All measurements were performed by three investigators, none of whom were involved in patient recruitment and all of whom were blinded to patient group assignment. Patients were stratified by age, sex, presence of osteoporosis (indirectly assessed by osteoporosis-specific drug consumption), fracture type (according to AO classification), and fracture stability (according to Lafontaine's criteria) [19]. At the final follow-up visit, patients were asked to complete DASH and SF-12 questionnaires and elbow range of movement (ROM) after cast removal was also recorded[20,21]. Protocol details have been published previously[22] and are available at https://clinicaltrials.gov/ct2/show/NCT03468023.

Statistical analysis

For the study to have 80% power to show a difference between the treatments with a two-sided type 1 error rate of 5%, we calculated that approximately 150 patients would be required for each group using a 2 mm difference in RL and a 3° difference in RI and VT as noninferiority thresholds. These estimates of minimal clinically important differences were based on previous reports of interobserver variability of up to 3° in radiographic parameter measurement and considerable deterioration of clinical outcome when shortening of RL was > 5 mm[15,23,24]. We included 53 additional patients to make up for a predicted 15% dropout rate. Since our aim was to identify the real treatment efficacy under optimal conditions, we conducted a per-protocol analysis. In noninferiority trials, both intention-to-treat and



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Figure 1 Above elbow cast (long arm cast) on the left side and below-elbow cast (short arm cast) on the right side. A and C: Long arm cast; B and D: Short arm cast.

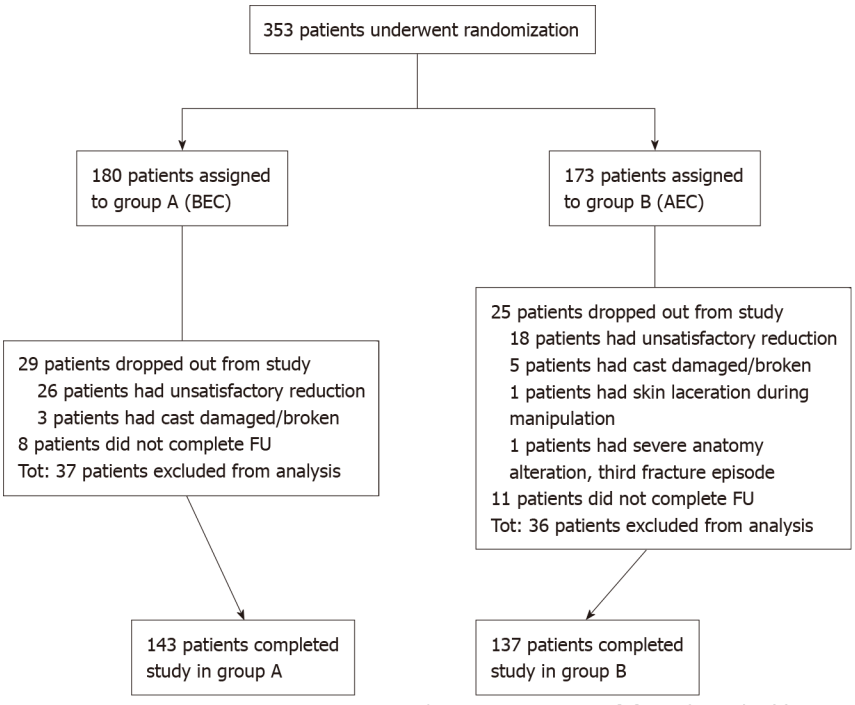
per-protocol analyses are recommended[25]. In this trial, we did not include dropouts in the final analysis, since doing so would have introduced a confounding effect of surgery. We did not use baseline differences to decide whether and which covariates should be used to adjust treatment effect because we assumed that, in RCTs, any baseline difference between the two groups is attributable to chance and thus negligible[26]. The 95%CI was calculated for continuous variables following a normal distribution. Noninferiority *t*-tests were used to compare radiological parameters, and chi-squared tests were used to compare percentages of loss of reduction between the two groups. DASH and SF-12 scores between the BEC and AEC groups were compared using superiority *t*-tests. All variables included in the analysis were complete, with no missing data. Analyses were performed using SAS 9.4.

RESULTS

Between March 2017 and February 2020, 353 eligible patients were enrolled in the trial. Of these, 180 patients were randomly assigned to treatment group A (BEC) and 173 were randomly assigned to treatment group B (AEC). In group A, 29 patients dropped out of the study, and 8 did not complete the follow-up. In group B, 25 patients dropped out from the study, and 11 did not complete the follow-up (Figure 2). Dropouts (and dropout reasons) were similar between the groups. A total of 280 patients (143 in group A and 137 in group B) completed the study and were included in the analysis. The study groups were similar with respect to age, sex, osteoporosis, type of fracture (AO classification), and stability of fracture, as shown in Table 1. Cast index and three-point index were homogeneous between the groups ($\chi^2 = 1.72$, $P = 0.19$ and $\chi^2 = 0.06$, $P = 0.79$, respectively). Randomization resulted in two well-balanced study groups. The mean time of immobilization was 33 d (95%CI: 31.88-34.10) for BEC patients and 32.6 d (95%CI: 31.5-33.63) for AEC patients. Nine patients treated with BEC and ten treated with AEC lost reduction at 7 d. Seven were treated surgically, and two continued nonoperative treatment in the BEC group; seven were treated surgically, and three continued nonoperative treatment in the AEC group. Upon removal of cast at the final follow-up, the mean loss of RL was -1.59 mm for BEC *vs* -1.63 mm for AEC (between-group difference: 0.04 mm; 95%CI: -0.36-0.44); the mean loss of RI was -2.83° in BEC *vs* -2.54° in AEC (between-group difference: -0.29°; 95%CI: -1.03-0.45); the mean loss of VT was 4.11° in BEC *vs* 3.52° in AEC (between-group difference: 0.59°; 95%CI: -1.39-2.57). Differences in loss of RL, RI, and VT during treatment between the groups reached statistical significance when tested for noninferiority ($P < 0.0001$ for RL, $P < 0.0001$ for RI, and $P = 0.0087$ for VT), and all differences were below the prefixed thresholds outlined above. Differences between the final and baseline radiographic parameters are reported in Table 2. According to Graham's criteria, 99 (69%) out of 143 patients treated with BEC maintained satisfactory reduction as opposed to 106 (77%) out of 137 patients treated with AEC. This difference was not significant ($P = 0.12$; Table 3). Considering that the percentage of fractures labelled as "maintained" varies according to the criteria of acceptability of reduction used, we tested a further three sets of criteria as described above. In all cases, no statistically significant difference was

Table 1 Baseline patient demographics

Characteristic	Group A (below-elbow cast)	Group B (above-elbow cast)	*t*-test (*t*) or Chi-squared test (χ^2)	*P* value
Age (yr), mean ± SD	70.2 ± 13.7	69.5 ± 15.4	$t = 0.42$	$P = 0.68$
Sex, *n* (%)			$\chi^2 = 0.02$	$P = 0.89$
Male	19 (13)	19 (14)		
Female	124 (87)	118 (86)		
Osteoporosis, *n* (%)			$\chi^2 = 1.53$	$P = 0.46$
Yes	44 (31)	78 (57)		
No	84 (59)	38 (28)		
Missing	15 (10)	21 (15)		
Type of fracture (AO classification), *n* (%)			$\chi^2 = 0.20$	$P = 0.90$
Type A	48 (34)	43 (31)		
Type B	17 (12)	18 (13)		
Type C	78 (55)	76 (55)		
Stability of fracture (Lafontaine), *n* (%)			$\chi^2 = 0.12$	$P = 0.73$
Stable	68 (48)	68 (50)		
Unstable	75 (52)	69 (50)		



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Figure 2 Study flow chart. BEC: Below elbow cast; AEC: Above elbow cast.

observed (66% maintained in BEC *vs* 74% in AEC for type 2, 61% maintained in BEC *vs* 62% in AEC for type 3, and 62% maintained in BEC *vs* 61% in AEC for type 4; Table 3). DASH score, SF-12 [physical component summary (PCS) and mental component summary (MCS)] scores, and elbow ROM were collected for 122 out of 280 patients: 55 (38%) patients in group A and 67 (49%) patients in group B. DASH score for BEC patients was 59 (95%CI: 53.8-64.2) and 59.9 (95%CI: 55.6-64.3) for AEC patients; the mean PCS and MCS scores were 34.9 (95%CI: 32.9-36.9) and 43.6 (95%CI: 40.5-46.8), respectively, for BEC patients and 36.6 (95%CI: 34.9-38.2) and 41.8 (95%CI: 39.1-44.5) for AEC patients. No difference was

Table 2 Radiographic parameter comparison between below-elbow cast and above-elbow cast at baseline (post reduction) and at final control

Parameter	Group A (BEC), mean (95%CI)	Group B (AEC), mean (95%CI)	*t*-test (*t*) comparing groups	*P* value
Baseline (post reduction)				
RL	11.31 mm (11.03; 11.60)	11.35 mm (11.05; 11.64)	t = -0.17	P = 0.86
RI	20.90° (20.41; 21.39)	21.08° (20.58; 21.59)	t = -0.50	P = 0.62
VT	-8.06° (-9.11; -7.01)	-6.55° (-7.56; -5.55)	t = -2.05	P = 0.04
Final control (35 d)				
RL	9.73 mm (9.33; 10.12)	9.72 mm (9.35; 10.09)	t = 0.02	P = 0.99
RI	18.07° (17.42; 18.72)	18.54° (17.88; 19.19)	t = -1.01	P = 0.31
VT	-3.95° (-5.61; -2.29)	-3.03° (-4,35; -1,71)	t = -0.86	P = 0.39
Δ final control–baseline				
Parameter				
RL	-1.59 mm (-1.88; -1.29)	-1.63 mm (-1.89; -1.36)	t = 0.2	P = 0.84
RI	-2.83° (-3.37; -2.29)	-2.54° (-3.05; -2.03)	t = -0.77	P = 0.44
VT	4.11° (2.61; 5.61)	3.53° (2.22; 4.83)	t = 0.58	P = 0.56
Δ of loss of radiographic parameters during treatment (BEC–AEC)				
Parameter	Group A-B, mean (95%CI)			
RL	0.04 mm (-0.36; 0.44)			
RI	-0.29° (-1.03; 0.45)			
VT	0.59° (-1.39; 2.57)			

BEC: Below elbow cast; AEC: Above elbow cast; RL: Radial length; RI: Radial inclination; VT: Volar tilt.

Table 3 Radiographic criteria for acceptability of reduction and percentage of maintenance of reduction comparison between below elbow cast and above elbow cast

	Type I (Graham)	Type II (Gliatis)	Type III (Aro and Koivunen)	Type IV (Fernandez)
Radiographic criterion/acceptable measurement				
RL shortening	< 5 mm	< 5 mm	< 3 mm	< 3 mm
RI	≥ 15°	≥ 15°	≥ 15°	≥ 15°
VT	Between 15° and 20°	Between 10° and 20°	Between 15° and 20°	Between 10° and 20°
Maintenance, *n* (%)				
Group A (BEC)	99 (69)	95 (66)	87 (61)	89 (62)
Group B (AEC)	106 (77)	101 (74)	87 (63)	83 (61)
Chi-squared test (χ^2)	χ^2 = 2.36	χ^2 = 1.77	χ^2 = 0.21	χ^2 = 0.09
P value	P = 0.12	P = 0.18	P = 0.65	P = 0.75

BEC: Below elbow cast; AEC: Above elbow cast; RL: Radial length; RI: Radial inclination; VT: Volar tilt.

observed between patient groups. Subgroup analysis for dominant side fracture did not change the result. Regarding elbow ROM, BEC patients exhibited a mean flexion of 123.6° (95%CI: 117.1-130.1), mean extension of 6.7° (95%CI: 2.5-10.8), mean pronation of 69.5° (95%CI: 63.8-75.3), and mean supination of 52.5° (95%CI: 45.6-59.3). AEC patients had similar ROM, with a mean flexion of 123.9° (95%CI: 118.9-128.9), mean extension of 5.5° (95%CI: 1.4-9.5), mean pronation of 72.1° (95%CI: 66.4-77.9), and mean supination of 52.9° (95%CI: 45.5-60.3). Again, no difference was observed between the groups.

DISCUSSION

Noninferiority tests are the most appropriate way to evaluate the hypothesis that BEC and AEC have similar efficacy. They are based on minimal clinically important thresholds that are established *a priori* by drawing on empirical assumptions. When observed between-treatment differences fall below these thresholds, treatments can be considered equivalent. Statistical superiority tests, for example, the percentage of fractures that maintain reduction *vs* the percentage of fractures that lose reduction, can be misleading since they tell us nothing about equivalence[12]. Therefore, in the current study, we analysed both dichotomic variables (*i.e.*, percentage of reduction maintenance) and continuous variables (*i.e.*, radiographic radial parameters) for which noninferiority thresholds could be predetermined. By employing a noninferiority design, the current study showed that the efficacy of BEC in maintaining the reduction of manipulated DRFs is similar to that of AEC. According to our model, when clinicians have to choose between using BEC or AEC to immobilize a DRF, the maximum predictable outcome difference between the two treatments does not exceed 2 mm in terms of RL loss and 3° in terms of RI and VT loss. Maintenance of reduction of DRFs is more likely to depend on factors other than length of cast used, for example, patient age and stability or type of fracture. SLA-VER has some limitations that warrant discussion. Quality of reduction was not assessed and could have potentially influenced the difference between BEC and AEC. Given that no computerized tomography was carried out, we may not have accurately measured every articular gap, and it is possible that its prevalence might be different between the study groups. However, our approach is consistent with general clinical practice. Furthermore, we limited our investigation to radiological outcomes only and did not include clinical outcome measures. SLA-VER aimed only at ascertaining whether the type of casting used affects the likelihood of fracture maintenance. A large amount of data about factors associated with loss of reduction risk and clinical outcome has already been published[16,27-39]. Only a small number of patients completed the DASH and SF-12 questionnaires and received elbow ROM measurements, even though this was a secondary study endpoint. Our data did not reveal a clear difference in patient comfort between BEC and AEC and this remained true even after subgroup analysis of dominant side fractures. Surprisingly, elbow range of motion was not affected by the type of cast as one would have expected. One explanation could be that the time of immobilization may have been too short to result in significant elbow stiffness or that the absence of elbow injury might have contributed to preserving joint mobility. This finding is also reported by Okamura *et al*[11]. Finally, it may be that DASH scores are not the most appropriate way to assess cast comfort. Bong *et al*[7] found better DASH scores in below-elbow splints, although to a lesser degree than expected, suggesting that DASH might not be able to specifically address the comfort level of the two constructs. Furthermore, Caruso *et al*[10] did not find any difference in DASH scores between BEC and AEC at the 4 wk follow-up but reported a significant difference in favour of BEC using the Mayo elbow score. Similarly, Park *et al*[8] did not find any difference in DASH score between BEC and AEC, although they found a correlation with the dominant side and a higher incidence of shoulder pain in the latter group. Nevertheless, BEC is broadly considered more comfortable and preferable than AEC[8].

CONCLUSION

Data from this trial lead us to conclude that BEC performs as well as AEC in maintaining reduction of a manipulated DRF. When clinicians have to choose between BEC and AEC, the maximum predictable difference does not exceed 2 mm in terms of RL loss and 3° in terms of RI and VT loss. We recommend BEC over AEC for its non-inferior performance and better tolerability.

ARTICLE HIGHLIGHTS

Research background

Distal radius fracture (DRF) treatment is a common challenge in orthopaedic trauma care. Uncertainty exists on how best to immobilize a DRF.

Research motivation

The necessity of blocking the elbow when immobilizing a DRF is still a matter of debate.

Research objectives

To test the hypothesis that blocking the elbow is not necessary and that a below arm cast (BEC) performs as well as an above elbow cast (AEC).

Research methods

A noninferiority randomized clinical trial was conducted on 280 patients diagnosed with a DRF managed nonsurgically. Loss of reduction was evaluated considering variation in radiographic parameters [radial length (RL), radial inclination (RI), and volar tilt (VT)].

Research results

Rates of loss of reduction were similar between BEC and AEC. Variation of radiographic parameters (RL, RI, and VT) was similar between BEC and AEC and fell within the predetermined noninferiority thresholds.

Research conclusions

BEC performs as well as AEC in maintaining reduction of a manipulated DRF.

Research perspectives

Further large population randomized controlled trials and meta-analyses are required to confirm the hypothesis that BEC should become the option of choice for DRF treatment.

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FOOTNOTES

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Clinical trial registration statement: This study was registered on ClinicalTrials.org (NCT03468023).

Informed consent statement: All study participants provided informed written consent prior to study enrollment.

Conflict-of-interest statement: Each author certifies that he or she has no conflict of interest in connection with the submitted article.

Data sharing statement: Dataset and statistical code is available from the corresponding author on request.

CONSORT 2010 statement: The authors have read the CONSORT 2010 statement, and the manuscript was prepared and revised according to the CONSORT 2010 statement.

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REFERENCES

1 **Sarmiento A**, Pratt GW, Berry NC, Sinclair WF. Colles' fractures. Functional bracing in supination. *J Bone Joint Surg Am* 1975; **57**: 311-317 [PMID: 1123382]
2 **Sarmiento A**. The brachioradialis as a deforming force in Colles' fractures. *Clin Orthop Relat Res* 1965; **38**: 86-92 [PMID: 5889097]
3 **Bünger C**, Sølund K, Rasmussen P. Early results after Colles' fracture: functional bracing in supination vs dorsal plaster immobilization. *Arch Orthop Trauma Surg (1978)* 1984; **103**: 251-256 [PMID: 6391415 DOI: 10.1007/BF00387330]
4 **Wahlström O**. Treatment of Colles' fracture. A prospective comparison of three different positions of immobilization. *Acta Orthop Scand* 1982; **53**: 225-228 [PMID: 7136568 DOI: 10.3109/17453678208992206]
5 **Lichtman DM**, Bindra RR, Boyer MI, Putnam MD, Ring D, Slutsky DJ, Taras JS, Watters WC 3rd, Goldberg MJ, Keith M, Turkelson CM, Wies JL, Haralson RH 3rd, Boyer KM, Hitchcock K, Raymond L. Treatment of distal radius fractures. *J Am Acad Orthop Surg* 2010; **18**: 180-189 [PMID: 20190108 DOI: 10.5435/00124635-201003000-00007]
6 **Sahin M**, Taşbaş BA, Dağlar B, Bayrakci K, Savaş MS, Günel U. [The effect of long- or short-arm casting on the stability of reduction and bone mineral density in conservative treatment of Colles' fractures]. *Acta Orthop Traumatol Turc* 2005; **39**: 30-34 [PMID: 15805751]
7 **Bong MR**, Egol KA, Leibman M, Koval KJ. A comparison of immediate postreduction splinting constructs for controlling initial displacement of fractures of the distal radius: a prospective randomized study of long-arm versus short-arm splinting. *J Hand Surg Am* 2006; **31**: 766-770 [PMID: 16713840 DOI: 10.1016/j.jhsa.2006.01.016]
8 **Park MJ**, Kim JP, Lee HI, Lim TK, Jung HS, Lee JS. Is a short arm cast appropriate for stable distal radius fractures in patients older than 55 years? *J Hand Surg Eur Vol* 2017; **42**: 487-492 [PMID: 28490225 DOI: 10.1177/1753193417690464]
9 **Gamba C**, Fernandez FAM, Llavall MC, Diez XL, Perez FS. Which immobilization is better for distal radius fracture? *Int Orthop* 2017; **41**: 1723-1727 [PMID: 28578470 DOI: 10.1007/s00264-017-3518-y]
10 **Caruso G**, Tonon F, Gildone A, Andreotti M, Altavilla R, Valentini A, Valpiani G, Massari L. Below-elbow or above-elbow cast for conservative treatment of extra-articular distal radius fractures with dorsal displacement: a prospective randomized trial. *J Orthop Surg Res* 2019; **14**: 477 [PMID: 31888682 DOI: 10.1186/s13018-019-1530-1]
11 **Okamura A**, de Moraes VY, Neto JR, Tamaoki MJ, Faloppa F, Belloti JC. No benefit for elbow blocking on conservative treatment of distal radius fractures: A 6-month randomized controlled trial. *PLoS One* 2021; **16**: e0252667 [PMID: 34111160 DOI: 10.1371/journal.pone.0252667]
12 **Harris AH**, Fernandes-Taylor S, Giori N. "Not statistically different" does not necessarily mean "the same": the important but underappreciated distinction between difference and equivalence studies. *J Bone Joint Surg Am* 2012; **94**: e29 [PMID: 22398743 DOI: 10.2106/JBJS.K.00568]
13 **Graham TJ**. Surgical Correction of Malunited Fractures of the Distal Radius. *J Am Acad Orthop Surg* 1997; **5**: 270-281 [PMID: 10795063 DOI: 10.5435/00124635-199709000-00005]
14 **Slutsky DJ**. Principles and practice of wrist surgery. Philadelphia PA: Saunders Elsevier, 2010
15 **Johnson PG**, Szabo RM. Angle measurements of the distal radius: a cadaver study. *Skeletal Radiol* 1993; **22**: 243-246 [PMID: 8316865 DOI: 10.1007/BF00197667]
16 **Lafontaine M**, Hardy D, Delince P. Stability assessment of distal radius fractures. *Injury* 1989; **20**: 208-210 [PMID: 2592094 DOI: 10.1016/0020-1383(89)90113-7]
17 **Chess DG**, Hyndman JC, Leahey JL, Brown DC, Sinclair AM. Short arm plaster cast for distal pediatric forearm fractures. *J Pediatr Orthop* 1994; **14**: 211-213 [PMID: 8188836 DOI: 10.1097/01241398-199403000-00015]
18 **Alemdaroğlu KB**, Iltar S, Aydoğan NH, Say F, Kilinç CY, Tiftikçi U. Three-point index in predicting redisplacement of extra-articular distal radial fractures in adults. *Injury* 2010; **41**: 197-203 [PMID: 19782974 DOI: 10.1016/j.injury.2009.08.021]
19 **Müller ME**, Koch P, Nazarian S, Schatzker J. The Comprehensive Classification of Fractures of Long Bones. Berlin, Heidelberg: Springer Berlin Heidelberg, 1990
20 **Hudak PL**, Amadio PC, Bombardier C. Development of an upper extremity outcome measure: the DASH (disabilities of the arm, shoulder and hand) [corrected]. The Upper Extremity Collaborative Group (UECG). *Am J Ind Med* 1996; **29**: 602-608 [PMID: 8773720 DOI: 10.1002/(SICI)1097-0274(199606)29:6<602::AID-AJIM4>3.0.CO;2-L]
21 **Jenkinson C**, Layte R. Development and testing of the UK SF-12 (short form health survey). *J Health Serv Res Policy* 1997; **2**: 14-18 [PMID: 10180648 DOI: 10.1177/135581969700200105]
22 **Maluta T**, Cengarle M, Dib G, Bernasconi A, Lavini F, Ricci M, Vecchini E, Samaila EM, Magnan B. SLA-VER: study protocol description and preliminar results of the first italian RCT on conservative treatment of distal radial fractures. *Acta Biomed* 2019; **90**: 54-60 [PMID: 30714999 DOI: 10.23750/abm.v90i1-S.8083]
23 **DiBenedetto MR**, Lubbers LM, Ruff ME, Nappi JF, Coleman CR. Quantification of error in measurement of radial inclination angle and radial-carpal distance. *J Hand Surg Am* 1991; **16**: 399-400 [PMID: 1861017 DOI: 10.1016/0363-5023(91)90004-u]
24 **Aro HT**, Koivunen T. Minor axial shortening of the radius affects outcome of Colles' fracture treatment. *J Hand Surg Am* 1991; **16**: 392-398 [PMID: 1861016 DOI: 10.1016/0363-5023(91)90003-t]
25 **Shah PB**. Intention-to-treat and per-protocol analysis. *CMAJ* 2011; **183**: 696; author reply 696 [PMID: 21464181 DOI: 10.1503/cmaj.111-2033]
26 **Senn S**. Statistical issues in drug development. 2nd ed. Chichester, England, Hoboken, NJ: John Wiley & Sons, 2007
27 **Jaremko JL**, Lambert RG, Rowe BH, Johnson JA, Majumdar SR. Do radiographic indices of distal radius fracture reduction predict outcomes in older adults receiving conservative treatment? *Clin Radiol* 2007; **62**: 65-72 [PMID: 17145266 DOI: 10.1016/j.crad.2006.08.013]
28 **Bentohami A**, Bijlsma TS, Goslings JC, de Reuver P, Kaufmann L, Schep NW. Radiological criteria for acceptable reduction of extra-articular distal radial fractures are not predictive for patient-reported functional outcome. *J Hand Surg*

Eur Vol 2013; **38**: 524-529 [PMID: 23186862 DOI: 10.1177/1753193412468266]

29 **Cowie J**, Anakwe R, McQueen M. Factors associated with one-year outcome after distal radial fracture treatment. *J Orthop Surg (Hong Kong)* 2015; **23**: 24-28 [PMID: 25920638 DOI: 10.1177/230949901502300106]

30 **Maluta T**, Dib G, Cengarle M, Bernasconi A, Samaila E, Magnan B. Below- vs above-elbow cast for distal radius fractures: is elbow immobilization really effective for reduction maintenance? *Int Orthop* 2019; **43**: 2391-2397 [PMID: 30324309 DOI: 10.1007/s00264-018-4197-z]

31 **Wadsten MÅ**, Sayed-Noor AS, Englund E, Buttazzoni GG, Sjödén GO. Cortical comminution in distal radial fractures can predict the radiological outcome: a cohort multicentre study. *Bone Joint J* 2014; **96-B**: 978-983 [PMID: 24986954 DOI: 10.1302/0301-620X.96B7.32728]

32 **Walenkamp MM**, Aydin S, Mulders MA, Goslings JC, Schep NW. Predictors of unstable distal radius fractures: a systematic review and meta-analysis. *J Hand Surg Eur Vol* 2016; **41**: 501-515 [PMID: 26420817 DOI: 10.1177/1753193415604795]

33 **Leone J**, Bhandari M, Adili A, McKenzie S, Moro JK, Dunlop RB. Predictors of early and late instability following conservative treatment of extra-articular distal radius fractures. *Arch Orthop Trauma Surg* 2004; **124**: 38-41 [PMID: 14608466 DOI: 10.1007/s00402-003-0597-6]

34 **Gliatis JD**, Plessas SJ, Davis TR. Outcome of distal radial fractures in young adults. *J Hand Surg Br* 2000; **25**: 535-543 [PMID: 11106514 DOI: 10.1054/jhsb.2000.0373]

35 **Kodama N**, Takemura Y, Ueba H, Imai S, Matsusue Y. Acceptable parameters for alignment of distal radius fracture with conservative treatment in elderly patients. *J Orthop Sci* 2014; **19**: 292-297 [PMID: 24338051 DOI: 10.1007/s00776-013-0514-y]

36 **Mackenney PJ**, McQueen MM, Elton R. Prediction of instability in distal radial fractures. *J Bone Joint Surg Am* 2006; **88**: 1944-1951 [PMID: 16951109 DOI: 10.2106/JBJS.D.02520]

37 **Makhni EC**, Ewald TJ, Kelly S, Day CS. Effect of patient age on the radiographic outcomes of distal radius fractures subject to nonoperative treatment. *J Hand Surg Am* 2008; **33**: 1301-1308 [PMID: 18929192 DOI: 10.1016/j.jhsa.2008.04.031]

38 **Gutiérrez-Monclus R**, Gutiérrez-Espinoza H, Zavala-González J, Olguín-Huerta C, Rubio-Oyarzún D, Araya-Quintanilla F. Correlation Between Radiological Parameters and Functional Outcomes in Patients Older Than 60 Years of Age With Distal Radius Fracture. *Hand (N Y)* 2019; **14**: 770-775 [PMID: 29661068 DOI: 10.1177/1558944718770203]

39 **Nesbitt KS**, Failla JM, Les C. Assessment of instability factors in adult distal radius fractures. *J Hand Surg Am* 2004; **29**: 1128-1138 [PMID: 15576227 DOI: 10.1016/j.jhsa.2004.06.008]

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ORIGINAL ARTICLE

Observational Study

Revision anterior cruciate ligament reconstruction: Return to sports at a minimum 5-year follow-up

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Abstract

BACKGROUND

Between 43% and 75% of patients who undergo primary anterior cruciate ligament (ACL) surgery return to sport activity. However, after a revision ACL reconstruction (ACLR) the rate of return to sports is variable. A few publications have reported returns to sports incidence between 56% to 100% after revision ACLR.

AIM

To determine return to sports and functional outcomes after a single-stage revision ACLR with a 5-year minimum follow-up at a single institution.

METHODS

All patients operated between 2010 and 2016 with a minimum 5 years of follow-up were included. Type of sport, intensity, frequency, expectation, time to return to sport and failure rate were recorded. Lysholm, Tegner and International Knee Documentation Committee forms were evaluated prior to the first ACLR surgery, at 6 mo after primary surgery and after revision ACLR at 5 years minimum of follow-up. Objective stability was tested with the knee arthrometer test (KT-1000 knee arthrometer, Medmetric Corp).

RESULTS

A total of 41 patients who underwent revision ACLR during that period of time were contacted and available for follow-up. Median patient age at time of revision was 29 years old [interquartile range (IQR): 24.0-36.0], and 39 (95.0%) were male. The median time from revision procedure to follow-up was 70 mo (IQR: 58.0-81.0). Regarding return to sports, 16 (39.0%) were at the same level compared to preinjury period, and 25 patients (61.0%) returned at a lower level. Sixty-three percent categorized the sport as very important and 37.0% as important. One patient (2.4%) failed with a recurrent ACL torn. Mean preoperative Lysholm and

subjective International Knee Documentation Committee scores were 58.8 [standard deviation (SD) 16] and 50 (SD 11), respectively. At follow-up, mean Lysholm and subjective International Knee Documentation Committee scores were 89 (SD 8) and 82 (SD 9) (P = 0.0001). Mean Tegner score prior to primary ACLR was 6.7 (SD 1.3), 5.1 (1.5 SD) prior to revision ACLR and 5.6 (1.6 SD) at follow-up (P = 0.0002). Overall, knee arthrometer test measurement showed an average of 6 mm (IQR: 4.0-6.0) side-to-side difference of displacement prior to revision ACLR and 3mm (IQR: 1.5-4.0) after revision.

CONCLUSION

Almost 40.0% of patients returned to preinjury sports level and 60.0% to a lower level. These may be useful when counseling a patient regarding sports expectations after a revision ACLR.

Key Words: Return to sport; Revision anterior cruciate ligament; Arthroscopy; Knee; Functional outcome

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Core Tip: This was a retrospective case series with 41 patients seeking to evaluate return to sports and clinical outcomes after revision anterior cruciate ligament reconstruction at 5 years minimum of follow up. Retrospective analyzed data included physical examination, Tegner activity level, Lysholm, International Knee Documentation Committee, type of sport, intensity, frequency, expectation and time to return to sport. Objective stability was tested with the knee arthrometer test. All data were recorded at the base line and after a 5-year minimum follow-up.

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INTRODUCTION

Consequent to a substantial increase in the incidence of anterior cruciate ligament (ACL) ruptures, revision ACL reconstruction (ACLR) has also suffered an increase[1]. The ACL re-rupture rate is between 4% to 6%, with the event occurring in the first 2 years in more than half of the cases[2-4]. The rate of one-third of ACL ruptures is around 13% to 19% according to different publications[5-7]. In addition, these patients also present an increased risk of developing early arthritis[8].

Historically, return to sports (RTS) is defined as the return to the pre-injury activity in one or two seasons, at the same sporting level[9]. A recently published consensus described continuous RTS in three stages: return to participation, RTS and return to previous performance. Thus, return to participation refers to the return to training or to a lower sporting level than the one practiced by the patient previously. RTS refers to the return to the sport previously performed, although not at the desired level. Return to previous performance refers to the return to the same level or a higher level than before the injury[10].

Between 43% and 75% of patients who undergo primary ACL surgery RTS[11-15]. However, after a revision ACLR the reported rates of RTS are very variable[16]. Causes of non-RTS are multifactorial and include age, sex, psychological factors, type of sport, number of previous surgeries, time lapse between surgeries and graft choice[11-26]. Few publications report sports return rates after revision ACLR, both in the medium and long term, and they vary from 56% to 100%[27-31]. The purpose of this study was to evaluate the rate of RTS in patients with revision ACLR after 5 years of surgery. The secondary purpose was to report the functional outcomes.

MATERIALS AND METHODS

Study group

This study was approved by the Ethics Committee of our hospital. A retrospective study was performed including all patients who underwent a revision ACLR between 2010 and 2016. The inclusion criteria were patients with traumatic or atraumatic knee instability with a displacement equal to or larger than 5 mm anteroposterior compared to the contralateral knee measured with the KT-1000 arthrometer after primary ACL surgery and older than 18 years.

Patients with multiligament injuries (more than two ligaments injured at the same time), second ACL revision and patients with osteotomies at time of revision ACLR surgery were excluded (Table 1).

Surgical technique

A single stage revision ACLR was performed in the whole series. A diagnostic arthroscopy was performed in every case, and if necessary associated meniscal and cartilage lesions were treated. In 5 patients, allografts were used. The fixation technique was with 2 titanium screws for bone tendon bone, and in cases of hamstrings or anterior tibial allograft; fixation was performed with a cortical button in the femur and a biocomposite interferential screw in the tibia.

Postoperative rehabilitation

All patients entered the same rehabilitation protocol with rearrangements for individual needs. Partial loading was allowed for the first 3 wk. Passive flexion and extension range of motion were carried out. In special cases with complex meniscal sutures or cartilage treatment with mosaicoplasty, full loading was delayed until week 6. From the 4th month onwards, low impact workout exercises and progressive muscle strengthening were started. RTS was allowed after 10 mo depending on the sport practiced prior to the revision ACLR and based on an evaluation by our rehabilitation team.

Evaluation

Assessment was performed by a single evaluator in this study. Age, sex, follow-up time, injury mechanism prior to revision ACLR, time between primary surgery and re-rupture, time between revision ACLR and RTS, technique used in both primary surgery and revision ACLR and associated procedures were recorded.

All patients were asked about the type and level of sport practiced, the motivation to RTS and the expectation of returning to sport in three instances: prior to the first ACL reconstruction surgery, after primary surgery and after revision ACLR and RTS. RTS activity was considered to be the return to their sport prior to the last injury at the same level or below the previous level. Motivation was classified as: very important, important, moderately important, minimally important or not important. The expectation regarding RTS was classified as: return to the same sport level, return to a lower level or not returning to the same sport. The number of sports practices per week before and after the revision ACLR was recorded.

Using the Tegner score, the type of sport was classified into high impact, moderate and low impact, according to the classification published in 2015 by the American Heart Association[32]; high impact was considered those with Tegner greater or equal to 7, moderate impact with Tegner between 4 to 6 and low impact with Tegner between 1 to 3. Lysholm and International Knee Documentation Committee Knee (IKDC) scores were used prior to the revision ACLR and at the last follow-up. For an objective assessment, the KT-1000 arthrometer (Medmetric Corp) was used at the last follow-up.

We defined failure of revision ACLR surgery as ACL re-rupture, whether traumatic or atraumatic, associated with positive pivot shift and a difference in arthrometry with KT-1000 greater than or equal to 5 mm requiring new surgery.

Statistical analysis

Due to the small sample of patients non-sample size calculations were conducted. Continuous variables were described as median and interquartile ranges. Categorical variables were reported as proportions with their absolute frequency. Stata 14 software was used for the analysis. Statistical significance was considered to be $P = 0.05$.

RESULTS

A total of 87 revision ACLR were performed in the study period: 16 were excluded because of multiligamentary lesions, 8 were second revisions, and 10 were associated with osteotomy. Of the 53 patients who met the inclusion criteria, 12 patients were lost during follow-up. The series consisted of 41 patients with a median follow-up of 70 mo (IQR: 58.0-81.0) (Figure 1). Thirty-nine patients were male with a median age of 29 years (IQR: 24.0-36.0). Table 1 shows the demographic data.

Surgical data

A total of 27 (65.8%) patients had concomitant meniscal lesions. The medial meniscus was more frequently injured ($n = 26$); 20 (77.0%) were treated with meniscectomy, 6 (19.0%) with repair and 1 (4.0%) with meniscal transplantation. Lateral meniscus was injured in 14 patients; all were treated with partial meniscectomy. Chondral lesions were found in 5 (12.0%) patients; 3 (60.0%) were treated with microfractures and 2 (40.0%) with chondroplasty (Table 2).

Table 1 Demographics

Demographics	Results (*N* = 41)
Yr, median (IQR)	29 (24-36)
Male, *n* (%)	39 (95)
Follow up (mo) (IQR)	70 (58-81)
Period (a)	2010-2016
Injury mechanism prior revision ACLR	
Traumatic	26 (63.4%)
Atraumatic	15 (36.6%)
Time between (mo)	
ACL Primary surgery and retear	22 (22-39)
Revision ACLR and return to sport	13 (11-15)
Failure	1 (2.4%)

IQR: Interquartile range; ACLR: Anterior cruciate ligament reconstruction; ACL: Anterior cruciate ligament.

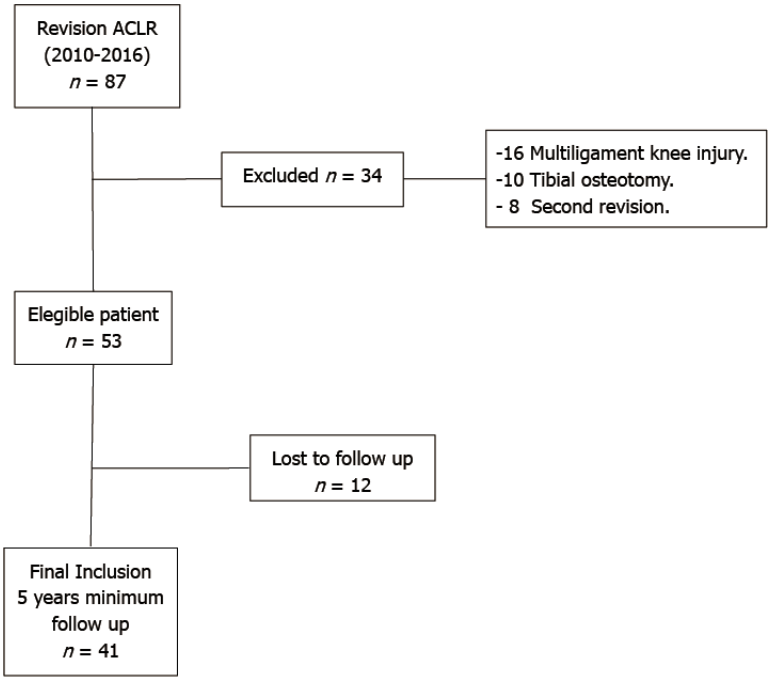
Table 2 Surgical technique and concomitant lesions

Graft	*n* (%)	Surgical technique	*n* (%)	Augmentation	*n* (%)
Primary ACL					
Hamstring	29 (70.7)	Monotunnel	36 (87.0)	-	-
BPTB	11(26.8)	Anatomic	5 (12.0)	-	-
Allograft	1 (2.4)				
Revision ACLR					
Hamstring	10 (24.3)	Anatomic	41 (100)	Lemaire	15 (36.0)
BTB	29 (70.3)			Allograft	2 (4.8)
Allograft	5 (2.0)			No Augmentation	24 (58.0)
Concomitant lesions					
Both meniscus	9 of 41 (21.0)				
Medial meniscus	26 of 41 (66.0)				
Meniscectomy	20 (77.0)				
Meniscal suture	5 (19.0)				
Meniscal transplantation	1 (4.0)				
Lateral meniscus					
Meniscectomy	14 of 41 (34.0)				
Chondral lesions	5 (12.0)				

BTB: Bone tendon bone; ACL: Anterior cruciate ligament; ACLR: Anterior cruciate ligament reconstruction; BPTB: Bone patellar tendon bone.

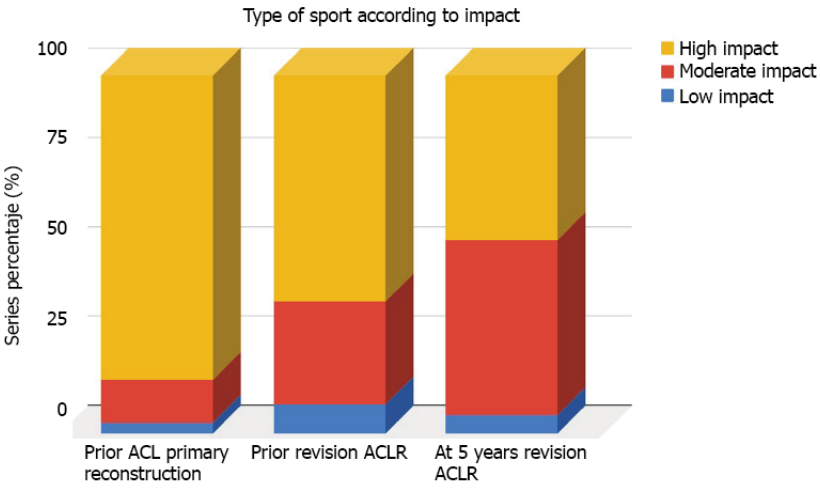
RTS

Prior to the first injury, 35 (85.0%) patients practiced high impact activities, 5 (12.0%) moderate and 1 (3.0%) low impact. After the first ACL surgery, 26 (63.0%) patients practiced high impact, 12 (29.0%) moderate and 3 (8.0%) low impact; 5 years after ACL revision, 19 (46.0%) continued to perform high impact, 20 (49.0%) moderate and 2 (5.0%) low impact (Figure 2). Prior to revision ACLR the patients practiced: soccer (24, 59.0%), running (9, 22.0%), gym (3, 7.0%), rugby (2, 5.0%), tennis (1, 2.0%), cycling (1, 2.0%) and other (1, 2.0%) other.



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Figure 1 Flowchart of patient inclusion. ACLR: Anterior cruciate ligament reconstruction.



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Figure 2 Type of sports at time of return. Lower sports impacts increased before revision anterior cruciate ligament reconstruction at the final follow-up. ACL: Anterior cruciate ligament; ACLR: Anterior cruciate ligament reconstruction.

After primary ACL surgery, 13 (31.0%) returned to the same level of sport, 26 (64.0%) to a lower level and 2 (5.0%) did not RTS. The rate of RTS for revision ACLR was 16 (39.0%) returning to the same level of sport and 25 (61.0%) to a lower level (Table 3). The time to RTS for both post-primary surgery and revision ACLR was 13 mo (IQR 11.0-15.0) (Figure 3).

Eighty percent (12/15) of patients without associated procedures and 73.0% (19/26) of patients with associated procedures returned to the same sports level, with no statistically significant differences (P = 0.61). Similarly, we found no association (P > 0.44) between the associated procedures performed at the time of revision ACLR surgery and the type of sport.

Regarding impact activity after revision surgery, it is interesting to note that 13.0%[7] modified their sports practice. When classifying sports according to impact based on Tegner, we recorded a 40.0% decrease from high impact to moderate impact activity and a 2.2% decrease from moderate to low impact after 5 years of follow-up after revision ACLR (Table 4) (Figure 2). Of those who played soccer, 1 patient changed to tennis, 1 to functional training and 1 to running. Of those who performed running, 1 began to perform a pivoting activity (soccer) and the other 2 modified it to a low-impact activity (bicycle

Table 3 Return to sport rate after primary anterior cruciate ligament surgery and before revision anterior cruciate ligament reconstruction after a 5-yr minimum follow-up

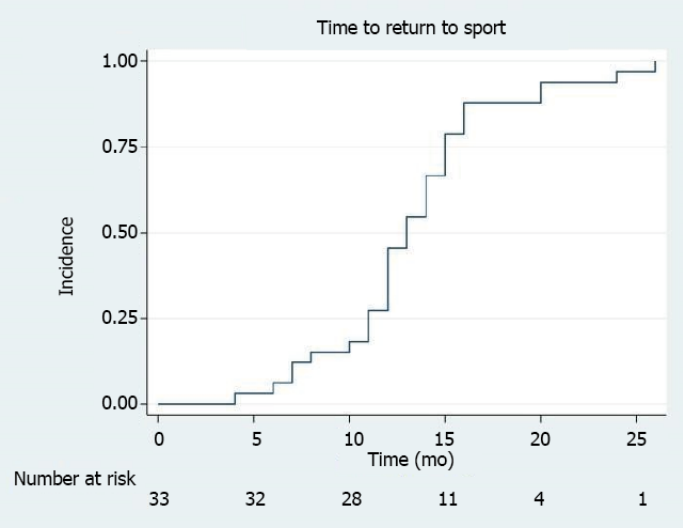
	Return to sports rate	
	Primary ACLR, %	Revision ACLR, %
Total return	95.0	100
Same level	31.7	39.0
Lower level	63.4	61.0

ACLR: Anterior cruciate ligament reconstruction.

Table 4 Activity sports impact and time evolution

Impact sport and Tegner	Prior to primary ACLR, *n* (%)	At 5 yr revision ACLR, *n* (%)
Low	1 (2.4)	2 (4.8)
Moderate	5 (12.2)	20 (48.7)
High	35 (85.3)	19 (46.3)

ACLR: Anterior cruciate ligament reconstruction.



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Figure 3 Time to return to sports (Kaplan - Meier). Fifty percent of the population returned to sport at some level 13 mo after revision anterior cruciate ligament reconstruction.

and yoga). This result was not modified for patients older than 40 years, in contrast to what it may be thought that in older patients (older than 40 years) the chances of modifying or abandoning sport is higher. The frequency with which they practiced sports in a week before and after the revision ACLR was maintained over time, being an average of twice a week (range 1-3); 26 (63.0%) patients practiced activities twice a week before the revision ACLR and 21 (51.0%) post-surgery.

When assessing motivation, 26 (63.0%) classified it as very important and 15 (37.0%) as important. When the patients were asked about their expectations regarding the RTS after their primary ACL surgery, 33 (80.0%) patients described their intention to return to the same sports level and 8 (20.0%) to return to a lower level. Regarding their expectation after revision ACLR surgery, 16 (39.0%) patients intended to return to the same level and 25 (61.0%) to a lower level (Table 3).

Clinical evaluation

According to the American Heart Association's classification in relation to Tegner score, a 40.0% decrease in impact activities at 5 years postoperatively was registered. Tegner score prior to primary

ACL surgery showed that 80.5% performed recreational physical activity, 9.8% performed their usual light work and 9.8% performed competitive sports activity. After primary ACL surgery, 58.5% performed their usual work, 36.6% performed recreational physical activity and 4.9% performed competitive sports activity. Post revision ACLR, 53.7% performed recreational physical activity, 41.5% performed their usual work/task and 4.9% performed competitive sports activity.

Prior to revision ACLR surgery the Lysholm score was good in 1.9% of the series, 35.8% were fair, and 62.3% were poor. For postoperative revision ACLR the score was excellent in 31.7% of the series, good in 56.1%, fair in 7.3% fair and poor in 4.9%. The Tegner, Lysholm and IKDC scores are summarized in Table 5. With the differential KT-1000 arthrometer the median values prior to ACL revision were 5 mm (IQR: 4.0-6.0) and at last follow-up 3 mm (IQR: 1.5-4.0). Finally, 1 patient had a failure after ACL revision surgery (2.4%) at 72 mo postoperatively.

DISCUSSION

The main finding of this study was that all patients returned to their sports practice after revision ACLR, 61.0% at a lower level and 39.0% at the same level prior to revision ACLR surgery. The rate of return to full sport, according to a systematic review of 48 studies with 5770 patients, is 82% in patients with primary ACL surgery. Only 63% returned to the same pre-injury sport, but 44% were able to do so at a competitive level[19]. Although the literature is more limited for RTS in revision ACLR surgery, a systematic review of 23 studies with a total of 1090 patients indicated that 85% of patients returned to sport, 53% to their previous sport and 51% to a competitive level[16]. According to another systematic review, the rate of RTS in patients with revision ACLR surgery ranged from 56% to 100%[33], similar to our series.

There are several factors that influence RTS: social, psychological and demographic factors. Age and sex are important factors. Men have a 10% higher rate of return than women, and young people (< 25 years) have a rate higher than 30% compared to adult patients[19,20,31,33]. The longer the time between ACL re-rupture and revision surgery, the lower the rates of RTS as well as an increase in associated injuries as revision surgery is delayed[19]. In the same way, the graft choice could be a determining factor in the RTS; however, it has not been studied in depth[27].

In our series, the time to RTS was the same (13 mo) with no significant differences found when dividing the series into those older than 25 years and those younger than 25 years as well as when differentiating between sex. The median time between ACL re-rupture and revision ACLR was 21 mo (IQR: 3.0-24.0). For patients who took more than 1 year to undergo a revision ACLR, the RTS was also at 13 mo on average (7 to 26) with no significant differences with the overall rate of sports return ($P = 0.64$).

Focusing on the graft choice, according to a meta-analysis of 32 studies comparing hamstring and bone tendon bone for revision surgeries, an increase in the IKDC, Lysholm and Tegner scores and a decrease in complications and reoperations was observed in favor of hamstrings[40]. In contrast to this, the authors of the study recommended that the graft choice should be based on the circumstances of each patient, the technique preferred by each surgeon, the tunnel widening, the type of graft previously used and the possible availability of allografts and not on the rate of RTS according to the type of graft [40]. All patients in our series were treated with autografts with the exception of 5 patients where allografts were used. We did not find significant differences in the time to return in patients where an allograft was used, being 13 mo for both groups. The preference of the authors of this study is to use an autograft from the same injured knee. This is due to the fact that, according to literature, series of patients with revision surgeries in which an autograft was used showed faster rates of RTS in comparison with those in which allografts were used[38,39]. The use of contralateral hamstring tendons for revision ACLR surgeries presented similar subjective and objective rates at 5.2 years of follow-up compared to revision surgeries in which patellar or Achilles tendon allograft was used[39]. In our series we do not have patients operated with contralateral knee grafts.

Several authors recommend that when evaluating series to assess the RTS the Lysholm score should be used together with the Tegner score to be able to more effectively evaluate the sports activity[34]. In our series, Lysholm score after revision ACLR increased by 30.0% for excellent results considered as greater than 95 points (0% preoperative to 31% postoperative) and decreased by 50.0% for poor results (62% preoperative to 4.9% postoperative).

For the Tegner scale we observed a decrease of 1.7 points between preoperative primary ACL surgery and postoperative revision ACLR ($P = 0.002$) showing the decrease in impact activity between primary surgery and revision ACLR. When comparing our series with the literature for both the Lysholm, Tegner and IKDC scores we found results that are close to the mean (Table 6).

When evaluating the expectation of patients regarding their intention to RTS after primary ACL surgery, 80.0% of our series intended to return to the same sport level, while 39.0% reported this intention prior to revision surgery (Tables 7-10 case examples). This 40.0% decrease in the expectation of RTS is consistent with the literature as shown by a study of 675 patients with a return expectation after primary surgery at 1 year of 84% and 63% for revision ACLR surgeries ($P < 0.001$ and $P = 0.08$, respectively). A multivariate logistic regression showed two determinant factors for abandoning sports

Table 5 Tegner, Lysholm and subjective International Knee Documentation Committee scores prior to revision anterior cruciate ligament reconstruction and at the 5-yr follow-up

	Preoperative	SD	5 yr postoperative	SD	Delta	SD	95%CI	*P* value
Tegner	6.7	(1.3)	5.6	(1.6)	-1.170	(1.8)	-1.739 to -0.602	0.002
Lysholm	58.8	(16.0)	89.0	(8.0)	30.121	(17.0)	24.736 to 35.507	< 0.001
IKDC	50.0	(11.0)	82.0	(9.0)	31.475	(15.0)	26.649 to 36.300	< 0.001

$\chi 2$ test was used to estimate the *P* value. SD: Standard deviation; IKDC: International Knee Documentation Committee; CI: Confidence interval.

Table 6 Comparing our series with the literature for the Lysholm, Tegner and International Knee Documentation Committee scores

Ref.	*N*	Years	F-up in yr	RTS	IKDC	Lysholm	Tegner	KT-1000, mm ± SD	KOOS
Battaglia *et al*[28], 2007	63	31	6.1	42 (66%) same level	G/E 36%; P 17%; F 11%	-	-	< 3	-
Diamantopoulos *et al*[29], 2008	107	39	6	39 (36%) same level	G/E 57%; P 34%; F 7%	88.5 ± 12.4	6.3 ± 1.8	0.93 ± 1.15	-
Gifstad *et al*[30], 2013	56	26	7.5	7 (13%) same level	-	80 ± 15	6 ± 4	3.3 ± 2.7	70 ± 21
Shelbourne *et al*[31], 2014	259	22	7.2	178 (68%) same level	Subjective 76 ± 18.3	-	-	2.3 ± 1.7	-
Ortiz *et al*, 2022	41	29	5.8	61% same level & 39% lower level	G/E 43%; P 53%; F 4%	89 ± 8	5.6 ± 1.6	3 ± 1.2	-

N: Number of patients; F-up: Follow up; RTS: Return to sport; IKDC: International Knee Documentation Committee; G/E: Good to excellent; P: Poor; F: Fair; SD: Standard deviation; KOOS: Knee Injury and Osteoarthritis Outcome Score.

Table 7 Five representative cases

Case	Sex	Years	Time between in min		Return to sport		Graft choice		Augmentation at revision ACLR	Concomitant lesions
			Primary ACLR and retear	Revision ACLR and last evaluation, F-up	To Primary ACLR	To Revision ACLR	Primary ACLR	Revision ACLR		
1	Male	30	36	126	17	20	Hamstring	BPTB	Lemaire	Medial meniscus tear
2	Male	42	12	131	14	13	Hamstring	BPTB	Lemaire	Medial meniscus tear
3	Male	29	48	107	13	11	Hamstring	BPTB	Lemaire	Chondral lesions
4	Male	35	22	115	10	14	Hamstring	BPTB	-	Chondral lesions
5	Female	28	13	103	14	16	Hamstring	BPTB	-	Medial meniscus tear

ACLR: Anterior cruciate ligament reconstruction; BPTB: Bone patellar tendon bone; F-up: Follow-up.

practice, which were having suffered a revision ACLR ($P < 0.0001$) and being female ($P = 0.02$). In our series, all patients returned to sports, and we did not obtain representative casuistry to make a comparison between sexes[34].

The association between chondral and meniscal lesions showed poor functional results in patients with revision ACLR surgery; the association of chondral lesions at the time of revision surgery showed lower values according to the Lysholm score in comparison with patients who did not present it. In the same way, patients who presented this lesion modified their intensity in RTS[34-37]. Another study showed poor results in Marx, Knee Injury and Osteoarthritis Outcome Score-quality of life and IKDC

Table 8 Return to sport was considered to be the return to their sport prior to the last injury, at the same level or below the previous level

Case	Sex	Years	Return to sport		Type of Sports			Training frequency	
			After					Days per week	
			Primary ACLR	Revision ACLR	Prior ACLR	Prior revision ACLR	After revision ACLR	Prior revision ACLR	After revision ACLR
1	Male	30	Lower level	Lower level	Soccer	Running	Running	2	1
2	Male	42	Same level	Same level	Soccer	Soccer	Tennis	2	1
3	Male	29	Lower level	Same level	Soccer	Running	Soccer	2	2
4	Male	35	Lower level	Same level	Soccer	Soccer	Soccer	2	2
5	Female	28	Lower level	Same level	Martial arts	Tennis	Tennis	2	2

ACLR: Anterior cruciate ligament reconstruction.

Table 9 Motivation was classified as very important, important, moderately important, minimally important or not important and expectation was classified as return to the same sport level, return to a lower level or not returning to the same sport

Case	Sex	Year	Motivation	Expectation	
				After primary ACLR	After revision ACLR
1	Male	30	Important	Same level	Lower level
2	Male	42	Very important	Same level	Same level
3	Male	29	Very important	Same level	Lower level
4	Male	35	Very important	Same level	Lower level
5	Female	28	Very important	Same level	Same level

ACLR: Anterior cruciate ligament reconstruction.

Table 10 Knee function and sports activity level

Case	Sex	Year	Tegner		Lysholm		IKDC	
			Prior revision ACLR	At 5-yr F-up revision ACLR	Prior revision ACLR	At 5-yr F-up revision ACLR	Prior revision ACLR	At 5-yr F-up revision ACLR
1	Male	30	7	4	47	65	62	71
2	Male	42	7	7	61	84	49	89
3	Male	29	7	4	39	86	59	90
4	Male	35	7	4	80	95	37	97
5	Female	28	7	6	38	86	49	86

ACLR: Anterior cruciate ligament reconstruction; F-up: Follow-up; IKDC: International Knee Documentation Committee.

activity scores after revision ACLR surgery in patients with chondral lesions and low scores for the Marx and Knee Injury and Osteoarthritis Outcome Score-quality of life scores in patients with medial meniscus lesions[29]. The level of RTS practice was equal or lower in patients who had associated injuries *vs* patients who did not have associated injuries at the time of revision ACLR surgery. Twelve patients returned to the same level; 3 patients returned to a lower level out of a total of 15 patients who underwent an associated procedure. In our series, 80.0% (12/15) of the patients without associated procedures and 73.0% (19/26) of the patients with associated procedures returned to the same sports level, with no statistically significant differences (P = 0.61).

Limitations

Among the limitations of our retrospective study, there was no control group of patients with high sports performance nor a numerical scale detailing the level of RTS practice, being this a subjective response of patients. No pre- and postoperative strength or resistance test was performed to determine the "level of muscle strength at their return." The series was a heterogeneous group of patients in terms of age and type of sport performed. Although the size of the series is close to those reported in international literature, the number is small. The strength of the study is that it is a case series operated in a single institution with a 5-year follow-up after revision ACLR.

CONCLUSION

Five years after a revision ACLR, 39.0% of patients returned to the same level of sport as before revision ACLR surgery and 61.0% to a lower level. The 13.2% (n = 7) of the series who changed their sports practice was a 40.0% decrease of high impact activity at the time of return. These data could be used to advise patients on the level and timing of sports return.

ARTICLE HIGHLIGHTS

Research background

Between 43% and 75% of patients who undergo primary anterior cruciate ligament (ACL) surgery return to sport activity. However, after a revision ACL reconstruction (ACLR) rate of return to sport are variable. Few publications report return to sports incidence between 56% to 100% after revision ACLR. Five-year minimum follow-up after revision ACLR is a good mid/long-term period evaluation to report return to sport of a case series patients.

Research motivation

Return to sports is a frequent question from patients during the first consultation. We believe this research could help other knee surgeons answer these types of questions. Motivation and expectation must be asked by surgeons during the consultation so as to give the patient a more detailed and realistic response to that question.

Research objectives

The objective was to report functional clinical outcomes and return to sport at a mid/long-term period after revision ACLR.

Research methods

A retrospective and observational study was performed to describe return to sport of an amateur case series of patients. The entire cohort was asked about motivation, expectation, intensity, frequency and level of return to sport after a 5-year follow-up after revision ACLR.

Research results

Thirty-nine percent of the cohort returned at the same level compared to the pre-injury period. Sixty-one percent returned at a lower level. Sixty-three percent categorized the sport as very important and 37.0% as important. One patient (2.4%) failed with a recurrent torn ACL.

Research conclusions

Almost 40.0% of patients returned to their pre-injury sport level and 60.0% to a lower level after 5 years of follow-up after revision ACLR.

Research perspectives

The direction of future research must be to compare return to sport of professional elite patients against amateur patients.

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FOOTNOTES

Author contributions: Ortiz E and Zicaro JP designed the research study; Ortiz E performed the research; Yacuzzi C and Costa Paz M contributed new reagents; Garcia Mansilla I contributed with analytic tools; Ortiz E and Zicaro JP analyzed the data and wrote the manuscript; All authors have read and approved the final manuscript.

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REFERENCES

1 **Liechti DJ**, Chahla J, Dean CS, Mitchell JJ, Slette E, Menge TJ, LaPrade RF. Outcomes and Risk Factors of Rerevision Anterior Cruciate Ligament Reconstruction: A Systematic Review. *Arthroscopy* 2016; **32**: 2151-2159 [PMID: 27289278 DOI: 10.1016/j.arthro.2016.04.017]
2 **Paterno MV**, Rauh MJ, Schmitt LC, Ford KR, Hewett TE. Incidence of Second ACL Injuries 2 Years After Primary ACL Reconstruction and Return to Sport. *Am J Sports Med* 2014; **42**: 1567-1573 [PMID: 24753238 DOI: 10.1177/0363546514530088]
3 **Wiggins AJ**, Grandhi RK, Schneider DK, Stanfield D, Webster KE, Myer GD. Risk of Secondary Injury in Younger Athletes After Anterior Cruciate Ligament Reconstruction: A Systematic Review and Meta-analysis. *Am J Sports Med* 2016; **44**: 1861-1876 [PMID: 26772611 DOI: 10.1177/0363546515621554]
4 **Lewis PB**, Parameswaran AD, Rue JP, Bach BR Jr. Systematic review of single-bundle anterior cruciate ligament reconstruction outcomes: a baseline assessment for consideration of double-bundle techniques. *Am J Sports Med* 2008; **36**: 2028-2036 [PMID: 18757764 DOI: 10.1177/0363546508322892]
5 **MARS Group**. , Ding DY, Zhang AL, Allen CR, Anderson AF, Cooper DE, DeBerardino TM, Dunn WR, Haas AK, Huston LJ, Lantz BBA, Mann B, Spindler KP, Stuart MJ, Wright RW, Albright JP, Amendola AN, Andrish JT, Annunziata CC, Arciero RA, Bach BR Jr, Baker CL 3rd, Bartolozzi AR, Baumgarten KM, Bechler JR, Berg JH, Bernas GA, Brockmeier SF, Brophy RH, Bush-Joseph CA, Butler JB 5th, Campbell JD, Carey JL, Carpenter JE, Cole BJ, Cooper JM, Cox CL, Creighton RA, Dahm DL, David TS, Flanigan DC, Frederick RW, Ganley TJ, Garofoli EA, Gatt CJ Jr, Gecha SR, Giffin JR, Hame SL, Hannafin JA, Harner CD, Harris NL Jr, Hechtman KS, Hershman EB, Hoellrich RG, Hosea TM, Johnson DC, Johnson TS, Jones MH, Kaeding CC, Kamath GV, Klootwyk TE, Levy BA, Ma CB, Maiers GP 2nd, Marx RG, Matava MJ, Mathien GM, McAllister DR, McCarty EC, McCormack RG, Miller BS, Nissen CW, O'Neill DF, Owens BD, Parker RD, Purnell ML, Ramappa AJ, Rauh MA, Rettig AC, Sekiya JK, Shea KG, Sherman OH, Slauterbeck JR, Smith MV, Spang JT, Svoboda SJ, Taft TN, Tenuta JJ, Tingstad EM, Vidal AF, Viskontas DG, White RA, Williams JS Jr, Wolcott ML, Wolf BR, York JJ. Subsequent Surgery After Revision Anterior Cruciate Ligament Reconstruction: Rates and Risk Factors From a Multicenter Cohort. *Am J Sports Med* 2017; **45**: 2068-2076 [PMID: 28557557 DOI: 10.1177/0363546517707207]
6 **Paterno MV**, Rauh MJ, Schmitt LC, Ford KR, Hewett TE. Incidence of contralateral and ipsilateral anterior cruciate ligament (ACL) injury after primary ACL reconstruction and return to sport. *Clin J Sport Med* 2012; **22**: 116-121 [PMID: 22343967 DOI: 10.1097/JSM.0b013e318246ef9e]
7 **Hettrich CM**, Dunn WR, Reinke EK; MOON Group, Spindler KP. The rate of subsequent surgery and predictors after anterior cruciate ligament reconstruction: two- and 6-year follow-up results from a multicenter cohort. *Am J Sports Med* 2013; **41**: 1534-1540 [PMID: 23722056 DOI: 10.1177/0363546513490277]
8 **Costa-Paz M**, Garcia-Mansilla I, Marciano S, Ayerza MA, Muscolo DL. Knee-related quality of life, functional results and osteoarthritis at a minimum of 20 years' follow-up after anterior cruciate ligament reconstruction. *Knee* 2019; **26**: 666-672 [PMID: 31103415 DOI: 10.1016/j.knee.2019.04.010]
9 **Lynch AD**, Logerstedt DS, Grindem H, Eitzen I, Hicks GE, Axe MJ, Engebretsen L, Risberg MA, Snyder-Mackler L.

Consensus criteria for defining 'successful outcome' after ACL injury and reconstruction: a Delaware-Oslo ACL cohort investigation. *Br J Sports Med* 2015; **49**: 335-342 [PMID: 23881894 DOI: 10.1136/bjsports-2013-092299]

10 **Ardern CL**, Glasgow P, Schneiders A, Witvrouw E, Clarsen B, Cools A, Gojanovic B, Griffin S, Khan KM, Moksnes H, Mutch SA, Phillips N, Reurink G, Sadler R, Silbernagel KG, Thorborg K, Wangensteen A, Wilk KE, Bizzini M. 2016 Consensus statement on return to sport from the First World Congress in Sports Physical Therapy, Bern. *Br J Sports Med* 2016; **50**: 853-864 [PMID: 27226389 DOI: 10.1136/bjsports-2016-096278]

11 **Ardern CL**, Österberg A, Tagesson S, Gauffin H, Webster KE, Kvist J. The impact of psychological readiness to return to sport and recreational activities after anterior cruciate ligament reconstruction. *Br J Sports Med* 2014; **48**: 1613-1619 [PMID: 25293342 DOI: 10.1136/bjsports-2014-093842]

12 **Ardern CL**, Taylor NF, Feller JA, Webster KE. Return-to-sport outcomes at 2 to 7 years after anterior cruciate ligament reconstruction surgery. *Am J Sports Med* 2012; **40**: 41-48 [PMID: 21946441 DOI: 10.1177/0363546511422999]

13 **Brophy RH**, Schmitz L, Wright RW, Dunn WR, Parker RD, Andrish JT, McCarty EC, Spindler KP. Return to play and future ACL injury risk after ACL reconstruction in soccer athletes from the Multicenter Orthopaedic Outcomes Network (MOON) group. *Am J Sports Med* 2012; **40**: 2517-2522 [PMID: 23002201 DOI: 10.1177/0363546512459476]

14 **Erickson BJ**, Harris JD, Cvetanovich GL, Bach BR, Bush-Joseph CA, Abrams GD, Gupta AK, McCormick FM, Cole BJ. Performance and Return to Sport After Anterior Cruciate Ligament Reconstruction in Male Major League Soccer Players. *Orthop J Sports Med* 2013; **1**: 2325967113497189 [PMID: 26535238 DOI: 10.1177/2325967113497189]

15 **Musahl V**, Karlsson J, Krutsch W, Mandelbaum BR, Espregueira-Mendes J, d'Hooghe P. Return to Play in Football: An Evidence-based Approach. Springer; 2018. 987 p. [DOI: 10.1007/978-3-662-55713-6]

16 **Grassi A**, Zaffagnini S, Marcheggiani Muccioli GM, Neri MP, Della Villa S, Marcacci M. After revision anterior cruciate ligament reconstruction, who returns to sport? *Br J Sports Med* 2015; **49**: 1295-1304 [PMID: 26062956 DOI: 10.1136/bjsports-2014-094089]

17 **Feller J**, Webster KE. Return to sport following anterior cruciate ligament reconstruction. *Int Orthop* 2013; **37**: 285-290 [PMID: 23138966 DOI: 10.1007/s00264-012-1690-7]

18 **Webster KE**, Feller JA, Leigh WB, Richmond AK. Younger Patients Are at Increased Risk for Graft Rupture and Contralateral Injury After Anterior Cruciate Ligament Reconstruction [DOI: 10.1177/0363546513517540]

19 **Ardern CL**, Webster KE, Taylor NF, Feller JA. Return to sport following anterior cruciate ligament reconstruction surgery: a systematic review and meta-analysis of the state of play. *Br J Sports Med* 2011; **45**: 596-606 [PMID: 21398310 DOI: 10.1136/bjsm.2010.076364]

20 **Ardern CL**, Taylor NF, Feller JA, Webster KE. Fifty-five per cent return to competitive sport following anterior cruciate ligament reconstruction surgery: an updated systematic review and meta-analysis including aspects of physical functioning and contextual factors. *Br J Sports Med* 2014; **48**: 1543-1552 [PMID: 25157180 DOI: 10.1136/bjsports-2013-093398]

21 **Lai CCH**, Ardern CL, Feller JA, Webster KE. Eighty-three per cent of elite athletes return to preinjury sport after anterior cruciate ligament reconstruction: a systematic review with meta-analysis of return to sport rates, graft rupture rates and performance outcomes. *Br J Sports Med* 2018; **52**: 128-138 [PMID: 28223305 DOI: 10.1136/bjsports-2016-096836]

22 **Ardern CL**, Taylor NF, Feller JA, Whitehead TS, Webster KE. Psychological responses matter in returning to preinjury level of sport after anterior cruciate ligament reconstruction surgery. *Am J Sports Med* 2013; **41**: 1549-1558 [PMID: 23733635 DOI: 10.1177/0363546513489284]

23 **Kvist J**, Österberg A, Gauffin H, Tagesson S, Webster K, Ardern C. Translation and measurement properties of the Swedish version of ACL-Return to Sports after Injury questionnaire. *Scand J Med Sci Sports* 2013; **23**: 568-575 [PMID: 22257241 DOI: 10.1111/j.1600-0838.2011.01438.x]

24 **Webster KE**, Feller JA, Lambros C. Development and preliminary validation of a scale to measure the psychological impact of returning to sport following anterior cruciate ligament reconstruction surgery. *Phys Ther Sport* 2008; **9**: 9-15 [PMID: 19083699 DOI: 10.1016/j.ptsp.2007.09.003]

25 **Langford JL**, Webster KE, Feller JA. A prospective longitudinal study to assess psychological changes following anterior cruciate ligament reconstruction surgery. *Br J Sports Med* 2009; **43**: 377-381 [PMID: 19019910 DOI: 10.1136/bjsm.2007.044818]

26 **Sonesson S**, Kvist J, Ardern C, Österberg A, Silbernagel KG. Psychological factors are important to return to pre-injury sport activity after anterior cruciate ligament reconstruction: expect and motivate to satisfy. *Knee Surg Sports Traumatol Arthrosc* 2017; **25**: 1375-1384 [PMID: 27562372 DOI: 10.1007/s00167-016-4294-8]

27 **Saper M**, Pearce S, Shung J, Zondervan R, Ostrander R, Andrews JR. Outcomes and Return to Sport After Revision Anterior Cruciate Ligament Reconstruction in Adolescent Athletes. *Orthop J Sports Med* 2018; **6**: 2325967118764884 [PMID: 29662910 DOI: 10.1177/2325967118764884]

28 **Battaglia MJ 2nd**, Cordasco FA, Hannafin JA, Rodeo SA, O'Brien SJ, Altchek DW, Cavanaugh J, Wickiewicz TL, Warren RF. Results of revision anterior cruciate ligament surgery. *Am J Sports Med* 2007; **35**: 2057-2066 [PMID: 17932401 DOI: 10.1177/0363546507307391]

29 **Diamantopoulos AP**, Lorbach O, Paessler HH. Anterior cruciate ligament revision reconstruction: results in 107 patients. *Am J Sports Med* 2008; **36**: 851-860 [PMID: 18272793 DOI: 10.1177/0363546507312381]

30 **Gifstad T**, Drogset JO, Viset A, Grøntvedt T, Hortemo GS. Inferior results after revision ACL reconstructions: a comparison with primary ACL reconstructions. *Knee Surg Sports Traumatol Arthrosc* 2013; **21**: 2011-2018 [PMID: 23238924 DOI: 10.1007/s00167-012-2336-4]

31 **Shelbourne KD**, Benner RW, Gray T. Return to Sports and Subsequent Injury Rates After Revision Anterior Cruciate Ligament Reconstruction With Patellar Tendon Autograft. *Am J Sports Med* 2014; **42**: 1395-1400 [PMID: 24627577 DOI: 10.1177/0363546514524921]

32 **Levine BD**, Baggish AL, Kovacs RJ, Link MS, Maron MS, Mitchell JH, et al Eligibility and Disqualification Recommendations for Competitive Athletes With Cardiovascular Abnormalities: Task Force 1: Classification of Sports: Dynamic, Static; and Impact: A Scientific Statement From the American Heart Association and American College of Cardiology. Circulation. 2015 Dec 1;132(22):e262–6. [DOI: 10.1161/cir.0000000000000237]

33 **Anand BS**, Feller JA, Richmond AK, Webster KE. Return-to-Sport Outcomes After Revision Anterior Cruciate Ligament

Reconstruction Surgery. *Am J Sports Med* 2016; **44**: 580-584 [PMID: 26672024 DOI: 10.1177/0363546515618381]

34 **Webster KE**, Feller JA. Expectations for Return to Preinjury Sport Before and After Anterior Cruciate Ligament Reconstruction. *Am J Sports Med* 2019; **47**: 578-583 [PMID: 30649903 DOI: 10.1177/0363546518819454]

35 **Webster KE**, Feller JA, Kimp A, Devitt BM. Medial meniscal and chondral pathology at the time of revision anterior cruciate ligament reconstruction results in inferior mid-term patient-reported outcomes. *Knee Surg Sports Traumatol Arthrosc* 2018; **26**: 1059-1064 [PMID: 29516122 DOI: 10.1007/s00167-018-4880-z]

36 **MARS Group**. Meniscal and Articular Cartilage Predictors of Clinical Outcome After Revision Anterior Cruciate Ligament Reconstruction. *Am J Sports Med* 2016; **44**: 1671-1679 [PMID: 27161867 DOI: 10.1177/0363546516644218]

37 **MARS Group**. , Wright RW, Huston LJ, Haas AK, Allen CR, Anderson AF, Cooper DE, DeBerardino TM, Dunn WR, Lantz BBA, Mann B, Spindler KP, Stuart MJ, Nwosu SK, Albright JP, Amendola AN, Andrish JT, Annunziata CC, Arciero RA, Bach BR Jr, Baker CL 3rd, Bartolozzi AR, Baumgarten KM, Bechler JR, Berg JH, Bernas GA, Brockmeier SF, Brophy RH, Bush-Joseph CA, Brad Butler V J, Campbell JD, Carey JL, Carpenter JE, Cole BJ, Cooper JM, Cox CL, Creighton RA, Dahm DL, David TS, Flanigan DC, Frederick RW, Ganley TJ, Garofoli EA, Gatt CJ Jr, Gecha SR, Giffin JR, Hame SL, Hannafin JA, Harner CD, Harris NL Jr, Hechtman KS, Hershman EB, Hoellrich RG, Hosea TM, Johnson DC, Johnson TS, Jones MH, Kaeding CC, Kamath GV, Klootwyk TE, Levy BA, Ma CB, Maiers GP 2nd, Marx RG, Matava MJ, Mathien GM, McAllister DR, McCarty EC, McCormack RG, Miller BS, Nissen CW, O'Neill DF, Owens BD, Parker RD, Purnell ML, Ramappa AJ, Rauh MA, Rettig AC, Sekiya JK, Shea KG, Sherman OH, Slauterbeck JR, Smith MV, Spang JT, Svoboda LSJ, Taft TN, Tenuta JJ, Tingstad EM, Vidal AF, Viskontas DG, White RA, Williams JS Jr, Wolcott ML, Wolf BR, York JJ. Predictors of Patient-Reported Outcomes at 2 Years After Revision Anterior Cruciate Ligament Reconstruction. *Am J Sports Med* 2019; **47**: 2394-2401 [PMID: 31318611 DOI: 10.1177/0363546519862279]

38 **Group M**; Mars Group, Wright RW. Effect of Graft Choice on the 6 Year Outcome of Revision Anterior Cruciate Ligament Reconstruction in the Multicenter ACL Revision Study (MARS) Cohort [DOI: 10.1177/2325967119s00281]

39 **Legnani C**, Zini S, Borgo E, Ventura A. Can graft choice affect return to sport following revision anterior cruciate ligament reconstruction surgery? *Arch Orthop Trauma Surg* 2016; **136**: 527-531 [PMID: 26768744 DOI: 10.1007/s00402-015-2387-3]

40 **Grassi A**, Nitri M, Moulton SG, Marcheggiani Muccioli GM, Bondi A, Romagnoli M, Zaffagnini S. Does the type of graft affect the outcome of revision anterior cruciate ligament reconstruction? *Bone Joint J* 2017; **99-B**: 714-723 [PMID: 28566389 DOI: 10.1302/0301-620X.99B6.BJJ-2016-0929.R2]

41 **Grassi A**, Vascellari A, Combi A, Tomaello L, Canata GL, Zaffagnini S; SIGASCOT Sports Committee. Return to sport after ACL reconstruction: a survey between the Italian Society of Knee, Arthroscopy, Sport, Cartilage and Orthopaedic Technologies (SIGASCOT) members. *Eur J Orthop Surg Traumatol* 2016; **26**: 509-516 [PMID: 26972570 DOI: 10.1007/s00590-016-1756-0]

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SYSTEMATIC REVIEWS

Fragility of statistically significant findings from randomized clinical trials of surgical treatment of humeral shaft fractures: A systematic review

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Abstract

BACKGROUND

Despite recent meta-analyses of randomized controlled trials (RCTs), there remains no consensus regarding the preferred surgical treatment for humeral shaft fractures. The fragility index (FI) is an emerging tool used to evaluate the robustness of RCTs by quantifying the number of participants in a study group that would need to switch outcomes in order to reverse the study conclusions.

AIM

To investigate the fragility index of randomized control trials assessing outcomes of operative fixation in proximal humerus fractures.

METHODS

We completed a systematic review of RCTs evaluating the surgical treatment of humeral shaft fractures. Inclusion criteria included: articles published in English; patients randomized and allotted in 1:1 ratio to 2 parallel arms; and dichotomous outcome variables. The FI was calculated for total complications, each

complication individually, and secondary surgeries using the Fisher exact test, as previously published.

RESULTS

Fifteen RCTs were included in the analysis comparing open reduction plate osteosynthesis with dynamic compression plate or locking compression plate, intramedullary nail, and minimally invasive plate osteosynthesis. The median FI was 0 for all parameters analyzed. Regarding individual outcomes, the FI was 0 for 81/91 (89%) of outcomes. The FI exceeded the number lost to follow up in only 2/91 (2%) outcomes.

CONCLUSION

The FI shows that data from RCTs regarding operative treatment of humeral shaft fractures are fragile and does not demonstrate superiority of any particular surgical technique.

Key Words: Humerus fracture; Open reduction internal fixation; Intramedullary nail; Fragility index; Complications; Fragility index

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Core Tip: Humerus shaft fractures have been managed with intramedullary nail fixation and plate osteosynthesis. Multiple randomized control trials have been performed to compare outcomes, complications, reoperations, and union rates between both treatment modalities. Despite multiple randomized control trials, there remains a lack of consensus from the existing literature regarding surgical treatment of humeral shaft fractures. This manuscript aims to further assess the quality of the literature that guides treatment decisions by employing a new metric, the fragility index.

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INTRODUCTION

Humeral shaft fractures represent approximately 3% of all long-bone fractures[1] with an incidence around 13 per 100000 people per year[2]. While the vast majority may be managed nonoperatively[1-5], surgical treatment is generally indicated for open fractures, polytrauma patients, ipsilateral humeral shaft and forearm fractures (floating elbow), segmental fractures, and cases of failed treatment in functional brace[3]. However, it is important to note that there are currently no defined gold standards for the treatment of humeral shaft fractures[6,7]. Surgical treatment options include external fixation, open reduction and plate osteosynthesis (ORPO), minimally invasive plate osteosynthesis (MIPO), and intramedullary nail (IMN). Implant options for both ORPO and MIPO include dynamic compression plate (DCP) and locking compression plate (LCP). Numerous recent systematic reviews, meta-analysis, and network meta-analysis (NMA) review papers have been published aiming to determine the efficacy of these treatment options in order to provide reliable evidence to guide clinical decision making[6,8-13]. Based on the lack of consensus from the existing literature regarding surgical treatment of humeral shaft fractures, this manuscript aims to further assess the quality of the literature that guides treatment decisions by employing a new metric, the fragility index (FI). The FI has been introduced to further evaluate the robustness (or fragility) of randomized control trial (RCT) results[14,15].

The evaluation of RCTs *via* systematic review, meta-analysis, or NMA represents level I evidence; however, the fact remains that many RCTs in orthopaedics, despite demonstrating statistically significant effects, are limited by small sample sizes and few outcome events[16-19]. Clinical studies are classically evaluated for statistical significance in the form of *P* values, and 95% confidence intervals, which help determine how likely observed effects would occur based solely on chance[20-22]. The FI represents the required number of participants in the RCT whose outcome would have to change from nonevent to event in order to convert a statistically significant result to nonsignificant. The FI is calculated by sequentially calculating the *P* value using the Fisher exact test while changing an outcome from nonevent to event between cycles until the calculated *P* value is not significant, or $P > 0.05$. Basically, the FI quantifies how many patients would be required to switch outcomes in order to change the study conclusions. In the case where a study reports a statistically significant result, but the FI is

calculated to be zero, this would indicate that the Fisher's exact test did not find a P value < 0.05, whereas the statistical method used in the paper did. In addition, the FI may be lower than the number of patients lost to follow-up, limiting the confidence one may have in the study conclusion[14]. The higher the FI the more confidence the reader can have that the result is robust. While there is no defined cut off for the FI value, if the FI is zero or less than the number of patients lost to follow up, then any statistically significant result should be considered fragile and interpreted with caution. By applying the FI metric to RCTs evaluating surgical outcomes in humeral shaft fractures we can determine how much confidence these studies should be given in guiding treatment decisions.

Due to this added value, the FI has been gaining traction in the literature with studies published across numerous medical specialties[15,23,32-35,24-31], in addition to orthopaedic subspecialties[25,36-40]. This valuable, new tool, the FI, can serve to increase our understanding of the literature regarding treatment of humeral shaft fractures, aiding in clinical decision making. Our primary objective was to determine the robustness of statistically significant findings in RCTs of the surgical treatment of humeral shaft fractures by systematically applying the FI. We sought to accomplish this objective by testing our hypothesis that the median FI in these RCTs would be less than the number lost to follow up and therefore would indicate fragile results.

MATERIALS AND METHODS

The systematic review was completed, and results reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines statement[41]. We began by evaluating all review articles about humeral shaft fractures published from 2000 to 2019[6,8-12] and extracting from those studies all included RCTs for analysis. We then performed a systematic review of the literature to identify randomized controlled trials dealing with surgical treatment of humeral shaft fractures that had been published since the most recent review articles. The Medline and EMBASE databases were searched for the dates of January 1, 2016 to April 1, 2019 using the following Medical Subject Headings terms: “humeral fractures”. The Reference Citation Analysis (RCA) was also used to ensure high quality studies were included in the analysis. These dates were selected to identify new RCTs that would not have been included in prior systematic review articles. Titles and abstracts were screened, and full text manuscripts reviewed. Inclusion criteria included the following: patients randomized to 2 parallel arms, articles published in English, patient allocated to treatment and control arms in 1:1 ratio, reported statistical significance for dichotomous variables. Exclusion criteria included: published abstract only; studies without available full text, (non-English manuscripts; studies reporting patient data published previously; retrospective studies; and prospective studies that were not randomized.

Data was extracted from the included studies by individual review of each study by the primary author. Accuracy of data extraction was confirmed by independent review by the remaining authors separately, with any discrepancy resolved by group consensus. An electronic data form was developed and the following data were extracted for each included study: First author, journal, publication year, comparison groups, randomization parameters, initial sample size, total patients lost to follow up, final sample size, patients in study group 1, patients in study group 2, patients lost to follow up in group 1, patients lost to follow up in group 2, presence of power analysis, as well as the number of events for each outcome in each group and reported p-value for dichotomous outcomes (delayed union/nonunion, iatrogenic radial nerve palsy, infection, malunion, shoulder impingement, elbow stiffness, secondary surgeries). For our study lost to follow up included any patients initially enrolled in the study but not included in final analysis for any reason. The total number of events for all complications was defined as the sum of delayed union/nonunion, iatrogenic radial nerve palsy, infection, malunion, shoulder impingement, and elbow stiffness. The total number of events for all complications was calculated for each study group within each included study.

For each study the FI was then calculated for all complications, secondary surgeries, as well as each complication individually. The FI was calculated *via* the method described previously by Walsh *et al*[14] using a publicly available calculator found at http://clincalc.com/Stats/FragilityIndex.aspx. After inputting the total number of patients in the control group, experimental group, control group with primary endpoint, and experimental group with primary endpoint, this tool calculates the P value using the Fisher exact test. If the P value is significant (< 0.05), the tool incrementally converts 1 outcome from nonevent to event and recalculates the P value until the P value increases above 0.05 and the result becomes insignificant. The methodological quality of each RCT was also assessed by calculating the Jadad scale[42], also known as the Oxford Quality Scoring System, for each trial.

RESULTS

Our review of RCTs from recent review articles as well as systemic search strategy produced 415 records screened and 28 full text articles assessed (Figure 1). Of these, 15 studies met inclusion criteria (Table 1)[43-57]. The primary outcome was only defined in two studies, shoulder function defined by

Table 1 Included randomized controlled trials with characteristics

First author (last name)	Journal	Year	Comparison	Patients enrolled	Patients lost to follow up	Final study, *n*	JADAD score	Power analysis
Kim	*J Orthop Trauma*	2015	ORPO (LCP) *vs* MIPO	72	4	68	3	Yes
Esmailiejah	*Trauma Mon*	2015	ORPO (DCP) *vs* MIPO	68	3	65	3	No
Fan	*Orthopedics*	2015	ORPO (LCP) *vs* IMN	60	0	60	2	Yes
Hadhoud	*Menoufia Medical Journal*	2015	ORPO (LCP) *vs* MIPO	30	0	30	2	No
Wali	*Strategies Trauma Limb Reconstr*	2014	ORPO (DCP) *vs* IMN	50	0	50	2	No
Benegas	*J Shoulder Elbow Surg*	2014	MIPO *vs* IMN	41	1	40	3	Yes
Lian	*Orthopedics*	2013	MIPO *vs* IMN	56	9	47	3	No
Li	*J Shoulder Elbow Surg*	2011	ORPO (LCP) *vs* IMN	50	5	45	3	Yes
Iqbal	*Annals of King Edward Medical University*	2011	ORPO (DCP) *vs* IMN	40	0	40	3	No
Singisetti	*Int Orthop*	2010	ORPO (DCP) *vs* IMN	45	9	36	1	No
Putti	*J Orthop Surg (Hong Kong)*	2009	ORPO (DCP) *vs* IMN	34	0	34	2	No
Changulani	*Int Orthop*	2007	ORPO (DCP) *vs* IMN	47	2	45	3	No
Kesemenli	*Acta Orthop Traumatol Turc*	2003	ORPO (DCP) *vs* IMN	60	0	60	2	No
McCormack	*J Bone Joint Surg (Br)*	2000	ORPO (DCP) *vs* IMN	44	3	41	2	No
Chapman	*J Orthop Trauma*	2000	ORPO (DCP) *vs* IMN	89	5	84	3	No

ORPO: Open reduction and plate osteosynthesis; DCP: Dynamic compression plate; LCP: Locking compression plate; IMN: Intramedullary nail; MIPO: Minimally invasive plate osteosynthesis.

University of California, Los Angeles (UCLA) scoring system in one study[43] and shoulder function defined by the American Shoulder and Elbow Surgeons (ASES) score in the other[56]. Table 2 contains summary characteristics for these trials. The mean initial sample size was 52.4 (range 30-89), mean lost to follow up of 2.7 (range 0-9), while the mean final sample size was 49.7 (range 30-84). The mean Jadad scale score was 2.5 (range 1-3). Power analysis was only reported in 4 studies (26.7%).

The most common comparison was between ORPO with DCP and IMN, found in 8 studies (53.3%). ORPO with LCP *vs* IMN, MIPO *vs* IMN, and ORPO with DCP *vs* IMN were the comparison groups of 2 studies each (13.3% each), and 1 study (6.7%) compared ORPO with DCP and MIPO. All 15 studies evaluated both the outcomes of delayed union/nonunion and iatrogenic radial nerve palsy. The majority of studies also reported incidence for infection (14 studies, 93.3%), secondary surgeries (11 studies, 73.3%), and shoulder impingement (10 studies, 66.7%). Malunion was a reported outcome in 7 studies (46.7%), while only 4 studies (26.7%) reported the outcome of elbow stiffness.

The cumulative FI values for each outcome within each study are listed in Table 3 and presented graphically (Figure 2). The FI was found to be 0 for all individual outcomes except for iatrogenic nerve palsy in 1 out of 14 studies (higher rate with DCP compared with IMN), malunion in 1 of 7 studies (higher rate in IMN compared with LCP), shoulder impingement in 4 of 10 studies (higher rate in IMN compared with MIPO or DCP), elbow stiffness in 1 of 4 studies (higher rate in DCP compared with IMN), and secondary surgeries in 1 of 11 studies (higher rate with IMN compared with DCP). When totaling all complications for each study, the FI was >0 in 2 out of the 15 studies, with higher complication rates in IMN compared with MIPO or DCP. Overall, the FI was greater than 0 in only 9.8% (9/91) and was greater than the number lost to follow up in 2% (2/91) of outcomes studied.

The relationship between enrolled initial sample size and FI for all complications (Figure 3) was calculated using the Spearman correlation coefficient and was found to not be significant with a *P* value of 0.830. The majority of included RCTs reported continuous variable outcomes such as operative time,

Table 2 Summary characteristics of included randomized controlled trials

Characteristic	No.	% or range
Initial sample size, mean No.	52.4	(30-89)
Lost to follow up, mean No.	2.7	(0-9)
Final sample size, mean No.	49.7	(30-84)
Power analysis	4	26.7%
Comparison groups		
ORPO (DCP) *vs* IMN	8	53.3%
ORPO (LCP) *vs* IMN	2	13.3%
MIPO *vs* IMN	2	13.3%
ORPO (LCP) *vs* MIPO	2	13.3%
ORPO (DCP) *vs* MIPO	1	6.7%
Outcome assessed		
Delayed union/nonunion	15	100.0%
Iatrogenic radial nerve palsy	15	100.0%
Infection	14	93.3%
Secondary surgeries	11	73.3%
Shoulder impingement	10	66.7%
Malunion	7	46.7%
Elbow stiffness	4	26.7%

ORPO: Open reduction and plate osteosynthesis; DCP: Dynamic compression plate; LCP: Locking compression plate; IMN: Intramedullary nail; MIPO: Minimally invasive plate osteosynthesis.

radiation exposure time, operative blood loss, length of hospital stay, time to union, and functional outcome scores such as the UCLA scoring system, Mayo elbow performance index, and the ASES score. The outcomes with reported differences between groups are summarized in Table 4.

DISCUSSION

Our systemic review looked at randomized control trials (RCTs) of the surgical treatment of humeral shaft fractures and discovered that the median FI for all outcomes was 0. In the studies with data leading to FI > 0, the FI exceeded the number lost to follow up in only two instances (2%): (1) Lower incidence of iatrogenic radial nerve palsy with IMN compared with ORPO[45]; and (2) Lower rate of overall total complication with ORPO compared with IMN[56]. Therefore, all evaluated outcomes (nonunion, radial nerve palsy, infections, malunion, malrotation, shoulder impingement, elbow stiffness, secondary surgeries, and overall complications) were extremely fragile and did not demonstrate superiority of one intervention (ORPO, MIPO, IMN) over another.

In analyzing all outcomes individually for humeral shaft fractures, the median FI was 0, and remained so when calculating median FI for all outcomes combined. This result is not surprising given the median FI ≤ 3 reported in the orthopaedic literature previously[36-40]. A recent study used FI to explore the literature on the treatment of clavicular fractures and found the median FI to be 2, with 46.7% of trials reporting the number of patients lost to follow-up exceeded the FI[40]. Sample sizes in an operative population are inherently lower. In addition, the cost, time, and resources required to complete RCTs with sufficiently large sample sizes often pose a significant challenge in orthopaedics, where the incidence of desired exposures and events can be low[18,58]. Simply increasing sample size alone, however, is not sufficient to guarantee increased FI values, as even very large sample size studies can still have fragile results if the between-group difference is very small[14].

While the FI was found to be > 0 in 9 outcomes total, the fact that the number lost to follow up exceeded the FI in 89/91 (98%) instances further confirms that those outcomes are quite fragile, and the significance of those conclusions should be called into question. When the number lost to follow up exceeds the FI this indicates that inclusion of the patients lost to follow up alone could have resulted in a nonsignificant *P* value. Kesemenli *et al*[45] reported significantly higher rate of iatrogenic radial nerve

Table 3 Fragility index values for each outcome for included randomized controlled trials

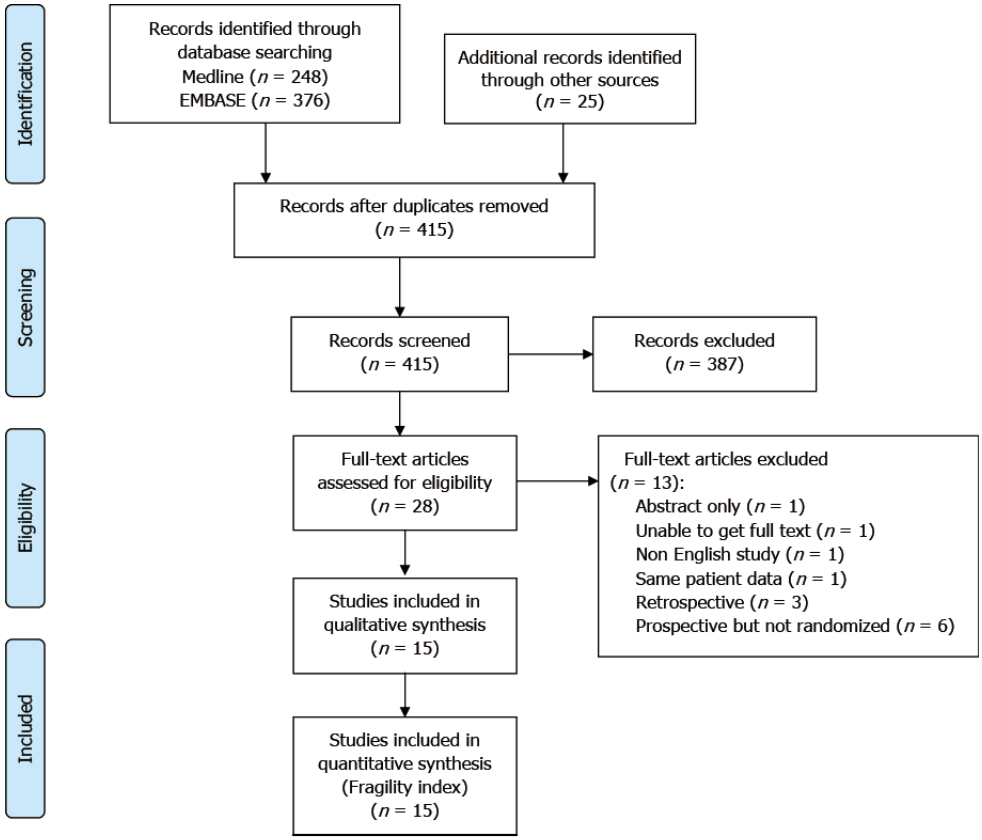
First author (last name)	Comparison	Delayed union/ Nonunion	Iatrogenic radial nerve palsy	Infection	Malunion	Shoulder Impingement	Elbow Stiffness	All complications	Secondary surgeries
Kim	ORPO (LCP) *vs* MIPO	0	0	0	0	NA	NA	0	0
Esmailiejah	ORPO (DCP) *vs* MIPO	0	0	0	0	NA	NA	0	0
Fan	ORPO (LCP) *vs* IMN	0	0	NA	NA	NA	NA	0	NA
Hadhoud	ORPO (LCP) *vs* MIPO	0	0	0	NA	NA	NA	0	NA
Wali	ORPO (DCP) *vs* IMN	0	0	0	NA	0	0	0	0
Benegas	MIPO *vs* IMN	0	0	0	0	0	NA	0	0
Lian	MIPO *vs* IMN	0	0	0	0	1	0	4	NA
Li	ORPO (LCP) *vs* IMN	0	0	0	2	NA	NA	0	NA
Iqbal	ORPO (DCP) *vs* IMN	0	0	0	NA	0	NA	0	0
Singisetti	ORPO (DCP) *vs* IMN	0	0	0	NA	0	0	0	0
Putti	ORPO (DCP) *vs* IMN	0	0	0	NA	0	NA	0	0
Changulani	ORPO (DCP) *vs* IMN	0	0	0	NA	1	NA	0	0
Kesemenli	ORPO (DCP) *vs* IMN	0	1	0	NA	0	NA	0	0
McCormack	ORPO (DCP) *vs* IMN	0	0	0	0	2	NA	6	1
Chapman	ORPO (DCP) *vs* IMN	0	0	0	0	2	1	0	0

ORPO: Open reduction and plate osteosynthesis; DCP: Dynamic compression plate; LCP: Locking compression plate; IMN: Intramedullary nail; MIPO: Minimally invasive plate osteosynthesis.

palsy among the DCP group compared with the IMN group. Of note, this study reported no patients lost to follow up. While this suggests a robust outcome, the fact remains that the other 14/15 studies showed no difference among treatment groups regarding iatrogenic radial nerve palsy. Regarding all complications combined, two studies[55,56] resulted in FI > 0, but the FI exceeded the number lost to follow up in only one[56].

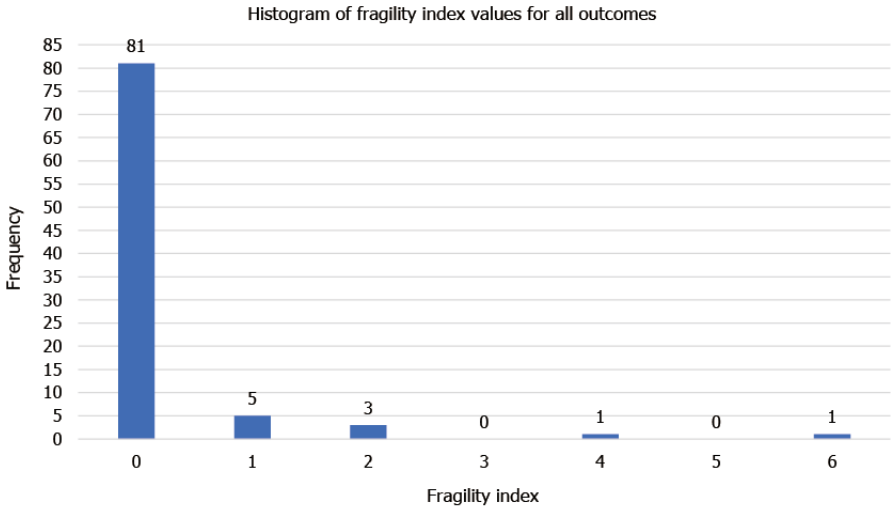
The difference between treatment options may possibly be captured only by continuous variables, and not by dichotomous variables. There is precedence for this in the orthopaedic literature, as Bhandari *et al*[58] recommended that when orthopaedic surgeons anticipate small sample sizes they can optimize their study's statistical power by choosing a continuous outcome variable. In reviewing 76 orthopaedic RCTs, these authors found significantly greater study power in RCTs reporting continuous variables compared with studies reporting dichotomous variables ($P = 0.042$), despite similar mean sample size in each group ($P > 0.05$). The difference in treatment options for humeral shaft fractures, however, has been reported and analyzed by continuous variables previously. As summarized in this review in Table 4, the majority of included RCTs reported on continuous variable outcomes. The FI is not designed to evaluate continuous variables, and therefore all these continuous outcomes fell outside the scope of our review. As such, application of the FI does not add to the commentary favoring any one treatment over the others on the basis of these continuous variables.

Our study has potential weaknesses, with some inherent to the requirements of the FI. In order to calculate an FI, a study must compare 2 treatment arms, randomize patients to those arms in 1:1 ratio, and report dichotomous outcomes. These inclusion criteria limit both the number of studies that can be included for analysis, as well as the number of outcomes or results that can be analyzed from the included studies. Another requirement of the FI is that a study must be a prospective, randomized trial.



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Figure 1 Preferred reporting items for systematic reviews and meta-analyses (PRISMA) flow diagram of included studies.



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Figure 2 Distribution of fragility indices from all studies and for all outcomes.

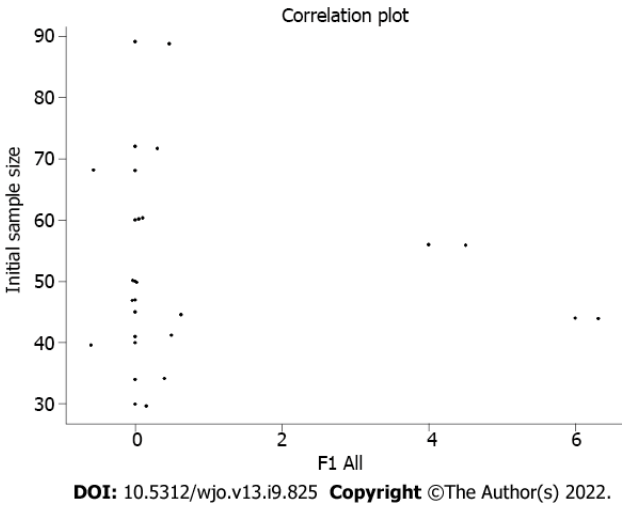
Due to this requirement, we excluded 3 retrospective studies and another 9 prospective studies that were not randomized. While this represents a loss in the number of included studies, and associated decrease in number of included patient outcomes, we do not feel this represents a significant loss as it means that the included studies represent the highest level of data availability.

Another potential weakness relates to the FI itself, which is not without inherent weakness or controversy. RCTs with small samples and in which the event of interest is rare, are common in orthopaedics and tend to be inherently fragile. The FI revolves around the statistical threshold of using $P < 0.05$ as a strict criterion of correct inference. While this cutoff is necessary for making statistical determinations, the actual judging of the quality of inference is a complex activity with more nuance

Table 4 Summary of outcomes with reported differences between groups

Continuous variable	Superior treatment	Inferior treatment	First author (last name)
Time to union	IMN	ORPO	Changulani
Time to union	IMN	ORPO	Fan
Operative time	IMN	ORPO	Fan
Operative time	IMN	ORPO	Wali
Operative time	MIPO	IMN	Lian
Operative time	MIPO	ORPO	Hadhoud
Intraoperative blood loss	IMN	ORPO	Fan
Intraoperative blood loss	IMN	ORPO	Wali
Intraoperative blood loss	MIPO	IMN	Lian
Hospital stay	IMN	ORPO	Fan
Hospital stay	IMN	ORPO	Wali
Constant scores	MIPO	IMN	Li
Rodriguez-Merchan criteria	DCP	IMN	Singisetti
Shoulder ROM	MIPO	IMN	Li
Shoulder ROM	DCP	IMN	Chapman
Elbow ROM	IMN	DCP	Chapman

ORPO: Open reduction and plate osteosynthesis; DCP: Dynamic compression plate; LCP: Locking compression plate; IMN: Intramedullary nail; MIPO: Minimally invasive plate osteosynthesis.



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Figure 3 Relationship between initial sample size and FI for all outcomes.

than is afforded in having a *P* value slightly greater of less than 0.05[59]. The misinterpretation of statistical tests extends beyond just the FI[60].

CONCLUSION

The FI represents a valuable tool that can aid in the interpretation of results from RCTs. Along with *P* value and confidence intervals, the FI provides a quantitative metric regarding the robustness of the reportedly significant results. In applying the FI to RCTs comparing surgical treatment options for humeral shaft fractures, this study has shown that there is a significant lack of robust data to recommend one treatment option over another on the basis of delayed union/nonunion, iatrogenic

radial nerve palsy, infection, malunion, shoulder impingement, elbow stiffness, or secondary surgeries. The results published in the literature for treatment of humeral shaft fractures should be interpreted cautiously. This study, while limited in the analysis of functional outcome, suggests no clear benefit of one surgical technique over another with respect to dichotomous outcomes. Plate and nail techniques should both be considered as options for surgical treatment of humeral shaft fractures.

ARTICLE HIGHLIGHTS

Research background

Humeral shaft fractures are a common injury which could be managed non-operatively or operatively. There is a lack of clear evidence to support open reduction internal fixation *vs* intramedullary nail fixation.

Research motivation

Identify the fragility index, which identifies the number of patients have a change in outcome from a significant to non-significant. This is important as higher level studies guide management in orthopedics.

Research objectives

Applying the fragility index to humeral shaft fractures will aid in clinical decision making on treatment of humeral shaft fractures.

Research methods

A systematic review of randomized controlled trials (RCTs) evaluating the surgical treatment of humeral shaft fractures was conducted. The fragility index (FI) was calculated for total complications, each complication individually, and secondary surgeries using the Fisher exact test, as previously published.

Research results

Fifteen RCTs were included in the analysis comparing open reduction plate osteosynthesis with dynamic compression plate or locking compression plate, intramedullary nail, and minimally invasive plate osteosynthesis. The median FI was 0 for all parameters analyzed. Regarding individual outcomes, the FI was 0 for 81/91 (89%) of outcomes. The FI exceeded the number lost to follow up in only 2/91 (2%) outcomes.

Research conclusions

The FI shows that data from RCTs regarding operative treatment of humeral shaft fractures are fragile and does not demonstrate superiority of any particular surgical technique.

Research perspectives

Further research is needed to delineate whether open reduction internal fixation or intramedullary nail fixation is superior in the management of humeral shaft fractures.

FOOTNOTES

Author contributions: Morris SC is responsible for the data collection; Morris SC and Gowd AK analyze the data; Phipatanakul WP, Liu JN and Amin NH are responsible for the study conception; all authors participate in the manuscript preparation.

Conflict-of-interest statement: All authors report no relevant conflict of interest for this article.

PRISMA 2009 Checklist statement: The authors have read the PRISMA 2009 Checklist, and the manuscript was prepared and revised according to the PRISMA 2009 Checklist.

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REFERENCES

1 **Attum B**, Obremskey W. Treatment of Humeral Shaft Fractures: A Critical Analysis Review. *JBJS Rev* 2015; **3** [PMID: 27490668 DOI: 10.2106/JBJS.RVW.N.00119]
2 **Updegrove GF**, Mourad W, Abboud JA. Humeral shaft fractures. *J Shoulder Elbow Surg* 2018; **27**: e87-e97 [PMID: 29292035 DOI: 10.1016/j.jse.2017.10.028]
3 **Walker M**, Palumbo B, Badman B, Brooks J, Van Gelderen J, Mighell M. Humeral shaft fractures: a review. *J Shoulder Elbow Surg* 2011; **20**: 833-844 [PMID: 21393016 DOI: 10.1016/j.jse.2010.11.030]
4 **Klenerman L**. Fractures of the shaft of the humerus. *J Bone Joint Surg Br* 1966; **48**: 105-111 [DOI: 10.1302/0301-620X.48B1.105]
5 **Sarmiento A**, Zagorski JB, Zych GA, Latta LL, Capps CA. Functional bracing for the treatment of fractures of the humeral diaphysis. *J Bone Joint Surg Am* 2000; **82**: 478-486 [PMID: 10761938 DOI: 10.2106/00004623-200004000-00003]
6 **Ouyang H**, Xiong J, Xiang P, Cui Z, Chen L, Yu B. Plate versus intramedullary nail fixation in the treatment of humeral shaft fractures: an updated meta-analysis. *J Shoulder Elbow Surg* 2013; **22**: 387-395 [PMID: 22947239 DOI: 10.1016/j.jse.2012.06.007]
7 **Gosler MW**, Testroote M, Morrenhof JW, Janzing HM. Surgical versus non-surgical interventions for treating humeral shaft fractures in adults. *Cochrane Database Syst Rev* 2012; **1**: CD008832 [PMID: 22258990 DOI: 10.1002/14651858.CD008832.pub2]
8 **Kurup H**, Hossain M, Andrew JG. Dynamic compression plating versus locked intramedullary nailing for humeral shaft fractures in adults. *Cochrane Database Syst Rev* 2011; CD005959 [PMID: 21678350 DOI: 10.1002/14651858.CD005959.pub2]
9 **Hu X**, Xu S, Lu H, Chen B, Zhou X, He X, Dai J, Zhang Z, Gong S. Minimally invasive plate osteosynthesis vs conventional fixation techniques for surgically treated humeral shaft fractures: a meta-analysis. *J Orthop Surg Res* 2016; **11**: 59 [PMID: 27169580 DOI: 10.1186/s13018-016-0394-x]
10 **Hohmann E**, Glatt V, Tetsworth K. Minimally invasive plating versus either open reduction and plate fixation or intramedullary nailing of humeral shaft fractures: a systematic review and meta-analysis of randomized controlled trials. *J Shoulder Elbow Surg* 2016; **25**: 1634-1642 [PMID: 27522336 DOI: 10.1016/j.jse.2016.05.014]
11 **Zhao Y**, Wang J, Yao W, Cai Q, Wang Y, Yuan W, Gao S. Interventions for humeral shaft fractures: mixed treatment comparisons of clinical trials. *Osteoporos Int* 2017; **28**: 3229-3237 [PMID: 28780727 DOI: 10.1007/s00198-017-4174-1]
12 **Zhao JG**, Wang J, Meng XH, Zeng XT, Kan SL. Surgical interventions to treat humerus shaft fractures: A network meta-analysis of randomized controlled trials. *PLoS One* 2017; **12**: e0173634 [PMID: 28333947 DOI: 10.1371/journal.pone.0173634]
13 **Qiu H**, Wei Z, Liu Y, Dong J, Zhou X, Yin L, Zhang M, Lu M. A Bayesian network meta-analysis of three different surgical procedures for the treatment of humeral shaft fractures. *Medicine (Baltimore)* 2016; **95**: e5464 [PMID: 28002327 DOI: 10.1097/MD.0000000000005464]
14 **Walsh M**, Srinathan SK, McAuley DF, Mrkobrada M, Levine O, Ribic C, Molnar AO, Dattani ND, Burke A, Guyatt G, Thabane L, Walter SD, Pogue J, Devereaux PJ. The statistical significance of randomized controlled trial results is frequently fragile: a case for a Fragility Index. *J Clin Epidemiol* 2014; **67**: 622-628 [PMID: 24508144 DOI: 10.1016/j.jclinepi.2013.10.019]
15 **Tignanelli CJ**, Napolitano LM. The Fragility Index in Randomized Clinical Trials as a Means of Optimizing Patient Care. *JAMA Surg* 2019; **154**: 74-79 [PMID: 30422256 DOI: 10.1001/jamasurg.2018.4318]
16 **Freedman KB**, Back S, Bernstein J. Sample size and statistical power of randomised, controlled trials in orthopaedics. *J Bone Joint Surg Br* 2001; **83**: 397-402 [PMID: 11341427 DOI: 10.1302/0301-620x.83b3.10582]
17 **Sabharwal S**, Patel NK, Holloway I, Athanasiou T. Sample size calculations in orthopaedics randomised controlled trials: revisiting research practices. *Acta Orthop Belg* 2015; **81**: 115-122 [PMID: 26280864]
18 **Abdullah L**, Davis DE, Fabricant PD, Baldwin K, Namdari S. Is There Truly "No Significant Difference"? *J Bone Joint Surg Am* 2015; **97**: 2068-2073 [PMID: 26677241 DOI: 10.2106/JBJS.O.00012]
19 **Mundi R**, Chaudhry H, Mundi S, Godin K, Bhandari M. Design and execution of clinical trials in orthopaedic surgery. *Bone Joint Res* 2014; **3**: 161-168 [PMID: 24869465 DOI: 10.1302/2046-3758.35.2000280]
20 **Dorey F**. Statistics in brief: Interpretation and use of p values: all p values are not equal. *Clin Orthop Relat Res* 2011; **469**: 3259-3261 [PMID: 21918804 DOI: 10.1007/s11999-011-2053-1]
21 **Porcher R**. Reporting results of orthopaedic research: confidence intervals and p values. *Clin Orthop Relat Res* 2009; **467**: 2736-2737 [PMID: 19565303 DOI: 10.1007/s11999-009-0952-1]
22 **Parisien RL**, Trofa DP, Dashe J, Cronin PK, Curry EJ, Fu FH, Li X. Statistical Fragility and the Role of P Values in the Sports Medicine Literature. *J Am Acad Orthop Surg* 2019; **27**: e324-e329 [PMID: 30325880 DOI: 10.5435/JAAOS-D-17-00636]
23 **Brown J**, Lane A, Cooper C, Vassar M. The Results of Randomized Controlled Trials in Emergency Medicine Are Frequently Fragile. *Ann Emerg Med* 2019; **73**: 565-576 [PMID: 30551894 DOI: 10.1016/j.annemergmed.2018.10.037]

24 **Gnech M**, Lovatt CA, McGrath M, Rickard M, Sanger S, Lorenzo AJ, Braga LH. Quality of reporting and fragility index for randomized controlled trials in the vesicoureteral reflux literature: where do we stand? *J Pediatr Urol* 2019; **15**: 204-212 [PMID: 31060965 DOI: 10.1016/j.jpurol.2019.02.014]

25 **Grolleau F**, Collins GS, Smarandache A, Pirracchio R, Gakuba C, Boutron I, Busse JW, Devereaux PJ, Le Manach Y. The Fragility and Reliability of Conclusions of Anesthesia and Critical Care Randomized Trials With Statistically Significant Findings: A Systematic Review. *Crit Care Med* 2019; **47**: 456-462 [PMID: 30394920 DOI: 10.1097/CCM.0000000000003527]

26 **Matics TJ**, Khan N, Jani P, Kane JM. The Fragility of Statistically Significant Findings in Pediatric Critical Care Randomized Controlled Trials. *Pediatr Crit Care Med* 2019; **20**: e258-e262 [PMID: 31013262 DOI: 10.1097/PCC.0000000000001922]

27 **Matics TJ**, Khan N, Jani P, Kane JM. The Fragility Index in a Cohort of Pediatric Randomized Controlled Trials. *J Clin Med* 2017; **6** [PMID: 28805717 DOI: 10.3390/jcm6080079]

28 **Narayan VM**, Gandhi S, Chrouser K, Evaniew N, Dahm P. The fragility of statistically significant findings from randomised controlled trials in the urological literature. *BJU Int* 2018; **122**: 160-166 [PMID: 29569390 DOI: 10.1111/bju.14210]

29 **Noel CW**, McMullen C, Yao C, Monteiro E, Goldstein DP, Eskander A, de Almeida JR. The fragility of statistically significant findings from randomized trials in head and neck surgery. *Laryngoscope* 2018; **128**: 2094-2100 [PMID: 29683494 DOI: 10.1002/lary.27183]

30 **Ridgeon EE**, Young PJ, Bellomo R, Mucchetti M, Lembo R, Landoni G. The Fragility Index in Multicenter Randomized Controlled Critical Care Trials. *Crit Care Med* 2016; **44**: 1278-1284 [PMID: 26963326 DOI: 10.1097/CCM.0000000000001670]

31 **Sato K**, Toda T, Iwata A. Fragility Index in Randomized Controlled Trials of Ischemic Stroke. *J Stroke Cerebrovasc Dis* 2019; **28**: 1290-1294 [PMID: 30765294 DOI: 10.1016/j.jstrokecerebrovasdis.2019.01.015]

32 **Shen C**, Shamsudeen I, Farrokhyar F, Sabri K. Fragility of Results in Ophthalmology Randomized Controlled Trials: A Systematic Review. *Ophthalmology* 2018; **125**: 642-648 [PMID: 29241744 DOI: 10.1016/j.ophtha.2017.11.015]

33 **Skinner M**, Tritz D, Farahani C, Ross A, Hamilton T, Vassar M. The fragility of statistically significant results in otolaryngology randomized trials. *Am J Otolaryngol* 2019; **40**: 61-66 [PMID: 30472124 DOI: 10.1016/j.amjoto.2018.10.011]

34 **Wayant C**, Meyer C, Gupton R, Som M, Baker D, Vassar M. The Fragility Index in a Cohort of HIV/AIDS Randomized Controlled Trials. *J Gen Intern Med* 2019; **34**: 1236-1243 [PMID: 31037544 DOI: 10.1007/s11606-019-04928-5]

35 **Shen Y**, Cheng X, Zhang W. The fragility of randomized controlled trials in intracranial hemorrhage. *Neurosurg Rev* 2019; **42**: 9-14 [PMID: 28634832 DOI: 10.1007/s10143-017-0870-8]

36 **Evaniew N**, Files C, Smith C, Bhandari M, Ghert M, Walsh M, Devereaux PJ, Guyatt G. The fragility of statistically significant findings from randomized trials in spine surgery: a systematic survey. *Spine J* 2015; **15**: 2188-2197 [PMID: 26072464 DOI: 10.1016/j.spinee.2015.06.004]

37 **Khan M**, Evaniew N, Gichuru M, Habib A, Ayeni OR, Bedi A, Walsh M, Devereaux PJ, Bhandari M. The Fragility of Statistically Significant Findings From Randomized Trials in Sports Surgery: A Systematic Survey. *Am J Sports Med* 2017; **45**: 2164-2170 [PMID: 27895038 DOI: 10.1177/0363546516674469]

38 **Khormaee S**, Choe J, Ruzbarsky JJ, Agarwal KN, Blanco JS, Doyle SM, Dodwell ER. The Fragility of Statistically Significant Results in Pediatric Orthopaedic Randomized Controlled Trials as Quantified by the Fragility Index: A Systematic Review. *J Pediatr Orthop* 2018; **38**: e418-e423 [PMID: 29979332 DOI: 10.1097/BPO.0000000000001201]

39 **Ruzbarsky JJ**, Khormaee S, Daluiski A. The Fragility Index in Hand Surgery Randomized Controlled Trials. *J Hand Surg Am* 2019; **44**: 698.e1-698.e7 [PMID: 30420197 DOI: 10.1016/j.jhsa.2018.10.005]

40 **Ruzbarsky JJ**, Khormaee S, Rauck RC, Warren RF. Fragility of randomized clinical trials of treatment of clavicular fractures. *J Shoulder Elbow Surg* 2019; **28**: 415-422 [PMID: 30771826 DOI: 10.1016/j.jse.2018.11.039]

41 **Panic N**, Leoncini E, de Belvis G, Ricciardi W, Boccia S. Evaluation of the endorsement of the preferred reporting items for systematic reviews and meta-analysis (PRISMA) statement on the quality of published systematic review and meta-analyses. *PLoS One* 2013; **8**: e83138 [PMID: 24386151 DOI: 10.1371/journal.pone.0083138]

42 **Jadad AR**, Moore RA, Carroll D, Jenkinson C, Reynolds DJM, Gavaghan DJ. Assessing the quality of reports of randomized clinical trials: Is blinding necessary? *Control Clin Trials* 1996; **17**: 1-12 [DOI: 10.1016/0197-2456(95)00134-4]

43 **Benegas E**, Ferreira Neto AA, Gracitelli ME, Malavolta EA, Assunção JH, Prada Fde S, Bolliger Neto R, Mattar R Jr. Shoulder function after surgical treatment of displaced fractures of the humeral shaft: a randomized trial comparing antegrade intramedullary nailing with minimally invasive plate osteosynthesis. *J Shoulder Elbow Surg* 2014; **23**: 767-774 [PMID: 24768221 DOI: 10.1016/j.jse.2014.02.010]

44 **Changulani M**, Jain UK, Keswani T. Comparison of the use of the humerus intramedullary nail and dynamic compression plate for the management of diaphyseal fractures of the humerus. A randomised controlled study. *Int Orthop* 2007; **31**: 391-395 [PMID: 16900354 DOI: 10.1007/s00264-006-0200-1]

45 **Kesemenli CC**, Subaşi M, Arslan H, Necmioğlu S, Kapukaya A. [Comparison between the results of intramedullary nailing and compression plate fixation in the treatment of humerus fractures]. *Acta Orthop Traumatol Turc* 2003; **37**: 120-125 [PMID: 12704250]

46 **Putti AB**, Uppin RB, Putti BB. Locked intramedullary nailing versus dynamic compression plating for humeral shaft fractures. *J Orthop Surg (Hong Kong)* 2009; **17**: 139-141 [PMID: 19721138 DOI: 10.1177/230949900901700202]

47 **Singisetti K**, Ambedkar M. Nailing versus plating in humerus shaft fractures: a prospective comparative study. *Int Orthop* 2010; **34**: 571-576 [PMID: 19506868 DOI: 10.1007/s00264-009-0813-2]

48 **Wali MG**, Baba AN, Latoo IA, Bhat NA, Baba OK, Sharma S. Internal fixation of shaft humerus fractures by dynamic compression plate or interlocking intramedullary nail: a prospective, randomised study. *Strategies Trauma Limb Reconstr* 2014; **9**: 133-140 [PMID: 25408496 DOI: 10.1007/s11751-014-0204-0]

49 **Hadhoud MM**, Darwish AE MM. Minimally invasive plate osteosynthesis vs open reduction and plate fixation of humeral

shaft fractures. *Menoufia Med J* 2015; **28**: 154-161 [DOI: 10.4103/1110-2098.155974]

50 **Chapman JR**, Henley MB, Agel J, Benca PJ. Randomized prospective study of humeral shaft fracture fixation: intramedullary nails versus plates. *J Orthop Trauma* 2000; **14**: 162-166 [PMID: 10791665 DOI: 10.1097/00005131-200003000-00002]

51 **Esmailiejah AA**, Abbasian MR, Safdari F, Ashoori K. Treatment of Humeral Shaft Fractures: Minimally Invasive Plate Osteosynthesis Versus Open Reduction and Internal Fixation. *Trauma Mon* 2015; **20**: e26271 [PMID: 26543844 DOI: 10.5812/traumamon.26271v2]

52 **Fan Y**, Li YW, Zhang HB, Liu JF, Han XM, Chang X, Weng XS, Lin J, Zhang BZ. Management of Humeral Shaft Fractures With Intramedullary Interlocking Nail Versus Locking Compression Plate. *Orthopedics* 2015; **38**: e825-e829 [PMID: 26375542 DOI: 10.3928/01477447-20150902-62]

53 **Kim JW**, Oh CW, Byun YS, Kim JJ, Park KC. A prospective randomized study of operative treatment for noncomminuted humeral shaft fractures: conventional open plating versus minimal invasive plate osteosynthesis. *J Orthop Trauma* 2015; **29**: 189-194 [PMID: 25210833 DOI: 10.1097/BOT.0000000000000232]

54 **Li Y**, Wang C, Wang M, Huang L, Huang Q. Postoperative malrotation of humeral shaft fracture after plating compared with intramedullary nailing. *J Shoulder Elbow Surg* 2011; **20**: 947-954 [PMID: 21440461 DOI: 10.1016/j.jse.2010.12.016]

55 **Lian K**, Wang L, Lin D, Chen Z. Minimally invasive plating osteosynthesis for mid-distal third humeral shaft fractures. *Orthopedics* 2013; **36**: e1025-e1032 [PMID: 23937748 DOI: 10.3928/01477447-20130724-18]

56 **McCormack RG**, Brien D, Buckley RE, McKee MD, Powell J, Schemitsch EH. Fixation of fractures of the shaft of the humerus by dynamic compression plate or intramedullary nail. A prospective, randomised trial. *J Bone Joint Surg Br* 2000; **82**: 336-339 [PMID: 10813165 DOI: 10.1302/0301-620x.82b3.9675]

57 **Iqbal M**, Nawaz A, Mahmood T, Manzoor S, Siddiq AB. A Comparative Study of Treatment of Humeral Shaft Fractures using Interlocking Nail vs. AO Dynamic Compression Plate Fixation. *Ann KING EDWARD Med Univ* 2011; **17** [DOI: 10.21649/akemu.v22i1.793]

58 **Bhandari M**, Lochner H, Tornetta P 3rd. Effect of continuous versus dichotomous outcome variables on study power when sample sizes of orthopaedic randomized trials are small. *Arch Orthop Trauma Surg* 2002; **122**: 96-98 [PMID: 11880910 DOI: 10.1007/s004020100347]

59 **Andrade C**. The Use and Limitations of the Fragility Index in the Interpretation of Clinical Trial Findings. *J Clin Psychiatry* 2020; **81** [PMID: 32237291 DOI: 10.4088/JCP.20f13334]

60 **Greenland S**, Senn SJ, Rothman KJ, Carlin JB, Poole C, Goodman SN, Altman DG. Statistical tests, P values, confidence intervals, and power: a guide to misinterpretations. *Eur J Epidemiol* 2016; **31**: 337-350 [PMID: 27209009 DOI: 10.1007/s10654-016-0149-3]

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SYSTEMATIC REVIEWS

Return to work following shoulder arthroplasty: A systematic review

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Abstract

BACKGROUND

Many patients prioritize the ability to return to work (RTW) after shoulder replacement surgeries such as total shoulder arthroplasty (TSA), reverse TSA (rTSA), and shoulder hemiarthroplasty (HA). Due to satisfactory clinical and functional long-term outcomes, the number of shoulder replacements performed will continue to rise into this next decade. With younger individuals who compose a significant amount of the workforce receiving shoulder replacements, patients will begin to place a higher priority on their ability to RTW following shoulder arthroplasty.

AIM

To summarize RTW outcomes following TSA, rTSA, and HA, and analyze the effects of workers' compensation status on RTW rates and ability.

METHODS

This systematic review and analysis was performed in accordance with Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines. A literature search regarding RTW following shoulder arthroplasty was performed using four databases (PubMed, Scopus, Embase, and Cochrane Library), and the *Reference Citation Analysis* (https://www.referencecitationanalysis.com/). All studies in English relevant to shoulder arthroplasty and RTW through January 2021 that had a level of evidence I to IV were included. Nonclinical studies, literature reviews, case reports, and those not reporting on RTW after shoulder arthroplasty were excluded.

RESULTS

The majority of patients undergoing TSA, rTSA, or HA were able to RTW between

one to four months, depending on work demand stratification. While sedentary or light demand jobs generally have higher rates of RTW, moderate or heavy demand jobs tend to have poorer rates of return. The rates of RTW following TSA (71%-93%) were consistently higher than those reported for HA (69%-82%) and rTSA (56%-65%). Furthermore, workers' compensation status negatively influenced clinical outcomes following shoulder arthroplasty. Through a pooled means analysis, we proposed guidelines for the average time to RTW after TSA, rTSA, and HA. For TSA, rTSA, and HA, the average time to RTW regardless of work demand stratification was 1.93 ± 3.74 mo, 2.3 ± 2.4 mo, and 2.29 ± 3.66 mo, respectively.

CONCLUSION

The majority of patients are able to RTW following shoulder arthroplasty. Understanding outcomes for rates of RTW following shoulder arthroplasty would assist in managing expectations in clinical practice.

Key Words: Shoulder replacement; Total shoulder arthroplasty; Reverse total shoulder arthroplasty; Hemiarthroplasty; Return to work

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Core Tip: Many patients prioritize the ability to return to work after shoulder replacement surgeries such as total shoulder arthroplasty, reverse total shoulder arthroplasty, and shoulder hemiarthroplasty. While rates of return to work have been studied in the literature following shoulder arthroplasty, a consensus on which is the most effective treatment is still controversial. Information about the ability to return to work following any type of shoulder arthroplasty would assist patients and surgeons in managing expectations and put into place evidence-based guidelines. This systematic review examines how return to work following shoulder arthroplasty has been studied and reported in the literature.

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INTRODUCTION

Over the last two decades, the number of shoulder arthroplasties, including total shoulder arthroplasty (TSA), reverse TSA (rTSA), and shoulder hemiarthroplasty (HA), has increased at exponential rates[1-4]. TSA has typically been indicated for end-stage shoulder conditions in individuals with intact rotator cuff and sufficient glenoid bone stock to allow for stable glenoid component implantation[1-4]. The TSA procedure involves replacing the humeral head and glenoid with similarly shaped prosthetic components. rTSA, on the other hand, was historically indicated for patients with massive rotator cuff tears and involves using a convex glenoid hemispheric ball and a concave humerus articulating cup to reconstruct the glenohumeral joint. HA has traditionally been indicated in patients with glenohumeral arthritis where the glenoid bone stock is inadequate for TSA[1-4]. This procedure involves removing the humeral articular surface and replacing it with a stemmed humeral component.

Due to satisfactory clinical and functional long-term outcomes, the number of shoulder replacements performed will continue to rise into this next decade, with models predicting between 174810 and 350558 procedures by 2025[2,5,6]. Historically, shoulder replacements have been performed in elderly patients for degenerative shoulder conditions; however, these procedures are becoming more prevalent in younger and more active populations[5-8]. Furthermore, individuals born between 1981 and 1996 make up the largest generation of workers in the U.S. Labor Force[9]. With younger individuals who compose a significant amount of the workforce receiving shoulder replacements, patients will begin to place a higher priority on their ability to return to work (RTW) following shoulder arthroplasty.

Prior studies have shown varying levels of RTW after shoulder arthroplasty based on arthroplasty type, diagnosis, and work intensity[10-12]. While informative, a compilation comparing various demographics, arthroplasty types, diagnoses, and work intensities has not been performed in recent years. The purpose of this systematic literature review and analysis is to summarize outcomes of RTW following TSA, rTSA, and HA as well as analyze the effects of workers' compensation (WC) status on rates and ability to RTW.

MATERIALS AND METHODS

In accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines, a systematic review and analysis was performed[13,14]. The PubMed, Scopus, Embase, and Cochrane Library databases was queried using the search terms "shoulder arthroplasty", "shoulder replacement", "shoulder hemiarthroplasty", or "humeral resurfacing" combined with "return to work". The *Reference Citation Analysis* (https://www.referencecitationanalysis.com/) software was also used to identify any additional studies. The final search was performed on January 8, 2021. Additionally, the references of each study were manually assessed as well for potential inclusion in this investigation. The flow diagram summarizes the progression of the literature review with 12 total references meeting the inclusion criteria (Figure 1).

Clinical studies were evaluated and included if they were in English, had level of evidence I to IV, and reported on RTW after shoulder arthroplasty. Nonclinical studies, literature reviews, case reports, and those not reporting on RTW after shoulder arthroplasty were excluded. Title and abstract reviews were performed by two of the study authors (Lalehzarian SP and Liu JN). The full texts of articles meeting inclusion criteria based on title and abstract were then reviewed by two of the study authors (Lalehzarian SP and Agarwalla A) for final inclusion in the study. As referenced in Figure 1, 23 references were initially identified by the keyword search terms described above. After the title review, 8 references were excluded as 7 were irrelevant to the topic of discussion and 1 was a case report. One reference was excluded after abstract review as it was a review article and two references were excluded after full text review as they did not include RTW data. Following the review process, there were 12 references left and all were included in this review.

Included studies were evaluated using the Methodological Index for Non-Randomized Studies (MINORS) checklist[15]. Studies were evaluated on 8 items to 12 items, with each scored 0 (not reported), 1 (reported but poorly or inadequately done), or 2 (reported, well done and adequate), with a maximum score of 16 and 24 for noncomparative and comparative studies, respectively. Articles were scored by one of the study authors (Lalehzarian SP) and confirmed by two of the study authors (Agarwalla A and Liu JN). An analysis of the 12 total articles is shown in Tables 1-3.

RESULTS

RTW after TSA

TSA has shown to be a highly effective treatment for degenerative shoulder disease with adequate long-term outcomes, low revision rates, and high implant survivorship[7,16]. The number of anatomic total shoulder arthroplasties has increased from 29414 in 2011 to 40750 in 2017 partly due to an increased demand from younger populations and expanded indications[2,17-20]. With this increase in demand and volume, RTW following anatomic TSA is an important metric for many employed patients.

In a study by Bülhoff *et al*[10], 57 TSA patients were analyzed after meeting inclusion criteria. At the most recent follow-up, 22 total patients (39%) returned to work. It is important to note that 6 patients (11%) cited their inability to pursue work at the time of most recent follow-up due to shoulder problems. While the authors concluded that approximately 61% of their patients did not retire or cease their vocation because of TSA, a large number of patients who were not working at final follow-up had retired from work[10]. This major limitation could be responsible for a low rate of RTW.

Liu *et al*[12] reported on 52 patients (54 shoulders), who were 55 years or younger at the time of surgery, worked in the 3 years leading up to surgery, and were available for a minimum follow-up of 2 years. Forty-eight patients (92%) were able to RTW postoperatively at an average of 2.1 mo after surgery. In addition to calculating the rate of RTW, the authors stratified patients by intensity of work: sedentary, light, moderate, or heavy. Forty one of 41 (100%) patients who had sedentary, light, or moderate work preoperatively were able to return to the same level of work. However, only 7 of 11 (64%) patients who had heavy-intensity work preoperatively were able to RTW. Of the 4 patients who did not RTW, only one patient cited shoulder pain and limited range of motion as the reason[12]. Additionally, the intensity of work was positively correlated with time to RTW. The authors found a statistically greater time to RTW when comparing heavy intensity (4.2 mo) to sedentary, light, and moderate intensity, respectively.

Cvetanovich *et al*[21] analyzed 27 shoulders (24 patients) that underwent anatomic TSA with an inlay glenoid component and stemless ovoid humeral head component. Twenty five (93%) of 27 patients were able to RTW with an average duration of 3.7 mo following surgery. Of the 2 patients who were not able to return, one patient cited reasons unrelated to the shoulder and the other patient cited back issues. When stratified by job intensity preoperatively, the rates of RTW were as follows: 5/5 for sedentary, 2/2 for light, 9/9 for moderate, and 9/11 for heavy. Furthermore, of the 25 patients who returned to work, 19 (76%) were able to return to their preoperative occupational demands. The 6 patients who returned to work at a lower intensity held heavy intensity occupations[21]. In addition to corroborating high rates of RTW for patients undergoing TSA, the authors found that patients with heavier demand jobs were less likely to RTW at the same occupational level postoperatively than patients in the other work

Table 1 Study characteristics

Ref.	Design	No. of groups	Level of evidence	Mean follow-up (range), yr	MINORS score
Bülhoff *et al*[10], 2015	Retrospective	1	IV	6.2 (2.6-12.6)	7/16
Jawa *et al*[56], 2015	Retrospective	2	III	3.9 (2.0-5.6)	17/24
Morris *et al*[55], 2015	Retrospective	2	III	3.5 (2-8)	20/24
Garcia *et al*[28], 2016	Retrospective	1	IV	2.6 (1-4.7)	10/16
Garcia *et al*[36], 2016	Retrospective	1	IV	5.1 (1-7.5)	10/16
Hurwit *et al*[11], 2017	Retrospective	2	III	HHA: 5.3 (1.1-7.5); rTSA[1]: 2.7 (1.0-4.9)	16/24
Liu *et al*[12], 2018	Retrospective	1	IV	5.4 (2.5-8.6)	10/16
Kurowicki *et al*[41], 2018	Retrospective	2	III	2.4 (0.5-7.6)	17/24
Gowd *et al*[48], 2019	Retrospective	2	III	Hemi RR: 5.7 (SD ± 2.0); aTSA: 5.8 (SD ± 2.2)	17/24
Cvetanovich *et al*[21], 2020	Retrospective	1	IV	3.4 (1.9-5.0)	9/16
Jayasekara *et al*[22], 2020[2]	Retrospective	3	IV	NR	NA
Liu *et al*[49], 2020	Retrospective	2	III	HHA: 5.2 (2.0-7.5); aTSA: 5.18 (2.0-7.49)	16/24

[1]Represents duplicate data from Garcia *et al*[28]; not included in meta-analysis.
[2]Numbers are relevant to groups who underwent total shoulder arthroplasty, reverse total shoulder arthroplasty, and hemiarthroplasty.
MINORS: Methodological Index for Non-Randomized Studies; HHA: Humeral hemiarthroplasty; rTSA: Reverse total shoulder arthroplasty; NR: Not reported; NA: Not available; Hemi RR: Hemiarthroplasty with ream-and-run resurfacing; aTSA: Anatomic total shoulder arthroplasty.

demand classes.

In a large clinical series by Jayasekara *et al*[22], 1773 patients were examined. TSA was one of the twelve surgeries analyzed with a total number of 38 patients. At the six month follow-up, 27 (71%) patients were able to return to some type of work: 14 (37%) patients returned with full duty, 13 (34%) patients returned with lighter duty, and 11 (29%) patients were unable to RTW. Of the twelve surgeries analyzed, TSA at 71% was shown to have a lower rate of RTW compared to surgeries such as HA and rTSA which had 82% and 56%, respectively[22]. This lower rate of RTW may have been due to a higher average age of patients who underwent TSA compared to those in previous studies; therefore, the age of the patients may have negatively influenced their desire and ability to RTW[22].

In summary, the majority of studies cited a rate of RTW between 71% and 93% with an average duration of 1 mo to 4 mo following TSA[12,21]. Furthermore, most patients who undergo TSA are able to RTW at the same preoperative intensity level with the exception of those patients in heavy intensity jobs who are less likely to RTW after TSA.

RTW after rTSA

In 2003, the United States Food and Drug Administration approved the use of rTSA for rotator cuff arthropathy[1,23]. Since that time, the volume of rTSA has drastically increased, from 21916 in 2011 to 63845 in 2017, in part due to its encouraging results and expanded indications to cover proximal humerus fracture and previous failures of arthroplasty[24-27]. When comparing the number of rTSA to the total number of shoulder replacements from 2011 and 2017, the percentage has increased from 33% to 58%[2]. Due to the exponential increase in rTSA use, a clinical review outlining the rate of RTW after rTSA will assist orthopedic surgeons in treating future patients with shoulder conditions.

Garcia *et al*[28] conducted a study on 40 patients who had undergone rTSA. Of the 40 patients analyzed, 26 (65%) of them were able to RTW with an average time of 2.3 mo. From the 14 patients who did not RTW, only two of them retired due to shoulder reasons while the other 12 retired due to nonorthopedic causes. When stratified into intensity level, rates were comparable to the overall rate of RTW with 17 (68%) of 25 patients returning in the sedentary class and 9 (60%) of 15 returning in the light class. Additionally, patients with sedentary jobs returned to work more quickly than those with light work (1.4 mo *vs* 4.0 mo).

Jayasekara *et al*[22] evaluated 34 rTSA patients, with 19 (56%) of them able to return to some type of work at the 6 mo follow-up. Eight of the 19 patients who returned to work were able to RTW with full duties and the other eleven returned to work with lighter duties. From the twelve surgeries included in the study, rTSA was associated with the lowest rate of RTW at 56%. Jayasekara *et al*[22] concluded that this percentage is consistent with prior studies which cited a 65% rate of RTW[11,28].

Table 2 Characteristics of the patients

Ref.	No. of shoulders	Mean age (range), yr	Gender (M/F), *n*	Dominant/nondominant, *n*	BMI, kg/m^2 (range)	WC/NWC	RTW (%)	Work intensity
Bülhoff *et al*[10], 2015	154	72 (33-88)	35/119	103/51	NR	NR	22/57 (38.6)[1]	NR
Jawa *et al*[56], 2015	13	55.9 (39-74)	13/0	NR	NR	13/0	4/13 (30.8)	1 light, 12 heavy
Morris *et al*[55], 2015	28	WC: 58.8 (49-69); NWC: 63.4 (50-72)	20/8	19/9	WC: 32.0 (SD ± 8.4); NWC: 27.1 (SD ± 5.3)	14/14	WC: 2/14 (14.3); NWC: 5/11 (45.5)[1]	WC: 8 sedentary/light, 6 heavy/strenuous; NWC: 3 retired, 7 sedentary/light, 4 heavy/strenuous
Garcia *et al*[28], 2016 (rTSA)	40	74.7 (56-82)	16/24	26/14	28.8 (14.8-46.2)	0/40	26/40 (65)	25 sedentary, 15 light
Garcia *et al*[36], 2016 (HHA)	79	69 (27.6-97.1)	24/55	62/17	28.3 (19.8-49.3)	0/79	34/49 (69.4)[1]	20 sedentary, 25 light, 4 moderate
Hurwit *et al*[11], 2017	81	HHA: 60.8 (40-88); rTSA: 68.6 (41-48)	33/48	52/29	HHA: 28.9; rTSA: 29.5	NR	55/81 (84.6)	44 sedentary, 33 light, 4 heavy
Liu *et al*[12], 2018	52	67.2 (56-96)	38/14	24/28	28.0 (18.1-52.9)	5/47	48/52 (92)	10 sedentary, 14 light, 17 moderate, 11 heavy
Kurowicki *et al* [41], 2018[2]	265	aTSA: 69; rTSA: 75	NR	NR	NR	NR	21% higher difference in ability to RTW following aTSA than rTSA	115 retired, 72 housework, 49 desk job, 16 prolonged standing, 11 yard work, 9 creative jobs, 5 requires lifting, 4 carpenter/construction, 5 cook/food prep
Gowd *et al*[48], 2019	53	Hemi RR: 52.8 ± 7.7; aTSA: 53.3 ± 9.2	48/5	28/25	Hemi RR: 28.5 ± 3.5; aTSA: 31.1 ± 5.7	4/49	50/53 (94.3)	17 sedentary, 12 light, 13 moderate, 11 heavy
Cvetanovich *et al* [21], 2020	27	52.1 ± 6 (42-63)	25/2	NR	NR	3/24	25/27 (92.6)	5 sedentary, 2 light, 9 moderate, 11 heavy
Jayasekara *et al* [22], 2020[3]	83	TSA: 65 ± 1.6 (48-86); rTSA: 72 ± 1.6 (54-91); Hemi: 72 ± 2.7 (57-84)	42/41	NR	NR	3/83	55/83 (66.3)	28 full duty, 27 lighter duty
Liu *et al*[49], 2020	49	HHA: 62.4 (42.7-87.7); aTSA: 61.7 (47.7-75.6)	22/27	30/19	HHA: 29.8 ± 7.1; aTSA: 29.2 ± 6.5	NR	36/49 (73.5)	20 sedentary, 21 light, 6 heavy

[1]Excluding those who were retired preoperatively, retired due to medical concerns, or retired due to non-specified reasons.
[2]Only includes individuals who responded to question 10 of the ASES questionnaire in regards to work.
[3]Numbers are relevant to groups who underwent total shoulder arthroplasty, reverse total shoulder arthroplasty, and hemiarthroplasty.
M: Male; F: Female; BMI: Body mass index; WC: Workers' compensation; NWC: Non-workers' compensation; RTW: Return to work; NR: Not reported; aTSA: Anatomic total shoulder arthroplasty; rTSA: Reverse total shoulder arthroplasty; HHA: Humeral hemiarthroplasty.

Table 3 Diagnosis and surgical characteristics

Ref.	Diagnosis	Surgery	Mean time out of work (range), mo	Complications
Bülhoff *et al* [10], 2015	Primary OA, 154 (100%)	aTSA	NR	NR
Jawa *et al*[56], 2015	OA, 11 (84.6%); capsulorrhaphy arthropathy, 2 (15.4%)	aTSA	4.2 (2.9-6.0)	NR
Morris *et al* [55], 2015	CTA, 14; massive RCT, 8; post-traumatic malunion, 4; failed prior arthroplasty, 2	rTSA	NR	WC (4): postoperative anterior dislocation (2), intraoperative humeral shaft fracture, postoperative periprosthetic infection; NWC (2): postoperative anterior dislocation
Garcia *et al*[28], 2016 (rTSA)	CTA, 21 (53.5%); OA, 10 (25%); PHFx, 7 (17.5%); RA, 2 (5%)	rTSA	2.3 (0.5-11)	NR
Garcia *et al*[36], 2016 (HHA)	OA, 40 (50.6%); PHFx, 17 (21.5%); AVN, 11 (13.9%); CTA, 8 (10.1%); RA, 3 (3.8%)	HHA	1.4 (0.25-24)	8 complications: 4 revision HHA (2 for dislocation, 2 for periprosthetic fracture after fall); 3 HHA revised to TSA; 1 HHA revised to rTSA for continued pain/glenoid wear
Hurwit *et al* [11], 2017	CTA, 63 (77.8%); RA, 14 (17.2%); PHFx, 2 (2.5%)	rTSA; HHA	rTSA: 3.1; HHA: 2.3	rTSA: 20 chronic pain and stiffness/limited mobility; 1 returned to OR; HHA: 4 chronic pain and stiffness/limited mobility; 5 returned to OR
Liu *et al*[12], 2018	OA, 42 (81%); failed prior arthroplasty, 7 (13%); AVN, 2 (4%); RA, 1 (2%)	aTSA	2.1 (SD: 1.7)	22 complications: 17 postoperative stiffness, 6 chronic pain, 3 instability, 4 returned to OR
Kurowicki *et al* [41], 2018	NR	aTSA; rTSA	NR	NR
Gowd *et al*[48], 2019	End-stage glenohumeral OA, 53 (100%)	Hemi RR; aTSA	Hemi RR: 2.5 ± 4.8; aTSA: 1.98 ± 2.6	Hemi RR: 3 chronic pain, 1 felt unstable, 5 postoperative stiffness, 1 nagging soreness, 1 acute pain, 2 conversion to aTSA, 1 received arthroscopic debridement; aTSA: 1 chronic pain, 2 weakness, 6 postoperative stiffness, 1 subscapularis repair, 1 revision with glenoid explantation due to loosening
Cvetanovich *et al*[21], 2020	Glenohumeral OA, 23 (85.1%); post-traumatic OA, 4 (14.9%)	aTSA	3.7 ± 5.2	1 hematoma, 1 pulmonary embolism
Jayasekara *et al* [22], 2020[1]	NR	aTSA; rTSA; HHA	NR	NR
Liu *et al*[49], 2020	End-stage glenohumeral OA, 49 (100%)	HHA; aTSA	HHA: 1.9 ± 2.3; aTSA: 1.3 ± 1.0	HHA: 15 chronic pain, 8 postoperative stiffness, 2 conversion to aTSA, 2 conversion to rTSA; aTSA: 3 postoperative stiffness

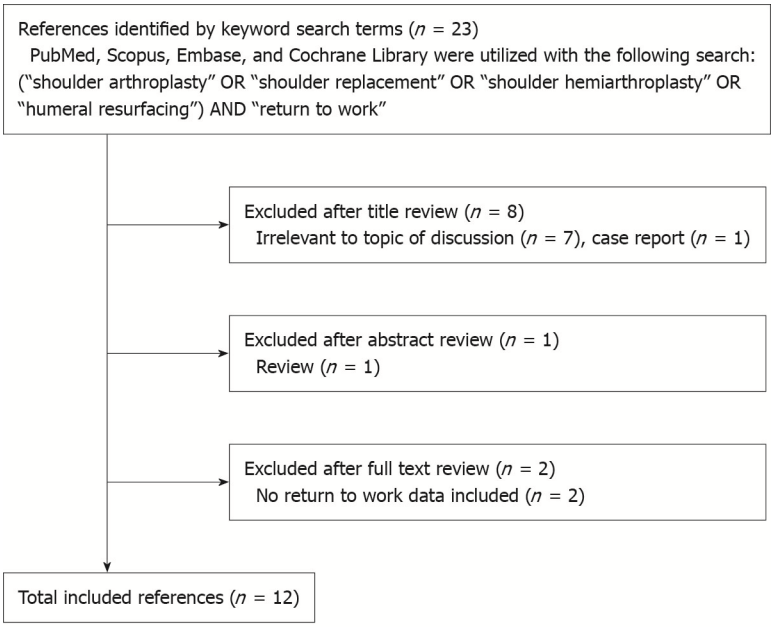
[1]Numbers are relevant to groups who underwent total shoulder arthroplasty, reverse total shoulder arthroplasty, and hemiarthroplasty.
OA: Osteoarthritis; CTA: Cuff tear arthropathy; RCT: Rotator cuff tear; PHFx: Proximal humerus fracture; RA: Rheumatoid arthritis; AVN: Avascular necrosis; aTSA: Anatomic total shoulder arthroplasty; rTSA: Reverse total shoulder arthroplasty; HHA: Humeral hemiarthroplasty; TSA: Total shoulder arthroplasty; NR: Not reported; WC: Workers' compensation; NWC: Non-workers compensation; OR: Operating room.

The available data suggests that the majority of patients who undergo rTSA are able to RTW at rates between 56% and 65%. Despite this low percentage, the volume of rTSA continues to rise due to expanding indications[2].

RTW after HA

Traditionally, HA was considered a safer option compared to TSA or rTSA for patients who wished to remain active following surgery due to its low failure rate and utilization of an intact glenoid[29]. Despite exponential rises in TSA and RTSA, the rate of HA procedures has steadily declined from 15860 in 2011 to 6150 in 2017[2]. This is in part due to the increase in rTSA for shoulder replacement. Since the indications for rTSA have been expanded to include fractures, the rate of HA for fracture use has decreased by nearly 30%[30-32]. Additionally, recent studies have shown that clinical outcomes from HA are significantly inferior to that of TSA and that patients undergoing HA had statistically significantly worse functional scores[11,33-35]. With this steady decline over the last decade, there is much necessity for a clinical review that examines all available literature regarding the rates of RTW for HA.

Garcia *et al*[36] examined 49 patients who worked preoperatively and underwent HA. Thirty-four (69.4%) patients were able to return to previous employment at an average duration of 1.4 mo. Preoper-



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Figure 1 Flow diagram illustrating systematic literature review process.

atively, 20 (41%) patients classified their jobs as sedentary, 25 (51%) patients as light physical work, and 4 (8%) patients as moderate physical work. Following HA, 15 of 20 (75%) patients returned as sedentary, 17 of 25 (68%) patients as light physical work, and 2 of 4 (50%) patients as moderate physical work. While no patients changed job demand level postoperatively, the average time to return to employment varied: 1.9 mo for sedentary, 2.6 mo for light, and 13.1 mo for moderate. As one of the first studies to analyze the rates of RTW following HA, Garcia *et al*[36] was able to quantify evidence that aided physicians in managing expectations of patients undergoing shoulder HA.

Jayasekara *et al*[22] included 11 patients who underwent shoulder HA. Nine (82%) patients were able to return to some type of work at 6 mo follow-up with 6 (55%) patients able to return to full duties, 3 (27%) able to return to lighter duties, and 2 (18%) unable to RTW. While the reason for not returning to work was not cited, it may be due to the fact that the average age of patients undergoing HA in this cohort was 72 years of age. Although a limitation of this study was a smaller size, Jayasekara *et al*[22] found higher rates of RTW despite an average age much higher than previous studies[11,36].

Recent literature has shown rates of RTW for shoulder HA between 69% and 82% compared to both TSA and rTSA[22,36]. Despite higher rates of RTW for HA compared to rTSA, the number of HA cases continues to decline with poor functional outcomes at long-term follow-up[11,37].

Comparison of RTW between TSA and rTSA

In patients with end-stage glenohumeral arthritis and an intact rotator cuff, TSA has shown to be a highly effective treatment with high rates of functional recovery[5]. While the original indication for rTSA was rotator cuff arthropathy, the indications for rTSA have expanded to include conditions such as TSA and HA implant failures, complex proximal humerus fractures, asymmetric glenoid wear, posterior humeral head subluxation in patients with intact rotator cuffs, and irreparable rotator cuff tears in the absence of arthritis[38-40]. Similarly, the indications for TSA have also expanded to now include a more diverse and active patient population[41]. As younger patients undergo shoulder replacements, many patients cite their ability to work as instrumental in their decision to have surgery. With increased indications for both surgeries, assessing the ability of patients to RTW following TSA and rTSA is imperative to educate future patients and manage expectations.

In one recent study, Kurowicki *et al*[41], evaluated 159 patients undergoing TSA (average age 69) and 106 patients undergoing rTSA (average age 75). Authors used the American Shoulder and Elbow Surgeons (ASES) Assessment Form as a way to track patients' ability to RTW. Among usually reported work, it is important to note that 43% of patients cited retirement as their work, with housework (27%) and desk jobs (18%) as the second and third most cited, respectively. Kurowicki *et al*[41] reported a 21% higher difference in overall ability to work for patients following TSA compared to those patients who underwent rTSA. In particular, statistically significant differences were found between TSA and rTSA amongst patients who cited their work as housework or gardening.

Kurowicki *et al*[41] is the only study that compares the ability of TSA patients to RTW to rTSA patients. Based on this study, authors concluded that returning to work after TSA is more favorable than rTSA in fields of work that require low-demand activities such as housework and gardening[41]. This

study was limited by its reporting bias from survey-based studies, small sample size within work subgroups, and population representation differences particularly in age. Regardless, comparisons among these groups hold importance in defining patient and surgeon expectations after surgery.

Comparison of RTW between TSA and HA

If non-operative treatment for glenohumeral osteoarthritis with intact rotator cuff integrity fails, patients are often told to consider HA or TSA. While the optimal surgical treatment remains controversial, there are benefits to both procedures. Multiple studies have shown that patients with glenohumeral arthritis who undergo TSA have improved pain relief, higher functional scores, and more range of motion compared to those who undergo HA[35,36,42-44]. However, TSA also has an increased operative time, more blood loss, more technical difficulty, and incurs the risk of glenoid loosening[45]. On the other hand, while HA has the benefits of decreased operative time, decreased blood loss, and less technical difficulty, there is some concern regarding the progression of arthritic changes especially with bone loss and the need for future revision surgeries such as conversion to TSA[45,46]. Furthermore, many patients have lifting restrictions after TSA, which may limit their ability to RTW[47].

Gowd *et al*[48] analyzed 53 total patients with glenohumeral arthritis. Twenty five patients (average age of 52.8 years) received HA with ream-and-run resurfacing and 28 patients (average age of 53.3 years) received TSA. Of the 25 patients undergoing HA, all 25 (100%) were able to RTW at an average duration of 1.98 mo. On the other hand, 25 (89%) of 28 patients receiving TSA were able to RTW with an average time of 2.5 mo following surgery. When HA patients were stratified preoperatively into work demand level, 7 patients were categorized as sedentary, 7 were light, 4 were moderate, and 7 were heavy. For TSA, 10 patients were categorized as sedentary, 5 were light, 9 were moderate, and 4 were heavy. Postoperatively, all HA patients (100%) in sedentary, light, and moderate were able to RTW. For TSA, 9 (90%) of 10 returned to sedentary work, while all (100%) light and moderate duty patients returned to work. For the heavy category, 7 (100%) of 7 HA patients were able to return compared to 2 (50%) of 4 TSA patients demonstrating that heavy duty workers undergoing HA had a significantly higher rate of RTW[48]. Of the 2 TSA heavy duty patients who were unable to RTW, only one reported permanent restriction with overhead lifting. Despite this difference, authors concluded near equivalent rates of RTW between HA and TSA.

Liu *et al*[49] evaluated 49 total patients with end-stage glenohumeral osteoarthritis. Twenty-six patients underwent HA (average age of 62.4 years) and 23 patients underwent TSA (average age 61.7). Sixteen (62%) of 26 HA patients were able to RTW at an average duration of 1.88 mo following surgery. Of the patients undergoing TSA, 20 (87%) were able to RTW at an average time of 1.29 mo following surgery. From the 10 HA patients who did not RTW, only one had retired postoperatively due to shoulder issues. The other nine patients retired preoperatively due to the shoulder, other medical reasons, or postoperatively due to non-specified reasons. Of the three TSA patients who did not RTW, zero had retired postoperatively due to the shoulder. Patients either retired preoperatively due to the shoulder, other medical concerns, or non-specified reasons. For patients who underwent TSA, 7 (100%) of 7 returned to a sedentary work demand level, 9 (82%) of 11 returned to a light work demand level, and 3 (100%) of 3 returned to a heavy work demand level (Table 4). For patients who underwent HA, 8 (62%) of 13 returned to a sedentary work demand level, 7 (70%) of 10 returned to a light work demand level, and 1 (33%) of 3 returned to a heavy work demand level (Table 4). (68%) of 25 returned to a sedentary work level and 9 (60%) of 15 returned to a light work demand level (Table 4). Liu *et al*[49] concluded that patients with osteoarthritis undergoing TSA have higher rates of RTW and function compared to those undergoing HA.

From these two studies, there is still a discrepancy in terms of ability to RTW between HA and TSA. The mixed results could potentially be due to the limitations of each study. For example, in Gowd *et al*[48], surgeons counseled their TSA patients that they would have permanent overhead lifting restrictions, whereas those who underwent HA would not receive these restrictions. Comparatively, in Liu *et al*[49], surgeons placed no postoperative work restrictions on either group. Furthermore, the average age of individuals in Gowd *et al*[48] (52.8 and 53.3 years of age) was significantly lower than the average of individuals in Liu *et al*[49] (62.4 and 61.7 years of age) possibly indicating that older patients either hold more sedentary, less demanding occupations or may benefit more in their ability to RTW following TSA compared to HA[48,49].

Comparison of RTW between HA and rTSA

When TSA is contraindicated, in cases such as rotator cuff or deltoid dysfunction, deficiencies in glenoid bone stock, or proximal humerus fractures, patients must be educated on the benefits and drawbacks of HA *vs* rTSA[50]. Many studies over the last decade have shown more predictable and superior outcomes for rTSA compared to HA[51-53]. Yet, in the younger population, especially those who want to remain employed following surgery, surgeons often feel more comfortable recommending HA given the theoretical risk of glenoid component loosening or failure in rTSA[54]. Furthermore, surgeons tend to place more activity restrictions on patients who undergo rTSA, which could significantly limit their ability to RTW.

Table 4 Return to work after total shoulder arthroplasty *vs* hemiarthroplasty[49]

Occupation intensity	RTW after TSA (%)	RTW after HA (%)
Sedentary	7/7 (100)	8/13 (62)
Light	9/11 (82)	7/10 (70)
Heavy	3/3 (100)	1/3 (33)
Total	20/23 (87)	16/26 (62)

RTW: Return to work; TSA: Total shoulder arthroplasty; HA: Hemiarthroplasty.

Hurwit *et al*[11] compared 40 rTSA patients (average age of 68.6 years) to 41 HA patients (average age of 60.8 years) all of whom had end-stage glenohumeral arthritis with rotator cuff dysfunction, deficiencies in glenoid bone stock that prohibited the insertion of an anatomic glenoid component, or proximal humerus fracture. Of the patients who underwent rTSA, 26 (65%) of them were able to RTW at an average duration of 2.3 mo following surgery. Only two patients who were unable to RTW cited their main reason as issues with the shoulder following surgery, while the other twelve either retired preoperatively due to medical reasons or non-specified reasons. Twenty-nine (71%) of the 41 HA patients were able to RTW at an average time of 3.1 mo after surgery. In this cohort, only one patient retired postoperatively due to shoulder issues. The other eleven had retired preoperatively due to the shoulder, medical reasons, or non-specified reasons. For patients who underwent HA, 14 (74%) of 19 were able to return to a sedentary work demand level, 13 (72%) of 18 returned to a light demand level, and 2 (50%) of 4 returned to work at a heavy work level (Table 5). For patients who underwent rTSA, 17 (68%) of 25 returned to a sedentary work level and 9 (60%) of 15 returned to a light work demand level (Table 5). Hurwit *et al*[11] concluded no significant difference between the two groups in terms of return to low- and moderate-intensity work, despite an older age for patients undergoing rTSA.

Despite a higher rate of RTW for HA patients, no significant differences were found by Hurwit *et al*[11]. A potential limitation with this study was the significant difference in average age of each cohort (68.6 years for rTSA patients and 60.8 years for HA patients), even though this did not affect RTW rates[11]. Furthermore, this study only had sufficient sample sizes for sedentary and light duty workers. Due to the lack of heavy duty workers, especially in rTSA, it is possible to hypothesize that heavy laborers may have experienced more difficulty in returning to work.

Comparison of RTW between WC and non-WC

Work-related injuries are a common cause of disability in the United States and have significant implications for workers, employers, insurers, and physicians[18,55,56]. WC status has shown to have a detrimental effect on clinical outcomes following orthopedic surgery[57,58]. The impact of WC status on postoperative outcomes is an important consideration for patients undergoing shoulder arthroplasty.

Morris *et al*[55] compared 14 WC patients who underwent rTSA to a matched cohort of 14 patients without WC status who also underwent rTSA. From the patients with WC claims, only 2 (14%) of 14 were able to RTW. Of the 12 patients who were not able to RTW, one was unemployed and seeking employment at the time of follow-up, five were disabled, and six had retired following rTSA. In the matched cohort of non-WC patients, only 11 patients had worked prior to the surgery. From these 11 patients, 5 (46%) were able to RTW, one was disabled, and five had retired after rTSA. No patients, WC or non-WC, were able to return to heavy/strenuous work demands after rTSA. Despite significant improvement from preoperative to final follow-up outcomes, WC patients had significantly worse Constant scores, ASES scores, Western Ontario Osteoarthritis of the Shoulder Index scores, and less external rotation compared with the matched cohort group. Morris *et al*[55] reported that while WC patients had significant improvements following rTSA, they achieved significantly worse outcomes compared to non-WC patients after rTSA.

In Jawa *et al*[56], a cohort of 13 WC patients (average age of 55.9 years) who underwent TSA were compared to a control group of 63 patients (average age of 63.2 years) who also underwent TSA. While RTW rates were not cited for the control group, only 4 (31%) of the 13 WC patients were able to RTW following TSA. Of the four patients who returned, one returned to the same job with lifting restrictions and the other three changed jobs to those that require less lifting. From the nine patients who did not return, 7 did not return due to functional restrictions after the surgery and 2 had retired. Additionally, Jawa *et al*[56] found the ASES score to be significantly lower in the WC cohort compared to the control group. From this study, authors concluded no WC patients were able to return to full duty work at their current job and that WC patients receiving TSA had poorer outcomes compared to non-WC patients.

Despite the lack of difference in RTW rates following shoulder arthroplasty for patients with or without WC claims, many studies in orthopedic literature have found poorer outcomes, lower satisfaction rates, and more pain in patients with WC status after shoulder arthroplasty[55,56,59,60]. Similar findings exist in the shoulder literature outside of shoulder arthroplasty. For example, in

Table 5 Return to work after hemiarthroplasty vs reverse total shoulder arthroplasty[11]

Occupation intensity	RTW after HA (%)	RTW after rTSA (%)
Sedentary	14/19 (74)	17/25 (68)
Light	13/18 (72)	9/15 (60)
Heavy[1]	2/4 (50)	-
Total	29/41 (71)	26/40 (65)

[1]No reverse total shoulder arthroplasty patients were classified into the heavy work category.
RTW: Return to work; rTSA: Reverse total shoulder arthroplasty; HA: Hemiarthroplasty.

numerous rotator cuff studies, patients with WC status have been found to be significantly less compliant with postoperative protocols and have less improvement in functional outcomes and pain after controlling for confounding factors such as age, marital status, education level, preoperative expectations, work demands, smoking, comorbidities, duration of symptoms, size of tear, and repair technique[61-64]. Furthermore, other similar results have been found in WC cohorts undergoing acromioplasty, superior labral anterior-posterior tear, and biceps tenodesis for failed superior labral anterior-posterior repair[65-68]. Regardless of procedure type, the differences in pain and outcomes persist, suggesting that WC status may play a crucial role in inferior outcomes.

DISCUSSION

RTW guidelines

While the decision to RTW depends on a variety of factors, all physicians have the goal of returning patients to maximal function in the shortest period of time with the least residual disability[69,70]. Based on the available literature, guidelines can be proposed for average time to RTW for each work demand level within each type of shoulder arthroplasty (Table 6). We determined these averages through a pooled analysis[71].

Throughout the rehabilitation process, physicians must assess patients, especially those with WC status, in terms of work restrictions and limitations. Given the little published evidence for guidelines regarding physical restrictions after shoulder arthroplasty, the work restrictions are commonly based on the physician's clinical judgment[69]. On the other hand, work limitations are easier to define as they are based on the patient's ability to perform a certain task[69].

Particularly for WC patients who undergo shoulder replacement and rehabilitation and have still failed to RTW at their desired work demand level, work conditioning or work hardening therapy regimens can be prescribed[69,72]. Work conditioning, a task simulation program lasting two to four hours per day for three to five days per week, is meant to develop a patient's ability to tolerate specific tasks they would typically encounter at work. Work hardening has the same goal in mind with a higher intensity lasting up to eight hours per day for five days per week[69].

When recovery from shoulder arthroplasty has reached a therapeutic plateau for either non-WC or WC patients, a physician must rate the residual permanent impairment and individually assess how long each injured patient should remain on this plateau before considering them at maximum medical improvement (MMI)[69]. MMI is established when no further treatment will significantly change the patient's outcome; at this point, a patient can be recovered completely without any residual impairment or have some permanent impairment[69,73]. Specifically for TSA, Cabarcas *et al*[74] established MMI at twelve months postoperatively. While Puzzitiello *et al*[75] established MMI for rTSA at twelve months following surgery, Matar *et al*[76] found patients undergoing rTSA may reach MMI as early as six months after surgery. If a patient has reached MMI, but has failed to achieve their pre-injury or prior level of work status, then a physician can utilize a functional capacity evaluation to determine the patient's ability and impose final work restrictions[69]. Although the results of the FCE are often used to set work limitations, some studies have questioned its utility as FCE does not take biopsychosocial factors into account and possibly measures a patient's tolerance to an activity as opposed to the patient's true ability[69,77,78].

After MMI has been reached, there are two outcomes: (1) The patient is able to RTW with or without permanent restrictions at the same job; or (2) The patient finds a new job because the employer cannot accommodate the patient's work limitations[69]. Using evidence-based guidelines to determine MMI for TSA, rTSA, and HA is important not only for counseling patients, but also modifying their expectations prior to surgery.

Table 6 Time to return to work (mo)

	Intensity[1]				
	Sedentary	Light	Moderate	Heavy	Overall
TSA					
Gowd *et al*[48], 2019	2.1 ± 3.8	1.3 ± 1.2	2.1 ± 2.0	3.0 ± 2.8	2.0 ± 2.6
Liu *et al*[12], 2018	1.3 ± 1.2	1.6 ± 1.3	2 ± 1.7	4.2 ± 2.0	2.1 ± 1.7
Liu *et al*[49], 2020	1.04 ± 0.87	1.06 ± 0.73	-	1.83 ± 1.04	1.29 ± 0.96
Cvetanovich *et al*[21], 2020	-	-	-	-	3.7 ± 5.2
Average[2]	1.19 ± 1.24	1.25 ± 0.99	2.03 ± 1.79	2.96 ± 3.23	1.93 ± 3.74
rTSA					
Garcia et al[28], 2016/ Hurwit *et al*[11], 2017[3]	1.38 ± 0.93	4 ± 3.4	-	-	2.3 ± 2.4
HA					
Hurwit *et al*[11], 2017/Garcia *et al*[24], 2015[4]	1.96 ± 3.0	2.72 ± 2.6	-	13.13 ± 15.4	3.1 ± 4.9
Gowd *et al*[48], 2019	0.9 ± 1.1	1.0 ± 1.7	6.8 ± 11.5	3.1 ± 2.3	2.5 ± 4.8
Liu *et al*[49], 2020	1.06 ± 0.98	2.76 ± 3.27	-	2.25[5]	1.88 ± 2.34
Average[2]	1.09 ± 1.36	2.00 ± 3.36	6.8 ± 11.5	3.16 ± 2.74	2.29 ± 3.66

[1]Intensity as based on US Department of Labor[56].
[2]Pooled means using meta analysis[57].
[3]Both studies used the same reverse total shoulder arthroplasty population.
[4]Both studies used the same hemiarthroplasty population.
[5]Only one patient in the heavy group, so no standard deviation available.
TSA: Total shoulder arthroplasty; rTSA: Reverse total shoulder arthroplasty; HA: Hemiarthroplasty.

Limitations and future research directions

Our narrative systematic review and analysis has several limitations. First, identification and inclusion of references utilized for this review relied on the previously described search strategy in 4 different databases. We searched 4 different databases in order to limit the possibility of overlooking studies related to shoulder arthroplasty and RTW. Second, our data relied on the data reported in the included studies. Therefore, we are limited by the clarity of the results reported as well as the study design and level of evidence. As a result, we utilized the MINORS score to evaluate the quality of the 12 included studies and any potential publication bias. We found that the 12 studies were of acceptable quality and determined no findings suggestive of publication bias. Additionally, our data shows a high level of heterogeneity which may lead to treatment bias effect. Similarly, with regard to work intensity, our study is limited by what was reported and those studies may exclude important nuances that could have led to functional consequences. Furthermore, the heterogeneity of our data is reflective of the reality of clinical practice and often most accurately represents what orthopedic surgeons encounter in the clinical setting[79-81]. Despite these limitations, the findings in our study provide important data that help orthopedic surgeons manage patient expectations about RTW following TSA, rTSA, or HA.

In the future, systematic reviews and analyses regarding shoulder arthroplasty and RTW will hopefully have access to references that are more homogenous with higher levels of evidence. Although the reality that a high level of heterogeneity may be inevitable in the clinical research setting, additional research should be conducted that compares short- and long-term outcomes following TSA, rTSA, and HA and a patients' ability to RTW. Furthermore, revision arthroplasty and ability to RTW may be a topic worth exploring as the average age of patients undergoing shoulder replacement is decreasing.

CONCLUSION

The majority of patients are able to RTW following TSA, rTSA, and shoulder HA. The rates of RTW following TSA (71%-93%) seem to be consistently higher than those reported for HA (69%-82%) and rTSA (56%-65%), although this may reflect demographic differences such as age in patient populations. Sedentary, light demand jobs generally have higher rates of RTW than moderate or heavy demand jobs. On average, most patients who underwent TSA, rTSA, or HA were able to RTW at an average duration between 1 mo to 4 mo depending on work demand level. Furthermore, WC status negatively influenced clinical outcomes following shoulder arthroplasty.

ARTICLE HIGHLIGHTS

Research background

Over the last two decades, the number of shoulder arthroplasties, including total shoulder arthroplasty (TSA), reverse TSA (rTSA), and shoulder hemiarthroplasty (HA), has increased at exponential rates. Due to satisfactory clinical and functional long-term outcomes, the number of shoulder replacements performed will continue to rise into this next decade. Additionally, these procedures are becoming more prevalent in younger and more active populations. With younger individuals who compose a significant amount of the workforce receiving shoulder replacements, patients will begin to place a higher priority on their ability to return to work following shoulder arthroplasty.

Research motivation

Prior studies have shown varying levels of return to work after shoulder arthroplasty based on arthroplasty type, diagnosis, and work intensity. While informative, a compilation comparing various demographics, arthroplasty types, diagnoses, and work intensities has not been performed in recent years.

Research objectives

The aim of the review article was to summarize return to work outcomes following TSA, rTSA, and HA, and analyze the effects of workers' compensation status on return to work rates and ability.

Research methods

This systematic review and analysis was performed in accordance with Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines. A literature search regarding return to work following shoulder arthroplasty was performed using four databases through January 2021. All studies included in this review were analyzed by at least two authors. Included studies were then evaluated using the Methodological Index for Non-Randomized Studies checklist.

Research results

The majority of patients undergoing TSA, rTSA, or HA were able to return to work between one to four months, depending on work demand stratification. While sedentary or light demand jobs generally have higher rates of return to work, moderate or heavy demand jobs tend to have poorer rates of return. Furthermore, workers' compensation status negatively influenced clinical outcomes following shoulder arthroplasty. Through a pooled means analysis, we proposed guidelines for the average time to return to work following TSA, rTSA, and HA.

Research conclusions

The majority of patients were able to return to work following TSA, rTSA, or HA. Understanding outcomes for rates of return to work following shoulder arthroplasty should assist surgeons and patients in managing expectations in clinical practice.

Research perspectives

Further research and analyses comparing short- and long-term outcomes following TSA, rTSA, and HA and a patients' ability to return to work would provide tremendous benefit. Additionally, revision arthroplasty and ability to return to work may be a topic worth exploring as the average age of patients undergoing shoulder replacement is decreasing.

FOOTNOTES

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REFERENCES

1 **Kim SH**, Wise BL, Zhang Y, Szabo RM. Increasing incidence of shoulder arthroplasty in the United States. *J Bone Joint Surg Am* 2011; **93**: 2249-2254 [PMID: 22258770 DOI: 10.2106/JBJS.J.01994]
2 **Wagner ER**, Farley KX, Higgins I, Wilson JM, Daly CA, Gottschalk MB. The incidence of shoulder arthroplasty: rise and future projections compared with hip and knee arthroplasty. *J Shoulder Elbow Surg* 2020; **29**: 2601-2609 [PMID: 33190759 DOI: 10.1016/j.jse.2020.03.049]
3 **Jain NB**, Yamaguchi K. The contribution of reverse shoulder arthroplasty to utilization of primary shoulder arthroplasty. *J Shoulder Elbow Surg* 2014; **23**: 1905-1912 [PMID: 25304043 DOI: 10.1016/j.jse.2014.06.055]
4 **Schairer WW**, Nwachukwu BU, Lyman S, Craig EV, Gulotta LV. National utilization of reverse total shoulder arthroplasty in the United States. *J Shoulder Elbow Surg* 2015; **24**: 91-97 [PMID: 25440519 DOI: 10.1016/j.jse.2014.08.026]
5 **Fehringer EV**, Kopjar B, Boorman RS, Churchill RS, Smith KL, Matsen FA 3rd. Characterizing the functional improvement after total shoulder arthroplasty for osteoarthritis. *J Bone Joint Surg Am* 2002; **84**: 1349-1353 [PMID: 12177264 DOI: 10.2106/00004623-200208000-00009]
6 **Haines JF**, Trail IA, Nuttall D, Birch A, Barrow A. The results of arthroplasty in osteoarthritis of the shoulder. *J Bone Joint Surg Br* 2006; **88**: 496-501 [PMID: 16567785 DOI: 10.1302/0301-620X.88B4.16604]
7 **Deshmukh AV**, Koris M, Zurakowski D, Thornhill TS. Total shoulder arthroplasty: long-term survivorship, functional outcome, and quality of life. *J Shoulder Elbow Surg* 2005; **14**: 471-479 [PMID: 16194737 DOI: 10.1016/j.jse.2005.02.009]
8 **Padegimas EM**, Maltenfort M, Lazarus MD, Ramsey ML, Williams GR, Namdari S. Future patient demand for shoulder arthroplasty by younger patients: national projections. *Clin Orthop Relat Res* 2015; **473**: 1860-1867 [PMID: 25758376 DOI: 10.1007/s11999-015-4231-z]
9 **Fry R**. Millennials are the largest generation in the U.S. labor force. Pew Research Center: Fact Tank. [cited 31 January 2021]. In: Pew Research Center [Internet]. Available from: https://www.pewresearch.org/fact-tank/2018/04/11/millennials-largest-generation-us-labor-force/
10 **Bülhoff M**, Sattler P, Bruckner T, Loew M, Zeifang F, Raiss P. Do patients return to sports and work after total shoulder replacement surgery? *Am J Sports Med* 2015; **43**: 423-427 [PMID: 25406301 DOI: 10.1177/0363546514557940]
11 **Hurwit DJ**, Liu JN, Garcia GH, Mahony G, Wu HH, Dines DM, Warren RF, Gulotta LV. A comparative analysis of work-related outcomes after humeral hemiarthroplasty and reverse total shoulder arthroplasty. *J Shoulder Elbow Surg* 2017; **26**: 954-959 [PMID: 28089256 DOI: 10.1016/j.jse.2016.10.004]
12 **Liu JN**, Garcia GH, Wong AC, Sinatro A, Wu HH, Dines DM, Warren RF, Gulotta LV. Return to Work After Anatomic Total Shoulder Arthroplasty for Patients 55 Years and Younger at Average 5-Year Follow-up. *Orthopedics* 2018; **41**: e310-e315 [PMID: 29451941 DOI: 10.3928/01477447-20180213-08]
13 **McInnes MDF**, Moher D, Thombs BD, McGrath TA, Bossuyt PM; and the PRISMA-DTA Group, Clifford T, Cohen JF, Deeks JJ, Gatsonis C, Hooft L, Hunt HA, Hyde CJ, Korevaar DA, Leeflang MMG, Macaskill P, Reitsma JB, Rodin R, Rutjes AWS, Salameh JP, Stevens A, Takwoingi Y, Tonelli M, Weeks L, Whiting P, Willis BH. Preferred Reporting Items for a Systematic Review and Meta-analysis of Diagnostic Test Accuracy Studies: The PRISMA-DTA Statement. *JAMA* 2018; **319**: 388-396 [PMID: 29362800 DOI: 10.1001/jama.2017.19163]
14 **Salameh JP**, Bossuyt PM, McGrath TA, Thombs BD, Hyde CJ, Macaskill P, Deeks JJ, Leeflang M, Korevaar DA, Whiting P, Takwoingi Y, Reitsma JB, Cohen JF, Frank RA, Hunt HA, Hooft L, Rutjes AWS, Willis BH, Gatsonis C, Levis B, Moher D, McInnes MDF. Preferred reporting items for systematic review and meta-analysis of diagnostic test accuracy studies (PRISMA-DTA): explanation, elaboration, and checklist. *BMJ* 2020; **370**: m2632 [PMID: 32816740 DOI: 10.1136/bmj.m2632]
15 **Slim K**, Nini E, Forestier D, Kwiatkowski F, Panis Y, Chipponi J. Methodological index for non-randomized studies (minors): development and validation of a new instrument. *ANZ J Surg* 2003; **73**: 712-716 [PMID: 12956787 DOI: 10.1046/j.1445-2197.2003.02748.x]
16 **Roberson TA**, Bentley JC, Griscom JT, Kissenberth MJ, Tolan SJ, Hawkins RJ, Tokish JM. Outcomes of total shoulder arthroplasty in patients younger than 65 years: a systematic review. *J Shoulder Elbow Surg* 2017; **26**: 1298-1306 [PMID: 28209327 DOI: 10.1016/j.jse.2016.12.069]
17 **Steinhaus ME**, Gowd AK, Hurwit DJ, Lieber AC, Liu JN. Return to work after shoulder arthroplasty: a systematic review and meta-analysis. *J Shoulder Elbow Surg* 2019; **28**: 998-1008 [PMID: 30885548 DOI: 10.1016/j.jse.2018.12.011]
18 **Riffkin R**. Americans Settling on Older Retirement Age. Gallup. [cited 31 January 2021]. In: News Gallup [Internet]. Available from: https://news.gallup.com/poll/182939/americans-settling-older-retirement-age.aspx
19 **Mattei L**, Mortera S, Arrigoni C, Castoldi F. Anatomic shoulder arthroplasty: an update on indications, technique, results

and complication rates. *Joints* 2015; **3**: 72-77 [PMID: 26605254 DOI: 10.11138/jts/2015.3.2.072]
20 **Walch G**, Boileau P, Noël E. Shoulder arthroplasty: evolving techniques and indications. *Joint Bone Spine* 2010; **77**: 501-505 [PMID: 20961793 DOI: 10.1016/j.jbspin.2010.09.004]
21 **Cvetanovich GL**, Naylor AJ, O'Brien MC, Waterman BR, Garcia GH, Nicholson GP. Anatomic total shoulder arthroplasty with an inlay glenoid component: clinical outcomes and return to activity. *J Shoulder Elbow Surg* 2020; **29**: 1188-1196 [PMID: 31899092 DOI: 10.1016/j.jse.2019.10.003]
22 **Jayasekara M**, Lam PH, Murrell GAC. Return to Work Following Shoulder Surgery: An Analysis of 1,773 Cases. *JB JS Open Access* 2020; **5** [PMID: 32803105 DOI: 10.2106/JBJS.OA.19.00081]
23 **Westermann RW**, Pugely AJ, Martin CT, Gao Y, Wolf BR, Hettrich CM. Reverse Shoulder Arthroplasty in the United States: A Comparison of National Volume, Patient Demographics, Complications, and Surgical Indications. *Iowa Orthop J* 2015; **35**: 1-7 [PMID: 26361437]
24 **Garcia GH**, Taylor SA, DePalma BJ, Mahony GT, Grawe BM, Nguyen J, Dines JS, Dines DM, Warren RF, Craig EV, Gulotta LV. Patient Activity Levels After Reverse Total Shoulder Arthroplasty: What Are Patients Doing? *Am J Sports Med* 2015; **43**: 2816-2821 [PMID: 26316610 DOI: 10.1177/0363546515597673]
25 **Nam D**, Kepler CK, Neviaser AS, Jones KJ, Wright TM, Craig EV, Warren RF. Reverse total shoulder arthroplasty: current concepts, results, and component wear analysis. *J Bone Joint Surg Am* 2010; **92** Suppl 2: 23-35 [PMID: 21189245 DOI: 10.2106/JBJS.J.00769]
26 **Hyun YS**, Huri G, Garbis NG, McFarland EG. Uncommon indications for reverse total shoulder arthroplasty. *Clin Orthop Surg* 2013; **5**: 243-255 [PMID: 24340143 DOI: 10.4055/cios.2013.5.4.243]
27 **Drake GN**, O'Connor DP, Edwards TB. Indications for reverse total shoulder arthroplasty in rotator cuff disease. *Clin Orthop Relat Res* 2010; **468**: 1526-1533 [PMID: 20049573 DOI: 10.1007/s11999-009-1188-9]
28 **Garcia GH**, Taylor SA, Mahony GT, DePalma BJ, Grawe BM, Nguyen J, Dines JS, Dines DM, Warren RF, Craig EV, Gulotta LV. Reverse Total Shoulder Arthroplasty and Work-Related Outcomes. *Orthopedics* 2016; **39**: e230-e235 [PMID: 26811957 DOI: 10.3928/01477447-20160119-03]
29 **Simovitch RW**, Gerard BK, Brees JA, Fullick R, Kearse JC. Outcomes of reverse total shoulder arthroplasty in a senior athletic population. *J Shoulder Elbow Surg* 2015; **24**: 1481-1485 [PMID: 25958214 DOI: 10.1016/j.jse.2015.03.011]
30 **Palsis JA**, Simpson KN, Matthews JH, Traven S, Eichinger JK, Friedman RJ. Current Trends in the Use of Shoulder Arthroplasty in the United States. *Orthopedics* 2018; **41**: e416-e423 [PMID: 29658976 DOI: 10.3928/01477447-20180409-05]
31 **Gadea F**, Alami G, Pape G, Boileau P, Favard L. Shoulder hemiarthroplasty: outcomes and long-term survival analysis according to etiology. *Orthop Traumatol Surg Res* 2012; **98**: 659-665 [PMID: 22944393 DOI: 10.1016/j.otsr.2012.03.020]
32 **Schultz BJ**, Lowe DT, Egol KA, Zuckerman JD. Shoulder Hemiarthroplasty for Proximal Humerus Fracture. *J Orthop Trauma* 2021; **35**: S3-S4 [PMID: 34227587 DOI: 10.1097/BOT.0000000000002158]
33 **Garcia GH**, Liu JN, Mahony GT, Sinatro A, Wu HH, Craig EV, Warren RF, Dines DM, Gulotta LV. Hemiarthroplasty Versus Total Shoulder Arthroplasty for Shoulder Osteoarthritis: A Matched Comparison of Return to Sports. *Am J Sports Med* 2016; **44**: 1417-1422 [PMID: 26960913 DOI: 10.1177/0363546516632527]
34 **Sowa B**, Thierjung H, Bülhoff M, Loew M, Zeifang F, Bruckner T, Raiss P. Functional results of hemi- and total shoulder arthroplasty according to diagnosis and patient age at surgery. *Acta Orthop* 2017; **88**: 310-314 [PMID: 28121220 DOI: 10.1080/17453674.2017.1280656]
35 **Singh JA**, Sperling J, Buchbinder R, McMaken K. Surgery for shoulder osteoarthritis: a Cochrane systematic review. *J Rheumatol* 2011; **38**: 598-605 [PMID: 21239751 DOI: 10.3899/jrheum.101008]
36 **Garcia GH**, Mahony GT, Fabricant PD, Wu HH, Dines DM, Warren RF, Craig EV, Gulotta LV. Sports- and Work-Related Outcomes After Shoulder Hemiarthroplasty. *Am J Sports Med* 2016; **44**: 490-496 [PMID: 26657261 DOI: 10.1177/0363546515613077]
37 **Levine WN**, Fischer CR, Nguyen D, Flatow EL, Ahmad CS, Bigliani LU. Long-term follow-up of shoulder hemiarthroplasty for glenohumeral osteoarthritis. *J Bone Joint Surg Am* 2012; **94**: e164 [PMID: 23172331 DOI: 10.2106/JBJS.K.00603]
38 **Botros M**, Curry EJ, Yin J, Jawa A, Eichinger JK, Li X. Reverse shoulder arthroplasty has higher perioperative implant complications and transfusion rates than total shoulder arthroplasty. *JSES Open Access* 2019; **3**: 108-112 [PMID: 31334437 DOI: 10.1016/j.jses.2019.03.001]
39 **Wierks C**, Skolasky RL, Ji JH, McFarland EG. Reverse total shoulder replacement: intraoperative and early postoperative complications. *Clin Orthop Relat Res* 2009; **467**: 225-234 [PMID: 18685908 DOI: 10.1007/s11999-008-0406-1]
40 **Flurin PH**, Roche CP, Wright TW, Marczuk Y, Zuckerman JD. A Comparison and Correlation of Clinical Outcome Metrics in Anatomic and Reverse Total Shoulder Arthroplasty. *Bull Hosp Jt Dis (2013)* 2015; **73** Suppl 1: S118-S123 [PMID: 26631207]
41 **Kurowicki J**, Rosas S, Law TY, Levy JC. Participation in Work and Sport Following Reverse and Total Shoulder Arthroplasty. *Am J Orthop (Belle Mead NJ)* 2018; **47** [PMID: 29883508 DOI: 10.12788/ajo.2018.0034]
42 **Bryant D**, Litchfield R, Sandow M, Gartsman GM, Guyatt G, Kirkley A. A comparison of pain, strength, range of motion, and functional outcomes after hemiarthroplasty and total shoulder arthroplasty in patients with osteoarthritis of the shoulder. A systematic review and meta-analysis. *J Bone Joint Surg Am* 2005; **87**: 1947-1956 [PMID: 16140808 DOI: 10.2106/JBJS.D.02854]
43 **Edwards TB**, Kadakia NR, Boulahia A, Kempf JF, Boileau P, Némoz C, Walch G. A comparison of hemiarthroplasty and total shoulder arthroplasty in the treatment of primary glenohumeral osteoarthritis: results of a multicenter study. *J Shoulder Elbow Surg* 2003; **12**: 207-213 [PMID: 12851570 DOI: 10.1016/s1058-2746(02)86804-5]
44 **Radnay CS**, Setter KJ, Chambers L, Levine WN, Bigliani LU, Ahmad CS. Total shoulder replacement compared with humeral head replacement for the treatment of primary glenohumeral osteoarthritis: a systematic review. *J Shoulder Elbow Surg* 2007; **16**: 396-402 [PMID: 17582789 DOI: 10.1016/j.jse.2006.10.017]
45 **van den Bekerom MP**, Geervliet PC, Somford MP, van den Borne MP, Boer R. Total shoulder arthroplasty *vs* hemiarthroplasty for glenohumeral arthritis: A systematic review of the literature at long-term follow-up. *Int J Shoulder*

Surg 2013; **7**: 110-115 [PMID: 24167403 DOI: 10.4103/0973-6042.118915]
46 **Carroll RM**, Izquierdo R, Vazquez M, Blaine TA, Levine WN, Bigliani LU. Conversion of painful hemiarthroplasty to total shoulder arthroplasty: long-term results. *J Shoulder Elbow Surg* 2004; **13**: 599-603 [PMID: 15570227 DOI: 10.1016/j.jse.2004.03.016]
47 **Golant A**, Christoforou D, Zuckerman JD, Kwon YW. Return to sports after shoulder arthroplasty: a survey of surgeons' preferences. *J Shoulder Elbow Surg* 2012; **21**: 554-560 [PMID: 21393018 DOI: 10.1016/j.jse.2010.11.021]
48 **Gowd AK**, Garcia GH, Liu JN, Malaret MR, Cabarcas BC, Romeo AA. Comparative analysis of work-related outcomes in hemiarthroplasty with concentric glenoid reaming and total shoulder arthroplasty. *J Shoulder Elbow Surg* 2019; **28**: 244-251 [PMID: 30269934 DOI: 10.1016/j.jse.2018.07.026]
49 **Liu JN**, Garcia GH, Gowd AK, Mahony G, Sinatro A, Wu HH, Dines DM, Warren RF, Gulotta LV. Return to Work After Shoulder Replacement for Glenohumeral Osteoarthritis Is Similar When Hemiarthroplasty Is Compared to Total Shoulder Arthroplasty. *HSS J* 2020; **16**: 212-217 [PMID: 33088235 DOI: 10.1007/s11420-019-09692-0]
50 **Lin DJ**, Wong TT, Kazam JK. Shoulder Arthroplasty, from Indications to Complications: What the Radiologist Needs to Know. *Radiographics* 2016; **36**: 192-208 [PMID: 26761537 DOI: 10.1148/rg.2016150055]
51 **Alentorn-Geli E**, Guirro P, Santana F, Torrens C. Treatment of fracture sequelae of the proximal humerus: comparison of hemiarthroplasty and reverse total shoulder arthroplasty. *Arch Orthop Trauma Surg* 2014; **134**: 1545-1550 [PMID: 25138037 DOI: 10.1007/s00402-014-2074-9]
52 **Boyle MJ**, Youn SM, Frampton CM, Ball CM. Functional outcomes of reverse shoulder arthroplasty compared with hemiarthroplasty for acute proximal humeral fractures. *J Shoulder Elbow Surg* 2013; **22**: 32-37 [PMID: 22652065 DOI: 10.1016/j.jse.2012.03.006]
53 **Leung B**, Horodyski M, Struk AM, Wright TW. Functional outcome of hemiarthroplasty compared with reverse total shoulder arthroplasty in the treatment of rotator cuff tear arthropathy. *J Shoulder Elbow Surg* 2012; **21**: 319-323 [PMID: 21872496 DOI: 10.1016/j.jse.2011.05.023]
54 **Magnussen RA**, Mallon WJ, Willems WJ, Moorman CT 3rd. Long-term activity restrictions after shoulder arthroplasty: an international survey of experienced shoulder surgeons. *J Shoulder Elbow Surg* 2011; **20**: 281-289 [PMID: 21051242 DOI: 10.1016/j.jse.2010.07.021]
55 **Morris BJ**, Haigler RE, Laughlin MS, Elkousy HA, Gartsman GM, Edwards TB. Workers' compensation claims and outcomes after reverse shoulder arthroplasty. *J Shoulder Elbow Surg* 2015; **24**: 453-459 [PMID: 25306491 DOI: 10.1016/j.jse.2014.07.009]
56 **Jawa A**, Dasti UR, Fasulo SM, Vaickus MH, Curtis AS, Miller SL. Anatomic total shoulder arthroplasty for patients receiving workers' compensation. *J Shoulder Elbow Surg* 2015; **24**: 1694-1697 [PMID: 26159842 DOI: 10.1016/j.jse.2015.04.017]
57 **Gruson KI**, Huang K, Wanich T, Depalma AA. Workers' compensation and outcomes of upper extremity surgery. *J Am Acad Orthop Surg* 2013; **21**: 67-77 [PMID: 23378370 DOI: 10.5435/JAAOS-21-02-67]
58 **Harris I**, Mulford J, Solomon M, van Gelder JM, Young J. Association between compensation status and outcome after surgery: a meta-analysis. *JAMA* 2005; **293**: 1644-1652 [PMID: 15811984 DOI: 10.1001/jama.293.13.1644]
59 **Chen AL**, Bain EB, Horan MP, Hawkins RJ. Determinants of patient satisfaction with outcome after shoulder arthroplasty. *J Shoulder Elbow Surg* 2007; **16**: 25-30 [PMID: 17097315 DOI: 10.1016/j.jse.2006.04.013]
60 **Vajapey SP**, Cvetanovich GL, Bishop JY, Neviaser AS. Psychosocial factors affecting outcomes after shoulder arthroplasty: a systematic review. *J Shoulder Elbow Surg* 2020; **29**: e175-e184 [PMID: 31899094 DOI: 10.1016/j.jse.2019.09.043]
61 **Cuff DJ**, Pupello DR. Prospective evaluation of postoperative compliance and outcomes after rotator cuff repair in patients with and without workers' compensation claims. *J Shoulder Elbow Surg* 2012; **21**: 1728-1733 [PMID: 22652063 DOI: 10.1016/j.jse.2012.03.002]
62 **Henn RF 3rd**, Tashjian RZ, Kang L, Green A. Patients with workers' compensation claims have worse outcomes after rotator cuff repair. *J Bone Joint Surg Am* 2008; **90**: 2105-2113 [PMID: 18829907 DOI: 10.2106/JBJS.F.00260]
63 **Holtby R**, Razmjou H. Impact of work-related compensation claims on surgical outcome of patients with rotator cuff related pathologies: a matched case-control study. *J Shoulder Elbow Surg* 2010; **19**: 452-460 [PMID: 19766021 DOI: 10.1016/j.jse.2009.06.011]
64 **Razmjou H**, Henry P, Costa G, Dwyer T, Holtby R. Effect of arthroscopic rotator cuff surgery in patients with preoperative restricted range of motion. *BMC Musculoskelet Disord* 2016; **17**: 99 [PMID: 26911157 DOI: 10.1186/s12891-016-0956-4]
65 **Nicholson GP**. Arthroscopic acromioplasty: a comparison between workers' compensation and non-workers' compensation populations. *J Bone Joint Surg Am* 2003; **85**: 682-689 [PMID: 12672845]
66 **Denard PJ**, Lädermann A, Burkhart SS. Long-term outcome after arthroscopic repair of type II SLAP lesions: results according to age and workers' compensation status. *Arthroscopy* 2012; **28**: 451-457 [PMID: 22264832 DOI: 10.1016/j.arthro.2011.09.005]
67 **Verma NN**, Garretson R, Romeo AA. Outcome of arthroscopic repair of type II SLAP lesions in worker's compensation patients. *HSS J* 2007; **3**: 58-62 [PMID: 18751771 DOI: 10.1007/s11420-006-9023-2]
68 **Werner BC**, Pehlivan HC, Hart JM, Lyons ML, Gilmore CJ, Garrett CB, Carson EW, Diduch DR, Miller MD, Brockmeier SF. Biceps tenodesis is a viable option for salvage of failed SLAP repair. *J Shoulder Elbow Surg* 2014; **23**: e179-e184 [PMID: 24332800 DOI: 10.1016/j.jse.2013.11.020]
69 **Bible JE**, Spengler DM, Mir HR. A primer for workers' compensation. *Spine J* 2014; **14**: 1325-1331 [PMID: 24462532 DOI: 10.1016/j.spinee.2014.01.030]
70 **US Department of Labor**, Office of Administrative Law Judges. Dictionary of occupational titles, revised 4th ed. [cited 31 January 2021]. In: United States Department of Labor [Internet]. Available from: https://www.oalj.dol.gov/PUBLIC/DOT/REFERENCES/DOTAPPC.HTM
71 **Wallace BC**, Dahabreh IJ, Trikalinos TA, Lau J, Trow P, Schmid CH. Closing the Gap between Methodologists and End-Users: R as a Computational Back-End. *J Stat Softw* 2012; **49**: 1-15 [DOI: 10.18637/jss.v049.i05]
72 **Voss MR**, Homa JK, Singh M, Seidl JA, Griffitt WE. Outcomes of an interdisciplinary work rehabilitation program. *Work*

2019; **64**: 507-514 [PMID: 31658084 DOI: 10.3233/WOR-193012]

73 **Knoblauch DK**, Cassaro S. Workers Compensation. [cited 31 January 2021]. In: StatPearls [Internet]. Available from: https://www.ncbi.nlm.nih.gov/books/NBK448106/

74 **Cabarcas BC**, Gowd AK, Liu JN, Cvetanovich GL, Erickson BJ, Romeo AA, Verma NN. Establishing maximum medical improvement following reverse total shoulder arthroplasty for rotator cuff deficiency. *J Shoulder Elbow Surg* 2018; **27**: 1721-1731 [PMID: 30030030 DOI: 10.1016/j.jse.2018.05.029]

75 **Puzzitiello RN**, Agarwalla A, Liu JN, Cvetanovich GL, Romeo AA, Forsythe B, Verma NN. Establishing maximal medical improvement after anatomic total shoulder arthroplasty. *J Shoulder Elbow Surg* 2018; **27**: 1711-1720 [PMID: 29730138 DOI: 10.1016/j.jse.2018.03.007]

76 **Matar RN**, Gardner TJ, Kassam F, Grawe BM. When do patients truly reach maximal medical improvement after undergoing reverse shoulder arthroplasty? *JSES Int* 2020; **4**: 675-679 [PMID: 32939505 DOI: 10.1016/j.jseint.2020.03.010]

77 **Ansuategui Echeita J**, Bethge M, van Holland BJ, Gross DP, Kool J, Oesch P, Trippolini MA, Chapman E, Cheng ASK, Sellars R, Spavins M, Streibelt M, van der Wurff P, Reneman MF. Correction to: Functional Capacity Evaluation in Different Societal Contexts: Results of a Multicountry Study. *J Occup Rehabil* 2019; **29**: 237-238 [PMID: 29946814 DOI: 10.1007/s10926-018-9797-3]

78 **Ansuategui Echeita J**, Bethge M, van Holland BJ, Gross DP, Kool J, Oesch P, Trippolini MA, Chapman E, Cheng ASK, Sellars R, Spavins M, Streibelt M, van der Wurff P, Reneman MF. Functional Capacity Evaluation in Different Societal Contexts: Results of a Multicountry Study. *J Occup Rehabil* 2019; **29**: 222-236 [PMID: 29802582 DOI: 10.1007/s10926-018-9782-x]

79 **Borm GF**, Lemmers O, Fransen J, Donders R. The evidence provided by a single trial is less reliable than its statistical analysis suggests. *J Clin Epidemiol* 2009; **62**: 711-715.e1 [PMID: 19171462 DOI: 10.1016/j.jclinepi.2008.09.013]

80 **Rücker G**, Schwarzer G, Schumacher M, Carpenter J. Are large trials less reliable than small trials? *J Clin Epidemiol* 2009; **62**: 886-7; author reply 887 [PMID: 19481419 DOI: 10.1016/j.jclinepi.2009.03.007]

81 **Shrier I**, Platt RW, Steele RJ. Mega-trials vs. meta-analysis: precision vs. heterogeneity? *Contemp Clin Trials* 2007; **28**: 324-328 [PMID: 17188025 DOI: 10.1016/j.cct.2006.11.007]

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SCIENTOMETRICS

Evolution of evidence in spinal surgery – past, present and future Scientometric analysis of randomized controlled trials in spinal surgery

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Abstract

BACKGROUND

Spine surgery is evolving and in the due course of its evolution, it is useful to have a comprehensive summary of the process to have a greater understanding to refine our future directives. With the multiple domains of research in the spine, it has become difficult for a surgeon to find the potential hotspots in research or identify the emerging research frontiers.

AIM

To analyze RCTs (1990–2019) for potential research domains along with their research networks and identify the hot topics for future research.

METHODS

A comprehensive and systematic analysis of all the RCTs published on spinal surgery from 1990 to 2019 retrieved from the Web of Science Core Collection database. Scientometric and visual analysis of their characteristics, cooperation networks, keywords, and citations were made using CiteSpace software. Journal and article impact index were retrieved from *Reference Citation Analysis* (*RCA*) Database.

RESULTS

A total of 696 RCTs were published on spinal surgery from 1990 to 2019; of which,

the United States (n = 263) and China (n = 71) made a significant contribution. Thomas Jefferson University (n = 16) was the leading contributor to RCTs on spinal surgery. Weinstein JN was the most cited author in the field followed by Deyo RA. *Spine* (n = 559) remained the top-cited journal for RCTs on spinal surgery. On literature co-citation analysis, spinal stenosis, anterior cervical discectomy and fusion, degenerative disc disease, and minimally invasive decompression were identified as the hotspots and potential research frontiers.

CONCLUSION

The identified hotspots that extending the frontiers in the management of degenerative disorders of the spine through further research holds the potential for advancement in spinal care.

Key Words: Randomized controlled trials; Scientometrics; Spine surgery

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Core Tip: The evolutionary process of a field is analyzed through various parameters like citation metrics, keywords and author networks in Scientometrics. With advances in the field of spinal surgery, surgeons find it difficult to identify the potential hotspots for their prospective research. We noted that research cooperation among the developed and developing nations remains crucial and needs to be strengthened. On literature co-citation analysis, spinal stenosis, anterior cervical discectomy and fusion, degenerative disc disease, and minimally invasive decompression were identified as the hotspots and potential research frontiers in the field of spinal surgery.

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INTRODUCTION

The safety and efficacy of the evolving treatment methods in clinical practice are assessed by randomized controlled trials (RCTs), are is considered the gold standard research method on the top of the evidence pyramid[1]. With the ongoing drive of the evidence-based approach in spinal surgery, RCTs are used to generate clinically important findings with valid conclusions on the prognosis and diagnosis of varied clinical conditions and effectiveness of their treatment methods[2]. Hence, by analyzing the research trend of RCTs in spinal surgery one could determine the evolution of evidence in the field.

With the rapid evolution in the advancements in spinal surgery, in order to have a better understanding of the advancements for streamlining our future directives, we need to have a comprehensive summary of the evolutionary process. Research with regards to spinal surgery has expanded to various domains and surgeons find it difficult to identify the potential hotspots in its advancement to direct their prospective research. Visualization of the evolutionary process in a field is possible with the current technological developments like information analytics, graphic drawing and data mining, combined with computational statistics. The evolutionary process in a field is analyzed through various parameters like citation metrics, keyword and author networks in scientometrics[3]. Using knowledge maps in scientometrics, one can visualize this panorama of information to explore hotspots in research [4]. This methodology has been established to study the evolution of fields such as orthopedics[5], public health[6], and artificial intelligence[7].

With a newer perspective, scientometric tools including text mining, co-word analysis, word frequency analysis, co-citation analysis, cluster analysis, and network analysis were used to do a systematic and comprehensive review to assess the potential research domains and research trend of RCTs published on spinal surgery for the past three decades (1990–2019) apart from analyzing their research networks to identify the hot topics for future research.

MATERIALS AND METHODS

Data sources

Various databases such as PubMed, Scopus, Google Scholar and Web of Science (WoS) were used by the

researchers. Each has its own merits and demerits. While Google Scholar has wider literature coverage, it is limited by the quality of results and duplication[8]. PubMed is rich in medical literature but lacks wider coverage in other subject areas[9]. Scopus and WoS are considered complementary databases without many differences. However, it was noted that for visual analysis and knowledge mapping with software such as CiteSpace, WoS was considered to be better[9,10]. Hence, WoS was used as the source for data retrieval. Among the WoS databases, WoS Core Collection with indexes SCI-EXPANDED, SSCI, and A&HCI were used for data extraction. The detailed data retrieval strategy is given in Figure 1. Preliminary data were standardized with deduplication and merge functions in CiteSpace. The literature search date was August 24, 2020. The resultant core dataset on the subject is subjected to natural language processing, network analyses using CiteSpace and thematic cluster knowledge maps were developed and individual clusters are analyzed using semantic network of author keywords and their hierarchy and key results are synthesized. Journal and article impact index was retrieved from *RCA* database[11].

Data visualization and analysis

Scientometric and visualization analysis was performed with CiteSpace (5.7.R1). CiteSpace was used to visualize the structure, regularity, and distribution of research domains in spinal surgery and analyze the article co-citation data to mine the knowledge clustering and citation space distribution. The co-occurrence between the additional research units such as cooperation among various authors, institutions, and countries in the field of spinal surgery was also analyzed. Consolidating the results of the analysis, a comprehensive knowledge map elaborating on the emerging research trend with the potential research domain from RCTs published in spinal surgery was built.

The scientometric analysis results are depicted as knowledge maps with the key parameters detailed as follows. The knowledge map depicts the time interval between its components with warm and cold colors. With time close to 2019, the components are depicted in warm colors and time close to 1990 in cold colors. The size of the nodes in the knowledge graphs indicates the frequency of authors, institutions and countries, while the connection between them indicates that they are from the same article[12]. When two or more authors or institutions or countries are noted in the same article, it is considered a scientific cooperative relationship between the group of authors or institutions or countries [13].

The scientometric analysis uses certain parameters for evaluation. H-index is used to quantify the academic output from researchers and institutions where h indicates the number of papers of the author/institution having ≥ h citations of all the papers published by the author/institution[14]. The degree indicates the total connection between the authors, institution, or country in the analyses of their co-occurrences. A high value denotes strong cooperation and communication among the group of authors, institutions or countries. The importance of nodes in the research cooperation network is indicated by the degree, whereas the half-life represents the continuum of institutional research on a timeline[15].

RESULTS

The database search recovered 696 RCTs published on spinal surgery from the global literature from 24 256 articles that included 20 458 non-RCTs, 2206 reviews, 583 proceedings papers, and 313 meeting abstracts from 1990 to 2019. Figure 2 shows the output of the RCTs published in the field of spinal surgery. The first two decades (1990–2009) had an average of three RCTs published per year, which later increased to 51 RCTs per year in the last decade (2010–2019). There was an overall rising trend in the scientific output on spinal surgery (Figure 2). This increasing trend in publication of RCTs shows the increased attention paid in the field of spinal surgery by surgeons and researchers to improve the standard of care. It is also evident from Figure 2 that the other types of research communication documents such as original articles, reviews and proceedings papers, and meeting abstracts also had a proportionate growing trend.

Journal analysis

The number of citations that the RCTs published in a journal receive reflects the importance and influence of a journal in the field. CiteSpace was used to analyze the list of journals where the retrieved RCTs were published and generated a map of journals that cited them (Figure 3). The journal citation network had 52 nodes and 358 links among them. Based on the citation frequency, the top 10 journals were selected and tabulated (Table 1). With due consideration to the impact factor, H-index, centrality, and citation frequency of the journals, the top five journals in spinal surgery were *Spine* (IF: 2.646, H-index: 243), *European Spine J* (IF: 2.458, H-index:128), *J Bone Joint Surg Am* (IF: 4.578, H-index: 322), *Spine J* (IF: 3.191, H-index: 102), *J Neurosurg-Spine* (IF: 3.011, H-index: 205). As shown in Figure 3, the node circles of *Spine, European Spine J, J Bone Joint Surg Am, Spine J, J Neurosurg-Spine* were larger and there were cool-tone areas within them. However, node circles of *J Spinal Disord Tech, Neurosurgery, New Engl J Med*, and *JAMA* were mostly depicted in warm colors. Early critical RCTs in spinal surgery were

Table 1 Top 10 journals in spinal surgery based on the co-citation network frequency

Rank	Source	Cited frequency	Impact factor	H-index	Degree	Centrality	2022 JAII
1	*Spine*	559	2.646	243	42	0.53	44.770
2	*Eur Spine J*	371	2.458	128	24	0.05	-
3	*J Bone Joint Surg Am*	322	4.578	249	33	0.24	55.199
4	*Spine J*	269	3.191	102	13	0.01	16.013
5	*J Neurosurg-Spine*	205	3.011	93	13	0	18.692
6	*Clin Orthop Relat R*	198	4.329	197	23	0.05	25.424
7	*J Spinal Disord Tech*	156	1.594	79	11	0	4.831
8	*Neurosurgery*	143	4.853	192	23	0.04	23.060
9	*New Engl J Med*	137	74.699	987	17	0.08	110.705
10	*J-J Am Med Assoc*	120	45.540	654	19	0.04	38.773

JAII: Journal Article Influence Index.

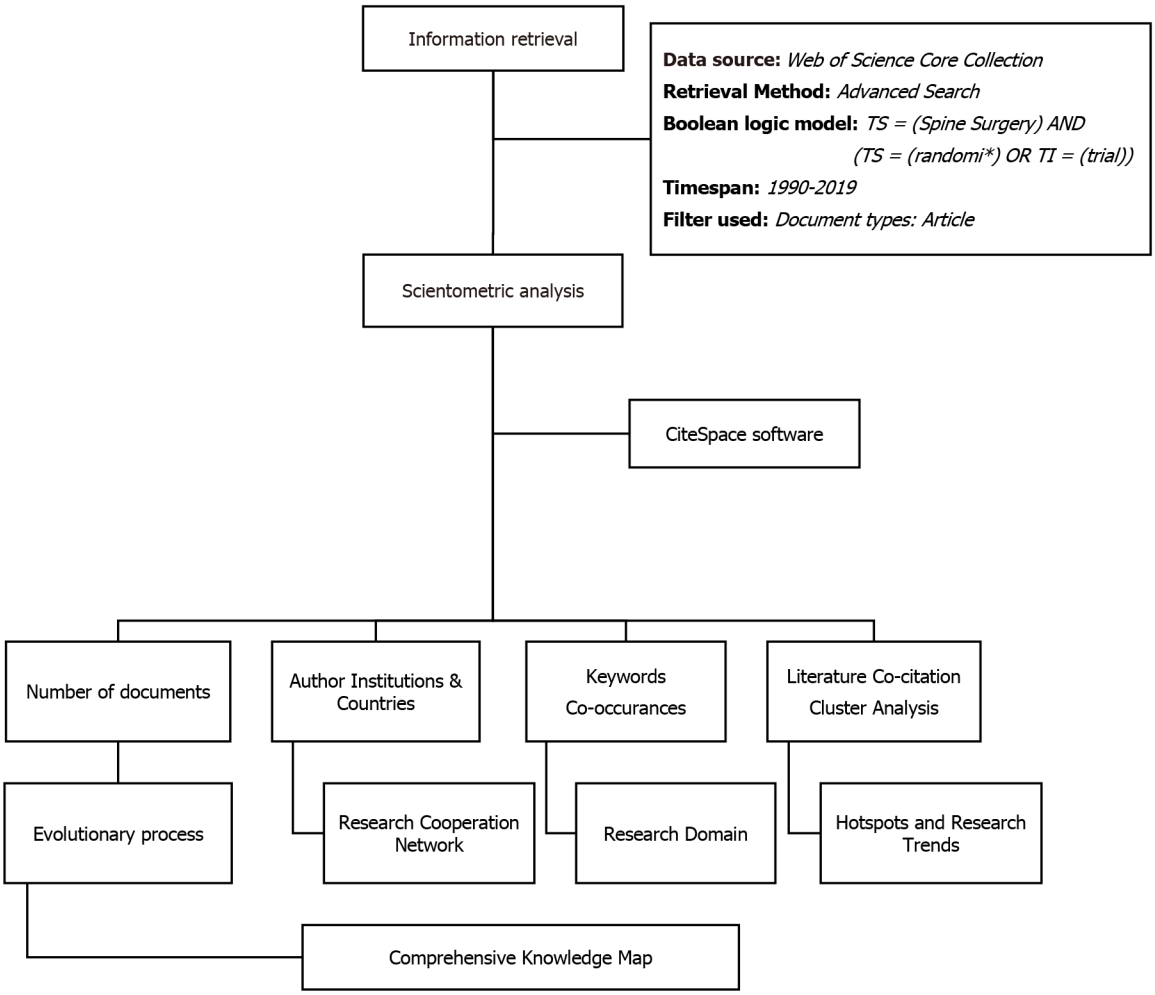


Figure 1 Scientometric analysis framework.

published in *Spine, European Spine J, J Bone Joint Surg Am, Spine J* and *J Neurosurg-Spine*. It is also worth noting that the top five journals on spinal surgery came from the United States (*Spine, J Bone Joint Surg Am, Spine J, J Neurosurg-Spine)* and Germany (*European Spine J*).

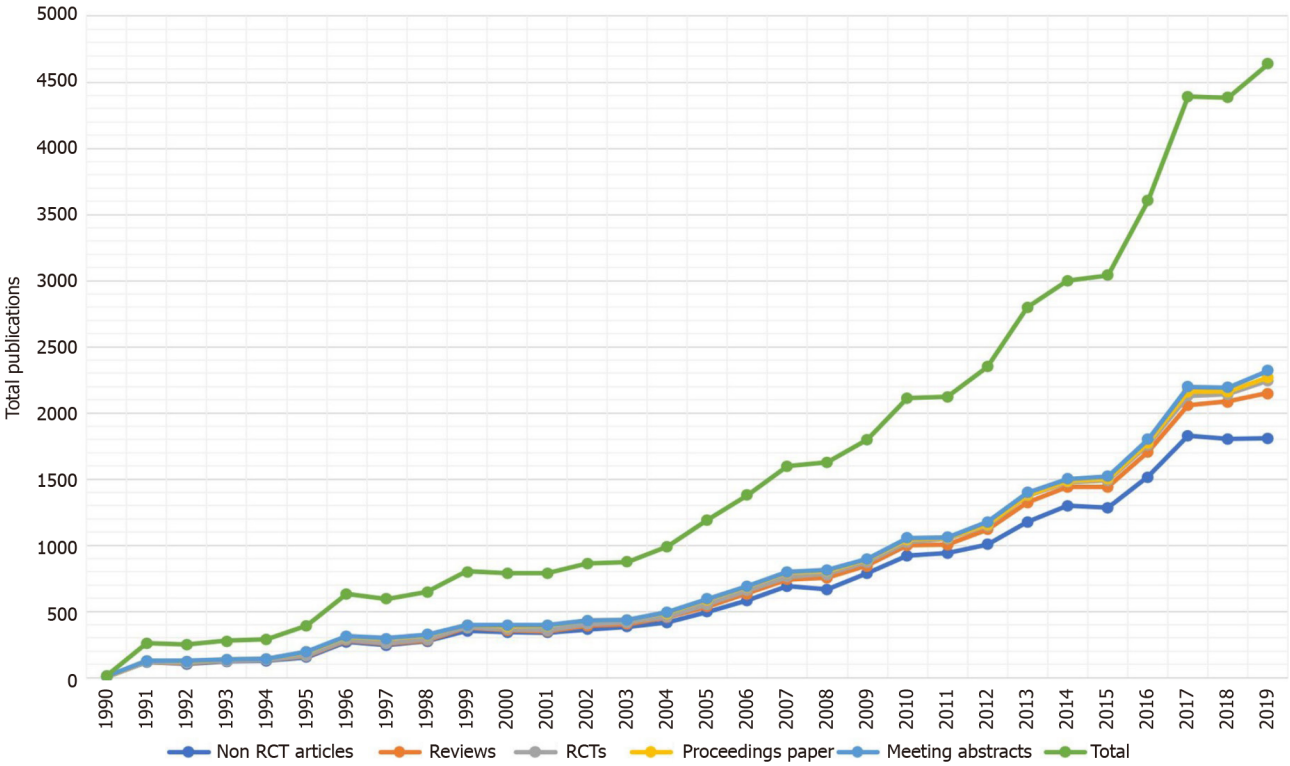


Figure 2 Scientific output in stem cell therapy for diabetes from 1990–2019. RCT: Randomized controlled trials.

Scientific cooperation network analysis

Coauthor analysis: The author co-occurrence network map had 245 nodes, and 1128 connections with a network density of 0.0377 (Figure 4). On the whole, the authors in the network map had a fair connection strength among each other; however, there were some poorly connected islands of author groups that need global strengthening (Figure 4).

The research cooperation group with the closest communication was from Weinstein JN, Deyo RA, Atlas SJ, Ware JE and Fairbank JCT. The details of the top 10 authors who published RCTs on spinal surgery are shown in Table 2. Weinstein JN published the highest number of RCTs in spinal surgery, with a degree value of 35 and H-index of 68. His research spanned several areas in spinal surgery. Weinstein JN was principal investigator in various outcome trials involving disc herniation, spinal stenosis and degenerative spondylolisthesis, and investigated the role of surgery and conservative therapy in these conditions. He also did a lot of work on pain and first developed the lumbar radiculopathy model. Deyo RA (degree: 55; H-index: 116), being a member of the Cochrane Review Group on Back Disorders, conducted trials mostly on clinical intervention and patient aids for spinal surgery. Atlas SJ concentrated on sciatica and spinal stenosis in spinal surgery. The other two authors in the top five were Ware JE and Fairbank JCT, who did pioneering works on quality of life measures in spinal surgery and Oswestry Disability Index, respectively.

Co-institutional analysis: The co-institutional network is presented in Figure 5, and consisted of 95 nodes and 118 links with a network density of 0.0264. There was weak collaboration among the institutions globally, but the network of domestic institutions seemed closer. The top 10 list of institutions that published maximum RCTs are listed in Table 3. Thomas Jefferson University (16 RCTs), Seoul National University (11 RCTs), University of California San Francisco (10 RCTs), Dartmouth Medical School (8 RCTs), and Dartmouth Institute of Health Policy & Clinical Practice (8 RCTs) were the predominant institutions with major contributions. These institutions made a central contribution to the RCTs in spinal surgery. Six of the top 10 institutions were from the United States (3 universities, 2 institutes, and 1 School), Sweden came second with two institutions (1 university and 1 institute). The contribution of United States and Sweden in the field of spinal surgery has been shown to be exceptional in this analysis.

Co-country analysis: In the co-country map depicted in Figure 6, 25 nodes and 64 links were noted with a network density of 0.2133. From a global standpoint, the density of the network as depicted in Figure 6 was weak with few connections between the countries in terms of conducting RCTs in spinal surgery. Further global cooperation is needed for research in spinal surgery. With the rising demand for advancement in the management of spinal ailments, countries must try to solve the problem by coordinating their efforts together for conducting RCTs. Table 4 shows the top 10 countries publishing

Table 2 Top 10 authors in spinal surgery based on the co-citation network frequency

Rank	Author	Cited frequency	H-index	Degree	Centrality
1	Weinstein JN	94	68	35	0.06
2	Deyo RA	83	116	55	0.21
3	Atlas SJ	57	43	37	0.08
4	Ware JE	55	78	47	0.27
5	Fairbank JCT	37	38	28	0.04
6	Fritzell P	35	15	38	0.18
7	Akbarnia BA	26	42	10	0
8	Carragee EJ	24	50	18	0.06
9	Zdeblick TA	22	41	38	0.21
10	Cloward RB	22	23	37	0.06

Table 3 Co-institution collaboration network map in spinal surgery

Rank	Institutions	Publications	Degree	Centrality	Half-life
1	Thomas Jefferson Univ	16	8	0.02	1.5
2	Seoul National Univ	11	4	0	0.5
3	Univ California San Francisco	10	5	0.02	6.5
4	Dartmouth Med School	8	10	0.05	3.5
5	Dartmouth Inst Health Policy & Clinical Practice	8	5	0	0.5
6	Rush Univ	8	5	0.02	2.5
7	Linkoping Univ	8	10	0.01	3.5
8	Dartmouth Hitchcock Med Cen	8	5	0.01	0.5
9	Karolinska Inst	8	9	0	3.5
10	Leiden Univ	8	2	0	7.5

Table 4 Co-country collaboration network map in spinal surgery

Rank	Country	Publications	Percent	Degree	Burst	Half-life
1	United States	263	37.8	15	5.11	16.5
2	China	71	10.2	5	-	8.5
3	Germany	59	8.5	9	4.18	13.5
4	South Korea	36	5.2	1	-	5.5
5	Sweden	35	5	10	4.71	14.5
6	England	27	3.9	12	5.72	7.5
7	Netherlands	23	3.3	4	-	8.5
8	Canada	20	2.9	5	-	5.5
9	Japan	15	2.2	0	-	2.5
10	Denmark	13	1.9	7	-	9.5

RCTs in spinal surgery. The United States has contributed most to the field of spinal surgery, with 263 RCTs, accounting for 37.8% of the global contribution. Other countries contributing to the publication of RCTs in spinal surgery included China (71 RCTs, 10.2%), Germany (59 RCTs, 8.5%), South Korea (36 RCTs, 5.2%), and Sweden (35 RCTs, 5%). Developed nations like the United States had a cold tone in

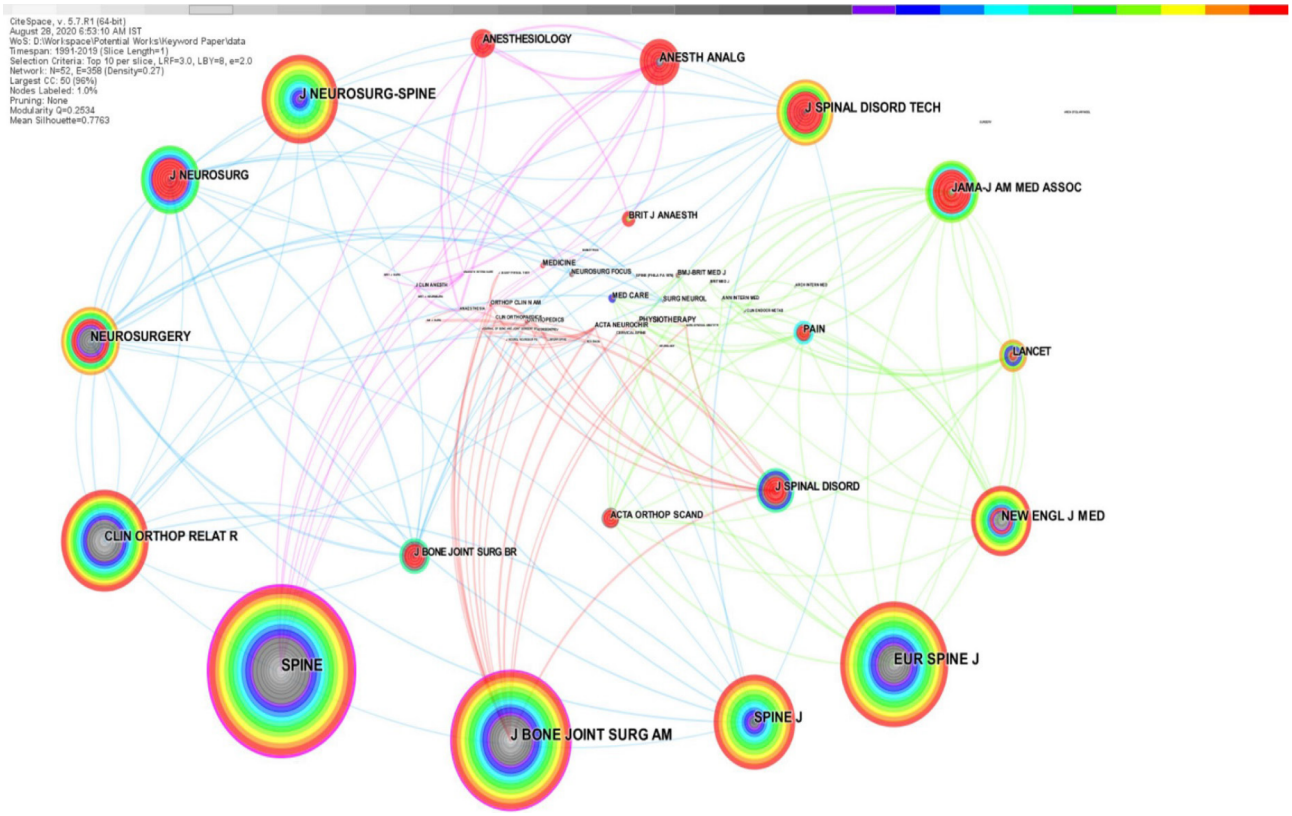


Figure 3 Journal citation network on stem cell therapy for diabetes. Journals with more than 750 co-citations were labelled.

their node circle whereas China, as a developing country, which conducted RCTs later than the developed nations, had a warm tone in their nodes (Figure 6). Despite having 71 RCTs published by China, none of their authors or institutions were in the top 10 list of contributors. It indicates that despite the late start of research in the field in China, it has developed at a rapid rate to achieve the current number of published RCTs.

Keyword analysis

We analyzed the co-occurrence network of the key words used in the field and their summary and classification based on research direction and frequency is given in Table 5. The keywords were manually sorted into five major topics. The first topic included localizing keywords such as "spine (133)", "lumbar spine (42)" and "cervical spine (7)". It focused mainly on the region of the spine involved in RCTs. Topic 2 included keywords related to disease pathology involved in RCTs such as "spondylolisthesis (11)", "disease (9)", "spinal disease (7)", degenerative spondylolisthesis (5)", *etc.* The third topic of keywords involved symptomatology such as "low back pain (104)", "pain (36)", "radiculopathy (10)" and "sciatica (7)". The fourth topic involved keywords related to management methods such as "surgery (208)", "fusion (91)", "spinal surgery (87)", "outcome (79)", "management (62)", "complications (59)", *etc.* The fifth topic was concerned with the outcome measure keywords such as "efficacy (40)", "reliability (9)", "risk (6)", "safety (6)", *etc.*

Co-citation analysis

It is a common practice for the researchers to cite the evidences from the results of RCTs in their research work as references. Scientific development is made through such mutual citations of scholarly works in the field.[16] The citation network of RCTs published in the 1990s looks relatively sparse while the network of RCTs published around the 2000s and 2010s look denser (Figure 7). It is also noted that highly cited RCTs are from the middle and late periods. Based on Figure 7, the top 10 RCTs cited by frequency are presented in Table 6. The frequency of citation of these RCTs was limited to the mutual citations between the 696 included RCTs, which was different from the citation frequency available in WoS. The article "Surgical *vs* nonoperative treatment for lumbar disk herniation – The Spine Patient Outcomes Research Trial (SPORT) observational cohort" by Weinstein JN is the most frequently cited RCT in spinal surgery. This pioneering work established the equivalence in the effectiveness of surgical and conservative treatment for lumbar disc herniation. The burst value in the table shows that these articles had been the focus of research for a period of time. The highest burst value was noted for the same article mentioned above by Weinstein JN. It is also noted from the table that *JAMA*, *Spine* and *New*

Table 5 Keyword analysis in spinal surgery

Topic	Keyword	Frequency	Centrality	Degree	Burst
1	Spine	133	0.27	22	-
	Lumbar spine	42	0.1	14	3.53
	Cervical spine	7	0.03	5	3.84
2	Spondylolisthesis	11	0.09	6	-
	Disease	9	0	5	4.7
	Spinal stenosis	7	0.01	6	-
	Stenosis	6	0	4	3.73
	Degenerative spondylolisthesis	5	0	4	-
	Herniation	5	0.01	6	-
	Intervertebral disc	5	0	2	-
	Scoliosis	5	0	2	-
3	Low back pain	104	0.2	21	-
	Pain	36	0.14	13	3.67
	Radiculopathy	10	0	4	4.35
	Sciatica	7	0.05	6	3.94
4	Surgery	208	0.2	18	-
	Fusion	91	0.3	24	-
	Spine surgery	87	0.09	14	-
	Outcome	79	0.09	16	-
	Management	62	0.16	16	7.22
	Complication	59	0.2	18	-
	Follow-up	42	0.16	19	5.11
	Diskectomy	32	0.19	19	5.65
	Spinal fusion	20	0.03	8	3.58
	Decompression	20	0.09	11	4.05
	Arthrodesis	19	0.16	14	3.48
	Interbody fusion	15	0.05	7	-
	Nonoperative treatment	14	0.02	9	7.77
	Postoperative pain	12	0	5	-
	Analgesia	8	0	2	-
	Discectomy	7	0.02	8	3.47
	Instrumentation	7	0.01	4	4.36
	Nonsurgical management	7	0.01	7	-
	Tranexamic acid	6	0	5	-
	Rehabilitation	6	0	2	-
	Bone graft	5	0	4	-
	Laminectomy	5	0	3	-
	Arthroplasty	5	0	2	-
	Total disc replacement	5	0.01	3	-
5	Efficacy	40	0.07	15	-
	Reliability	9	0.07	8	-

	Randomized controlled trial	8	0	2	-
	Risk	6	0.01	4	-
	Safety	6	0	5	-
	Children	5	0	2	-

Table 6 Top 10 cited literature in spinal surgery

Rank	Frequency	Author	Journal	Year	Burst	Half-life	Impact index
1	24	Weinstein JN	*JAMA*	2006	8.79	4.5	44.9
2	24	Heller JG	*Spine*	2009	5.39	3.5	26.9
3	22	Weinstein JN	*JAMA*	2006	7.75	3.5	31.1
4	21	Murrey D	*Spine J*	2009	5.66	4.5	26.3
5	20	Akbarnia BA	*Spine*	2013	7.3	3.5	16.3
6	19	Cheung KMC	*Lancet*	2012	7.6	4.5	19.1
7	19	Weinstein JN	*New Engl J Med*	2008	4.66	2.5	48.2
8	19	Weinstein JN	*New Engl J Med*	2007	5.37	3.5	37.2
9	16	Bess S	*J Bone Joint Surg Am*	2010	7.67	6.5	29.1
10	16	Dannawi Z	*Bone Joint J*	2013	7.67	3.5	13.3

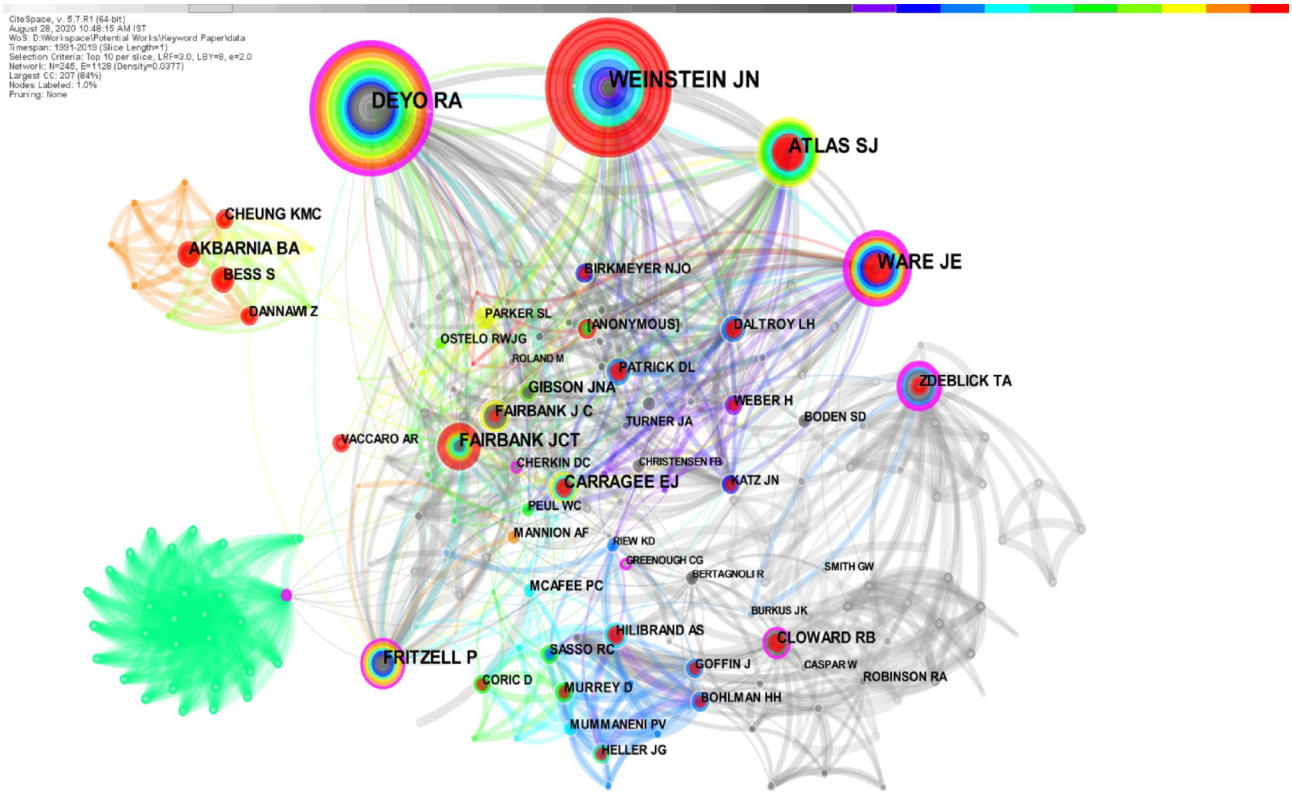


Figure 4 Coauthor collaboration network in spinal surgery.

Engl J Med each contributed two articles to the top 10 list. Of the top 10 articles, three RCTs compared surgical and conservative treatment for lumbar disc disease, three RCTs evaluated the role of growth rods in early-onset scoliosis, and three RCTs compared the results of fusion and arthroplasty for cervical disc disease.

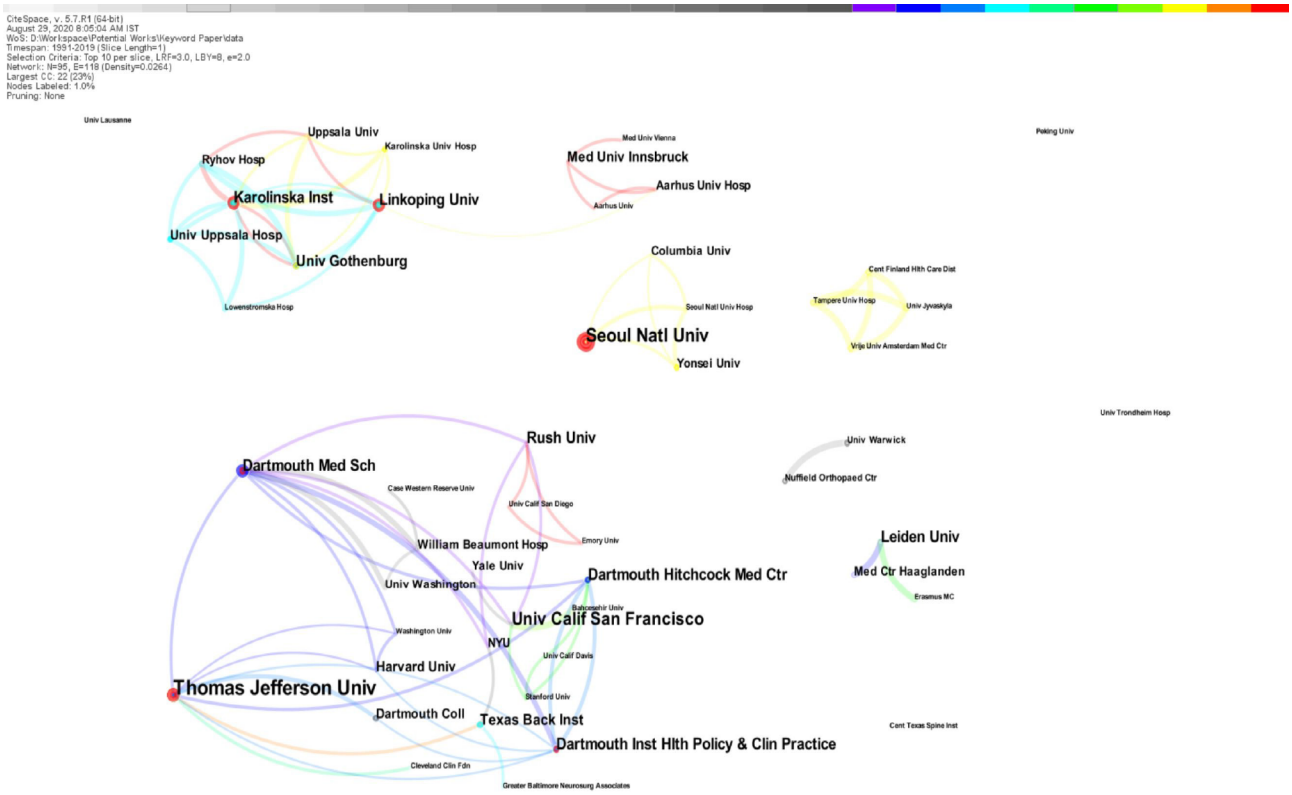


Figure 5 Co-institution collaboration network in spinal surgery.

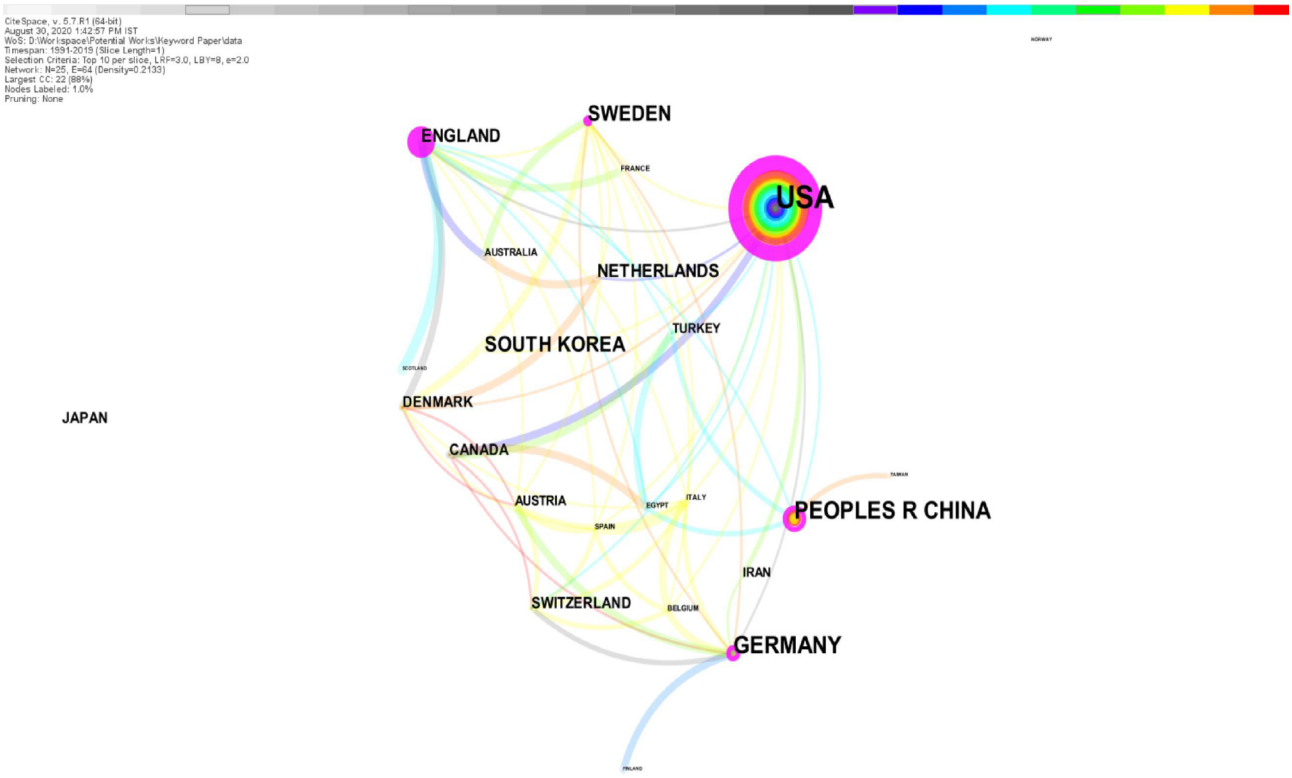


Figure 6 Co-country collaboration network in spinal surgery.

Cluster analysis of co-citation network

Using exploratory data mining techniques, analysis of the data clusters enables the identification of important topics, and their evolutionary trends. A comprehensive clustering of the RCTs published in a given theme is done in cluster analysis and an objective projection of the principle content is visualized

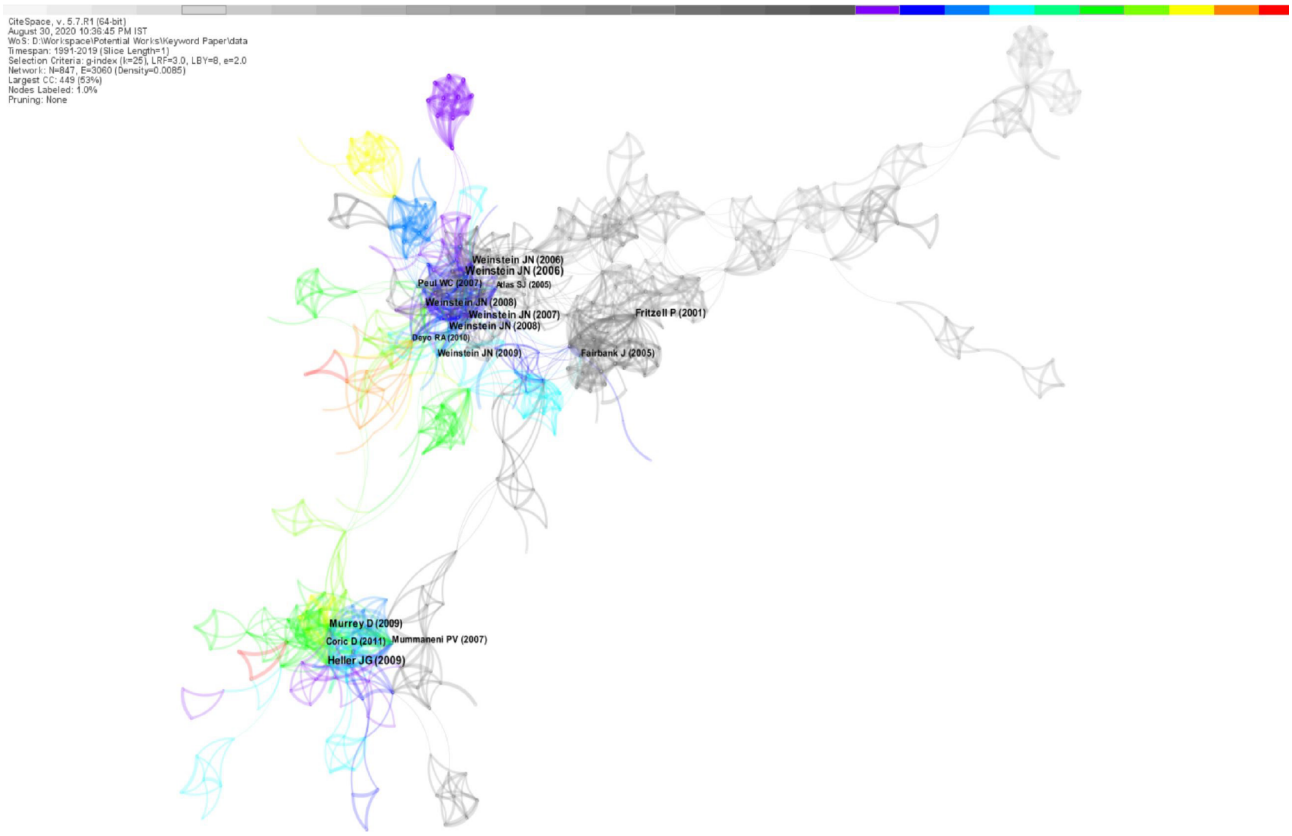


Figure 7 Co-citation network in spinal surgery. The studies depicted in the network are the top 50 per slice and labeled with a threshold frequency of 10 citations and the largest citation subnetwork is displayed.

[17]. The RCT cluster map on spinal surgery is depicted in Figure 8. The time needed for clustering from far to near is depicted as the color of the clusters from cold to warm. The articles with high burst values are presented as cluster blocks with red nodes. The higher the presence of red nodes in a cluster it denotes that the clustered topic is a research frontier and hot spot in the field. We summarized the information of the clusters in Table 7. Considering the cluster analysis from Figure 8 and Table 7, "spinal stenosis", "anterior cervical discectomy and fusion", "degenerative disc disease" and "minimally invasive decompression" were the hotspots in the field of spinal surgery and considered as the potential research frontiers that need further research.

Category co-occurrence analysis

Based on the category co-occurrence analysis, one can intuitively understand the main subjects of research in the field of concern[18]. The categories used for classification were taken from the WoS core collection database. As shown in Figure 9, the highlighted circle on the nodes indicate that it has high–intermediate values of centrality. Table 8 gives the list of top 10 categories in spinal surgery with high co-occurrence frequency. From Figure 9 and Table 8 it is evident that the research categories involve multiple disciplines and fields. The comprehensive knowledge map in spine surgery research from 1990 to 2019 is depicted in Figure 10.

DISCUSSION

We noted a rising trend in the number of published studies on spinal surgery based on the research outputs analyzed. We also noted an increase in the academic activities in the field of spinal surgery through a proportionate increase in the number of proceeding papers and meeting abstracts. This denoted an increase in international attention for innovation in the field of spinal surgery and improvisation of the existing standards of care. With the advances in technology, we noted an increase in survival period and proportionate increase in the aging population[19], which raises a concern to increase our focus on degenerative disorders of the spine.

Some of the landmark papers in spinal surgery research were published in *JAMA* and *New Engl J Med* , which were in the publishing field for more than a century with a high academic reputation. They have laid a foundation for spinal surgery research and paved the way for the field-specific journals to cater to the subsequent research in spinal surgery. Among the specific journals recognized in the field, *Spine, Eur*

Table 7 Cluster summary of co-citation network

Cluster ID	Size	Silhouette	Mean (Year)	Label (LLR)
0	69	0.925	2006	Spinal stenosis, sciatica
1	63	0.982	2009	Anterior cervical discectomy and fusion, clinical outcome
3	57	0.952	2002	Chronic low back pain, degenerative disc disease
5	22	0.968	2003	Cloward, nerve injury
6	21	0.991	2011	Spine Patient Outcomes Research Trial (SPORT), National Surgical Quality Improvement Project (NSQIP)
9	13	0.963	2010	Minimally invasive decompression, multicenter study
11	11	1	2005	Discogenic, Prospective randomized multicenter clinical study
14	6	0.995	2008	Biologics, extreme lateral interbody fusion

Silhouette is a parameter in CiteSpace software to analyze the clustering effect in terms of homogeneity of the network. A value closer to 1 means higher homogeneity and results more than 0.7 has high reliability.

Table 8 Top 10 subject categories in spinal surgery

Rank	Category	Frequency	Centrality	Burst
1	Neurosciences and neurology	390	0.03	7.18
2	Clinical neurology	389	0.03	7.23
3	Orthopedics	367	0.04	11.42
4	Surgery	151	0.06	-
5	Anesthesiology	67	0.05	-
6	General and internal medicine	53	0.03	-
7	Research and experimental medicine	26	0.01	-
8	Rheumatology	14	0.02	-
9	Rehabilitation	13	0.01	-
10	Pharmacology and pharmacy	5	0.00	-

Spine J, J Bone Joint Surg Am, and *Spine J* were affiliated with various regional, national, international societies and associations and have been in publication for > 40 years and have contributed to progress in the field of spinal surgery. Most of the hotspots in spinal surgery arose from RCTs published in these high-impact journals. Researchers interested in spinal surgery should closely follow the high-quality trials published by these journals in real time.

Our revies explored the research cooperation in spinal surgery from three perspectives, namely, small-author cooperation network, intermediate-institutional cooperation network, and large-national cooperation network. We noted academic cooperation mostly among the predominant institutions in a particular country and prominent authors in an institution. In the publication of RCTs, developed nations like the United States and Germany were leading the way, while in developing countries like China, although they had more publications, they were not from prominent institutions or authors. Hence, increased research collaboration with the developing countries will be conducive to advancement of spinal surgery.

The potential research topics and emerging trends have been revealed by analyzing the keyword co-occurrences and literature co-citations in spinal surgery. Keywords are one of the research data that gives an idea about the main themes of research in a particular article. With the advanced scientometric techniques such as text mining and keyword co-occurrence analysis, we can visualize the research trends in a field and identify the hotspots of research[20]. From the result of such analysis, the five main research topics in spinal surgery include regional localization such as cervical and lumbar surgery; disease pathology like spondylolisthesis, stenosis, intervertebral disc, and scoliosis; surgical treatment methods like fusion surgery, decompression surgery, instrumentation surgery, and arthroplasty; outcome measures like efficacy, risks, safety and reliability of the treatment methods.

Literature co-citation analysis noted that spinal stenosis, anterior cervical discectomy and fusion, degenerative disc disease, and minimally invasive decompression are the current hotspots and research

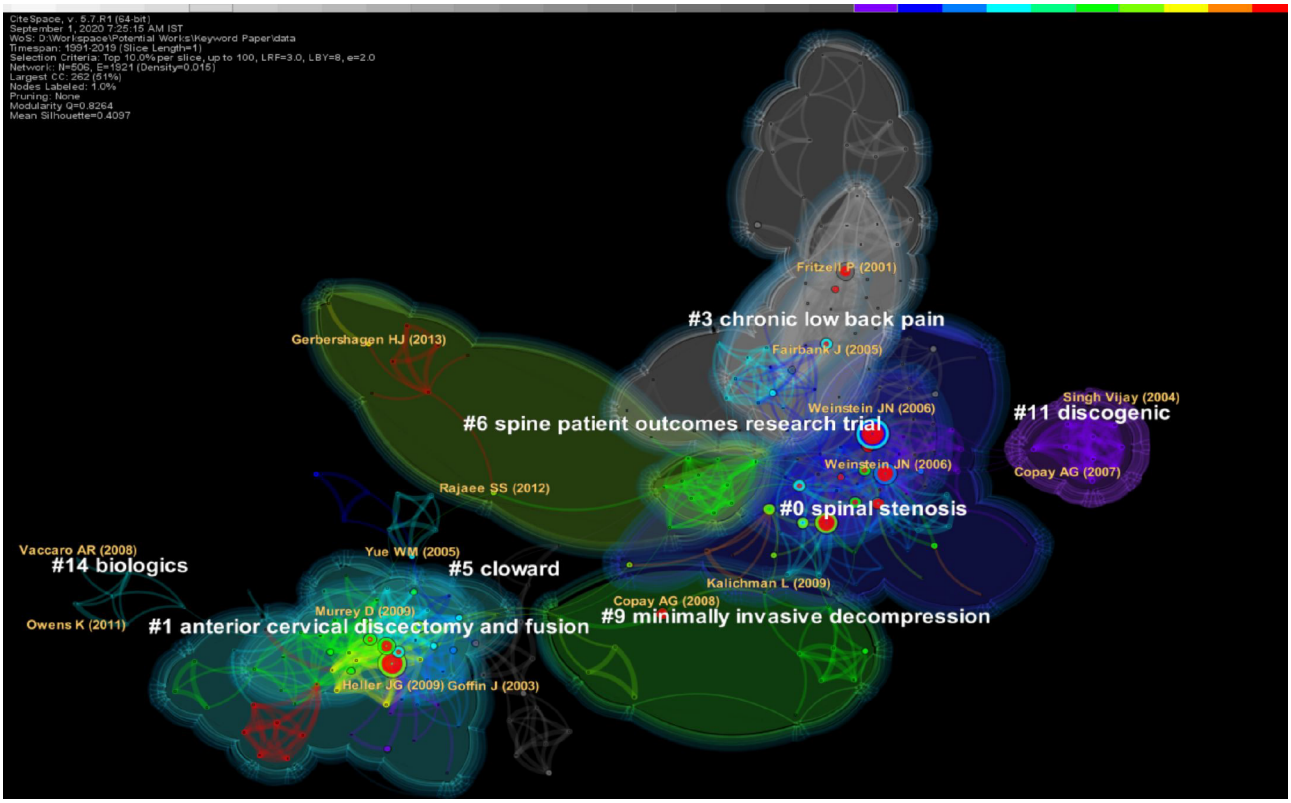


Figure 8 Cluster map of literature in spinal surgery. The clusters are named in CiteSpace based on the keywords used in articles along with a log-likelihood algorithm.

frontiers. With the global aging population > 60 years expected to outnumber children younger than 5 years by 2020[19], spinal stenosis and its fusion procedures have become one of the major research frontiers. With the drive for minimally invasive surgical procedures considering their lower morbidity with minimal hospitalization period[21], much of the research efforts are being directed towards making such surgical procedures safer for these aging patients and simpler for surgeons.

Spinal surgery has made technological advancements in recent years in terms of intraoperative imaging, 3D navigated operations, materials with nanoscale architecture, *etc.*[22-25]. Material science research has brought about a revolution in the instrumentation options involved in spinal surgery. The development of materials with high biocompatibility and biomechanical characteristics comparable to those of the native has resulted in a faster and more physiological ossification when used in spinal fusion[26]. Hence, topics such as discogenic pain, nerve injury, clinical outcome, biologics and extreme lateral interbody fusion (XLIF) have been the important research topics directing the progress of spinal surgery.

Our study had a few limitations. The core data used for analysis were from the WoS Core Collection database and *RCA* database. We had an English language restriction for the published RCTs. We did not consider the grey literature such as unpublished conference documents, scientific reports, dissertations, scientific archives, *etc.*, for analysis of the research trend. From a visual analysis perspective, all the available information was not incorporated into the knowledge map.

Our analysis revealed the key areas of ongoing research in spinal surgery to advance the management of spinal diseases like spinal cord injury, spondylolisthesis, spinal stenosis, intervertebral disc disease, and scoliosis. Since arthroplasty is a sought-after field of research in the orthopedic forum, the spine is no exception. However, recent trials are being conducted on surgical treatment methods like fusion surgery, decompression surgery, instrumentation surgery, and arthroplasty. With the current abundance of evidence on novel treatment methods using regenerative principles and mesenchymal stromal cells and their derivatives to combat various inflammatory and degenerative disorders, we except more upcoming trials investigating their role in spinal surgery too. The current research hotspots are presented in the PICO format as Table 9.

CONCLUSION

Spinal surgery research was extensive with multidisciplinary methods and technologies and its development needs the involvement of researchers from various fields. We recommend strengthening

Table 9 Research hotspots in spinal surgery

Category	Hotspot
Patient	Spinal cord injury
	Spondylolisthesis
	Spinal stenosis
	Intervertebral disc disease
	Scoliosis
Intervention	Arthroplasty
	Fusion surgery
	Decompression surgery
	Instrumentation surgery
	Biological therapy
Comparator	Conventional treatment methods
Outcome	Clinical outcome
	Patient reported outcome measures

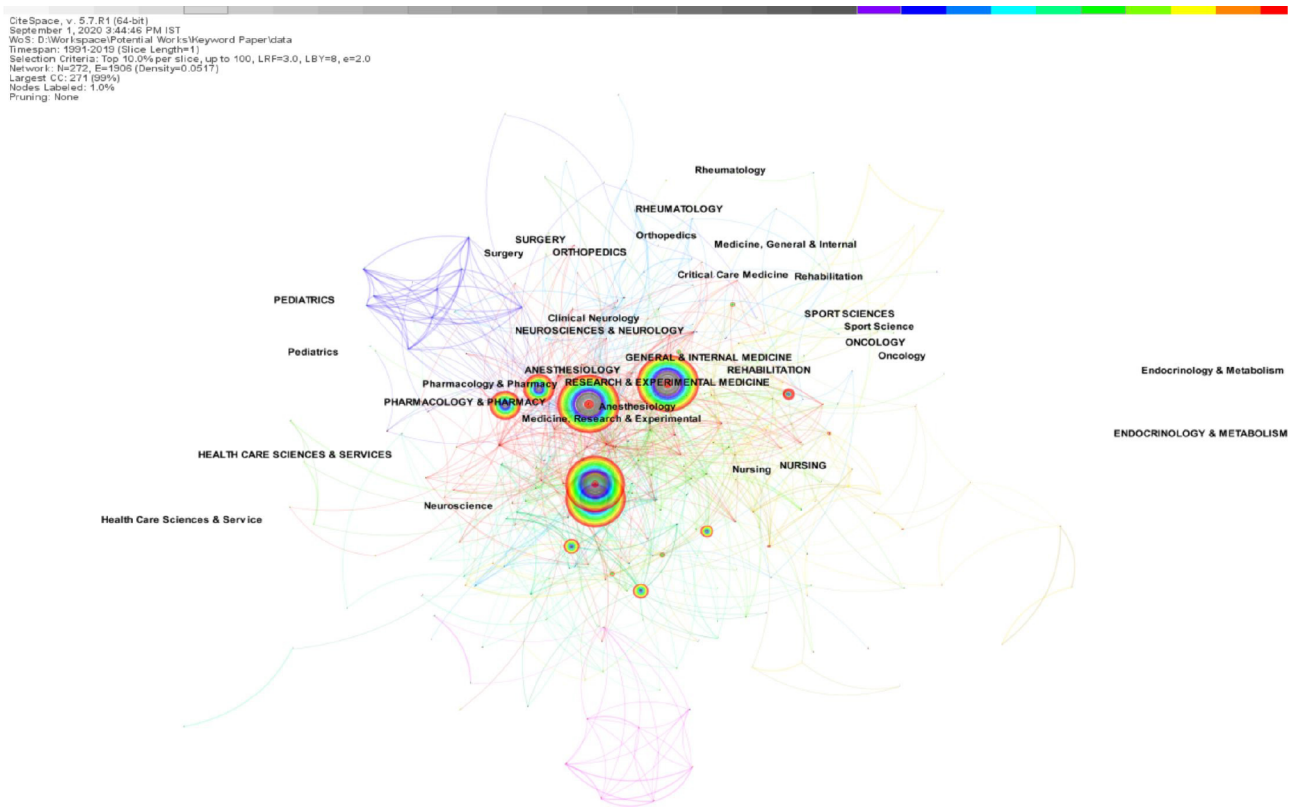


Figure 9 Co-occurrence network of research categories in spinal surgery.

research cooperation among the developed and developing nations. This study provides an overview of research fields in spinal surgery through a systematic and comprehensive scientometric analysis of published RCTs and identified the emerging trends and research hotspots. It was evident from the identified hotspots that degenerative disorders remain the potential frontier in spinal surgery that holds the promise for future advancements.

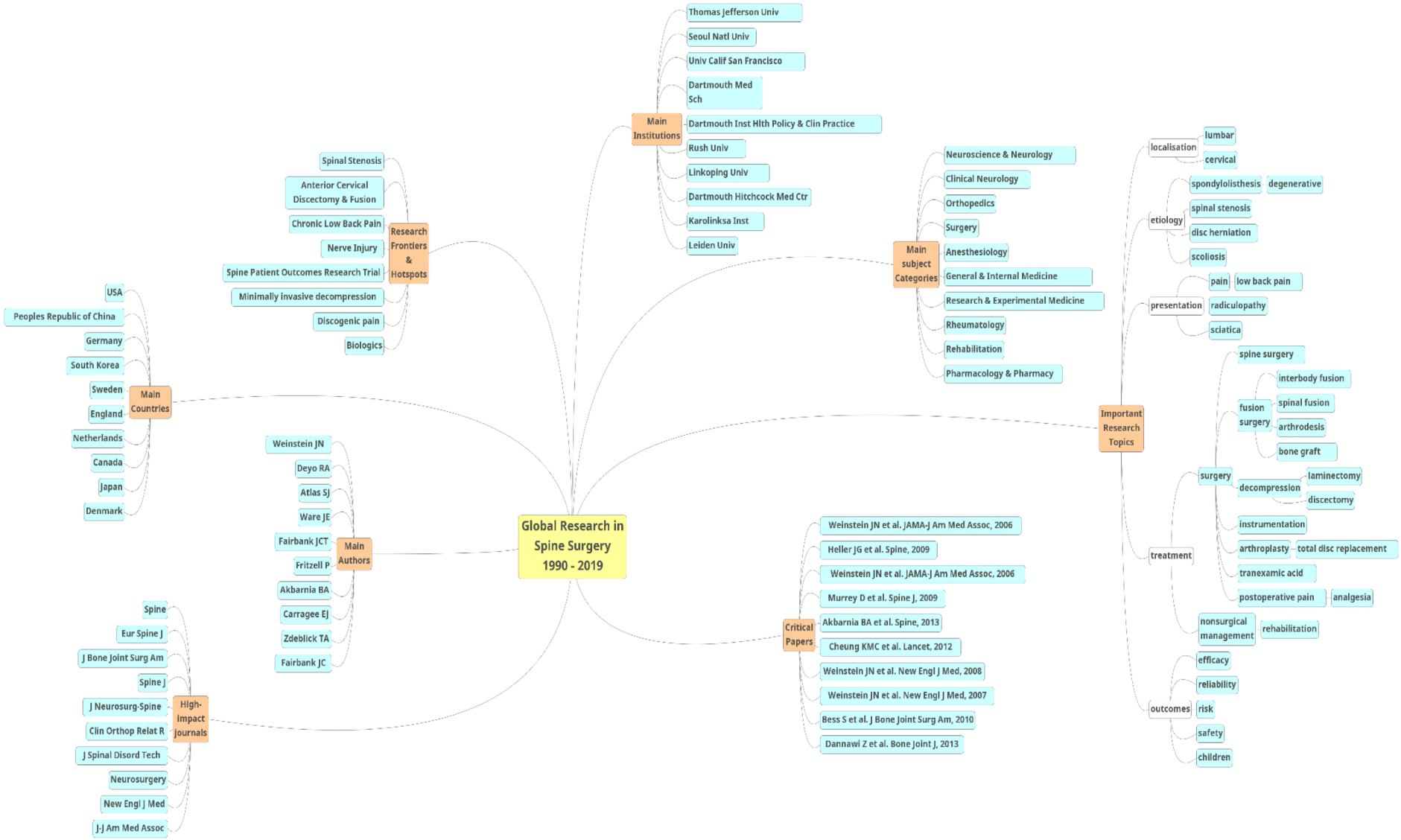


Figure 10 Comprehensive knowledge map in spinal surgery research: 1990–2019.

ARTICLE HIGHLIGHTS

Research background

Spinal surgery is evolving and in the due course of its evolution, it is useful to have a comprehensive summary of the process to have a greater understanding to refine our future directives.

Research motivation

With the multiple domains of research on the spine, it has become difficult for surgeons to find the potential hotspots in research or identify the emerging research frontiers.

Research objectives

To assess the potential research domains of randomized controlled trials (RCTs) for the past three decades (1990–2019), along with their research networks, and to identify the hot topics for future research.

Research methods

A comprehensive and systematic analysis of all the RCTs published on spinal surgery from 1990 to 2019 retrieved from the Web of Science Core Collection database. Scientometric and visual analysis of their characteristics, cooperation networks, keywords, and citations were made using CiteSpace software.

Research results

A total of 696 RCTs were published on spinal surgery from 1990 to 2019; of which, the United States (n = 263) and China (n = 71) made a significant contribution. Thomas Jefferson University (n = 16) was the leading contributor to RCTs. Weinstein JN was the most cited author in the field followed by Deyo RA. *Spine* (n = 559) remained the top-cited journal for RCTs on spinal surgery. On literature co-citation analysis, spinal stenosis, anterior cervical discectomy and fusion, degenerative disc disease, and minimally invasive decompression were identified as the hotspots and potential research frontiers.

Research conclusions

Research cooperation among developed and developing nations remains crucial and needs to be strengthened. It was evident from the identified hotspots that extending the frontiers in the management of degenerative disorders of the spine through further research holds the potential for advancement in spinal care.

Research perspectives

Our analysis revealed the key areas of ongoing research in spinal surgery to advance the management of spinal diseases like spinal cord injury, spondylolisthesis, spinal stenosis, intervertebral disc disease, and scoliosis. Since arthroplasty is a sought-after field of research in the orthopedic forum, the spine is no exception. However, recent trial are being conducted on surgical treatment methods like fusion surgery, decompression surgery, instrumentation surgery, and arthroplasty. With the current abundance of evidence on novel treatment methods using regenerative principles and mesenchymal stromal cells and their derivatives to combat various inflammatory and degenerative disorders, we except more upcoming trials investigating their role in spinal surgery.

FOOTNOTES

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REFERENCES

1 **Kabisch M**, Ruckes C, Seibert-Grafe M, Blettner M. Randomized controlled trials: part 17 of a series on evaluation of scientific publications. *Dtsch Arztebl Int* 2011; **108**: 663-668 [PMID: 22013494 DOI: 10.3238/arztebl.2011.0663]
2 **Hanson B**, Kopjar B. Clinical studies in spinal surgery. *Eur Spine J* 2005; **14**: 721-725 [PMID: 15940476 DOI: 10.1007/s00586-005-0926-2]
3 **Mingers J**, Leydesdorff L. A review of theory and practice in scientometrics. *Eur J Oper Res* 2015; **246**: 1-19 [DOI: 10.1016/j.ejor.2015.04.002]
4 **Frenken K**, Hardeman S, Hoekman J. Spatial scientometrics: Towards a cumulative research program. *J Informetr* 2009; **3**: 222-232 [DOI: 10.1016/j.joi.2009.03.005]
5 **Gobbur A**, Konkathi VK, Suresh Babu G, Chellamuthu G, Muthu S, Jeyaraman M. Past, Present and Future of Arthroscopic Research: A Scientometric Analysis of Research Frontiers in Arthroscopy. *Indian J Orthop* 2022; **56**: 521-532 [PMID: 35342515 DOI: 10.1007/s43465-021-00586-0]
6 **Zacca-González G**, Chinchilla-Rodríguez Z, Vargas-Quesada B, de Moya-Anegón F. Bibliometric analysis of regional Latin America's scientific output in Public Health through SCImago Journal & Country Rank. *BMC Public Health* 2014; **14**: 632 [PMID: 24950735 DOI: 10.1186/1471-2458-14-632]
7 **Tran BX**, Latkin CA, Vu GT, Nguyen HLT, Nghiem S, Tan MX, Lim ZK, Ho CSH, Ho RCM. The Current Research Landscape of the Application of Artificial Intelligence in Managing Cerebrovascular and Heart Diseases: A Bibliometric and Content Analysis. *Int J Environ Res Public Health* 2019; **16** [PMID: 31362340 DOI: 10.3390/ijerph16152699]
8 **López-Cózar ED**, Orduna-Malea E, Martín-Martín A. Google Scholar as a data source for research assessment. ArXiv180604435 Cs (e-pub ahead of print 18 June 2018) [DOI: 10.31235/osf.io/pqr53]
9 **Falagas ME**, Pitsouni EI, Malietzis GA, Pappas G. Comparison of PubMed, Scopus, Web of Science, and Google Scholar: strengths and weaknesses. *FASEB J* 2008; **22**: 338-342 [PMID: 17884971 DOI: 10.1096/fj.07-9492LSF]
10 **Martín-Martín A**, Orduna-Malea E, Thelwall M, Delgado López-Cózar E. Google Scholar, Web of Science, and Scopus: A systematic comparison of citations in 252 subject categories. *J Informetr* 2018; **12**: 1160-1177 [DOI: 10.1016/j.joi.2018.09.002]
11 Reference Citation Analysis. Artificial intelligence based open multidisciplinary citation analysis database. Available from: https://www.referencecitationanalysis.com/
12 **Chen C**. Science Mapping: A Systematic Review of the Literature. *J Data Inf Sci* 2017; **2**: 1-40 [DOI: 10.1515/jdis-2017-0006]
13 **Katz JS**, Martin BR. What is research collaboration? *Res Policy* 1997; **26**: 1-18 [DOI: 10.1016/S0048-7333(96)00917-1]
14 **Hirsch JE**. An index to quantify an individual's scientific research output. *Proc Natl Acad Sci U S A* 2005; **102**: 16569-16572 [PMID: 16275915 DOI: 10.1073/pnas.0507655102]
15 **Chen C**. CiteSpace II: Detecting and visualizing emerging trends and transient patterns in scientific literature. *J Am Soc Inf Sci Technol* 2006; **57**: 359-377 [DOI: 10.1002/asi.20317]
16 **Small H**. Co-citation in the scientific literature: A new measure of the relationship between two documents. *J Am Soc Inf Sci* 1973; **24**: 265-269 [DOI: 10.1002/asi.4630240406]
17 **Chen C**, Ibekwe-SanJuan F, Hou J. The structure and dynamics of cocitation clusters: A multiple-perspective cocitation analysis. *J Am Soc Inf Sci Technol* 2010; **61**: 1386-1409 [DOI: 10.1002/asi.21309]
18 **Hou J**, Yang X, Chen C. Emerging trends and new developments in information science: a document co-citation analysis (2009–2016). *Scientometrics* 2018; **115**: 869-892 [DOI: 10.1007/s11192-018-2695-9]
19 **World Health Organization**. Ageing and health. Available from: https://www.who.int/news-room/fact-sheets/detail/ageing-and-health
20 **Chen C**, Dubin R, Kim MC. Orphan drugs and rare diseases: a scientometric review (2000 – 2014). *Expert Opin Orphan Drugs* 2014; **2**: 709-724 [DOI: 10.1517/21678707.2014.920251]
21 **Vaishnav AS**, Othman YA, Virk SS, Gang CH, Qureshi SA. Current state of minimally invasive spine surgery. *J Spine Surg* 2019; **5**: S2-S10 [PMID: 31380487 DOI: 10.21037/jss.2019.05.02]
22 **Viswanathan VK**, Rajaram Manoharan SR, Subramanian S, Moon A. Nanotechnology in Spine Surgery: A Current Update and Critical Review of the Literature. *World Neurosurg* 2019; **123**: 142-155 [PMID: 30447449 DOI: 10.1016/j.wneu.2018.11.035]
23 **Walker CT**, Kakarla UK, Chang SW, Sonntag VKH. History and advances in spinal neurosurgery. *J Neurosurg Spine* 2019; **31**: 775-785 [PMID: 31786543 DOI: 10.3171/2019.9.SPINE181362]
24 **Lopez CD**, Boddapati V, Lee NJ, Dyrszka MD, Sardar ZM, Lehman RA, Lenke LG. Three-Dimensional Printing for Preoperative Planning and Pedicle Screw Placement in Adult Spinal Deformity: A Systematic Review. *Global Spine J* 2021; **11**: 936-949 [PMID: 32762378 DOI: 10.1177/2192568220944170]
25 **Gan G**, Kaliya-Perumal AK, Yu CS, Nolan CP, Oh JY. Spinal Navigation for Cervical Pedicle Screws: Surgical Pearls and Pitfalls. *Global Spine J* 2021; **11**: 196-202 [PMID: 32875902 DOI: 10.1177/2192568220902093]
26 **Plantz MA**, Hsu WK. Recent Research Advances in Biologic Bone Graft Materials for Spine Surgery. *Curr Rev Musculoskelet Med* 2020; **13**: 318-325 [PMID: 32323248 DOI: 10.1007/s12178-020-09620-4]

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CASE REPORT

Calcium pyrophosphate dihydrate crystals in a 9-year-old with osteomyelitis of the knee: A case report

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Abstract

BACKGROUND

Calcium pyrophosphate dihydrate deposition disease (CPPD), or pseudogout, is an inflammatory arthritis common among elderly patients, but rarely seen in patients under the age of 40. In the rare cases presented of young patients with CPPD, genetic predisposition or related metabolic conditions were almost always identified.

CASE SUMMARY

The authors report the case of a 9-year-old boy with no past medical history who presented with acute knee pain and swelling after a cat scratch injury 5 d prior. Synovial fluid analysis identified calcium pyrophosphate dihydrate crystals. Further MRI analysis identified osteomyelitis and a small soft tissue abscess.

CONCLUSION

This case presents the extremely rare diagnostic finding of calcium pyrophosphate dihydrate crystals in a previously healthy pediatric patient. The presence of osteomyelitis presents a unique insight into the pathogenesis of these crystals in pediatric patients. More research needs to be done on the role of CPPD in pediatric arthritis and joint infection.

Key Words: Calcium pyrophosphate; Pseudogout; Pediatrics; Crystals; Osteomyelitis; Case report

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Core Tip: Calcium pyrophosphate dihydrate deposition disease (CPPD) is rarely seen in patients under the age of 40. This case represents a rare diagnostic finding of CPP crystals in a 9-year-old patient. Previously, the youngest patients ever described in case reports were 16 years old. In the rare cases presented of young patients with CPPD, genetic predisposition or related metabolic conditions were almost always identified. In this case, the presence of osteomyelitis presents a unique insight into the pathogenesis of these crystals in pediatric patients. This case highlights the need for more research on the pathogenesis of these crystals and their role in pediatric arthritis and joint infection.

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INTRODUCTION

Calcium pyrophosphate dihydrate deposition disease (CPPD), formerly known as pseudogout, is a common inflammatory arthritis that may asymptomatically present as chondrocalcinosis or as episodes of acute calcium pyrophosphate (CPP) crystal arthritis. Increasing age is one of the strongest risk factors for the condition, with the condition rarely seen before the age of 40 and common in patients over 80[1]. In cases where the condition has been identified in patients under 40, risk factors such as genetic predisposition or metabolic disorders are almost always present[2]. In this report, we present the case of a 9-year-old male with no past medical history developing CPP crystals in the synovial fluid of the knee during an episode of osteomyelitis caused by cat scratch injury. The patient's mother consented to the publication of this case report and accompanying images.

CASE PRESENTATION

Chief complaints

A 9-year-old, African American male presented to the emergency room accompanied by his mother with right knee pain of 5 d duration.

History of present illness

The patient stated that the pain began after he was scratched by a cat 5 d prior to presentation. His mother noticed her son was not bearing weight on the right lower extremity 2 d after the incident. He described the pain as constant and worsening and aggravated by both passive movement of the knee and weight bearing of the extremity. The patient and his mother denied any history of fever or drainage from the wound but did report antecedent upper respiratory infection symptoms one week prior. He had not trialed NSAIDs or acetaminophen for the injury. The patient was in the 2nd grade and lived with both parents. The orthopedics service was consulted to rule septic arthritis of the right knee.

History of past illness

The patient had no past medical history.

Personal and family history

The patient had no relevant family history, including no history of metabolic disorders such as hereditary hemochromatosis or hyperparathyroidism.

Physical examination

Focused examination of the right lower extremity demonstrated warmth and swelling across the knee. Superficial scratches were noted across the anterolateral leg. One punctate wound on the lateral knee was noted without erythema or drainage. Thigh and leg compartments were soft and compressible. Significant pain was reproduced with both axial loading and passive range of motion of the knee from 0°-40°. Sensation and motor function were intact in all nerve distributions with palpable distal pulses and brisk capillary refill in all toes.

Laboratory examinations

Initial laboratory studies showed a white blood cell count of 8.9, C-reactive protein of 1.1, and erythrocyte sedimentation rate of 39. The patient had a calcium level of 9.7 and alkaline phosphatase of

209. Due to the clinical concern for septic arthritis, joint aspiration was performed. Aspiration yielded 10 mL of cloudy, viscous, yellow fluid. Follow-up cell counts of the synovial fluid yielded a glucose of 99, protein of 4.9, and a WBC of 7,345 with 59% polymorphic neutrophils. Positively birefringent, rhomboid shaped crystals were present and identified as calcium pyrophosphate dihydrate crystals. Bacterial and fungal cultures of the fluid were both negative for any growth. This synovial fluid analysis was suggestive of an inflammatory origin and a preliminary diagnosis of CPP arthritis was made.

Imaging examinations

Radiographs of the right knee demonstrated a joint effusion within the suprapatellar recess and trace effusion within Hoffa's fat pad (Figure 1). No chondrocalcinosis was observed. Follow-up ultrasound of the right knee was performed for comparison, which showed a simple fluid collection in the knee joint.

The patient was placed in an ace wrap for compressive dressing, started on oral ibuprofen, intravenous (IV) ceftriaxone and clindamycin, and admitted for additional work-up. Pediatric infectious disease was consulted and elected to continue ongoing antibiotic management and perform Bartonella titers, which were negative. On the third day of admission, MRI with IV contrast was performed and significant for a focal, intra-synovial area of enhancing, 6 mm cortical defect at the lateral border of the lateral femoral condyle (Figure 2). Additionally, a small joint effusion and subcutaneous soft tissue edema overlying the proximal tibia, rim enhancement suggestive of synovitis, and a collection within the inflammatory changes of the vastus lateralis with rim enhancement suggesting small abscess formation were also found.

FINAL DIAGNOSIS

A diagnosis of osteomyelitis was made with a rare, incidental finding of calcium pyrophosphate dihydrate crystals in synovial fluid analysis of the knee.

TREATMENT

Antibiotic management was changed to IV ampicillin-sulbactam due to concern for Pasteurella secondary to cat scratch. A diagnosis of CPPD was considered very unlikely due to the patient's young age, lack of previous episodes or family history of CPPD, and absence of other medical issues considered risk factors for CPPD, such as hyperparathyroidism, hereditary hemochromatosis, chronic kidney disease, or loop diuretic use.

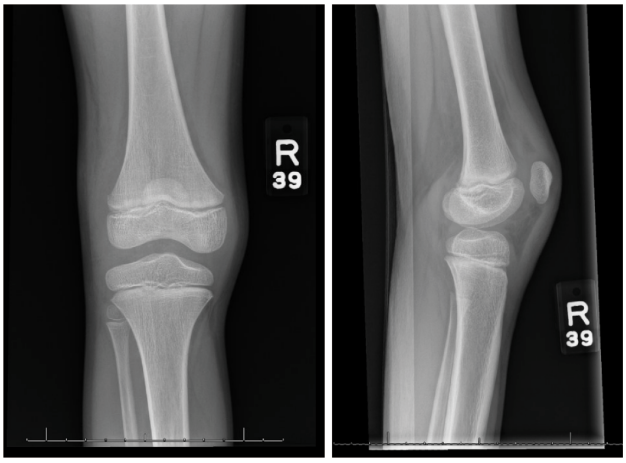
Debridement of the osteomyelitis and needle aspiration of the soft-tissue abscess were not performed due to the small size of the deformities and marked clinical improvement in the patient. Due to this, no cultures or drug sensitives of the abscess or bone were performed. By the fourth day of admission, the patient had remained afebrile, his CRP had decreased to less than 0.5, his right knee had become significantly less edematous, and he no longer endorsed pain or reduced range of motion. After final discussion with the infectious disease team, the decision was made to discharge the patient with a 4-wk supply of oral amoxicillin-clavulanate. The patient did not require physical therapy and was discharged without a walker. The patient was referred for follow-up in the infectious disease to ensure resolution of symptoms and monitor for side effects of antibiotic treatment. The mother was agreeable with the nonoperative management of her son and counseled to return to the emergency room if symptoms recurred.

OUTCOME AND FOLLOW-UP

At 6-wk follow-up, the patient was asymptomatic, had completed his course of oral antibiotics, and had returned to prior function. The patient's mother reported no ongoing noticeable disability or changes in her child. She reported overall satisfaction with the treatment of her child and the quality of care she received from the physician, nursing, and physical therapy staff during her son's hospitalization.

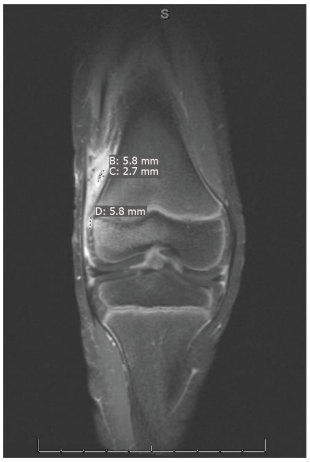
DISCUSSION

In this case, we present the rare finding of CPP crystals in the synovial fluid of a healthy 9-year old child with osteomyelitis and a soft-tissue abscess following minor knee trauma. CPPD is a common inflammatory arthritis with a strong association with increasing age. A community prevalence study in the United Kingdom found the mean age of individuals with the condition to be 63.7, with prevalence increasing from 3.7% in those aged 55-59 to 17.5% in those aged 80-84[3]. Cases are very rarely identified



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Figure 1 Anteroposterior (left) and lateral (right) radiographs of the right knee demonstrating evidence of a joint effusion within the suprapatellar recess and Hoffa's fat pad.



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Figure 2 Magnetic resonance imaging with intravenous contrast of the right knee demonstrating a small enhancing cortical defect along the lateral border of the lateral femoral condyle, measuring approximately 6 mm, suggestive of osteomyelitis. There is a collection within the inflammatory changes of the vastus lateralis demonstrating rim enhancement measuring approximately 0.6 cm × 0.2 cm representing tiny abscess formation.

in patients under the age of 40. In a study of a region encompassing one million people in Sweden, only 6 of 706 cases were identified in individuals under the age of 34, with the youngest patient being 20[4].

In the literature, few reports of CPPD in younger patients have been published, with most being associated with significant relevant co-morbidities[5-9]. The youngest cases of CPPD disease identified from the literature were two 16 year old patients in Germany[9]. The condition's occurrence in those younger than 55 has been linked to familial hereditary predisposition and metabolic conditions such as hyperparathyroidism, hemochromatosis, Wilson's disease, hypophosphatasia, and hypomagnesemia [2]. In two prior cases, patients presented with CPPD disease at age 24 and 31 despite no relevant co-morbidities or similar familial occurrence[6,7]. The patient in this case similarly demonstrated no metabolic or genetic abnormalities and lacked any similar family history. Acute attacks of CPPD are often found in the setting of acute joint trauma or illness, making this patients concomitant trauma and osteomyelitis a likely inciting factor[2]. However, the pathogenesis of this condition is still not fully understood, and this case highlights the need for more research on the role of join trauma and inflammation on the development of CPPD.

CPPD is frequently asymptomatic and believed to be severely underdiagnosed. One study found that CPP crystals were present in the synovial fluid of 30% of patients undergoing knee arthroplasty for osteoarthritis[10]. Diagnosis rates are dependent on methods of diagnosis. The identification of articular chondrocalcinosis on radiographs is a common means of diagnosis; however, studies of prevalence of the condition using this method vary widely based on the type and number of joints examined[1]. The most accurate form of diagnosis remains the identification of positively birefringent, rhomboid-shaped crystals in synovial fluid from the affected joint. In this study, no chondrocalcinosis was observed

despite the identification of CPP crystals in synovial fluid.

This study is limited by the short follow-up period. Further follow-up will be required to evaluate the significance of this finding in the setting of this young patient's acute injury. Additionally, this patient was not formally screened for several metabolic conditions associated with early-onset CPPD, such as hereditary hemochromatosis and hyperparathyroidism. Observation for repeat episodes of acute joint pain or the development of chondrocalcinosis will require further investigation for underlying causes of CPPD. However, this case report successfully presents findings of CPP crystals in a pediatric patient younger than any other previous reported in the literature. Further research could generate key findings on the pathogenesis of these crystals in the setting of trauma and infection in pediatric patients.

CONCLUSION

CPPD is a common form of arthritis with still relatively little known about its pathogenesis and prevalence. The condition is rarely identified in those under the age of 40. In this study, we present the rare case of a 9-year-old with CPP crystals in the synovial fluid of the knee during an episode of osteomyelitis. This rare finding presents further questions regarding the pathogenesis of the condition and its role in pediatric joint infection and arthritis. Future diagnostic studies among pediatric populations may identify additional cases of CPP crystals in children and shed new insights on the mechanisms of CPP deposition.

FOOTNOTES

Author contributions: Pavlis W is responsible for the data curation and write original draft; Constantinescu D is responsible for methodology; Pavlis W, Constantinescu D, Murgai R and Barnhill S participate in the investigation; Pavlis W and Constantinescu D are responsible for the project administration; Black B is responsible for supervision; all authors participate in the manuscript conceptualization, review and editing.

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REFERENCES

1 **Abhishek A**. Calcium pyrophosphate deposition disease: a review of epidemiologic findings. *Curr Opin Rheumatol* 2016; **28**: 133-139 [PMID: 26626724 DOI: 10.1097/BOR.0000000000000246]
2 **Rosenthal AK**, Ryan LM. Calcium Pyrophosphate Deposition Disease. *N Engl J Med* 2016; **374**: 2575-2584 [PMID: 27355536 DOI: 10.1056/NEJMra1511117]
3 **Neame RL**, Carr AJ, Muir K, Doherty M. UK community prevalence of knee chondrocalcinosis: evidence that correlation with osteoarthritis is through a shared association with osteophyte. *Ann Rheum Dis* 2003; **62**: 513-518 [PMID: 12759286 DOI: 10.1136/ard.62.6.513]
4 **Hameed M**, Turkiewicz A, Englund M, Jacobsson L, Kapetanovic MC. Prevalence and incidence of non-gout crystal arthropathy in southern Sweden. *Arthritis Res Ther* 2019; **21**: 291 [PMID: 31847885 DOI: 10.1186/s13075-019-2077-6]
5 **Bradley JD**. Pseudoseptic pseudogout in progressive pseudorheumatoid arthritis of childhood. *Ann Rheum Dis* 1987; **46**: 709-712 [PMID: 3675014 DOI: 10.1136/ard.46.9.709]

6 **Hammoudeh M**, Siam AR. Pseudogout in a young patient. *Clin Rheumatol* 1998; **17**: 242-245 [PMID: 9694062 DOI: 10.1007/BF01451057]

7 **Hayashi M**, Matsunaga T, Tanikawa H. Idiopathic widespread calcium pyrophosphate dihydrate crystal deposition disease in a young patient. *Skeletal Radiol* 2002; **31**: 246-250 [PMID: 11904695 DOI: 10.1007/s00256-002-0479-y]

8 **Unlu Z**, Tarhan S, Ozmen EM. An idiopathic case of calcium pyrophosphate dihydrate crystal deposition disease with crowned dens syndrome in a young patient. *South Med J* 2009; **102**: 949-951 [PMID: 19668044 DOI: 10.1097/SMJ.0b013e3181b08c26]

9 **Fuchsberger T**, Pillukat T, van Schoonhoven J, Prommersberger KJ. [Acute and chronic calcium pyrophosphate dihydrate deposition disease in young patients]. *Handchir Mikrochir Plast Chir* 2012; **44**: 181-183 [PMID: 22833073 DOI: 10.1055/s-0032-1321772]

10 **Derfus BA**, Kurian JB, Butler JJ, Daft LJ, Carrera GF, Ryan LM, Rosenthal AK. The high prevalence of pathologic calcium crystals in pre-operative knees. *J Rheumatol* 2002; **29**: 570-574 [PMID: 11908575]



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MINIREVIEWS

Hamstring autograft utilization in reconstructing anterior cruciate ligament: Review of harvesting techniques, graft preparation, and different fixation methods

Waleed Albishi, Baraa Baltow, Nora Albusayes, Ameer A Sayed, Hamza M Alrabai

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Abstract

Rupture of the anterior cruciate ligament (ACL) is a common orthopedic injury. Various graft options are available for the reconstruction of ruptured ACL. Using the hamstring muscle as an autograft was first described in 1934, and it remains a commonly harvested graft for ACL reconstruction. Hamstring autografts can be harvested using the traditional anteromedial approach or the newer postero-medial technique. An isolated semitendinosus tendon can be used or combined with the gracilis tendon. There are numerous methods for graft fixation, such as intra-tunnel or extra-tunnel fixation. This comprehensive review discusses the different hamstring muscle harvesting techniques and graft preparation options and fixation methods. It provides a comprehensive overview for choosing the optimal surgical technique when treating patients.

Key Words: Anterior cruciate ligament; Anterior cruciate ligament reconstruction; Graft fixation; Hamstring autograft; Infrapatellar nerve injury; Patient reported outcomes

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Core tip: Anterior cruciate ligament (ACL) rupture is a common orthopedic injury and various graft options are available for the reconstruction of a ruptured ACL. This comprehensive review discusses the different hamstring muscle harvesting techniques as well as graft preparation and fixation methods that can be used to guide clinicians in making evidence-based decisions when treating their patients.

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INTRODUCTION

The knee is a weight-bearing joint that gains stability through various supportive structures[1]. Limiting tibial translation, cruciate ligaments act as the greatest stabilizing force of the knee[2]. The anterior cruciate ligament (ACL) extends from the posteromedial aspect of the femoral lateral condyle to the tibial eminence in the anteromedial and posterolateral bundles. It functions by preventing anterior displacement of the tibia in the sagittal plane[1,2]. A common orthopedic complaint is the ACL injury. Sanders *et al*[3] reported in his 21-year population-based study that the annual incidence of ACL injury is 68.6 per 100 000 person-years.

The ACL can be injured by either a direct contact force to the knee or a noncontact mechanism by landing or deceleration motion which represents 70% of ACL cases[4]. Boden *et al*[5] described the event as a combination of the misdirected kinetic energies that results in the "twisting event" of a valgus knee and tibial internal rotation in addition to the columnar buckling effect.

Patients usually describe an ACL injury with an audible loud pop followed by an immediately swollen painful knee. Later, incidents of giving way to pivot movements may also occur[6,7]. Examination of the affected extremity is an effective diagnostic tool, whereas magnetic resonance imaging is the main diagnostic confirmatory tool. Although multiple factors influence the management of a patient with a ruptured ACL, limited data support the choice of a purely conservative management[6,8]. Various graft options are available for the reconstruction of a ruptured ACL. The two main graft categories are allografts [bone-patellar tendon-bone (BTB), hamstring, tibialis anterior and posterior, peroneal, Achilles] and autografts (BTB, quadriceps, and hamstring)[9]. The semitendinosus (ST) tendon, which is the hamstring tendon used for ACL rupture (ACLR), is found on the medial side of the knee between layer I (encompassing the sartorius muscle) and layer II (encompassing the superficial medial collateral ligament) as described by Warren *et al*[10] and Nichalas *et al*[11]. The insertion of the ST tendon is on the anteromedial aspect of the tibia on the conjoining structure of the pes anserinus together with the gracilis and sartorius tendons[12,13]. In general, better outcomes found in the literature support the use of autografts than allografts. Moreover, hamstring tendon autograft is one of the optimal choices for reconstructing a ruptured ACL. This is because of the lower failure rates in comparison to that of allografts and avoidance of anterior knee pain found with BTB grafts[9]. In 1934, Galliazi was the first orthopedic surgeon to describe the use of the hamstring tendon as an autograft for ACLR[14]. The aim of this review is to discuss the different hamstring muscle harvesting techniques, graft preparation options, and fixation methods.

The reference numbers will be superscripted in square brackets at the end of the sentence with the citation content or after the cited author's name, with no spaces.

METHOD/LITERATURE SEARCH

We searched for the following keywords in the PubMed database: hamstring autograft, hamstring harvest, infrapatellar branch of the saphenous nerve (IPBSN) injury, saphenous nerve injury, posteromedial hamstring harvest, semitendinosus autograft, gracilis tendon autograft, ACL fixation, and suspensory interference screws. The main review question was "What are the strategies of hamstring autografts available for ACL reconstruction?" and "How are they harvested, prepared, and fixated?" The article collection was not limited to PubMed search of the previously mentioned terms, and further studies were identified and retrieved through citations. Articles were assessed for relevance for inclusion in this review based on the titles and abstracts. The database was searched up to August 22, 2021. Non-English papers and case reports were excluded.

GRAFT HARVESTING

Anteromedial technique

Typically, the hamstring tendon is harvested using the anteromedial approach. The incision is performed medial to the anterior tibial tuberosity and 4–6 cm distal to the joint line. The direction and length of the incision differed based on the surgeon's preference. This is followed by dissection of the subcutaneous tissue until the sartorial tendon in layer I is exposed. Beneath this layer, the semitendinosus and gracilis tendons are found. Once the tendons are identified, harvesting can be performed in two ways: (1) Dissecting the tendons distally, stripping proximally with a closed stripper; and (2) using an open stripper proximally and then stripping distally with a closed stripper. In the first technique, a whip stitch is used for countertraction during harvest. Second, a right-angled retractor is used for countertraction while stripping the tendon[12,13,15,16].

Hamstring tendon harvest may be associated with complications including injury to the medial collateral ligament, premature amputation of the tendon, and injury to the infrapatellar saphenous nerve[12,13,17]. Several methods have been proposed to overcome these complications.

In dissecting through the sartorius tendon in layer I to reach the ST and GT, extreme caution and adequate anatomical knowledge are advocated to avoid injuring the superficial medial collateral ligament immediately below the two tendons in layer II[12,13]. In the new OLIBAS harvesting technique recently published, Olivos-Meza *et al*[17] proposed the use of the tibial tubercle and medial border of the tibia as landmarks for an easier harvest with fewer complications. MCL injury is suggested to be reduced by a couple of maneuvers in the dissection technique. First, the superficial dissection of the subcutaneous tissue using a No. 15 blade with a vertical incision line, followed by blunt dissection medially and laterally with retractors, and further cleaning of any remnants with 360° motion using wet gauze. Second, direct, safe access to the tendons between the sartorius tendon and MCL by blunt introduction of Kelly forceps into the over-elevation landmark representing the gracilis as seen through the incision while the knee is in 90º flexion. The semitendinosus tendon contains multiple accessory bands. Meticulous dissection of such bands is crucial to prevent harvesting of a graft shorter than expected. Before advancement of the stripper, scissors can be used to release bands while the tendon is taut forcefully by a Penrose drain if the surgeon has chosen a proximal to distal grafting direction or by the whip stitch if a distal to proximal direction is preferred[12,13]. Olivos-Meza *et al*[17] urged manual exploration of expansions by introducing the index finger along the tendon path and rotating it 360º. Any expansions felt should be exposed through the incision by a Kelly and cut. Colombet *et al*[18] described another approach in identifying all expansions. By pulling out expansions through the incision one by one using an alternative probe hook maneuver, more expansions are exposed. The stripper could be easily advanced 10 cm without resistance, indicating that no expansions were left. The direction of the stripper is proposed to reduce the risk of premature amputation when it is aimed at the origin of the ST, ischial tuberosity, or lesser trochanter when harvesting the GT[13]. Another issue that might require a surgeon to use another graft is retraction and loss of tendons during stripping. This complication is thought to be reduced in the OLIBAS technique by holding the tip of the tendon perpendicularly with strong forceps and rolling it multiple times until the knuckles of the surgeon's nondominant hand rest on the operated knee while advancing the stripper firmly and gently with the dominant hand[17].

The saphenous nerve gives rise to two branches as it exits the adductor canal: the infrapatellar and sartorial branches[19]. The IPBSN is a small cutaneous nerve supplying the anterior aspect of the knee, anterolateral aspect of the leg, and anteroinferior aspect of the knee joint capsule[20]. The sartorial branch provides sensory innervation to the medial aspect of the leg and ankle[19].

Injury to the IPBSN is a common complication of the anteromedial approach for ACL reconstruction. The reported prevalence of IPBSN injury using the anteromedial approach ranges from 21.1% to 83%[15,19-29]. This injury can cause hypoesthesia, dysesthesia, painful neuroma, and reflex sympathetic dystrophy[28]. Pagnani *et al*[12] and Solman *et al*[13] implemented a figure of four position with the knee flexed and the hip abducted and externally rotated during harvest. This position allows the saphenous nerve located on top of the gracilis at the posteromedial joint line to relax, reducing the risk of injury. Pękala *et al*[30] also recommended the use of a figure of four position. Despite the use of this configuration, Figueroa *et al*[28] in their prospective study found 77% of patients to have clinical hypoesthesia and electrophysiological denervation of the IPBSN postoperatively using a vertical incision. They concluded that this nerve injury must have occurred during the harvest since the saphenous nerve is far from the incision and would only be at risk during stripping where a sharp instrument is near. Mahmood *et al*[21] have conducted a similar study using an oblique anteromedial incision. They found that 24% of patients complained of hypoesthesia, and the same patients were found to have IPBSN injury on electrophysiological study. Sanders *et al*[15] performed a survey-based study of patients who underwent ACL reconstruction through a vertical anteromedial incision while also utilizing the figure of four position. Among the participants, 74% reported disturbed sensation. In their anatomical analysis, Sanders *et al*[15] concluded that injury to the SBSN and IPBSN can occur during tendon stripping, especially when using a mini-incision that obligates the surgeon to blindly harvest the tendons. An anatomical study aimed at describing the IPBSN course with regard to surgery around the knee was also conducted. The IPBSN was found to have a highly variable coarse, the most

common variant being the posterior pathway in 56% of the knees (arising along the inferior posterior border of the sartorius muscle), found alone in 28%, and in association with the intramuscular (piercing through the sartorius muscle) and/or the anterior pathway (anterior border of the sartorius muscle) in 28%. Walshaw *et al*[31] also concluded that the IPBSN is mostly damaged during tendon harvesting with the stripper owing to its close proximity to the ST and GT.

The lower prevalence of injury observed in the study by Mahmood *et al*[21] in comparison to Figueroa *et al*[28] and Sanders *et al*[15] can be attributed to the orientation of the incision. This may be attributed to the subcutaneous oblique course of the infrapatellar nerve inferior to the patella that occupies the anteromedial region of the knee with its multiple branches, as reported by Hunter *et al*[32]. Two meta-analyses found that the risk of IPBSN injury during ACL reconstruction was significantly higher with vertical incisions than with oblique incisions[30,33]. Pękala *et al*[34], by simulating differently directed incisions in an ultrasound study on healthy knees, have also documented a similar risk reduction for oblique incision over the vertical incision. Multiple randomized controlled trials have studied the effect of incision direction on this complication. Keyhani *et al*[25], Mousavi *et al*[27], Sabat *et al*[22], Joshi *et al*[23], and Luo *et al*[19] found a decreased risk of IPBSN injury using the oblique incision compared to that with a vertical traditional incision (Table 1).

In contrast, Chen *et al*[29] and Leiter *et al*[35] found no relationship between the incision direction and IPBSN injury. The larger incision length in these two studies may be the reason, as Luo *et al*[19] found that the average distance between the upper edge of the pes anserinus and IPBSN was 0.6 cm. Mahmood *et al*[21] found a significant association between incision length and risk of IPBSN injury. Moreover, the use of a shorter incision was strongly supported in the meta-analysis by Pękala *et al*[30] and Henry *et al*[20] in an anatomical study where they measured the safe distance between an incision and a nerve to be 0.82–0.87 cm (Table 1).

Shorter incisions with adequate access to the hamstring tendons have been proposed. In 2016, Colombet *et al*[18] suggested the use of a small 2-cm vertical incision over the palpable pes anserinus. This incision is intended to decrease the incidence of IPBSN injury and is the cosmetically preferred option. Direct access to the tendons can be achieved by a 3-cm horizontal incision over the fascia following careful soft tissue dissection using Metzenbaum scissors. In the OLIBAS technique, the unique anatomical landmark used for incision placement also plays a role in the use of a smaller vertical/oblique incision (1.5 cm), which allows for cosmetic benefit with direct access to the tendons. The incision is located on a horizontal line drawn between the two landmarks (tibial tubercle and medial border of the tibia) and divided into thirds, and a vertical or oblique incision is made in the second third. The risk of nerve injury is reduced during subcutaneous tissue dissection, as sharp dissection is only performed in a proximal–distal direction, while further medial–lateral dissection is performed bluntly with two Farabeuf retractors[17]. A unique inverted L-shaped incision of the sartorial fascia has been used by multiple surgeons to allow direct access to the hamstring tendons and reduce the risk of nerve injury[15,17,23]. In a cadaveric study, Tillett *et al*[36] proposed a uniquely placed incision, which is claimed to be located in a safe zone where neurological injury is prevented and direct access to tendons is achieved. This incision is inclined approximately 30° from the vertical, starting at a point 3 cm medial to the apex of the tibial tuberosity and ending 5 cm medial to it. The authors used this incision in 45 patients with no complications.

Ultrasound can readily visualize the IPBSN and its main trunks over the pes anserinus, which are at risk during skin incision. Therefore, preoperative identification of the anatomical distribution of the IPBSN by ultrasound is recommended to reduce the incidence of iatrogenic nerve injury by finding a safe area for the incision. However, smaller branches were not detected[30,34]. Regardless of the orientation of the incision, IPBSN iatrogenic injury remains an unavoidable complication of hamstring tendon harvesting using an anteromedial approach. The previous statement was supported by Leiter *et al*[35] since a safe zone to prevent IPBSN injury could not be found and nerve distribution was highly variable regarding the number and orientation of branches. Accordingly, an incision that is as small as possible and preferably oblique should always be the goal to limit the number of possibly injured branches[30,34,35]. Furthermore, multiple studies have demonstrated smaller areas of hypoesthesia in patients with oblique incisions than in those with vertical incision[19,22,35] (Table 1).

Posteromedial technique

To avoid some of the aforementioned complications, Franz *et al*[37] pioneered a new approach in harvesting the hamstring tendon from the popliteal fossa. Franz's technique starts with the leg in a figure of four position, with the knee in 60° flexion, allowing for relaxation and protection of the saphenous nerve. The incision is made horizontally on the popliteal crease on top of the semitendinosus tendon, which is palpable in the posteromedial aspect of the popliteal fossa. A visible anatomical landmark to help locate the incision is the Jobert's groove, which is described by Prenkopf, representing the space between the adductor muscle group from the ST. Vertical dissection of the fascia follows. A FiberTape suture is looped around the tendon. The tendon is pulled out through the incision while the knee is flexed to 90°, permitting visualization and dissection of the distal accessory insertions, and avoiding premature graft amputation. Distal-to-proximal harvesting is carried out with an open stripper first to release proximally. Afterwards, a closed tendon stripper is advanced to release the tendon from its insertion distally while palpating the stripper on the anteromedial aspect of the tibia with caution not

Table 1 Incision direction/length, neurological injury, area of hypoesthesia

Ref.	Direction/length of incision	Prevalence of IPBSN injury	Area of hypoesthesia
Keyhani *et al*[23], 2019	Vertical: 3.8 cm; Oblique: 2.7 cm	IPBSN 40%; Vertical 56.8%; Oblique 25%	Vertical 34.2 cm^2; Oblique 9.6 cm^2
Mousavi *et al*[25], 2018	Vertical: 5.1 cm; Oblique: 3.8 cm	IPBSN 83%; Vertical 95.8%; Oblique 61.3%	Vertical 59.9 cm^2; Oblique 11.5 cm^2
Sabat *et al*[29], 2012	Vertical: 4.1 cm; Oblique 3.8 cm	[1]IPBSN 48%; [1]Vertical 76%; [1]Oblique 32%	[1]Vertical: 44.6 cm^2; [1]Oblique: 14.4 cm^2
Joshi *et al*[23], 2016	Vertical: 3 cm; Oblique: 3 cm	IPBSN 21.1%; Vertical 25%; Oblique 16.36%	N/M
Luo *et al*[19], 2007	Vertical 3.4 cm; Oblique: 3.3 cm	IPBSN 48%; Vertical 65.7%; Oblique 24%	Vertical: 48 cm^2; Oblique: 8.4 cm^2
Sharaby *et al*[29], 2019	Vertical 5 cm; Oblique: 5.2 cm	IPBSN: 69.2%; Vertical: 39.5%; Oblique: 24%	N/M
Mahmood *et al*[21], 2020	Oblique: 2.9 cm	IPBSN: 24%	Oblique: 3.9 cm^2
Figueroa *et al*[28], 2008	Vertical: 1.8 cm	IPBSN: 77%	Vertical: 3.6 cm^2
Sanders *et al*[15], 2007	Vertical: 1.5-2 cm	IPBSN: 19%	N/M
Ochiai *et al*[24], 2017	Vertical: 1.8-2.5 cm	21.1%	N/M

[1]Six months postoperatively.
IPBSN: Infrapatellar branch of the saphenous nerve (total prevalence of hypoesthesia over the infrapatellar branch of the saphenous nerve distribution measured clinically); N/M: No mention.

to perforate the skin. The same incision can be used to harvest the gracilis if the surgeon chooses to follow the same procedure[37].

Kodkani *et al*[38] implemented a posteromedial technique with some modifications. A small incision (1–1.5 cm) was made horizontally at the same location as described by Franz. To grant better access to the tendons, the knee was flexed at 30° and externally rotated. Knee flexion was increased for optimal identification and cutting of distal fibrous bands. After freeing the tendon proximally, the distal insertion was released while the knee was completely flexed and internally rotated. In a review of eight cases, Kodkani *et al*[38] reported zero intraoperative and postoperative complications, and all patients had satisfactory cosmetic results. Letartre *et al*[39] further modified this technique. During the procedure, the surgeon conveniently faced the posterior aspect of the knee. This view was achieved while the hip was flexed, and the knee flexed at 20°. An assistant held the limb up by the foot and applied external rotation. A 3–4-cm horizontal incision over the palpable ST was then made. Proximally, the tendon was harvested at 120° flexion. Distal harvesting was performed using a closed, short stripper. In an evaluation of 90 patients prospectively, a complete failure of harvest was reported during their first attempt for the posteromedial approach that required conversion to the anterior approach. In another case, the gracilis was harvested mistakenly instead of the semitendinosus, while in two cases, the ST alone resulted in a weak graft that was reinforced by the gracilis. In addition, no premature ambulation of the graft or sensory deficit occurred in any of the patients.

Wilson *et al*[40] described a vertical posteromedial incision. This incision was made while the leg was in a figure of four position, starting from the popliteal crease where the ST was palpable and extended 2–3 cm proximally. The longitudinal orientation of the incision was thought to improve wound healing, prevent wound complications, and provide a cosmetically appealing option. The tendon was extracted from the wound, and fibrous extensions were dissected until no calf pinching was visible, which indicated missed bands. Proximal to distal stripping was then performed.

A double incision technique using both an anterior and a posterior incision was described by Prodromos *et al*[41] with a posterior 2-cm incision while the knee was in 30° flexion in a figure of four position. The incision could be performed vertically or horizontally using the ST as a starting point. Both the ST and GR were pulled out through the wound and held by Penrose drains. The anterior 2-cm incision was made at the ST insertion, as guided by the surgeon's index finger, following the course of the tendon from the posterior, and tenting the skin which marks the location. The incision was obliquely inclined at 45° in relation to the tibia and perpendicular to the pes anserinus. The tendon was harvested proximally with an open stripper from the anterior incision and passed through the posterior incision. At this point, the tendon could be delivered through an anterior incision, and distal release was initiated by cutting the periosteum along the superior and inferior edges of the pes anserinus with a scalpel. Strong pulling of the tendons resulted in periosteal elevation of 1 cm approximately along with the tendon. The attached part of the periosteum was incised sharply. This was thought to increase the length of the tendon by adding 1 cm of periosteum and approximately 2 cm of pes anserinus. Accessory tendons were cut with a no. 15 blade or Metzenbaum scissors as they obscured the advancement of the stripper. In a chart review of 175 patients who underwent this technique, no intraoperative difficulties or complications were encountered. The wounds healed without further complications except for one

Table 2 Advantages of using the posteriomedial approach to harvest hamstring tendons

Advantages of the posteriomedial hamstring harvesting approach over the anteromedial approach
Better cosmetic appearance
Lower risk of infrapatellar branch of the saphenous nerve injury
Direct visualization of the bands attached to the hamstring tendons which facilitate their release
Lower risk of premature amputation of the harvested grafts
Easier approach when harvesting of a single tendon is desired
Lower risk of medial collateral ligament injury
Smaller incision for the tibial drill guide with the advantage of placing the incision in the desired location

incidence of anterior cellulitis that was managed conservatively with antibiotics. Wound healing and cosmesis were thought to be superior in the posterior incision. In fact, 80% of patients thought they had a better scar appearance compared to that of others who underwent ACL reconstruction[41].

Khanna *et al*[42] recently described a posterior hamstring harvesting technique for pediatric and adolescent subjects. The incision was made horizontally 2–3 cm in length over the palpable ST, while the leg was abducted, and externally rotated. A proximal-to-distal harvest was adopted. The semitendinosus accessory band was excised and the gracilis was harvested in a similar manner. A total of 214 patients were followed up for a minimum of 6 mo for complication analysis. In all cases, the tendons were identified intraoperatively, and no incidence of premature graft transection was reported. No wound healing issues, painful scars, restriction of knee motion due to incision location, or neurovascular injuries were observed. The patient also reported no cosmetic concerns.

Anteromedial versus posteromedial technique

The traditional anteromedial hamstring harvest was compared with the posteromedial approach as described by Franz *et al*[37]. They conducted a randomized controlled trial (RCT) with 100 patients and found that the average ST harvest time was significantly lower in the posteromedial group. Although the harvested graft was sufficient in length for both groups, the average length was significantly longer in the anteromedial group with a 2-cm difference. Fourteen percent of patients in the anteromedial group reported sensory deficits along the distribution of the saphenous nerve, compared to zero sensory issues in the posteromedial group. Pain scores using the visual analog scale were similar in both groups. No wound complications were found in the posteromedial group, whereas one case in the anteromedial group had a superficial wound infection which was treated conservatively with oral antibiotics. Patients who underwent a posteromedial incision had a significantly smaller incision than those who underwent a vertical anteromedial incision.

Shu *et al*[43] retrospectively reviewed 29 patients who underwent a posteromedial harvest as described by Wilson *et al*[40]. Among these patients, 22 underwent an anteromedial harvest. Operative and tourniquet times were significantly lower in the posteromedial group. This could be explained by the ease of tendon and accessory band identification using the posteromedial approach. The posteromedial group also had a reduced risk of unintentionally harvesting the gracilis. Both groups had no incidence of premature tendon amputation or IPBSN injury. The patients were then contacted for subjective knee scores, including Knee Osteoarthritis and Outcomes Score, Western Ontario and McMaster Universities Osteoarthritis Index, and International Knee Documentation Committee score (IKDC). All scores showed no significant differences between the two groups.

In the posteromedial incision, tendons are readily identified, and adequate exposure of all extensions and accessory insertions can be achieved[38,40]. Specifically, the most important ST accessory insertion found in 90% of patients is attached to the medial head of gastrocnemius. This band is found 2.6 cm below the posterior incision and 7.6 cm away from the anterior approach[44]. Posterior direct access to the tendon can be achieved even in obese patients, as the tendons are palpable posteriorly and have little subcutaneous tissue coverage[37]. Roussignol *et al*[44] found that a 3-cm posterior incision was sufficient in identifying tendons and cutting accessory insertions with the complete avoidance of premature transection of the graft.

Neurological injury of the saphenous nerve and its branches is avoided in a posterior approach, as the nerve is protected from the sharp stripper by the sartorial fascia that is left intact in this technique[38,44]. Therefore, none of the studies included in this review reported such complications following the posteromedial approach (Table 2).

In a prospective clinical study, Ochiai *et al*[24] reported a low IPBSN injury rate of 21.1% following an anteromedial approach using a vertical incision. This may be explained by the long follow up of 24 mo compared with the 77% at 3 wk post reconstruction in the study by Figueroa *et al*[28]. Luo *et al*[19], Sabat *et al*[22], Leiter *et al*[35], and Chen *et al*[29] reported that the area of sensory disturbances healed over time. Similarly, Joshi *et al*[23] reported gradual improvement in paresthesia within a year. Recovery was

also noted to be faster with an oblique incision than with a vertical incision. A hypothesis generated to support the difference was that in the oblique incision, IPBSN injury results in neuropraxia, while the vertical incision results in a neurotmesis injury[23]. Sabat *et al*[22] and Mousavi *et al*[27] reported higher satisfaction rates in patients who underwent oblique incision than in those who underwent vertical incision. In contrast, Grassi *et al*[33] reported that the incision orientation had no impact on the Lysholm score or patient subjective satisfaction. Ochiai *et al*[24] reported no significant difference in Lysholm score, visual analog scale pain score, patient-based SF-36, and presence of anterior knee pain in relation to IPBSN injury. However, patients with IPBSN were found to be significantly less satisfied than patients without this complication[21]. Apart from the above-mentioned studies, Sanders *et al*[15], Keyhani *et al*[25], Figueroa *et al*[28], and Sabat *et al*[22] reported that the majority of patients with a neurological injury post-operatively thought that it had no significant effect on their daily activities.

GRAFT PREPARATION

Once the hamstring tendons are completely harvested, muscular remnants are removed. Based on the choice to harvest the semitendinosus alone or together with the gracilis, the preparation differs. For a four-strand (quadrupled) semitendinosus graft (4-ST), the ST is folded with a nonabsorbable suture in the middle, and the two ends are stitched with a nonabsorbable suture. The graft is folded again with a nonabsorbable suture in the middle, held on a suspensory device, and whipstitched from proximal to distal. In case both semitendinosus and gracilis (2ST-2GT) are harvested, a four-strand graft is created with both tendons folded and loaded on a suspensory device. A nonabsorbable suture is passed twice around the free ends, and the tendons are whipstitched with a nonabsorbable suture once from distal to proximal, and again from proximal to distal[45]. These graft options are most commonly used when hamstring autografts are preferred[46].

4ST versus 2ST-2GT hamstring autograft

To guide the choice between 4ST and 2ST-2GT autografts, multiple investigators have compared patient-reported outcomes as well as hamstring muscle strength following ACL reconstruction. Ardern *et al*[47] stated that harvesting the gracilis along with the semitendinosus resulted in a deficit in isometric strength at deep knee flexion angles. Furthermore, Sharma *et al*[46] also found a large difference between ST autograft subjects and STGT autograft subjects in isometric strength at deep flexion angles in a meta-analysis. A significant decrease in active knee flexion angle after STGT harvesting has been reported[46,47]. Similar with isometric strength, active knee flexion is evaluated while the hip is in relative extension, aiding in demonstrating hamstring muscle insufficiency. A significant difference in isokinetic peak torque was found by Chin *et al*[48]. This deficit is rarely found in the literature because the isokinetic flexion peak torque is generated at shallow angles that are produced by the contraction of the biceps femoris rather than the semitendinosus and/or gracilis. Additionally, the peak torque is measured while the hip is flexed to 90, a suboptimal position for the hamstring to flex the knee[47].

In an RCT, Tashiro *et al*[49] evaluated hamstring muscle strength and compared the results between patients who had both tendons harvested and patients with isolated ST harvest. The STGT group had significantly weaker isometric and isokinetic hamstring strength than the group with preserved gracilis. Both groups were found to have significantly weaker hamstrings at angles of 70° and deeper in isokinetic and isometric evaluations compared to the preoperative status. Similarly, Nakamura *et al*[50] found a significant hamstring strength deficit identified using isokinetic testing at 90° in both groups. However, no difference was observed between the STGT and ST groups. A significantly lower active knee flexion angle in the STGT group was found. Hu *et al*[51] reported a significantly higher strength deficit in the STGT group during isometric flexion at 90°. A trend of increasing deficit with increasing angle was also noted[49,51]. A loss in active knee flexion angle was significantly higher in the STGT group than in the ST group in a prospective review by Adachi *et al*[52]. However, no significant difference was reported in hamstring isokinetic strength evaluation[52]. Yosmaoglu *et al*[53] in another prospective review reported a significantly higher hamstring isokinetic deficit in flexion at 60° in subjects post-STGT autograft harvest than in subjects post-ST autograft harvest. Three RCTs by Carter *et al*[54], Karimi-Mobarakeh *et al*[55], and Gobbi *et al*[56]; two prospective cohort studies by Inagaki *et al*[57] and Segawa *et al*[58], and three retrospective studies by Ardern *et al*[59], Barenius *et al*[60], and Lipscomb *et al*[61] found no difference in flexion hamstring strength deficit after ACL reconstruction with an isolated ST harvest or a combined ST and GT harvest. Of the studies included in this review, only two investigated rotational muscle strength and compared patients after STGT autograft and ST autograft. Segawa *et al*[58] in their prospective review have reported a significantly higher deficit of internal rotation at 30° and 120° in the STGT group. This same strength deficit was found to be significantly more common in females than in males. Additionally, Gobbi *et al*[56] found a significantly greater deficit in isokinetic internal and external rotation at 60°.

The large number of articles with different study designs that reported no difference in hamstring strength between the two groups could be attributed to the method of strength evaluation used[47].

Table 3 Hamstring graft preparation techniques: summary of results

Graft preparation		
Ref.	**Study design**	**Results/conclusion**
Ardern *et al* [47], 2009	Systematic review	ST-GT autograft have a significantly higher deficit in isometric strength at knee flexion ≥ 70°. Significant standing knee flexion angle deficit in the ST-GT autograft group.
Sharma *et al* [46], 2015	Meta-analysis	ST-GT group had a significantly higher isokinetic hamstring strength deficit at 60°. ST-GT group had a significantly higher isometric hamstring strength deficit at 90°, 105°, 110°. ST-GT group had a significantly higher standing knee flexion angle deficit.
Chin *et al*[48], 2018	Meta-analysis	ST-GT group had a significantly increased s deficit in isokinetic peak torque when compared with ST group for flexion at 60°/s at 2-yr follow-up, and flexion at 180°/s at 1- and 2-yr follow-up.
Tashiro *et al* [49], 2003	RCT	ST-GT group had a significantly increased deficit in isokinetic peak torque measured at knee flexion 60°/s at 80°, 90°, 110° when compared with ST group at 18 mo postoperatively. ST-GT group had a significantly higher isometric hamstring strength deficit at 70° measured in sitting position at 18 mo postoperatively. ST-GT group had a significantly higher isometric hamstring strength deficit at 70° and 90° measured in prone position at 18 mo postoperatively. Both groups showed significant isometric and isokinetic strength deficit when compared to preoperative measures.
Nakamura *et al*[50], 2002	Consecutive sample, case–control study	ST-GT group had a significantly higher standing knee flexion angle deficit. Decreased isokinetic torque at 90° in both groups.
Hu *et al*[51], 2020	Retrospective comparative	ST-GT group had a significantly higher isometric hamstring strength deficit at 90° flexion. Significant difference in the KOOS pain score.
Adachi *et al* [52], 2003	Prospective review	ST-GT group had a significantly higher standing knee flexion angle deficit.
Yosmaoglu *et al*[53], 2011	Prospective review	ST-GT group had a significantly higher hamstring isokinetic flexion strength deficit at 60°/s.
Carter *et al* [54], 1999	RCT	No difference in isokinetic strength deficit between ST-GT and ST groups, measured at 180°/s and 300°/s. Majority of patients had activity limitation at 6 mo postoperatively.
Karimi-Mobarakeh *et al*[55], 2014	RCT	No difference in isometric strength deficit between ST-GT and ST groups, measured at 90° flexion, extension, adduction, or abduction. No difference in patient outcome measures between ST-GT and ST groups.
Gobbi *et al* [56], 2005	RCT	ST-GT group had a significantly higher hamstring isokinetic internal and external rotation strength deficit at 60°/s.
Inagaki *et al* [57], 2013	Prospective comparative	No difference in isokinetic strength deficit between ST-GT and ST groups, measured at 60°/s. No difference in anterior laxity, or knee ROM. No difference in patient reported outcomes.
Segawa *et al* [58], 2002	Prospective study	ST-GT group had a significantly higher hamstring isokinetic internal rotation at 120°/s and 30°/s.
Ardern *et al* [59], 2010	Retrospective comparative	No difference in isometric strength deficit between ST-GT and ST groups, at 30°, 90°, or 105°. No difference in isokinetic strength deficit between ST-GT and ST groups, measured at 60°, 90°, and 105° or 60°/s and 180°/s. No difference in standing nee flexion angle between ST-GT and ST groups.
Barenius *et al* [60], 2013	Retrospective study	No difference in isokinetic strength deficit between ST-GT and ST groups, at 20°, and 90° measured at 60°/s. No difference in isometric strength deficit between ST-GT and ST groups at 90°.
Lipscomb *et al* [61], 1982	Retrospective study	No difference in isokinetic strength deficit between ST-GT and ST groups, measured at 60°/s and 240°/s.

ST-GT: Semitendinosus and gracilis; ST: Semitendinosus; RCT: Randomized control trial; KOOS: Knee osteoarthritis and outcomes score.

Most studies assessed the strength deficit with isokinetic testing which was done in a sitting position while the hip was 90° flexed, a position that did not allow the ST and GT muscles to contract concentrically to produce knee flexion where a deficit could be spotted. Another explanation is that the isokinetic peak torque is usually measured at shallow angles. Here, knee flexion is elicited mostly by biceps femoris contraction, while the semitendinosus and gracilis muscle function is best evaluated at deeper angles[47]. In contrast, a reported strength deficit was elicited by Ardern *et al*[59] as a result of poor rehabilitation or early assessment, where the muscles have not recovered fully.

Despite the significance in hamstring strength, the previously mentioned studies reported no difference in subjective patient-reported outcome scores[46-49,55-60]. In addition, Hu *et al*[51] found a significant difference in the pain section of the knee injury and osteoarthritis outcome score. This can be attributed to the fact that the strength deficit is only observed in such deep angles and is not utilized by most people in their daily activities and is specifically used by athletes in gymnastics, judo, and wrestling (Table 3)[46,47,52].

GRAFT FIXATION

Currently, there are many methods for femoral-sided graft fixation in ACL reconstruction. They can be categorized into two main types: intra-tunnel fixation (interference screw) and extra tunnel fixation (cortical fixation devices or femoral loops). Fixation of soft tissue grafts is generally considered a weak point early in the postoperative course after ACL reconstruction[62]. Therefore, many different devices have been developed for soft-tissue femoral fixation[63]. Despite numerous options, the gold standard for femoral fixation has not yet been identified[63].

Suspensory fixation

Fixation methods can be categorized into compression, expansion, and suspension. Suspensory devices can be subdivided into cortical (metal plates with or without suture loops), cancellous, and corticocancellous devices[64]. Suspensory fixation devices can maximize the amount of graft in the femoral tunnel, thereby improving the outcomes of ACL reconstruction. Suspensory devices commonly feature a button that rests on the cortex of the femur and a loop that holds the folded soft tissue ACL graft in position until healing can occur[65-68]. This technique can avoid common problems that occur with interference screw fixation, such as divergent screw placement, laceration of sutures or grafts by screw threads, and increasing difficulty of revision surgery in the presence of screws[69].

Interference screw fixation

Because of its capacity to resist cyclic movements, one of the most efficient fixation devices are interference screws. The interference screw is a conical threaded device inserted into the bone tunnel, compressing the graft against the tunnel walls, and fixing it in the desired position. Although it is more commonly used on the tibial side; this screw can also be used for femoral fixation. Interference screws may be composed of metals or bioabsorbable materials[70]. A review article by Debieux *et al*[70] showed no difference in self-reported knee function and patients' postoperative activity levels when comparing bioabsorbable interference screws with metallic interference screws. However, bioabsorbable screws may be associated with overall treatment failures, including implant breakage during surgery.

Suspensory fixation versus interference screw fixation

There is no consensus on the best method to achieve hamstring autograft fixation during ACL reconstruction. Intra-tunnel fixation methods predominantly rely on the use of metal or bioresorbable interference screws. Extra-tunnel fixation methods rely on buttons, staples, or washer-post combinations placed outside the tunnel over the adjacent cortical bone surface[71]. Based on the literature review, each fixation has its own advantages and disadvantages for achieving early and long-term successful ACL reconstruction. Regarding the incidence of graft lengthening under cyclical loads after ACL reconstruction, Boutsiadis *et al*[72] assessed anterior knee laxity following primary ACLR. They found that the use of an adjustable loop suspensory fixation device for femoral fixation was associated with noninferior postoperative anterior knee laxity results compared with interference screw fixation at a minimum 2-years' follow-up. The operative pivot shift was the only significant risk factor for postoperative residual anterior knee laxity > 3 mm.

Regarding tunnel widening, a meta-analysis comparing the clinical results of the all-inside (ACLR) technique using suspensory cortical button fixation to a whole tibial tunnel drilling technique with interference screw fixation has shown that all-inside ACLR with suspensory cortical button fixation was not clinically superior in terms of functional outcomes, knee laxity measured with an arthrometer, or re-rupture rate. However, the advantage of using suspensory cortical button fixation is the ability to utilize a thicker graft and a lower rate of tibial tunnel widening[73]. In addition, Baumfeld *et al*[74] found significantly more femoral tunnel widening associated with the endobutton suspensory fixation system compared to double cross-pin fixation in the tunnel. However, they found a significant difference in the amount of tibial tunnel widening between the groups in this study[74]. A prospective comparative study by Sabat *et al*[75] compared the incidence of tunnel widening in patients who underwent ACL reconstruction with a quadrupled hamstring graft using either endobutton CL or Transfix on the femoral tunnel side and bioabsorbable interference screws in the tibial tunnel using computed tomography scans. Femoral tunnel widening was significantly lower in the Transfix group than in the EndoButton group. Regarding tunnel drilling techniques, Saygi *et al*[76] investigated the effect of tunnel undersizing (tight fit ACL reconstruction technique) on tunnel widening and overall clinical outcomes compared with conventional ACL reconstruction techniques. They concluded that undersized drilling might be preferred when using button fixation to reduce tunnel widening and improve clinical satisfaction.

Each fixation device has biomechanical properties that have been demonstrated in several studies. Shen *et al*[77] compared cross-pin to endobutton-CL femoral fixation and found that they are equally strong and safe fixation options for ACL reconstruction. However, cross-pin fixation has significantly less displacement of the femur-graft-tibia complex than endobutton-CL fixation in response to the cyclic loading test. Thus, it could be considered when early aggressive rehabilitation following ACL reconstruction is required. Milano *et al*[64] found that corticocancellous suspension fixation obtained

Table 4 Hamstring graft fixation techniques: summary of results

Graft fixation		
Ref.	**Study design**	**Results/conclusion**
Boutsiadis *et al* [72], 2018	Cohort study; level of evidence, 3	No difference in postoperative anterior knee laxity at a minimum 2 yr follow-up between interference screw and ALSF device for femoral fixation. The preoperative pivot shift is the only significant risk factor for postoperative residual anterior knee laxity more than 3 mm.
Shanmugaraj *et al*[81], 2020	Systematic review and meta-analysis	No significant differences in complication rates between femoral press-fit and femoral metal interference screw fixation. Press-fit fixation had significant improvements in functional outcome scores postoperatively and had significantly reduced postoperative bone tunnel enlargement compared to bioabsorbable fixation.
Debieux *et al* [70], 2016	Review	No difference in self-reported knee function and levels of activity between bioabsorbable and metallic interference screws. Bioabsorbable screws may be associated with more overall treatment failures, including implant breakage during surgery.
Han *et al*[62], 2012	Level II, systematic review of level I and II studies	At a minimum of 2 yr follow-up, comparable outcomes based on objective IKDC, Lysholm knee scale, and Tegner activity level survey results were found, as well as anterior knee joint laxity measurements between intra-tunnel and extra-tunnel fixation. Intra-tunnel fixation began jogging/running earlier than patients who received extra-tunnel fixation. However, return to sports timing was comparable between the groups.
Hu *et al*[80], 2017	Systematic review and meta-analysis	The significantly decreased instrumented side-to-side anterior–posterior laxity difference achieved by cross-pin transfixation appears to be of limited clinical significance when compared with interference screw fixation in primary hamstring ACLR.
Fu *et al*[73], 2020	Systematic review and meta-analysis	Suspensory cortical button fixation was not clinically superior to interference screw fixation in functional outcomes, knee laxity measured with arthrometer, or re-rupture rate. The advantage of using suspensory cortical button fixation was that a thicker graft could be used for reconstruction, and brought less tibia tunnel widening compared with bioabsorbable interference screw fixation.
Saccomanno *et al*[63], 2014	Systematic review of randomized controlled trials	There are no short- to medium-term differences in knee-specific outcome measures between cortical button femoral graft fixation and suspensory transfemoral fixation In addition, radiological evidence of tunnel widening does not seem to affect short- to medium-term clinical outcomes.
Speziali *et al* [79], 2014	Systematic review of level I and II therapeutic studies	Side-to-side anterior-posterior tibial translation was 1.9 ± 0.9, 1.5 ± 0.9, 1.5 ± 0.8, 2.2 ± 0.4 mm for metallic interference screw, bioabsorbable screw, cross-pin and suspensory device, respectively. Rate of failure was 6.1%, 3.3%, 1.7% and 1.2% for bioabsorbable interference screw, metallic interference screw, cross-pin and suspensory device, respectively.
Baumfeld *et al* [74], 2008	Retrospective review	There was significantly more femoral tunnel widening associated with the use of the endobutton suspensory fixation system compared to the use of double cross-pins fixation.
Milano *et al*[64], 2006	Biomechanical analysis	Corticocancellous suspension fixation offer the best results in terms of graft elongation, fixation strength, and stiffness. Cancellous suspension fixation was homogeneous with other suspension fixation mechanisms but significantly weaker. Interference screws, both metallic and absorbable, showed low failure load but greatest graft elongation.
Sabat *et al*[75], 2011	Level II, prospective comparative study	Femoral tunnel widening was significantly less in the Transfix group compared with the endobutton group.
Saygi *et al*[76], 2015	Therapeutic case series, level IV	Undersize drilling technique is preferred in button fixation in order to reduce tunnel widening and improve clinical satisfaction.
Shen *et al*[77], 2008	Biomechanical comparison study	The cross-pin fixation is a good option for early aggressive rehabilitation following ACL reconstruction due to has significantly less displacement of femur–graft–tibia complex than that of endobutton-CL fixation in response to the cyclic loading test.
Vertullo *et al* [78], 2019	Controlled laboratory study	The suspensory fixation constructs exhibited small yet statistically significant biomechanical differences among each other. Tibial screw fixation had lower ultimate failure load and higher total elongation.

ALSF: Adjustable-loop suspensory fixation; IKDC: International Knee Documentation Committee; ACLR: Anterior cruciate ligament rupture; ACL: Anterior cruciate ligament; CL: Cruciate ligament.

with transcondylar devices offered the best results in terms of graft elongation, fixation strength, and stiffness. Cancellous suspension fixation was homogeneous with other suspension fixation mechanisms but was significantly weaker. Interference screws, both metallic and absorbable, showed a low failure load but the greatest graft elongation. They concluded that the mechanical behavior of cortical suspension fixation was strictly correlated with the area of the contact surface between the hardware and cortical bone and the structural properties of the implant. Vertullo *et al*[78] conducted a biomechanical study comparing quadrupled tendon graft constructs with adjustable loop suspensory fixation to four-strand graft constructs secured with screws and a femoral fixed-loop device. They found small, yet significant, biomechanical differences between the different techniques. In addition, they found that tibial screw fixation resulted in a lower ultimate failure load and higher total graft elongation. Another study compared the different fixation techniques for ACLR. On the femoral side, a cross-pin, a metallic interference screw, a bioabsorbable interference screw, and a suspensory device were used in 32.3%, 27.3%, 24.8%, and 15.5% of the patients, respectively. On the tibial side, a metallic interference screw, a

bioabsorbable interference screw, a screw and plastic sheath, a screw post, and a cross-pin were used in 38.7%, 31%, 15.7%, 12.8%, and 1.7% of the patients, respectively. The side-to-side anterior–posterior tibial translation was 1.9 ± 0.9, 1.5 ± 0.9, 1.5 ± 0.8, and 2.2 ± 0.4 mm for metallic interference screw, bioabsorbable screw, cross-pin, and suspensory device, respectively. The rate of failure was 6.1%, 3.3%, 1.7%, and 1.2% for the bioabsorbable interference screw, metallic interference screw, cross-pin, and suspensory device, respectively. Two-thirds of the patients achieved good-to-excellent clinical outcomes. Several pitfalls that affect current fixation techniques, such as graft tensioning and graft tunnel motion, remain unaddressed[79]. Moreover, Saccomanno *et al*[63] compared the cortical button with transfemoral suspensory fixation. They suggested that there were no short- to medium-term differences in the knee-specific outcome measures. In contrast, a meta-analysis by Hu *et al*[80] found a decrease in instrumented side-to-side anteroposterior laxity when cross-pin transfixation was used. However, the difference appears to have limited clinical significance compared with interference screw fixation. In addition, a 2-year clinical outcome study found that patients who underwent ACL reconstruction with intra-tunnel or extra-tunnel fixation had comparable results based on objective IKDC, Lysholm knee scale, Tegner activity level survey, anterior knee joint laxity measurements, and time to resume sports. Patients who received intra-tunnel fixation began full weight-bearing, jogging, and running earlier than patients who received extra-tunnel fixation[62]. Finally, a meta-analysis showed that the overall graft failure and revision rates with press-fit fixation for ACLR were low. There were no significant differences in the complication rates between patients who underwent femoral press-fit or femoral metal interference screw fixation. Patients who underwent press-fit fixation for ACLR had significant improvements in functional outcome scores post-operatively and significantly lower postoperative bone tunnel enlargement than patients who underwent bioabsorbable fixation. Thus, early evidence suggests that press-fit fixation is a good option for patients undergoing ACLR (Table 4)[81].

CONCLUSION

Multiple surgical maneuvers and approaches have been reported to avoid complications when reconstructing a ruptured ACL. For a hamstring tendon autograft, a shorter oblique anteromedial incision has been suggested to reduce the incidence of local neurological injuries compared to that with a longer vertical incision. The posteromedial harvesting approach is associated with fewer complications and better cosmetic outcomes. Sparing the gracilis tendon when harvesting the hamstring tendon can reduce the strength deficit postoperatively at deeper angles utilized by athletes. Several hamstring autograft fixation methods are available, but the optimum method is yet to be determined. Further studies are required to establish a safer surgical approach.

FOOTNOTES

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REFERENCES

1 **Tompson JC**. Netter's Concise Orthopeaedic Anatomy. Elsevier, 2016
2 **Augustine RW**. The unstable knee. *Am J Surg* 1956; **92**: 380-388 [PMID: 13354860 DOI: 10.1016/s0002-9610(56)80110-4]
3 **Sanders TL**, Maradit Kremers H, Bryan AJ, Larson DR, Dahm DL, Levy BA, Stuart MJ, Krych AJ. Incidence of Anterior Cruciate Ligament Tears and Reconstruction: A 21-Year Population-Based Study. *Am J Sports Med* 2016; **44**: 1502-1507 [PMID: 26920430 DOI: 10.1177/0363546516629944]
4 **Griffin LY**, Agel J, Albohm MJ, Arendt EA, Dick RW, Garrett WE, Garrick JG, Hewett TE, Huston L, Ireland ML, Johnson RJ, Kibler WB, Lephart S, Lewis JL, Lindenfeld TN, Mandelbaum BR, Marchak P, Teitz CC, Wojtys EM. Noncontact anterior cruciate ligament injuries: risk factors and prevention strategies. *J Am Acad Orthop Surg* 2000; **8**: 141-150 [PMID: 10874221 DOI: 10.5435/00124635-200005000-00001]
5 **Boden BP**, Torg JS, Knowles SB, Hewett TE. Video analysis of anterior cruciate ligament injury: abnormalities in hip and ankle kinematics. *Am J Sports Med* 2009; **37**: 252-259 [PMID: 19182110 DOI: 10.1177/0363546508328107]
6 **Cimino F**, Volk BS, Setter D. Anterior cruciate ligament injury: diagnosis, management, and prevention. *Am Fam Physician* 2010; **82**: 917-922 [PMID: 20949884]
7 **Walsh WM**, McCarty EC, Madden CC. Knee Injuries. In: Madden C, Putukian M, McCarty E, Young C. Netter's Sports Medicine. Elsevier, 2021
8 **Shea KG**, Carey JL. Management of anterior cruciate ligament injuries: evidence-based guideline. *J Am Acad Orthop Surg* 2015; **23**: e1-e5 [PMID: 25795769 DOI: 10.5435/JAAOS-D-15-00094]
9 **Lin KM**, Boyle C, Marom N, Marx RG. Graft Selection in Anterior Cruciate Ligament Reconstruction. *Sports Med Arthrosc Rev* 2020; **28**: 41-48 [PMID: 32345925 DOI: 10.1097/JSA.0000000000000265]
10 **Warren LF**, Marshall JL. The supporting structures and layers on the medial side of the knee: an anatomical analysis. *J Bone Joint Surg Am* 1979; **61**: 56-62 [PMID: 759437]
11 **Nichalas JA**, Hershuran EB. The Lower Extremity and Spine in Sports Medicine. St. Louis: Mosby, 1995: 657-694
12 **Pagnani MJ**, Warner JJ, O'Brien SJ, Warren RF. Anatomic considerations in harvesting the semitendinosus and gracilis tendons and a technique of harvest. *Am J Sports Med* 1993; **21**: 565-571 [PMID: 8368418 DOI: 10.1177/036354659302100414]
13 **Solman CG Jr**, Pagnani MJ. Hamstring tendon harvesting. Reviewing anatomic relationships and avoiding pitfalls. *Orthop Clin North Am* 2003; **34**: 1-8 [PMID: 12735196 DOI: 10.1016/s0030-5898(02)00025-1]
14 **Davarinos N**, Neill BJO, Curtin W. A Brief History of Anterior Cruciate Ligament Reconstruction. *Adv In Orthop Surg* 2014 [DOI: 10.1155/2014/706042]
15 **Sanders B**, Rolf R, McClelland W, Xerogeanes J. Prevalence of saphenous nerve injury after autogenous hamstring harvest: an anatomic and clinical study of sartorial branch injury. *Arthroscopy* 2007; **23**: 956-963 [PMID: 17868834 DOI: 10.1016/j.arthro.2007.03.099]
16 **Miller MD**, Browne JA, Cole BJ, Cosgarea AJ, Owens BD. Operative Techniques: Knee Surgery: Second Edition. Elsevier, 2017: 1-393
17 **Olivos-Meza A**, Suarez-Ahedo C, Jiménez-Aroche CA, Pantanali N, Valdez-Chávez MV, Pérez-Jiménez FJ, Olivos-Díaz B, Olivos-Gárces NA, González-Hernández A, Ibarra C. Anatomic Considerations in Hamstring Tendon Harvesting for Ligament Reconstruction. *Arthrosc Tech* 2020; **9**: e191-e198 [PMID: 32021795 DOI: 10.1016/j.eats.2019.09.021]
18 **Colombet P**, Graveleau N. Minimally Invasive Anterior Semitendinosus Harvest: A Technique to Decrease Saphenous Nerve Injury. *Arthrosc Tech* 2016; **5**: e139-e142 [PMID: 27274445 DOI: 10.1016/j.eats.2015.10.011]
19 **Luo H**, Yu JK, Ao YF, Yu CL, Peng LB, Lin CY, Zhang JY, Fu X. Relationship between different skin incisions and the injury of the infrapatellar branch of the saphenous nerve during anterior cruciate ligament reconstruction. *Chin Med J (Engl)* 2007; **120**: 1127-1130 [PMID: 17637238 DOI: 10.1097/00029330-200707010-00002]
20 **Henry BM**, Tomaszewski KA, Pękala PA, Graves MJ, Pękala JR, Sanna B, Mizia E. Oblique incisions in hamstring tendon harvesting reduce iatrogenic injuries to the infrapatellar branch of the saphenous nerve. *Knee Surg Sports Traumatol Arthrosc* 2018; **26**: 1197-1203 [PMID: 28573437 DOI: 10.1007/s00167-017-4590-y]
21 **Mahmood A**, Nag H, Srivastava AK. Clinical and electrophysiological assessment of injury to infrapatellar branch(es) of saphenous nerve during anterior cruciate ligament reconstruction using oblique incision for hamstring graft harvest: A prospective study. *Knee* 2020; **27**: 709-716 [PMID: 32563427 DOI: 10.1016/j.knee.2020.04.021]
22 **Sabat D**, Kumar V. Nerve injury during hamstring graft harvest: a prospective comparative study of three different incisions. *Knee Surg Sports Traumatol Arthrosc* 2013; **21**: 2089-2095 [PMID: 23073817 DOI: 10.1007/s00167-012-2243-8]
23 **Joshi A**, Kayasth N, Shrestha S, Kc BR. Infra Patellar Branch of Saphenous Nerve Injury during Hamstring Graft Harvest: Vertical versus Oblique Incisions. *J Nepal Health Res Counc* 2016; **14**: 180-185 [PMID: 28327683]
24 **Ochiai S**, Hagino T, Senga S, Yamashita T, Oda K, Haro H. Injury to infrapatellar branch of saphenous nerve in anterior cruciate ligament reconstruction using vertical skin incision for hamstring harvesting: risk factors and the influence of treatment outcome. *J Orthop Surg Res* 2017; **12**: 101 [PMID: 28655325 DOI: 10.1186/s13018-017-0596-x]
25 **Keyhani S**, Kazemi SM, Sajjadi MM, Elmi A. A Comparison between Oblique and Vertical Incisions on the Hamstring Tendon Harvesting in Anterior Cruciate Ligament Reconstruction and Infrapatellar Branch Injury of the Saphenous Nerve. *Rev Bras Ortop (Sao Paulo)* 2020; **55**: 374-379 [PMID: 32616985 DOI: 10.1055/s-0039-1692695]
26 **Papastergiou SG**, Voulgaropoulos H, Mikalef P, Ziogas E, Pappis G, Giannakopoulos I. Injuries to the infrapatellar branch(es) of the saphenous nerve in anterior cruciate ligament reconstruction with four-strand hamstring tendon autograft: vertical versus horizontal incision for harvest. *Knee Surg Sports Traumatol Arthrosc* 2006; **14**: 789-793 [PMID: 16328463 DOI: 10.1007/s00167-005-0008-3]
27 **Mousavi H**, Mohammadi M, Aghdam HA. Injury to the Infrapatellar Branch of the Saphenous Nerve during ACL Reconstruction with Hamstring Tendon Autograft: A Comparison between Oblique and Vertical Incisions. *Arch Bone Jt*

Surg 2018; **6**: 52-56 [PMID: 29430496 DOI: 10.5812/atr.11146]
28 **Figueroa D**, Calvo R, Vaisman A, Campero M, Moraga C. Injury to the infrapatellar branch of the saphenous nerve in ACL reconstruction with the hamstrings technique: clinical and electrophysiological study. *Knee* 2008; **15**: 360-363 [PMID: 18583136 DOI: 10.1016/j.knee.2008.05.002]
29 **Chen X**, Bickham SR, Liu HF, Dosunmu OI, Hurley JE, Li MJ. 25 Gb/s transmission over 820 m of MMF using a multimode launch from an integrated silicon photonics transceiver. *Opt Express* 2014; **22**: 2070-2077 [PMID: 24515216 DOI: 10.1364/OE.22.002070]
30 **Pękala PA**, Tomaszewski KA, Henry BM, Ramakrishnan PK, Roy J, Mizia E, Walocha JA. Risk of iatrogenic injury to the infrapatellar branch of the saphenous nerve during hamstring tendon harvesting: A meta-analysis. *Muscle Nerve* 2017; **56**: 930-937 [PMID: 28120438 DOI: 10.1002/mus.25587]
31 **Walshaw T**, Karuppiah SV, Stewart I. Erratum to "The course and distribution of the infra patellar nerve in relation to ACL reconstruction" [Knee 22 (2015) 384-388]. *Knee* 2016; **23**: 1174 [PMID: 27681096 DOI: 10.1016/j.knee.2016.05.002]
32 **Hunter LY**, Louis DS, Ricciardi JR, O'Connor GA. The saphenous nerve: its course and importance in medial arthrotomy. *Am J Sports Med* 1979; **7**: 227-230 [PMID: 474860 DOI: 10.1177/036354657900700403]
33 **Grassi A**, Perdisa F, Samuelsson K, Svantesson E, Romagnoli M, Raggi F, Gaziano T, Mosca M, Ayeni O, Zaffagnini S. Association between incision technique for hamstring tendon harvest in anterior cruciate ligament reconstruction and the risk of injury to the infra-patellar branch of the saphenous nerve: a meta-analysis. *Knee Surg Sports Traumatol Arthrosc* 2018; **26**: 2410-2423 [PMID: 29423546 DOI: 10.1007/s00167-018-4858-x]
34 **Pękala PA**, Miza E, Henry BM, Popieluszko P, Loukas M, Tomaszewski KA. Injury to the infrapatellar branch of the saphenous nerve during tendon graft harvesting for knee ligament reconstruction: An ultrasound simulation study. *Clin Anat* 2017; **30**: 868-872 [PMID: 28514510 DOI: 10.1002/ca.22904]
35 **Leiter J**, Peeler J, McRae S, Wiens S, Hammond A, Froese W, MacDonald P. The Effect of Graft Harvest and Skin Incision Angle on Sensory Disturbance in ACL Reconstruction With Semitendinosus-Gracilis Tendon Graft: A Randomized Controlled Trial and Cadaveric Study. *Orthop J Sports Med* 2020; **8**: 2325967120948954 [PMID: 32974411 DOI: 10.1177/2325967120948954]
36 **Tillett E**, Madsen R, Rogers R, Nyland J. Localization of the semitendinosus-gracilis tendon bifurcation point relative to the tibial tuberosity: an aid to hamstring tendon harvest. *Arthroscopy* 2004; **20**: 51-54 [PMID: 14716279 DOI: 10.1016/j.arthro.2003.11.003]
37 **Franz W**, Baumann A. Minimally invasive semitendinosus tendon harvesting from the popliteal fossa versus conventional hamstring tendon harvesting for ACL reconstruction: A prospective, randomised controlled trial in 100 patients. *Knee* 2016; **23**: 106-110 [PMID: 26753501 DOI: 10.1016/j.knee.2015.09.001]
38 **Kodkani PS**, Govekar DP, Patankar HS. A new technique of graft harvest for anterior cruciate ligament reconstruction with quadruple semitendinosus tendon autograft. *Arthroscopy* 2004; **20**: e101-e104 [PMID: 15483531 DOI: 10.1016/j.arthro.2004.07.016]
39 **Letartre R**, Isida R, Pommepuy T, Miletic B. Horizontal posterior hamstring harvest. *Orthop Traumatol Surg Res* 2014; **100**: 959-961 [PMID: 25453925 DOI: 10.1016/j.otsr.2014.08.002]
40 **Wilson TJ**, Lubowitz JH. Minimally invasive posterior hamstring harvest. *Arthrosc Tech* 2013; **2**: e299-e301 [PMID: 24266003 DOI: 10.1016/j.eats.2013.04.008]
41 **Prodromos CC**, Han YS, Keller BL, Bolyard RJ. Posterior mini-incision technique for hamstring anterior cruciate ligament reconstruction graft harvest. *Arthroscopy* 2005; **21**: 130-137 [PMID: 15689860 DOI: 10.1016/j.arthro.2004.09.010]
42 **Khanna K**, Janghala A, Pandya NK. Use of Posterior Hamstring Harvest During Anterior Cruciate Ligament Reconstruction in the Pediatric and Adolescent Population. *Orthop J Sports Med* 2018; **6**: 2325967118775597 [PMID: 29900181 DOI: 10.1177/2325967118775597]
43 **Shu HT**, Bodendorfer BM, Michaelson EM, Argintar EH. Posteromedial versus Anteromedial Hamstring Tendon Harvest for Anterior Cruciate Ligament Reconstruction: A Retrospective Comparison of Accidental Gracilis Harvests, Outcomes, and Operative Times. *J Knee Surg* 2019; **32**: 1121-1127 [PMID: 30449022 DOI: 10.1055/s-0038-1675796]
44 **Roussignol X**, Bertiaux S, Rahali S, Potage D, Duparc F, Dujardin F. Minimally invasive posterior approach in the popliteal fossa for semitendinosus and gracilis tendon harvesting: an anatomic study. *Orthop Traumatol Surg Res* 2015; **101**: 167-172 [PMID: 25701163 DOI: 10.1016/j.otsr.2014.12.009]
45 **Vinagre G**, Kennedy NI, Chahla J, Cinque ME, Hussain ZB, Olesen ML, LaPrade RF. Hamstring Graft Preparation Techniques for Anterior Cruciate Ligament Reconstruction. *Arthrosc Tech* 2017; **6**: e2079-e2084 [PMID: 29349000 DOI: 10.1016/j.eats.2017.08.031]
46 **Sharma A**, Flanigan DC, Randall K, Magnussen RA. Does Gracilis Preservation Matter in Anterior Cruciate Ligament Reconstruction? *Arthroscopy* 2016; **32**: 1165-1173 [PMID: 26874800 DOI: 10.1016/j.arthro.2015.11.027]
47 **Ardern CL**, Webster KE. Knee flexor strength recovery following hamstring tendon harvest for anterior cruciate ligament reconstruction: a systematic review. *Orthop Rev (Pavia)* 2009; **1**: e12 [PMID: 21808674 DOI: 10.4081/or.2009.e12]
48 **Chin BZ**, Wee IJY, Syn NL, Krishna L. Arthroscopic Anterior Cruciate Ligament Reconstruction: A Meta-Analysis Comparing Semitendinosus Alone and Semitendinosus with Gracilis Tendon Autografts. *J Knee Surg* 2019; **32**: 796-803 [PMID: 30206911 DOI: 10.1055/s-0038-1669950]
49 **Tashiro T**, Kurosawa H, Kawakami A, Hikita A, Fukui N. Influence of medial hamstring tendon harvest on knee flexor strength after anterior cruciate ligament reconstruction. A detailed evaluation with comparison of single- and double-tendon harvest. *Am J Sports Med* 2003; **31**: 522-529 [PMID: 12860539 DOI: 10.1177/31.4.522]
50 **Nakamura N**, Horibe S, Sasaki S, Kitaguchi T, Tagami M, Mitsuoka T, Toritsuka Y, Hamada M, Shino K. Evaluation of active knee flexion and hamstring strength after anterior cruciate ligament reconstruction using hamstring tendons. *Arthroscopy* 2002; **18**: 598-602 [PMID: 12098120 DOI: 10.1053/jars.2002.32868]
51 **Hu A**, Lawton CD, Nelson P, Selley RS, Sweeney P, Tuttle J, Johnson DJ, Balderama ES, Gryzlo SM, Terry MA. Assessment of Flexion Strength Following Single- Versus Double-Hamstring Tendon Harvest for Anterior Cruciate Ligament Reconstruction. *Arthroscopy* 2020; **36**: 1409-1416 [PMID: 32001278 DOI: 10.1016/j.arthro.2020.01.019]

52 **Adachi N**, Ochi M, Uchio Y, Sakai Y, Kuriwaka M, Fujihara A. Harvesting hamstring tendons for ACL reconstruction influences postoperative hamstring muscle performance. *Arch Orthop Trauma Surg* 2003; **123**: 460-465 [PMID: 12920536 DOI: 10.1007/s00402-003-0572-2]

53 **Yosmaoglu HB**, Baltaci G, Ozer H, Atay A. Effects of additional gracilis tendon harvest on muscle torque, motor coordination, and knee laxity in ACL reconstruction. *Knee Surg Sports Traumatol Arthrosc* 2011; **19**: 1287-1292 [PMID: 21298255 DOI: 10.1007/s00167-011-1412-5]

54 **Carter TR**, Edinger S. Isokinetic evaluation of anterior cruciate ligament reconstruction: hamstring versus patellar tendon. *Arthroscopy* 1999; **15**: 169-172 [PMID: 10210074 DOI: 10.1053/ar.1999.v15.0150161]

55 **Karimi-Mobarakeh M**, Mardani-Kivi M, Mortazavi A, Saheb-Ekhtiari K, Hashemi-Motlagh K. Role of gracilis harvesting in four-strand hamstring tendon anterior cruciate ligament reconstruction: a double-blinded prospective randomized clinical trial. *Knee Surg Sports Traumatol Arthrosc* 2015; **23**: 1086-1091 [PMID: 24531357 DOI: 10.1007/s00167-014-2890-z]

56 **Gobbi A**, Domzalski M, Pascual J, Zanazzo M. Hamstring anterior cruciate ligament reconstruction: is it necessary to sacrifice the gracilis? *Arthroscopy* 2005; **21**: 275-280 [PMID: 15756179 DOI: 10.1016/j.arthro.2004.10.016]

57 **Inagaki Y**, Kondo E, Kitamura N, Onodera J, Yagi T, Tanaka Y, Yasuda K. Prospective clinical comparisons of semitendinosus versus semitendinosus and gracilis tendon autografts for anatomic double-bundle anterior cruciate ligament reconstruction. *J Orthop Sci* 2013; **18**: 754-761 [PMID: 23793303 DOI: 10.1007/s00776-013-0427-9]

58 **Segawa H**, Omori G, Koga Y, Kameo T, Iida S, Tanaka M. Rotational muscle strength of the limb after anterior cruciate ligament reconstruction using semitendinosus and gracilis tendon. *Arthroscopy* 2002; **18**: 177-182 [PMID: 11830812 DOI: 10.1053/jars.2002.29894]

59 **Ardern CL**, Webster KE, Taylor NF, Feller JA. Hamstring strength recovery after hamstring tendon harvest for anterior cruciate ligament reconstruction: a comparison between graft types. *Arthroscopy* 2010; **26**: 462-469 [PMID: 20362824 DOI: 10.1016/j.arthro.2009.08.018]

60 **Barenius B**, Webster WK, McClelland J, Feller J. Hamstring tendon anterior cruciate ligament reconstruction: does gracilis tendon harvest matter? *Int Orthop* 2013; **37**: 207-212 [PMID: 23052280 DOI: 10.1007/s00264-012-1672-9]

61 **Lipscomb AB**, Johnston RK, Snyder RB, Warburton MJ, Gilbert PP. Evaluation of hamstring strength following use of semitendinosus and gracilis tendons to reconstruct the anterior cruciate ligament. *Am J Sports Med* 1982; **10**: 340-342 [PMID: 7180953 DOI: 10.1177/036354658201000603]

62 **Han DL**, Nyland J, Kendzior M, Nawab A, Caborn DN. Intratunnel versus extratunnel fixation of hamstring autograft for anterior cruciate ligament reconstruction. *Arthroscopy* 2012; **28**: 1555-1566 [PMID: 22560484 DOI: 10.1016/j.arthro.2012.02.021]

63 **Saccomanno MF**, Shin JJ, Mascarenhas R, Haro M, Verma NN, Cole BJ, Bach BR Jr. Clinical and functional outcomes after anterior cruciate ligament reconstruction using cortical button fixation versus transfemoral suspensory fixation: a systematic review of randomized controlled trials. *Arthroscopy* 2014; **30**: 1491-1498 [PMID: 25064753 DOI: 10.1016/j.arthro.2014.05.028]

64 **Milano G**, Mulas PD, Ziranu F, Piras S, Manunta A, Fabbriciani C. Comparison between different femoral fixation devices for ACL reconstruction with doubled hamstring tendon graft: a biomechanical analysis. *Arthroscopy* 2006; **22**: 660-668 [PMID: 16762706 DOI: 10.1016/j.arthro.2006.04.082]

65 **Chang CB**, Choi JY, Koh IJ, Lee KJ, Lee KH, Kim TK. Comparisons of femoral tunnel position and length in anterior cruciate ligament reconstruction: modified transtibial versus anteromedial portal techniques. *Arthroscopy* 2011; **27**: 1389-1394 [PMID: 21889869 DOI: 10.1016/j.arthro.2011.06.013]

66 **Wang JH**, Kim JG, Lee DK, Lim HC, Ahn JH. Comparison of femoral graft bending angle and tunnel length between transtibial technique and transportal technique in anterior cruciate ligament reconstruction. *Knee Surg Sports Traumatol Arthrosc* 2012; **20**: 1584-1593 [PMID: 22120838 DOI: 10.1007/s00167-011-1781-9]

67 **Zantop T**, Ferretti M, Bell KM, Brucker PU, Gilbertson L, Fu FH. Effect of tunnel-graft length on the biomechanics of anterior cruciate ligament-reconstructed knees: intra-articular study in a goat model. *Am J Sports Med* 2008; **36**: 2158-2166 [PMID: 18669984 DOI: 10.1177/0363546508320572]

68 **Ekdahl M**, Wang JH, Ronga M, Fu FH. Graft healing in anterior cruciate ligament reconstruction. *Knee Surg Sports Traumatol Arthrosc* 2008; **16**: 935-947 [PMID: 18633596 DOI: 10.1007/s00167-008-0584-0]

69 **Barrett GR**, Noojin FK, Hartzog CW, Nash CR. Reconstruction of the anterior cruciate ligament in females: A comparison of hamstring versus patellar tendon autograft. *Arthroscopy* 2002; **18**: 46-54 [PMID: 11774141 DOI: 10.1053/jars.2002.25974]

70 **Debieux P**, Franciozi CES, Lenza M, Tamaoki MJ, Magnussen RA, Faloppa F. Bioabsorbable vs metallic interference screws for graft fixation in anterior cruciate ligament reconstruction. *Cochrane Database Syst Rev* 2016 [DOI: 10.1002/14651858.cd009772]

71 **Chen NC**, Brand JC Jr, Brown CH Jr. Biomechanics of intratunnel anterior cruciate ligament graft fixation. *Clin Sports Med* 2007; **26**: 695-714 [PMID: 17920961 DOI: 10.1016/j.csm.2007.06.009]

72 **Boutsiadis A**, Panisset JC, Devitt BM, Mauris F, Barthelemy R, Barth J. Anterior Laxity at 2 Years After Anterior Cruciate Ligament Reconstruction Is Comparable When Using Adjustable-Loop Suspensory Fixation and Interference Screw Fixation. *Am J Sports Med* 2018; **46**: 2366-2375 [PMID: 30015501 DOI: 10.1177/0363546518784005]

73 **Fu CW**, Chen WC, Lu YC. Is all-inside with suspensory cortical button fixation a superior technique for anterior cruciate ligament reconstruction surgery? *BMC Musculoskelet Disord* 2020; **21**: 445 [PMID: 32635920 DOI: 10.1186/s12891-020-03471-3]

74 **Baumfeld JA**, Diduch DR, Rubino LJ, Hart JA, Miller MD, Barr MS, Hart JM. Tunnel widening following anterior cruciate ligament reconstruction using hamstring autograft: a comparison between double cross-pin and suspensory graft fixation. *Knee Surg Sports Traumatol Arthrosc* 2008; **16**: 1108-1113 [PMID: 18791702 DOI: 10.1007/s00167-008-0606-y]

75 **Sabat D**, Kundu K, Arora S, Kumar V. Tunnel widening after anterior cruciate ligament reconstruction: a prospective randomized computed tomography--based study comparing 2 different femoral fixation methods for hamstring graft. *Arthroscopy* 2011; **27**: 776-783 [PMID: 21624672 DOI: 10.1016/j.arthro.2011.02.009]

76 **Saygi B**, Karaman O, Sirin E, Arslan I, Demir A, Oztermeli A. Comparison of different femoral fixation implants and fit

techniques for tunnel widening and clinical outcome in ACL reconstruction using hamstring autograft. *Arch Orthop Trauma Surg* 2016; **136**: 241-247 [PMID: 26471986 DOI: 10.1007/s00402-015-2348-x]

77 **Shen HC**, Chang JH, Lee CH, Shen PH, Yeh TT, Wu CC, Kuo CL. Biomechanical comparison of Cross-pin and Endobutton-CL femoral fixation of a flexor tendon graft for anterior cruciate ligament reconstruction--a porcine femur-graft-tibia complex study. *J Surg Res* 2010; **161**: 282-287 [PMID: 19524939 DOI: 10.1016/j.jss.2009.01.015]

78 **Vertullo CJ**, Piepenbrink M, Smith PA, Wilson AJ, Wijdicks CA. Biomechanical Testing of Three Alternative Quadrupled Tendon Graft Constructs With Adjustable Loop Suspensory Fixation for Anterior Cruciate Ligament Reconstruction Compared With Four-Strand Grafts Fixed With Screws and Femoral Fixed Loop Devices. *Am J Sports Med* 2019; **47**: 828-836 [PMID: 30789779 DOI: 10.1177/0363546518825256]

79 **Speziali A**, Delcogliano M, Tei M, Placella G, Bartoli M, Menghi A, Cerulli G. Fixation techniques for the anterior cruciate ligament reconstruction: early follow-up. A systematic review of level I and II therapeutic studies. *Musculoskelet Surg* 2014; **98**: 179-187 [PMID: 25269758 DOI: 10.1007/s12306-014-0338-8]

80 **Hu B**, Shen W, Zhou C, Meng J, Wu H, Yan S. Cross Pin Versus Interference Screw for Femoral Graft Fixation in Hamstring Anterior Cruciate Ligament Reconstruction: A Systematic Review and Meta-analysis of Clinical Outcomes. *Arthroscopy* 2018; **34**: 615-623 [PMID: 29066266 DOI: 10.1016/j.arthro.2017.07.031]

81 **Shanmugaraj A**, Mahendralingam M, Gohal C, Horner N, Simunovic N, Musahl V, Samuelsson K, Ayeni OR. Press-fit fixation in anterior cruciate ligament reconstruction yields low graft failure and revision rates: a systematic review and meta-analysis. *Knee Surg Sports Traumatol Arthrosc* 2021; **29**: 1750-1759 [PMID: 32785757 DOI: 10.1007/s00167-020-06173-4]

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Abstract

After three rounds of rigorous evaluation of core journals in orthopedics conducted by the *Reference Citation Analysis* (*RCA*) editorial team of Baishideng Publishing Group (Baishideng), the *RCA* database of Baishideng officially released the 2022 *Journal Article Influence Index* (2022 *JAII*) of 104 core journals and a list of high-quality academic journals in orthopedics, for the first time on August 9, 2022. The list of 104 core journals can be found at: https://www.referencecitationanalysis.com/SearchJournal. Among them, the highest 2022 *JAII* is 55.015 and the lowest is 3.076. This article introduces the 21 high-quality academic journals and describes the calculation method for the 2022 *JAII*, the evaluation process, and the inclusion principles for journals in the *RCA*. These steps are the underpinning of the *RCA*'s empirical journal academic evaluation service by which the digital platform addresses the needs of authors to select reliable journals for submission, readers to select high-quality literature for reading, and editors to track their own journal citation performance. As such, the *RCA* core journal list will serve as a useful Find-a-Journal tool. Any interested party is welcome to use this journal list and recommend it to their peers.

Key Words: *Reference Citation Analysis*; *Journal Article Influence Index*; Orthopedics; Journal list; Find a journal; Announcement

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Core Tip: The *Reference Citation Analysis* (*RCA*) database of Baishideng Publishing Group officially released the 2022 *Journal Article Influence Index* (2022 *JAII*) of 104 core journals and the list of high-quality academic journals in orthopedics, for the first time. This article highlights the top 21 journals, describes the calculation method for the 2022 *JAII*, the evaluation process, and the inclusion principles of *RCA* journals. The *RCA* journal academic evaluation service platform addresses the needs of authors to select reliable journals for submission, readers to select high-quality literature for reading, and editors to track their own journal citation performance, effectively serving as a useful Find-a-Journal tool. You are welcome to use this journal list and recommend it to your peers.

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DOI: https://dx.doi.org/10.5312/wjo.v13.i10.891

INTRODUCTION

We are very pleased to announce that the *Reference Citation Analysis* (*RCA*) database of Baishideng Publishing Group (Baishideng) has, for the first time, officially released the 2022 *Journal Article Influence Index* (2022 *JAII*) of 104 core journals in the field of orthopedics on August 9, 2022. The detailed information on these 104 core journals in orthopedics can be found at: https://www.referencecitation-analysis.com/SearchJournal.

RCA is an AI technology-based open multidisciplinary citation analysis database. As such, *RCA* will lead the development of wisdom, knowledge innovation, and emerging disciplines. The functions of *RCA* include: Find an Article (55334324), Find a Category (254), Find a Journal (14077), Find a Scholar (632), and Find an Academic Assistant (18) (Data collection: August 9, 2022)[1]. *RCA* updates its list of journals daily, according to relevant data including total number of articles, total citations, and the *JAII*. *RCA* acquires the newly released abstracts and references from Crossref and adds them to the *RCA* database weekly. *RCA* also acquires the abstracts and references released that year from Crossref and adds them to the *RCA* database monthly, and then updates the total number of articles, citations, and *JAII*. In this study, we introduce the top 21 journals ranked by the 2022 *JAII* from the total 104 core journals in the field of orthopedics included in *RCA*, the calculation method for the 2022 *JAII*, and the evaluation process and the inclusion principles of *RCA* journals.

TOP 21 JOURNALS RANKED BY THE 2022 *JAII* IN THE FIELD OF ORTHOPEDICS INCLUDED IN THE *RCA*

The *RCA* classifies academic journals with a *JAII* of 20.0 or above as high-quality academic journals, which will be highly recommended to authors and readers. There are 104 core journals in the field of orthopedics in the *RCA*, of which 21 were identified to be high-quality academic journals, accounting for 20.2%. These 21 high-quality academic journals, ranked by the *JAII* among the core journals in the field of orthopedics in the *RCA*, are described below.

2022 JAII and rankings of The Journal of Bone and Joint Surgery-American Volume

In the *RCA* database, the 2022 *JAII* for *The Journal of Bone and Joint Surgery-American Volume* is 55.015, ranking 1st among 104 core journals in the field of orthopedics included in the *RCA*, with a total of 1110044 citations (1/104) and a total of 20177 articles (2/104) (Figure 1). For more information on *The Journal of Bone and Joint Surgery-American Volume*, please visit: https://www.referencecitationanalysis.com/SearchJournal.

2022 JAII and rankings of The American Journal of Sports Medicine

In the *RCA* database, the 2022 *JAII* for *The American Journal of Sports Medicine* is 52.976, ranking 2nd among 104 core journals in the field of orthopedics included in the *RCA*, with a total of 589467 citations (4/104) and a total of 11127 articles (6/104) (Figure 2). For more information on *The American Journal of Sports Medicine*, please visit: https://www.referencecitationanalysis.com/SearchJournal.

2022 JAII and rankings of Spine

In the *RCA* database, the 2022 *JAII* for *Spine* is 44.570, ranking 3rd among 104 core journals in the field of



THE JOURNAL OF BONE AND JOINT SURGERY-AMERICAN VOLUME

Category Rank: Orthopedics

Total View: 5 (1/104)

Journal Article Influence Index: 55.015 (1/104)

Total Citations: 1110044 (1/104)

Cited by in F6Publishing: 643883 (1/104)

Total Articles: 20177 (2/104)

Number of Years: 74 (3/104)

Peer-Reviewed Journal: Yes

DOI: 10.5312/wjo.v13.i10.891 **Copyright** ©The Author(s) 2022.

Figure 1 2022 *Journal Article Influence Index* and rankings of *The Journal of Bone and Joint Surgery-American Volume*. The image of the journal cover is originally from the home page of the journal: https://journals.lww.com/jbjsjournal/pages/default.aspx.



THE AMERICAN JOURNAL OF SPORTS MEDICINE

Category Rank: Orthopedics

Total View: 4 (6/104)

Journal Article Influence Index: 52.976 (2/104)

Total Citations: 589467 (4/104)

Cited by in F6Publishing: 460196 (3/104)

Total Articles: 11127 (6/104)

Number of Years: 46 (14/104)

Peer-Reviewed Journal: Yes

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Figure 2 2022 *Journal Article Influence Index* and rankings of *The American Journal of Sports Medicine*. The image of the journal cover is originally from the home page of the journal: https://journals.sagepub.com/home/ajs.

orthopedics included in the *RCA*, with a total of 864839 citations (2/104) and a total of 19404 articles (3/104) (Figure 3). For more information on *Spine*, please visit: https://www.referencecitationanalysis.com/SearchJournal.

2022 JAII and rankings of European Cells & Materials

In the *RCA* database, the 2022 *JAII* for *European Cells & Materials* is 42.896, ranking 4th among 104 core journals in the field of orthopedics included in the *RCA*, with a total of 22735 citations (43/104) and a total of 530 articles (90/104) (Figure 4). For more information on *European Cells & Materials*, please visit: https://www.referencecitationanalysis.com/SearchJournal.

2022 JAII and rankings of Journal of Orthopaedic Research

In the *RCA* database, the 2022 *JAII* for *Journal of Orthopaedic Research* is 35.509, ranking 5th among 104 core journals in the field of orthopedics included in the *RCA*, with a total of 261809 citations (7/104) and a total of 7373 articles (14/104) (Figure 5). For more information on *Journal of Orthopaedic Research*, please visit: https://www.referencecitationanalysis.com/SearchJournal.

2022 JAII and rankings of Physical Therapy & Rehabilitation Journal

In the *RCA* database, the 2022 *JAII* for *Physical Therapy & Rehabilitation Journal* is 31.086, ranking 6th among 104 core journals in the field of orthopedics included in the *RCA*, with a total of 197801 citations (10/104) and a total of 6363 articles (20/104) (Figure 6). For more information on *Physical Therapy & Rehabilitation Journal*, please visit: https://www.referencecitationanalysis.com/SearchJournal.

2022 JAII and rankings of Arthroscopy

In the *RCA* database, the 2022 *JAII* for *Arthroscopy* is 29.982, ranking 7th among 104 core journals in the field of orthopedics included in the *RCA*, with a total of 285163 citations (5/104) and a total of 9511 articles (9/104) (Figure 7). For more information on *Arthroscopy*, please visit: https://www.referencecit-



SPINE

Category Rank: Orthopedics

Total View: 3 (31/104)

Journal Article Influence Index: 44.570 (3/104)

Total Citations: 864839 (2/104)

Cited by in F6Publishing: 558845 (2/104)

Total Articles: 19404 (3/104)

Number of Years: 46 (13/104)

Peer-Reviewed Journal: Yes

DOI: 10.5312/wjo.v13.i10.891 **Copyright** ©The Author(s) 2022.

Figure 3 2022 *Journal Article Influence Index* and rankings of *Spine*. The image of the journal cover is originally from the home page of the journal: https://journals.lww.com/spinejournal/pages/issuelist.aspx.

EUROPEAN CELLS & MATERIALS

Category Rank: Orthopedics

Total View: 5 (2/104)

Journal Article Influence Index: 42.896 (4/104)

Total Citations: 22735 (43/104)

Cited by in F6Publishing: 11264 (46/104)

Total Articles: 530 (90/104)

Number of Years: 21 (50/104)

Peer-Reviewed Journal: Yes

Free Access: Open

DOI: 10.5312/wjo.v13.i10.891 **Copyright** ©The Author(s) 2022.

Figure 4 2022 *Journal Article Influence Index* and rankings of *European Cells & Materials*. The image of the logo of AO Foundation is originally from the home page of the journal: http://www.ecmjournal.org/.



JOURNAL OF ORTHOPAEDIC RESEARCH

Category Rank: Orthopedics

Total View: 3 (17/104)

Journal Article Influence Index: 35.509 (5/104)

Total Citations: 261809 (7/104)

Cited by in F6Publishing: 204326 (5/104)

Total Articles: 7373 (14/104)

Number of Years: 39 (21/104)

Peer-Reviewed Journal: Yes

DOI: 10.5312/wjo.v13.i10.891 **Copyright** ©The Author(s) 2022.

Figure 5 2022 *Journal Article Influence Index* and rankings of *Journal of Orthopaedic Research*. The image of the journal cover is originally from the home page of the journal: https://onlinelibrary.wiley.com/journal/1554527x.

ationanalysis.com/SearchJournal.

2022 JAII and rankings of Osteoarthritis and Cartilage

In the *RCA* database, the 2022 *JAII* for *Osteoarthritis and Cartilage* is 28.691, ranking 8th among 104 core journals in the field of orthopedics included in the *RCA*, with a total of 194522 citations (12/104) and a total of 6780 articles (18/104) (Figure 8). For more information on *Osteoarthritis and Cartilage*, please visit: https://www.referencecitationanalysis.com/SearchJournal.



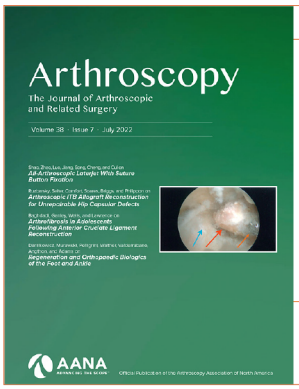
PHYSICAL THERAPY & REHABILITATION JOURNAL

Category Rank: Orthopedics
Total View: 3 (18/104)
Journal Article Influence Index: 31.086 (6/104)
Total Citations: 197801 (10/104)
Cited by in F6Publishing: 139123 (9/104)
Total Articles: 6363 (20/104)
Number of Years: 101 (2/104)

Peer-Reviewed Journal: Yes

DOI: 10.5312/wjo.v13.i10.891 **Copyright** ©The Author(s) 2022.

Figure 6 2022 *Journal Article Influence Index* and rankings of *Physical Therapy & Rehabilitation Journal*. The image of the journal cover is originally from the home page of the journal: https://academic.oup.com/ptj.



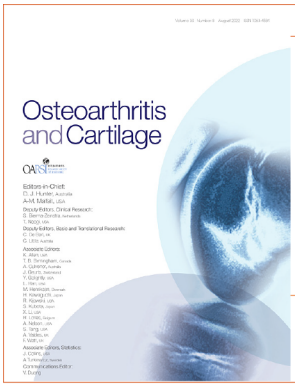
ARTHROSCOPY

Category Rank: Orthopedics
Total View: 2 (19/104)
Journal Article Influence Index: 29.982 (7/104)
Total Citations: 285163 (5/104)
Cited by in F6Publishing: 168924 (6/104)
Total Articles: 9511 (9/104)
Number of Years: 37 (24/104)

Peer-Reviewed Journal: Yes

DOI: 10.5312/wjo.v13.i10.891 **Copyright** ©The Author(s) 2022.

Figure 7 2022 *Journal Article Influence Index* and rankings of *Arthroscopy*. The image of the journal cover is originally from the home page of the journal: http://www.sciencedirect.com/science/journal/07498063.



OSTEOARTHRITIS AND CARTILAGE

Category Rank: Orthopedics
Total View: 3 (12/104)
Journal Article Influence Index: 28.691 (8/104)
Total Citations: 194522 (12/104)
Cited by in F6Publishing: 164493 (8/104)
Total Articles: 6780 (18/104)
Number of Years: 29 (38/104)

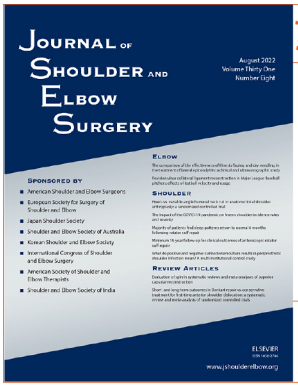
Peer-Reviewed Journal: Yes

DOI: 10.5312/wjo.v13.i10.891 **Copyright** ©The Author(s) 2022.

Figure 8 2022 *Journal Article Influence Index* and rankings of *Osteoarthritis and Cartilage*. The image of the journal cover is originally from the home page of the journal: http://www.sciencedirect.com/science/journal/10634584.

2022 JAII and rankings of Journal of Shoulder and Elbow Surgery

In the *RCA* database, the 2022 *JAII* for *Journal of Shoulder and Elbow Surgery* is 27.384, ranking 9th among 104 core journals in the field of orthopedics included in the *RCA*, with a total of 195354 citations (11/104) and a total of 7134 articles (16/104) (Figure 9). For more information on *Journal of Shoulder and Elbow Surgery*, please visit: https://www.referencecitationanalysis.com/SearchJournal.



JOURNAL OF SHOULDER AND ELBOW SURGERY

Category Rank: Orthopedics

Total View: 3 (13/104)

Journal Article Influence Index: 27.384 (9/104)

Total Citations: 195354 (11/104)

Cited by in F6Publishing: 117378 (12/104)

Total Articles: 7134 (16/104)

Number of Years: 30 (36/104)

Peer-Reviewed Journal: Yes

DOI: 10.5312/wjo.v13.i10.891 **Copyright** ©The Author(s) 2022.

Figure 9 2022 *Journal Article Influence Index* and rankings of *Journal of Shoulder and Elbow Surgery*. The image of the journal cover is originally from the home page of the journal: http://www.sciencedirect.com/science/journal/10582746.

2022 JAII and rankings of Journal of Orthopaedic & Sports Physical Therapy

In the *RCA* database, the 2022 *JAII* for *Journal of Orthopaedic & Sports Physical Therapy* is 26.966, ranking 10th among 104 core journals in the field of orthopedics included in the *RCA*, with a total of 105707 citations (20/104) and a total of 3920 articles (27/104) (Figure 10). For more information on *Journal of Orthopaedic & Sports Physical Therapy*, please visit: https://www.referencecitationanalysis.com/SearchJournal.

2022 JAII and rankings of The Journal of The American Academy of Orthopaedic Surgeons

In the *RCA* database, the 2022 *JAII* for *The Journal of The American Academy of Orthopaedic Surgeons* is 25.946, ranking 11th among 104 core journals in the field of orthopedics included in the *RCA*, with a total of 86581 citations (24/104) and a total of 3337 articles (33/104) (Figure 11). For more information on *The Journal of The American Academy of Orthopaedic Surgeons*, please visit: https://www.referencecitationanalysis.com/SearchJournal.

2022 JAII and rankings of The Gait & Posture

In the *RCA* database, the 2022 *JAII* for *Gait & Posture* is 25.815, ranking 12th among 104 core journals in the field of orthopedics included in the *RCA*, with a total of 165136 citations (14/104) and a total of 6397 articles (19/104) (Figure 12). For more information on *Gait & Posture*, please visit: https://www.referencecitationanalysis.com/SearchJournal.

2022 JAII and rankings of The Journal of Hand Surgery

In the *RCA* database, the 2022 *JAII* for *The Journal of Hand Surgery* is 25.713, ranking 13th among 104 core journals in the field of orthopedics included in the *RCA*, with a total of 270686 citations (6/104) and a total of 10527 articles (8/104) (Figure 13). For more information on *The Journal of Hand Surgery*, please visit: https://www.referencecitationanalysis.com/SearchJournal.

2022 JAII and rankings of Clinical Biomechanics

In the *RCA* database, the 2022 *JAII* for *Clinical Biomechanics* is 25.387, ranking 14th among 104 core journals in the field of orthopedics included in the *RCA*, with a total of 124397 citations (18/104) and a total of 4900 articles (26/104) (Figure 14). For more information on *Clinical Biomechanics*, please visit: https://www.referencecitationanalysis.com/SearchJournal.

2022 JAII and rankings of Foot & Ankle International

In the *RCA* database, the 2022 *JAII* for *Foot & Ankle International* is 25.123, ranking 15th among 104 core journals in the field of orthopedics included in the *RCA*, with a total of 142573 citations (16/1041) and a total of 5675 articles (16/104) (Figure 15). For more information on *Foot & Ankle International*, please visit: https://www.referencecitationanalysis.com/SearchJournal.

2022 JAII and rankings of Clinical Orthopaedics and Related Research

In the *RCA* database, the 2022 *JAII* for *Clinical Orthopaedics and Related Research* is 23.901, ranking 16th among 104 core journals in the field of orthopedics included in the *RCA*, with a total of 612124 citations (3/104) and a total of 25611 articles (1/104) (Figure 16). For more information on *Clinical Orthopaedics and Related Research*, please visit: https://www.referencecitationanalysis.com/SearchJournal.



JOURNAL OF ORTHOPAEDIC & SPORTS PHYSICAL THERAPY

Category Rank: Orthopedics
Total View: 3 (14/104)
Journal Article Influence Index: 26.966 (10/104)
Total Citations: 105707 (20/104)
Cited by in F6Publishing: 72730 (20/104)
Total Articles: 3920 (27/104)
Number of Years: 43 (18/104)

Peer-Reviewed Journal: Yes

DOI: 10.5312/wjo.v13.i10.891 **Copyright** ©The Author(s) 2022.

Figure 10 2022 *Journal Article Influence Index* and rankings of *Journal of Orthopaedic & Sports Physical Therapy*. The image of the journal cover is originally from the home page of the journal: http://www.jospt.org/.



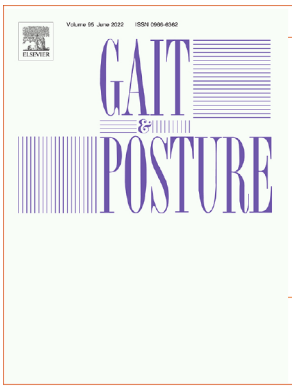
THE JOURNAL OF THE AMERICAN ACADEMY OF ORTHOPAEDIC SURGEONS

Category Rank: Orthopedics
Total View: 2 (22/104)
Journal Article Influence Index: 25.946 (11/104)
Total Citations: 86581 (24/104)
Cited by in F6Publishing: 50765 (25/104)
Total Articles: 3337 (33/104)
Number of Years: 29 (39/104)

Peer-Reviewed Journal: Yes

DOI: 10.5312/wjo.v13.i10.891 **Copyright** ©The Author(s) 2022.

Figure 11 2022 *Journal Article Influence Index* and rankings of *The Journal of The American Academy of Orthopaedic Surgeons*. The image of the journal cover is originally from the home page of the journal: https://journals.lww.com/jaaos.



GAIT & POSTURE

Category Rank: Orthopedics
Total View: 3 (15/104)
Journal Article Influence Index: 25.815 (12/104)
Total Citations: 165136 (14/104)
Cited by in F6Publishing: 98615 (14/104)
Total Articles: 6397 (19/104)
Number of Years: 29 (39/104)

Peer-Reviewed Journal: Yes

DOI: 10.5312/wjo.v13.i10.891 **Copyright** ©The Author(s) 2022.

Figure 12 2022 *Journal Article Influence Index* and rankings of *Gait & Posture*. The image of the journal cover is originally from the home page of the journal: https://www.sciencedirect.com/journal/gait-and-posture.

2022 JAII and rankings of Acta Orthopaedica

In the *RCA* database, the 2022 *JAII* for *Acta Orthopaedica* is 23.437, ranking 17th among 104 core journals in the field of orthopedics included in the *RCA*, with a total of 35953 citations (34/104) and a total of 1534 articles (56/104) (Figure 17). For more information on *Acta Orthopaedica*, please visit: https://www.referencecitationanalysis.com/SearchJournal.



THE JOURNAL OF HAND SURGERY

Category Rank: Orthopedics

Total View: 2 (21/104)

Journal Article Influence Index: 25.713 (13/104)

Total Citations: 270686 (6/104)

Cited by in F6Publishing: 112017 (13/104)

Total Articles: 10527 (8/104)

Number of Years: 46 (15/104)

Peer-Reviewed Journal: Yes

DOI: 10.5312/wjo.v13.i10.891 **Copyright** ©The Author(s) 2022.

Figure 13 2022 *Journal Article Influence Index* and rankings of *The Journal of Hand Surgery*. The image of the journal cover is originally from the home page of the journal: http://www.sciencedirect.com/science/journal/03635023.



CLINICAL BIOMECHANICS

Category Rank: Orthopedics

Total View: 1 (88/104)

Journal Article Influence Index: 25.387 (14/104)

Total Citations: 124397 (18/104)

Cited by in F6Publishing: 67321 (21/104)

Total Articles: 4900 (26/104)

Number of Years: 36 (26/104)

Peer-Reviewed Journal: Yes

DOI: 10.5312/wjo.v13.i10.891 **Copyright** ©The Author(s) 2022.

Figure 14 2022 *Journal Article Influence Index* and rankings of *Clinical Biomechanics*. The image of the journal cover is originally from the home page of the journal: https://www.sciencedirect.com/journal/clinical-biomechanics.



FOOT & ANKLE INTERNATIONAL

Category Rank: Orthopedics

Total View: 1 (89/104)

Journal Article Influence Index: 25.123 (154/104)

Total Citations: 142573 (16/104)

Cited by in F6Publishing: 82809 (15/104)

Total Articles: 5675 (23/104)

Number of Years: 28 (41/104)

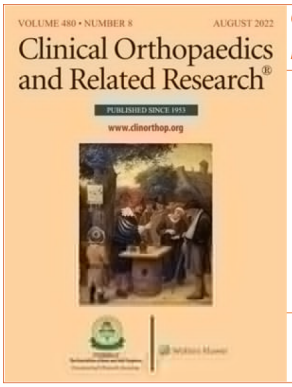
Peer-Reviewed Journal: Yes

DOI: 10.5312/wjo.v13.i10.891 **Copyright** ©The Author(s) 2022.

Figure 15 2022 *Journal Article Influence Index* and rankings of *Foot & Ankle International*. The image of the journal cover is originally from the home page of the journal: https://journals.sagepub.com/home/fai.

2022 JAII and rankings of Knee Surgery Sports Traumatology Arthroscopy

In the *RCA* database, the 2022 *JAII* for *Knee Surgery Sports Traumatology Arthroscopy* is 22.713, ranking 18th among 104 core journals in the field of orthopedics included in the *RCA*, with a total of 172777 citations (13/104) and a total of 7607 articles (13/104) (Figure 18). For more information on *Knee Surgery Sports Traumatology Arthroscopy*, please visit: https://www.referencecitationanalysis.com/Search-Journal.



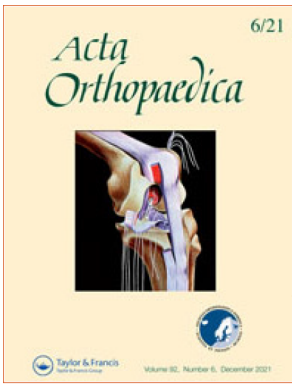
CLINICAL ORTHOPAEDICS AND RELATED RESEARCH

Category Rank: Orthopedics
Total View: 1 (90/104)
Journal Article Influence Index: 23.901 (16/104)
Total Citations: 612124 (3/104)
Cited by in F6Publishing: 407047 (4/104)
Total Articles: 25611 (1/104)
Number of Years: 59 (4/104)

Peer-Reviewed Journal: Yes

DOI: 10.5312/wjo.v13.i10.891 **Copyright** ©The Author(s) 2022.

Figure 16 2022 *Journal Article Influence Index* and rankings of *Clinical Orthopaedics and Related Research*. The image of the journal cover is originally from the home page of the journal: https://journals.lww.com/clinorthop/pages/default.aspx.



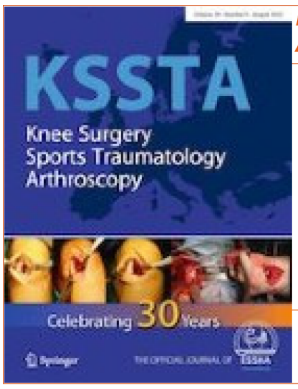
ACTA ORTHOPAEDICA

Category Rank: Orthopedics
Total View: 4 (3/104)
Journal Article Influence Index: 23.437 (17/104)
Total Citations: 35953 (34/104)
Cited by in F6Publishing: 31145 (29/104)
Total Articles: 1534 (56/104)
Number of Years: 34 (30/104)

Peer-Reviewed Journal: Yes
Free Access: Open

DOI: 10.5312/wjo.v13.i10.891 **Copyright** ©The Author(s) 2022.

Figure 17 2022 *Journal Article Influence Index* and rankings of *Acta Orthopaedica*. The image of the journal cover is originally from the home page of the journal: https://www.tandfonline.com/journals/iort20.



KNEE SURGERY SPORTS TRAUMATOLOGY ARTHROSCOPY

Category Rank: Orthopedics
Total View: 1 (87/104)
Journal Article Influence Index: 22.713 (18/104)
Total Citations: 172777 (13/104)
Cited by in F6Publishing: 127770 (10/104)
Total Articles: 7607 (10/104)
Number of Years: 29 (40/104)

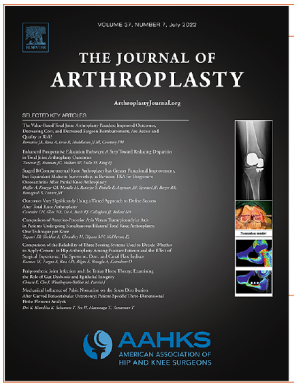
Peer-Reviewed Journal: Yes

DOI: 10.5312/wjo.v13.i10.891 **Copyright** ©The Author(s) 2022.

Figure 18 2022 *Journal Article Influence Index* and rankings of *Knee Surgery Sports Traumatology Arthroscopy*. The image of the journal cover is originally from the home page of the journal: https://Link.springer.com/journal/167.

2022 JAII and rankings of The Journal of Arthroplasty

In the *RCA* database, the 2022 *JAII* for *The Journal of Arthroplasty* is 22.683, ranking 19th among 104 core journals in the field of orthopedics included in the *RCA*, with a total of 257022 citations (8/104) and a total of 11322 articles (5/104) (Figure 19). For more information on *The Journal of Arthroplasty*, please visit: https://www.referencecitationanalysis.com/SearchJournal.



THE JOURNAL OF ARTHROPLASTY

Category Rank: Orthopedics

Total View: 2 (26/104)

Journal Article Influence Index: 22.683 (19/104)

Total Citations: 257022 (8/104)

Cited by in F6Publishing: 167335 (7/104)

Total Articles: 11331 (5/104)

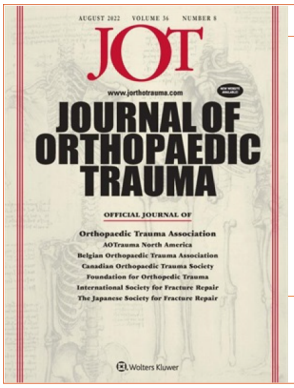
Number of Years: 36 (25/104)

Peer-Reviewed Journal: Yes

Free Access: Open

DOI: 10.5312/wjo.v13.i10.891 **Copyright** ©The Author(s) 2022.

Figure 19 2022 *Journal Article Influence Index* and rankings of *The Journal of Arthroplasty*. The image of the journal cover is originally from the home page of the journal: http://www.sciencedirect.com/science/journal/08835403.



JOURNAL OF ORTHOPAEDIC TRAUMA

Category Rank: Orthopedics

Total View: 1 (59/104)

Journal Article Influence Index: 22.363 (20/104)

Total Citations: 137263 (17/104)

Cited by in F6Publishing: 75584 (18/104)

Total Articles: 6138 (22/104)

Number of Years: 35 (28/104)

Peer-Reviewed Journal: Yes

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Figure 20 2022 *Journal Article Influence Index* and rankings of *Journal of Orthopaedic Trauma*. The image of the journal cover is originally from the home page of the journal: https://journals.lww.com/jorthotrauma/pages/issuelist.aspx.



CLINICAL JOURNAL OF SPORT MEDICINE

Category Rank: Orthopedics

Total View: 1 (65/104)

Journal Article Influence Index: 21.471 (21/104)

Total Citations: 55095 (27/104)

Cited by in F6Publishing: 30531 (31/104)

Total Articles: 2566 (41/104)

Number of Years: 31 (33/104)

Peer-Reviewed Journal: Yes

Free Access: Open

DOI: 10.5312/wjo.v13.i10.891 **Copyright** ©The Author(s) 2022.

Figure 21 2022 *Journal Article Influence Index* and rankings of *Clinical Journal of Sport Medicine*. The image of the journal cover is originally from the home page of the journal: https://journals.lww.com/cjsportsmed/pages/issuelist.aspx.

2022 JAII and rankings of Journal of Orthopaedic Trauma

In the *RCA* database, the 2022 *JAII* for *Journal of Orthopaedic Trauma* is 22.363, ranking 20th among 104 core journals in the field of orthopedics included in the *RCA*, with a total of 137263 citations (17/104) and a total of 6138 articles (22/104) (Figure 20). For more information on *Journal of Orthopaedic Trauma*, please visit: https://www.referencecitationanalysis.com/SearchJournal.

2022 JAII and rankings of Clinical Journal of Sport Medicine

In the *RCA* database, the 2022 *JAII* for *Clinical Journal of Sport Medicine* is 21.471, ranking 21st among 104 core journals in the field of orthopedics included in the *RCA*, with a total of 55095 citations (27/104) and a total of 2566 articles (41/104) (Figure 21). For more information on *Clinical Journal of Sport Medicine*, please visit: https://www.referencecitationanalysis.com/SearchJournal.

RCA'S MISSION

The mission of *RCA* is to provide a high-quality academic article evaluation service platform for various categories. At present, there are many evaluation methods for academic articles, but their calculation methods are complicated. The *RCA* is a new method of evaluating the quality of academic articles, which allows academic evaluation of journals, scholars, institutions, drugs, medical devices, and publishers based on the *JAII* of each article in the citation analysis database, thus greatly enriching the academic evaluation systems across different categories and guiding the healthy development of the academic community[2].

OPENNESS AND TRANSPARENCY OF RCA EVALUATION

RCA is unique in its objective, impartial, fair, and transparent release of citation analysis data of important academic journals to authors and readers, including evaluation data, evaluation indices, evaluation methods, and evaluation results, in order to ensure the reliability of academic evaluation[2].

CALCULATION METHOD FOR 2022 *JAII*

The 2022 *JAII*, calculated as Total citations/Total articles, is not a 2-year or 5-year average of citations, but is an average of citations for all articles since the journal was assigned its DOI number. Article types are not only limited to original articles and review articles, but for all types of articles. In this way, it is a more objective, fair, and transparent calculation of the academic influence index of an academic journal. Furthermore, the journal list itself is evaluated dynamically, with its bibliographic metrics being updated daily, including total number of articles, total citations, and *JAII*[2].

EVALUATION PROCESS OF *RCA* JOURNALS

The journals included in the *RCA* core journal list need to undergo three rounds of strict evaluation. The evaluation process is as follows[2]:

First-round evaluation: The basic information on the journal is verified, including Journal Name, Abbreviated Title, Print ISSN, Online ISSN, Language, Category, Peer-Reviewed Journal, Ownership, Publisher, Journal Website, Editorial Board Members, Submit a Manuscript, and Indexed by.

Second-round evaluation: The activity of the journal is verified, including Total Articles, Total Citations, Cited by in F6Publishing, and the *JAII*.

Third-round evaluation: Based on the reliability of journal information, the activity of publication data, whether the journal is a peer-reviewed journal or not, and *JAII*, the editorial team evaluates every journal, makes the decision to accept or reject the journal, and creates a list of core journals by category. The function of the list of core academic journals is to classify journals according to categories and rank them according to various bibliometrics, including Total Views, *JAII*, Total Citations, Cited by in F6Publishing, Total Articles, and Number of Years.

INCLUSION PRINCIPLES OF *RCA* JOURNALS

The *RCA* editorial team of Baishideng conducted three rounds of rigorous evaluation of core journals in orthopedics. The resultant *RCA* core journal list for the field of orthopedics includes a total of 104 journals, among which the highest 2022 *JAII* is 55.015 and the lowest *JAII* is 3.076, the highest total number of citations is 1110044 and the lowest is 678, and the highest total number of articles is 612124 and the lowest is 164. The *RCA* core journal list does not include any journals with a *JAII* lower than 3.0. We implement dynamic evaluation inclusively for the *RCA* core journal list. Evaluation is initiated once

an *RCA*-nonincluded journal receives a *JAII* over 3.0. Similarly, if a journal included in the *RCA* core journal list receives a *JAII* lower than 3.0, it will be excluded. The *RCA* core journal list is designed by publishers, scientific editors, and engineers for use by readers, authors, and editorial offices, and is free of charge to users[2].

Upon completion of the three rounds of rigorous evaluation of core journals in orthopedics by the *RCA* editorial team, all data in each journal are organized for public consumption according to category rank, including the 2022 *JAII*, total citations, cited by in F6Publishing, total articles, and the 2021 Journal Impact Factor™. All information in each journal, including Journal Name, Print ISSN, Online ISSN, Language, Free Access, Peer-Reviewed Journal, Ownership, Publisher, Journal Website, Editorial Board Members, Submit a Manuscript, and Indexed by, is made available in *RCA*. Moreover, the citations of each journal can be then ranked in *RCA* by the *Impact Index Per Article*, Cited by in Crossref, and Cited by in F6Publishing parameters. Results analysis available for each journal includes Year Published Analysis, Article Type Analysis, Journal Title Analysis, and Category Analysis. The references of each journal are also able to be refined by Year Published and Article Type. Each reference's citation information is displayed, including PMID, DOI, Cited by in Crossref, *Impact Index Per Article*, *RCA*, and Track Full Text[2].

CONCLUSION

The ultimate purpose of *RCA* is to provide an open, objective, fair, and reliable academic evaluation service platform for readers, authors, and journal editors, in order to address the needs of authors to select reliable journals for submission, readers to select high-quality literature for reading, and editors to track their own journal citation performance.

FOOTNOTES

Author contributions: Wang JL analyzed the data and drafted the manuscript; Ma YJ participated in the data collection; Ma LS revised the manuscript for important intellectual content; and all authors participated in manuscript revision.

Conflict-of-interest statement: The authors are all employees of the Baishideng Publishing Group Inc and declare that they have no other real or potential conflicts of interest to disclose.

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REFERENCES

1 **Baishideng Publishing Group Inc**. Welcome to the Reference Citation Analysis. Available from: https://www.referencecitationanalysis.com
2 **Baishideng Publishing Group Inc**. Reference Citation Analysis's evaluation process for inclusion of academic journals. [cited 19 August 2022]. Available from: https://www.wjgnet.com/bpg/GerInfo/303

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ORIGINAL ARTICLE

Retrospective Cohort Study

Preoperative and postoperative risk factors for periprosthetic joint infection in primary total hip arthroplasty: A 1-year experience

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Abstract

BACKGROUND

Periprosthetic joint infection (PJI) in primary total hip replacement (THR) is one of the most important threats in orthopedic surgery, so one important surgeon's target is to avoid or early diagnose a PJI. Although the incidence of PJI is very low (0.69%) in our department, with an average follow-up of 595 d, this infection poses a serious threat due to the difficulties of treatment and the lower functional outcomes after healing.

AIM

To study the incidence of PJI in all operations occurring in the year 2016 in our department to look for predictive signs of potential infection.

METHODS

We counted 583 THR for 578 patients and observed only 4 cases of infection (0.69%) with a mean follow-up of 596 d (min 30, max 1451). We reviewed all medical records to collect the data: duration and time of the surgery, presence, type and duration of the antibiotic therapy, preoperative diagnosis, blood values before and after surgery, transfusions, presence of preoperative drugs (in particularly anticoagulants and antiaggregant, corticosteroids and immunosuppressants), presence of some comorbidities (high body mass index, blood hypertension, chronic obstructive pulmonary disease, cardiac ischemia, diabetes, rheumatological conditions, previous local infections).

RESULTS

No preoperative, intraoperative, or postoperative analysis showed a higher

incidence of PJI. We did not find any class with evident major odds of PJI. In our study, we did not find any border value to predict PJI and all patients had similar values in both groups (non-PJI and PJI). Only some categories, such as female patients, showed more frequency of PJI, but this difference related to sex was not statistically significant.

CONCLUSION

We did not find any category with a higher risk of PJI in THR, probably due to the lack of few cases of infection.

Key Words: Primary total hip replacement; Periprosthetic joint infection; Preoperative risk factors; Postoperative risk factors; Preoperative and postoperative blood value; Total hip arthroplasty

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Core Tip: In this study, we evaluated the incidence of periprosthetic joint infection in all interventions occurring in the year 2016 at our department at IRCCS Istituto Ortopedico Rizzoli. We reviewed all operated patients to look for predictive signs of potential infection to explore methodological approaches that could better inform daily orthopedic practice. We reviewed the duration and time of surgery, presence, type and duration of antibiotic therapy, preoperative diagnosis, some blood values before and after surgery, transfusions, the presence of preoperative drugs, and the presence of some comorbidities.

Citation: Tella GF, Donadono C, Castagnini F, Bordini B, Cosentino M, Di Liddo M, Traina F. Preoperative and postoperative risk factors for periprosthetic joint infection in primary total hip arthroplasty: A 1-year experience. *World J Orthop* 2022; 13(10): 903-910

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INTRODUCTION

Periprosthetic joint infection (PJI) in primary total hip replacement (THR) is one of the most important threats in orthopedic surgery. When it occurs, many types of treatment are proposed[1-7] and different studies have reported similar odds of healing[1,3,7]. In this study, we evaluated the incidence of PJI in all interventions occurring in the year 2016 at our department. We counted 583 primary THR in 578 patients. We observed only four cases of infection with a minimum of 20 d to a maximum of 390 d after the THR. We reviewed all operated patients trying to look for predictive signs of potential infection. We reviewed the duration and time of surgery, presence, type and duration of antibiotic therapy, preoperative diagnosis, blood value before and after surgery, transfusions, presence of preoperative drugs (in particularly anticoagulants and antiaggregant, corticosteroids and immunosuppressants), presence of some comorbidities (high body mass index [BMI], blood hypertension, chronic obstructive pulmonary disease [COPD], cardiac ischemia, diabetes, rheumatological conditions, previous local infections). We tried to identify some values to predict or early diagnose PJI analyzing all data collected from surgeries occurring in 1 year.

MATERIALS AND METHODS

With agreement of the ethics committee of the Rizzoli Orthopedic Institute (Bologna, Italy), we reviewed all patients who had undergone total hip replacement (THR) in 2016. Categorical data were analyzed with use of the Fisher's test and χ^2 test and continuous data with the *t*-test. Level of significance was set at 0.05. There were 583 THR on 578 patients. Only 4 cases reported PJI (0.69%) and were re-operated. We reviewed all medical records to collect the data. All of these patients were visited at the hospital and in all authorized external clinics with the presence of a Rizzoli's doctor for follow-up. We had a mean follow-up of 595 d (min 30, max 1451). There were 320 females 54.9% and 263 males 45.1%, with a mean age of 62.2 years (min 17, max 88). The mean age for the 4 patients with infection was 62.8 age (min 51, max 69) (P = 0.98, t test) and included 3 females and 1 male (P = 0.63, Fisher's test). Differences in frequencies of infection for different BMI groups were not statistically significant (P = 0.455; χ^2 test). All patients received preoperative antibiotic therapy, 564 with cefazolin 2 g (96.9%) and 18 with clindamycin (3.1%); one case was lost. In the PJI group, all patients were treated with cefazolin (P = 1.00, Fisher's test). Twenty-one patients underwent further antibiotic treatment (see Table 1) with

Table 1 Patients' characteristics according to periprosthetic joint infection

Covariate	Infection (yes)	Infection (not)	*P* value
Age, mean (min-max)	62.8 (51-69)	62.8 (17-88)	$P = 0.98$; T-test
Sex			
Female (%)	3 (75.0)	317 (54.7)	$P = 0.63$; Fisher's test
Male (%)	1 (25.0)	262 (45.3)	
BMI			
Underweight (%)	-	4 (0.7)	$P = 0.455$; χ^2 test
Normal (%)	1 (25.0)	208 (36.0)	
Overweight (%)	1 (25.0)	259 (44.8)	
Obese (%)	2 (50.0)	107 (18.5)	
Antibiotic therapy			
Cefazolin (%)	4 (100.0)	560 (96.9)	$P = 1.00$; Fisher's test
Clindamycin (%)	-	18 (3.1)	
Additional antibiotic doses			
Yes (%)	1 (25.0)	20 (3.5)	$P = 0.137$; Fisher's test
Not (%)	3 (75.0)	559 (96.5)	
Diagnosis			
Coxartrosis (%)	3 (75.0)	370 (97.6)	$P = 1.00$; Fisher's test
Dysplasia (%)	1 (25.0)	9 (2.4)	
Bearings			
Cer-cer (%)	4 (100.0)	522 (90.2)	$P = 0.001$; χ^2 test
Cer-pol (%)	-	8 (1.4)	
Met-pol (%)	-	49 (8.5)	
Steroid			
Yes (%)	1 (25.0)	14 (2.4)	$P = 0.1$; Fisher's test
Not (%)	3 (75.0)	562 (97.6)	
Immunosuppressants			
Yes (%)	-	13 (2.3)	$P = 0.1$; Fisher's test
Not (%)	4 (100.0)	564 (97.7)	
Antiaggregant drugs			
Yes (%)	1 (25.0)	116 (20.1)	$P = 1.00$; Fisher's test
Not (%)	3 (75.0)	460 (79.9)	
Local surgery before the operation			
Yes (%)	-	66 (11.5)	$P = 1.00$; Fisher's test
Not (%)	4 (100.0)	507 (88.5)	
COPD			
Yes (%)	-	78 (13.5)	$P = 1.00$; Fisher's test
Not (%)	4 (100.0)	500 (86.5)	
Chronic renal insufficiency			
Yes (%)	1 (25.0)	20 (3.5)	$P = 0.137$; Fisher's test
Not (%)	3 (75.0)	558 (96.5)	
Preexisting heart ischemic conditions			

Yes (%)	1 (25.0)	51 (8.8)	P = 0.313; Fisher's test
Not (%)	3 (75.0)	527 (91.2)	
Diabetes			
Yes (%)	-	44 (7.6)	P = 1.00; Fisher's test
Not (%)	4 (100.0)	533 (92.4)	
Rheumatological conditions			
Yes (%)	-	12 (2.1)	P = 1.00; Fisher's test
Not (%)	4 (100.0)	565 (97.9)	
Previously local septic conditions			
Yes (%)	-	6 (1.0)	P = 1.00; Fisher's test
Not (%)	4 (100.0)	571 (99.1)	
Blood transfusion			
Yes (%)	1 (25.0)	98 (16.9)	P = 1.00; Fisher's test
Not (%)	3 (75.0)	468 (80.8)	
Prosthesis fixation			
Uncemented (%)	4 (100.0)	570 (98.4)	P = 1.00; Fisher's test
Cemented stem and uncemented cup (%)	-	9 (1.6)	
Time of intervention			
(07-12) (%)	4 (100.0)	442 (76.3)	P = 0.578; Fisher's test
(12-19) (%)	0	137 (23.7)	

Cer-Cer: Ceramic on ceramic; Cer-pol; Ceramic on polyethylene; COPD: Chronic obstructive pulmonary disease; Cup: Met-pol: Metal on polyethylene.

different types of drugs and doses, of whom one patient had a PJI. In the PJI group (see Table 1), 3 patients underwent THR for primary arthrosis and 1 for hip dysplasia (P = 1.00, Fisher's test). Regarding the bearing, 526 were ceramic on ceramic (90.2%), 8 were ceramics on polyethylene (1.4%), and 49 were metal on polyethylene (8.4%). In the PJI group, they were all ceramic on ceramic (P = 0.001, χ^2 test). Five hundred and seventy stems were uncemented (98.4%) and only nine were cemented (1.6%). All PJIs occurred in the prosthesis with uncemented stems. (P = 1.000, Fisher's test). Regarding the use of drugs, 565 patients (97.4%) did not use steroids and only 15 (2.6%) used them before surgery. In the PJI group, only 1 patient used drugs before intervention (P = 0.1, Fisher's test). Five hundred and sixty-eight patients (97.8%) did not use immunosuppressants and only thirteen (2.2%) used them before and after the intervention. In the PJI group, no patient used immunosuppressants (P = 0.1, Fisher's test). Four hundred and sixty-three patients (79.8%) did not use antiaggregant and one hundred and seventeen (20.2%) used it before intervention. In the PJI group, only 1 was using antiaggregant (P = 1.000, Fisher's test). Five hundred and eleven patients (88.6%) did not have local surgery before the operation and sixty-six did (11.4%). In the PJI group, none of the patients did (P = 1.000, Fisher's test). Considering the preoperative hemoglobin value, we found that it was less than 12 g/dL in 25 cases (4.3%) and higher in 557 cases (95.7%). In the PJI group, all patients had a value superior to 12 g/dL.

We considered the incidence of PJI in relation to COPD, and there were 504 cases (86.6%) without lung disease and 78 with COPD (13.4%). PJI occurred in all patients without COPD (P = 1.000, Fisher's test). Five hundred and sixty-one patients (96.4%) did not have chronic renal insufficiency (CRI) and twenty-one had CRI (3.6%); data were missing for one patient. In the PJI group, 3 patients suffered from CRI and 1 did not (P = 0.137, Fisher's test).

Considering the incidence of PJI in relation to preexisting heart ischemic conditions, 530 patients (91.1%) did not have heart disease before and after the operation, 52 patients (8.9%) had different degrees of ischemic condition preoperatively. For 1 patient, the data were missing. Only 1 patient with this comorbidity had PJI and the other 3 did not have any heart disease (P = 0.313, Fisher's test). Considering the incidence of PJI in relation of diabetes, there were 537 cases (92.4%) without diabetes and 44 with the disease (7.6%). The data were missing for 2 patients. We were not able to recognize the degree and type of the disease. PJIs occurred in all patients without diabetes (P = 1.000, Fisher's test). Considering the incidence of PJI in relation to rheumatological conditions, there were 569 cases (97.9%) without and 12 with rheumatological disease (2.1%). The data were missing for 2 patients. PJI patients did not suffer from/have any rheumatological condition (P = 1.000, Fisher's test). Considering the

incidence of PJI in relation to previously local septic conditions, there were 575 cases (99%) without previous septic conditions and 6 with them (1%). The data were missing for 2 patients. PJI was present in all patients without previous septic conditions (P = 1.000, Fisher's test). Laboratory data are summarized in Table 1.

For the erythrocyte sedimentation rate (ESR) value, the preoperative mean was 11.1 mm (the data were missing in 2 cases): 11.1 mm for all cases without PJI and 11 mm for cases with PJI. For the C-reactive protein (CRP) value, the preoperative mean was 0.9 mg/dL (data were missing in 16 cases): 0.9 mg/dL for all cases without PJI and 0.5 mg/dL for cases with PJI. For the WBC count, the preoperative mean was 7199.5 × 10^6/L (the data were missing in 20 cases): 7192.55 × 10^6/L for all cases without PJI and 8177.55 × 10^6/L for cases with PJI. For the Hb value, the preoperative mean was 13.9 g/dL (the data were missing in 16 cases): 13.9 g/dL for all cases without PJI and 14.6 g/dL for cases with PJI (see Table 2).

We analyzed the same parameters in the postoperative period: the day after surgery, the last day of hospitalization, and a random day between these days. We did not have these three parameters for all patients and many others had more than three values. In the last case, we picked up the lowest data. Analyses of the data showed that the average Hb value the day after the operation was 11.1 g/dL: 11.1 g/dL for all cases without PJI and 11.0 g/dL for the 4 cases with PJI (the data were missing for 2 patients). The average WBC count was 9804.5 × 10^6/L: 9821.5 × 10^6/L for cases without PJI and 7360.0 × 10^6/L for cases with PJI (see Table 2).

Analyses of the data showed that the average Hb value of the intermediate sample was 10.0 g/dL: 10.0 g/dL for all cases without PJI and 10.6 g/dL for the 4 cases with PJI (the data were missing for 33 patients). The intermediate average of WBC count was 8984.9 × 10^6/L: 8997.6 × 10^6/L for cases without PJI and 7257.5 × 10^6/L for cases with PJI. The samples on the last day of hospitalization showed that the average Hb value for all patients was 10.1 g/dL: 10.1 g/dL for all cases without PJI and 10.7 g/dL for the 4 cases with PJI. On the last day of hospitalization, the average WBC count was 7759.1 × 10^6/L: 7764.4 × 10^6/L for cases without PJI and 7764.4 × 10^6/L for cases with PJI (data were missing in 42 patients) (See Tables 1 and 2).

Regarding blood transfusion, 450 patients (77.2%) did not have a blood transfusion, 3 of whom were part of the PJI group, 133 (22.8%) had one or more homologous blood sack, only 1 had PJI (P = 1.000, Fisher's test). The average time of operation was 01:17:42 (min 00:37:00 max 04:03:00): 01:17:38 (min 00:37:00 max 04:03:00) for patients without PJI and 01:26:45 (min 00:56:00 max 02:31:00) for patients with PJI. Four hundred and forty-six patients (76.5%) were operated on between 07:00 and 12:00 and 137 (23.5%) between 12:00 to 19:00. All PJI patients were operated from 07:00 to 12:00.

RESULTS

Infections are classified according to their temporal appearance[4], even though many systems proposed are not always accepted[8]. We defined acute infection as symptoms lasting less than 4 wk, and chronic as lasting more than 4 wk. Many kinds of treatments have been proposed with different indications and results[2-6]. All surgeons agree with the difficulties of the different approaches to treat a PJI (surgery and drugs with multidisciplinary approaches)[4-6,9]. For these reasons, we reviewed all cases of THR treated in 2016 in our Department of Orthopedic Surgery to identify preoperative and postoperative signs to predict a PJI.

All cases were operated on by no more than 10 different surgeons at our department in the same operating room with laminar airflow. All cases underwent the same type of surgery: lateral approach with detachment of the gluteus minimus and medius and reconstruction of the hip capsule. All cases had the drainage removed within 24 h after surgery. Standard procedures of antibiotic prophylaxis were followed: cefazolin 2 g in most of the patients and clindamycin 600 mg in allergic patients.

Four patients had a PJI: two within 30 d, one 6 mo later, and one 13 mo later. All patients were surgically treated with deep or superficial debridement first[2]. One of these patients underwent a two-stage revision after this surgical procedure. Analyzing sex, we founded that PJI incidence was higher in females than men (see Table 1), but data were not statistically significant as in many other studies[10]. Regarding age (see Table 1), no differences were observed between the two groups, as previously reported[11].

Analyzing antibiotic therapy (see Table 1), all patients with PJI were treated with single-dose cefazolin 2 g before surgery. After surgery, many patients had postoperative antibiotic treatment (see Table 1), 1 of whom developed a PJI. Even in this case, we did not find a difference between the two groups. Regarding the indications that led to the operation, no category showed a higher risk than another. Analyses of the bearings and different types of prostheses did not show a difference in the incidence of PJI. Analyses of the use of drugs such as steroids, immunosuppressors, and anticoagulants showed that PJI did not have a higher incidence in any patient, which disagrees with a previous study [12]. We did not find differences in Hb value and WBC count between the two groups of patients (see Table 2). We did not analyze the CRP and ESR due to the lack of values for many patients.

Table 2 Blood values according to periprosthetic joint infection

	Infection (yes)				Infection (not)			
	Pre	T1	T2	Last	Pre	T1	T2	Last
Hemoglobin	14.6	11.0	10.6	10.7	13.9	11.1	10.0	10.1
White blood cells	8177.5	7360.0	7257.5	7040.0	7192.5	9821.5	8997.6	7764.4

Data are means.

In the analysis of blood transfusions in relation to PJI, 133 patients were transfused with one or more blood sacks, and 450 did not receive any transfusion. PJI occurred in 3 of the non-transfused patients and in 1 transfused patient. Analyses of the blood transfusions showed a higher incidence of PJI in transfused patients but it was not statistically significant, in disagreement with a previous study[13]. Analyzing the time of surgery, we divided the patients in two groups: 7.00 am to 12.00 and 12.00 to 19.00. All cases of PJI occurred in patients in the first group (7.00-12.00). There were no statistically significant differences in any of those groups, in disagreement with a previously study[12] (Table 1).

DISCUSSION

One of the most difficult and important targets in surgery is to avoid or early diagnose a PJI. Although the incidence of PJI is very low (0.69%) in our department, with an average follow-up of 595 d, this infection poses a serious threat due to the difficulties of treatment and the lower functional outcomes after healing[1]. We did not find any class with an evident major risk of PJI. In our study, we did not find any border value to predict PJI and all patients had similar parameters in both groups (non-PJI and PJI), in contrast to a previous study[14]. For some categories, such as sex, we observed a higher frequency of PJI in females than in males, but this difference was not statistically significant. Other authors have reported a higher incidence in males[12,15]. We did not find other studies with the control of blood values preoperatively and postoperatively in relation to the likelihood of PJI. Due to the lack of a sufficient number of patients, especially in the PJI group, we could not demonstrate a statistically significant difference between non-PJI patients and PJI ones. Maybe PJI has a multifactorial etiology[16] and our few cases of PJI could not demonstrate a higher incidence despite the reports in other studies[9,14,17,18]. Furthermore, we were unable to analyze other data such as urinary screening[19], which may also play a role in the prediction of a PJI, even though some authors have expressed doubts[20,21]. Some studies[20,21] have emphasized the increasing baseline risk of PJI with the increasing number of comorbidities. Another limit of this study was the inability to grade the severity of comorbidities. Many studies have reported different prognoses for different types and degrees of preexisting diseases[22]. All of these detailed analyses could not be carried out in our study, which is a limitation. The percentage of PJI was very low in our patients, and worldwide its incidence is decreasing due to surgical and drug management. Nonetheless, preoperative and postoperative THR surveillance needs to be more accurate in the future[23].

CONCLUSION

From the experience of all operations for THR performed at our department in the year 2016 we did not find any data that could help us avoid, predict, or early diagnose a PJI. This disagrees with other studies [14,16] and many accepted and undiscussed scientific convictions. The difference between our study and others may have been due to the low number of cases, especially in the PJI group (only 4 cases).

ARTICLE HIGHLIGHTS

Research background

Periprosthetic joint infection (PJI) in primary total hip replacement (THR) is one of the most important challenges in orthopedic surgery, so one important surgeon's goal is to avoid or diagnose a PJI early.

Research motivation

The incidence of PJI is very low (0.69%) in our department, with an average follow-up of 595 d. This infection poses a serious threat due to the difficulties of treatment and the lower functional outcomes

after healing.

Research objectives
We tried to identify predictive signs of potential infection with the goal of exploring methodological approaches that could better inform daily orthopedic practice.

Research methods
We counted 583 THR for 578 patients and observed only 4 cases of infection (0.69%) with a mean follow-up of 596 d (min 30 max 1451). We reviewed duration and time of the surgery, presence, type and duration of the antibiotic therapy, preoperative diagnosis, blood values before and after surgery, transfusions, presence of preoperative drugs, and presence of some comorbidities to look for statistically significant differences between the patients that did and did not develop a PJI.

Research results
No preoperative, intraoperative, or postoperative analysis showed a higher incidence of PJI. We did not find any class with evident major risk of PJI. Some categories, such as female patients, showed a higher frequency of PJI, but this difference related to sex was not statistically significant.

Research conclusions
We did not find any category with a higher risk of PJI in THR, probably due to the lack of few cases of infection.

Research perspectives
PJI is an important topic and more research about the subject is needed. Probably due to the low number of cases, especially in the PJI group (4 cases), we did not attain the results we were expecting. Future studies are needed to add new information to the scientific literature, for example, data spanning 5 years or combined from multiple centers.

FOOTNOTES

Author contributions: Tella GF, Donadono C, Castagnini F, Bordini B, Cosentino M, Di Liddo M, and Traina F contributed equally to all aspects of this work.

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REFERENCES

1 **Herman BV**, Nyland M, Somerville L, MacDonald SJ, Lanting BA, Howard JL. Functional outcomes of infected hip arthroplasty: a comparison of different surgical treatment options. *Hip Int* 2017; **27**: 245-250 [PMID: 27911455 DOI: 10.5301/hipint.5000455]

2 **Barros LH**, Barbosa TA, Esteves J, Abreu M, Soares D, Sousa R. Early Debridement, antibiotics and implant retention (DAIR) in patients with suspected acute infection after hip or knee arthroplasty - safe, effective and without negative functional impact. *J Bone Jt Infect* 2019; **4**: 300-305 [PMID: 31966962 DOI: 10.7150/jbji.39168]

3 **Castagnini F**, Tella G, Montalti M, Biondi F, Bordini B, Busanelli L, Toni A. Mid-term outcomes of a partial 2-stage approach in late chronic periprosthetic hip infections. *Hip Int* 2020; **30**: 327-332 [PMID: 31894700 DOI: 10.1177/1120700019855627]

4 **Renz N**, Trebse R, Akgün D, Perka C, Trampuz A. Enterococcal periprosthetic joint infection: clinical and microbiological findings from an 8-year retrospective cohort study. *BMC Infect Dis* 2019; **19**: 1083 [PMID: 31881851 DOI: 10.1186/s12879-019-4691-y]

5 **Shirai T**, Tsuchiya H, Terauchi R, Tsuchida S, Mizoshiri N, Mori Y, Takeuchi A, Hayashi K, Yamamoto N, Ikoma K, Kubo T. A retrospective study of antibacterial iodine-coated implants for postoperative infection. *Medicine (Baltimore)* 2019; **98**: e17932 [PMID: 31702678 DOI: 10.1097/MD.0000000000017932]

6 **Ebied AM**, Elseedy AI, Gamal O. Single-stage revision for periprosthetic hip infection using antibiotic loaded impaction graft. *Hip Int* 2016; **26**: 573-579 [PMID: 27739567 DOI: 10.5301/hipint.5000401]

7 **Gundtoft PH**, Pedersen AB, Schønheyder HC, Møller JK, Overgaard S. One-year incidence of prosthetic joint infection in total hip arthroplasty: a cohort study with linkage of the Danish Hip Arthroplasty Register and Danish Microbiology Databases. *Osteoarthritis Cartilage* 2017; **25**: 685-693 [PMID: 27986623 DOI: 10.1016/j.joca.2016.12.010]

8 **Guan H**, Fu J, Li X, Chai W, Hao L, Li R, Zhao J, Chen J. The 2018 new definition of periprosthetic joint infection improves the diagnostic efficiency in the Chinese population. *J Orthop Surg Res* 2019; **14**: 151 [PMID: 31126290 DOI: 10.1186/s13018-019-1185-y]

9 **Rosteius T**, Jansen O, Fehmer T, Baecker H, Citak M, Schildhauer TA, Geßmann J. Evaluating the microbial pattern of periprosthetic joint infections of the hip and knee. *J Med Microbiol* 2018; **67**: 1608-1613 [PMID: 30207518 DOI: 10.1099/jmm.0.000835]

10 **Yokoe DS**, Avery TR, Platt R, Huang SS. Reporting surgical site infections following total hip and knee arthroplasty: impact of limiting surveillance to the operative hospital. *Clin Infect Dis* 2013; **57**: 1282-1288 [PMID: 23912846 DOI: 10.1093/cid/cit516]

11 **Mei XY**, Gong YJ, Safir O, Gross A, Kuzyk P. Long-term outcomes of total hip arthroplasty in patients younger than 55 years: a systematic review of the contemporary literature. *Can J Surg* 2019; **62**: 249-258 [PMID: 31348632 DOI: 10.1503/cjs.013118]

12 **Ong KL**, Kurtz SM, Lau E, Bozic KJ, Berry DJ, Parvizi J. Prosthetic joint infection risk after total hip arthroplasty in the Medicare population. *J Arthroplasty* 2009; **24**: 105-109 [PMID: 19493644 DOI: 10.1016/j.arth.2009.04.027]

13 **Berbari EF**, Hanssen AD, Duffy MC, Steckelberg JM, Ilstrup DM, Harmsen WS, Osmon DR. Risk factors for prosthetic joint infection: case-control study. *Clin Infect Dis* 1998; **27**: 1247-1254 [PMID: 9827278 DOI: 10.1086/514991]

14 **Triantafyllopoulos GK**, Soranoglou VG, Memtsoudis SG, Sculco TP, Poultsides LA. Rate and Risk Factors for Periprosthetic Joint Infection Among 36,494 Primary Total Hip Arthroplasties. *J Arthroplasty* 2018; **33**: 1166-1170 [PMID: 29248486 DOI: 10.1016/j.arth.2017.11.040]

15 **McMaster Arthroplasty Collaborative (MAC)**. Risk Factors for Periprosthetic Joint Infection Following Primary Total Hip Arthroplasty: A 15-Year, Population-Based Cohort Study. *J Bone Joint Surg Am* 2020; **102**: 503-509 [PMID: 31876641 DOI: 10.2106/JBJS.19.00537]

16 **Saleh K**, Olson M, Resig S, Bershadsky B, Kuskowski M, Gioe T, Robinson H, Schmidt R, McElfresh E. Predictors of wound infection in hip and knee joint replacement: results from a 20 year surveillance program. *J Orthop Res* 2002; **20**: 506-515 [PMID: 12038624 DOI: 10.1016/S0736-0266(01)00153-X]

17 **Purcell RL**, Parks NL, Cody JP, Hamilton WG. Comparison of Wound Complications and Deep Infections With Direct Anterior and Posterior Approaches in Obese Hip Arthroplasty Patients. *J Arthroplasty* 2018; **33**: 220-223 [PMID: 28864031 DOI: 10.1016/j.arth.2017.07.047]

18 **de Jong L**, Klem TMAL, Kuijper TM, Roukema GR. Factors affecting the rate of surgical site infection in patients after hemiarthroplasty of the hip following a fracture of the neck of the femur. *Bone Joint J* 2017; **99-B**: 1088-1094 [PMID: 28768787 DOI: 10.1302/0301-620X.99B8.BJJ-2016-1119.R1]

19 **Sousa RJG**, Abreu MA, Wouthuyzen-Bakker M, Soriano AV. Is Routine Urinary Screening Indicated Prior To Elective Total Joint Arthroplasty? *J Arthroplasty* 2019; **34**: 1523-1530 [PMID: 30956050 DOI: 10.1016/j.arth.2019.03.034]

20 **Saeed K**, Dryden M, Bassetti M, Bonnet E, Bouza E, Chan M, Cortes N, Davis JS, Esposito S, Giordano G, Gould I, Hartwright D, Lye D, Marin M, Morgan-Jones R, Lajara-Marco F, Righi E, Romano CL, Segreti J, Unal S, Williams RL, Yalcin AN; International Society of Chemotherapy. Prosthetic joints: shining lights on challenging blind spots. *Int J Antimicrob Agents* 2017; **49**: 153-161 [PMID: 27939092 DOI: 10.1016/j.ijantimicag.2016.10.015]

21 **Lai K**, Bohm ER, Burnell C, Hedden DR. Presence of medical comorbidities in patients with infected primary hip or knee arthroplasties. *J Arthroplasty* 2007; **22**: 651-656 [PMID: 17689771 DOI: 10.1016/j.arth.2006.09.002]

22 **Duensing I**, Anderson MB, Meeks HD, Curtin K, Gililland JM. Patients with Type-1 Diabetes Are at Greater Risk of Periprosthetic Joint Infection: A Population-Based, Retrospective, Cohort Study. *J Bone Joint Surg Am* 2019; **101**: 1860-1867 [PMID: 31626011 DOI: 10.2106/JBJS.19.00080]

23 **Løwer HL**, Dale H, Eriksen HM, Aavitsland P, Skjeldestad FE. Surgical site infections after hip arthroplasty in Norway, 2005-2011: influence of duration and intensity of postdischarge surveillance. *Am J Infect Control* 2015; **43**: 323-328 [PMID: 25672951 DOI: 10.1016/j.ajic.2014.12.013]

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ORIGINAL ARTICLE

Retrospective Cohort Study

Adjunctive platelet-rich plasma and hyaluronic acid injection after arthroscopic debridement in Kellgren-Lawrence grade 3 and 4 knee osteoarthritis

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Abstract

BACKGROUND

Osteoarthritis (OA) is the most common cause of pain and disability, predominantly affecting the knee. The current management of knee OA falls short of completely stopping disease progression, particularly in Kellgren-Lawrence (KL) grade 3 and 4 knee OA. As such, joint replacement is often recommended, although only 15%-33% of candidates accept it. Alternative therapeutic options are still needed to prevent the progression of joint damage and delay the need for knee arthroplasty.

AIM

To investigate the effect of adjunctive platelet rich plasma (PRP) and hyaluronic acid (HA) after arthroscopic debridement in KL grade 3 and 4 knee OA.

METHODS

This retrospective cohort study used the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) score and WOMAC sub-scores (pain, stiffness, and function) to assess 21 patients, grouped according to medical record data of treatment received: Arthroscopic debridement (n = 7); arthroscopic debridement with PRP (n = 7); or arthroscopic debridement with HA (n = 7). WOMAC scores and sub-scores at baseline and at 3 mo and 5 mo posttreatment were recorded. The three-group data were statistically analyzed using the tests of paired t, one-way analysis of variance, and post hoc least significant difference.

RESULTS

All three treatment groups showed significant improvements in WOMAC score and sub-scores from before treatment to 3 mo and 5 mo after treatment. However,

the arthroscopic debridement with PRP treatment group, in particular, showed a significantly lower WOMAC pain score than the group who received arthroscopic debridement alone at 5 mo after the procedure (P = 0.03).

CONCLUSION
Compared to arthroscopic debridement alone, adjunctive PRP after arthroscopic debridement significantly lessened the patients' pain symptom.

Key Words: Arthroscopic debridement; Hyaluronic acid; Osteoarthritis; Platelet-rich plasma; Western Ontario and McMaster Universities Osteoarthritis Index; WOMAC score

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Core Tip: This manuscript highlights the alternative approaches in managing knee osteoarthritis of Kellgren-Lawrence grade 3 and 4. Outcomes of arthroscopic debridement, arthroscopic debridement with platelet-rich plasma (PRP), or arthroscopic debridement with hyaluronic acid were evaluated prior to treatment and at 3 mo and 5 mo after the procedure. According to the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) score and sub-scores (pain, stiffness, function), arthroscopic debridement with PRP provided significantly lower pain than arthroscopic debridement after treatment, however neither treatment was superior in the ability to improve total WOMAC score.

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INTRODUCTION

Osteoarthritis (OA) is the leading cause of pain and disability, with a 10-fold increased incidence and prevalence occurring in 30-years-old to 65-years-old age range[1-3]. In Indonesia, the prevalence of knee OA is appreciable, at 15.5% for men and 12.7% for women, with rates following the trend of increase with increased age[4].

To date, the management of knee OA is only capable of addressing symptomatic features and has been ineffective in halting progression of the disease itself. In the advanced stage of knee OA, joint replacement is the recommended management; since only 15%-33% of knee arthroplasty candidates are willing to submit themselves to the extensive surgery and recovery, an alternative treatment option is needed[5-8]. The proposed treatment involves adjunctive administration of platelet rich plasma (PRP) or hyaluronic acid (HA) following the knee arthroscopy. PRP is the blood's plasma component that has been prepared with a high concentration of platelets, which express the cytokines and growth factors to stimulate cartilage repair and inflammation decrease[6,7,9]. In knee OA, PRP has been shown to improve both the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) score and the 36-item Short Form survey (commonly known as the SF-36) score[10,11]. Intraarticular HA injection has shown the benefits of chondroprotective effect, pain decrease, inflammatory response modulation and endogenous HA synthesis increase, and its wide application has demonstrated success in decreasing knee OA symptoms[12-15].

In this study, we aimed to investigate whether adjunctive treatment with PRP or HA after arthroscopic debridement was able to provide better outcomes then arthroscopic debridement alone.

MATERIALS AND METHODS

This was a retrospective cohort study based on medical record data. All treatments were performed by a single orthopedic surgeon in Denpasar, Bali, Indonesia between January 2021 and December 2021. Data were collected at Sanglah General Hospital and Surya Husada Ubung Hospital (Denpasar, Bali, Indonesia). The study sample was made up of KL grade 3 and 4 knee OA patients who had undergone arthroscopic debridement, arthroscopic debridement with PRP, or arthroscopic debridement with HA. The inclusion criteria were KL grade 3 and 4 knee OA patients, with diagnosis based on American College of Rheumatology Clinical and Radiological Classification Criteria, of ages 40-years-old to 70-

years-old, and who had failed conservative treatment. Patients with knee deformity due to trauma or congenital knee deformity were excluded. The study sample size was calculated according to a false positive rate of 5% (α = 0.5) and 80% power (β = 0.2), and on a predicted difference 56.87 point on mean WOMAC score changes (standard deviation 37.26)[16]. Accordingly, for multiple-group comparison, a minimum of 6 patients per group were determined to be required, and we included 7 patients per group.

The total 21 patients (n = 7 per three treatment groups) underwent the standard arthroscopic debridement procedure under general anesthesia. As a minimally invasive procedure, arthroscopic debridement is performed by inserting arthroscopes through small incisions, followed by debridement and irrigation. Debridement of necrotic chondral tissue is carried out to remove it from the cartilage, with subsequent saline-solution washing by irrigation[17]. For our patients, either PRP or HA was administered at 1 wk postsurgically *via* intraarticular injection to the patelofemoral joint under aseptic conditions. The HA treatment consisted of 3 mL Hyajoint-plus® (Macopharma, Tourcoing, France) at 20 mg/mL, while the PRP preparation protocol consisted of RegenKit® (Regen Lab, New York, NY, United States) administered as 5 mL. Any meniscus tear found during surgery was recorded and noted for its potential to serve as a confounding factor. There were no adverse reactions noted in the medical record data for any of the total 21 patients.

Outcomes

WOMAC score is an assessment instrument specific to OA that is widely used to evaluate symptom improvement in knee OA. WOMAC sub-scores consist of pain, stiffness, and functional assessments. Overall, the WOMAC and its sub-scores are reputed as reliable, valid, and responsive to change in patients with OA symptoms[18]. The highest total score is 96, with a lower score indicating improvement in knee OA symptoms.

We did not use magnetic resonance imaging (MRI) assessment as outcome measurement since this imaging modality was not in routine use in our hospitals during the study period.

Analysis

Data were analyzed using the Statistical Package for Social Sciences software (IBM Corp., Armonk, NY, United States). The Shapiro-Wilks normality test was performed. One-way analysis of variance was used to compare WOMAC scores among the three groups, and post hoc analysis was conducted using the least significant difference (commonly known as LSD) test. The paired t-test was used to compare baseline and follow-up WOMAC scores. $P < 0.05$ was considered statistically significant.

RESULTS

Subjects' characteristics

Among the 21 total patients included in the study, 61.9% were female and 38.1% were male. The mean age of the patients was 59.29 ± 6.61 years. Sixty-six percent of the patients had right knee OA and the remaining patients had left knee OA. None of the subjects had bilateral knee OA. Seventy-one percent of the patients had KL grade 3, and meniscus tear was found in 10 patients (47.6%) during surgery. The subjects' characteristics are summarized in Table 1.

WOMAC score and sub-scores

Before/after treatment comparisons showed that patients in all three groups had significantly lower WOMAC scores at 3 mo and 5 mo follow-up (Table 2). In the arthroscopic debridement group, a significant reduction was also found in pain score and physical function score at 3 mo follow-up (P = 0.002 and 0.011 respectively) and 5 mo follow-up (P = 0.000 and 0.001 respectively) but not in stiffness score, which was not significantly reduced at either the 3 mo or 5 mo follow-up (P = 0.091 and 0.067 respectively). In the arthroscopic debridement with HA group, a significant reductions was found in pain score and physical function score at 3 mo follow-up (P = 0.001 and 0.004 respectively) and 5 mo follow-up (P =0.001 and 0.000 respectively). In this group, the stiffness score was significantly reduced at the 5 mo follow-up (P = 0.026) but not at the 3 mo follow-up (P = 0.160). The arthroscopic debridement with PRP group showed a significant reduction in all WOMAC sub-scores at the 3 mo follow-up (P = 0.000, 0.019, and 0.001) and 5 mo follow-up (P = 0.000, 0.011, and 0.001 for pain, stiffness, and physical function scores respectively). Results from the paired t-test analyses are detailed in Table 2.

We also performed between-group comparisons for WOMAC score and sub-scores before treatment (at baseline) and after treatment (at the 3 mo and 5 mo follow-up); the findings are illustrated in Figure 1. At baseline, the mean WOMAC score was statistically similar among all groups (P = 0.65), with the arthroscopic debridement group having a mean ± SD score of 49.43 ± 10.33, the arthroscopic debridement with HA group having a mean ± SD score of 54.43 ± 14.55, and the arthroscopic debridement with PRP group having a mean ± SD score of 49.86 ± 7.22. No treatment was superior to another for WOMAC score at either the 3 mo follow-up or the 5 mo follow-up (P = 0.23 and 0.56

Table 1 Patient characteristics

Characteristic		Mean	Arthroscopic debridement	Arthroscopic debridement + HA	Arthroscopic debridement + PRP	*P* value
Patients		7	7	7	7	N/A
Age (yr)		59.29 ± 6.61	58.29 ± 6.75	57.29 ± 7.16	62.29 ± 5.71	0.34
Sex	Male	8 (38.1%)	3 (42.9%)	2 (28.6%)	3 (42.9%)	0.82
	Female	13 (61.9%)	4 (57.2%)	5 (71.4%)	4 (57.2%)	
Affected knee	Right	14 (66.7%)	5 (71.4%)	6 (85.7%)	3 (42.9%)	0.22
	Left	7 (33.3%)	2 (28.6%)	1 (14.3%)	4 (57.2%)	
KL grade	3	15 (71.4%)	7 (100%)	2 (28.6%)	6 (85.7%)	0.01
	4	6 (28.6%)	0	5 (71.4%)	1 (14.3%)	
Meniscus tear	Yes	10 (47.6%)	2 (28.6%)	5 (71.4%)	3 (42.9%)	0.25
	No	11 (52.4%)	5 (71.4%)	2 (28.6%)	4 (57.1%)	

Data are presented as *n* (%) or mean ± SD. HA: Hyaluronic acid; KL: Kellgren-Lawrence; N/A: Not applicable; PRP: Platelet-rich plasma.

Table 2 Paired *t*-test analysis of Western Ontario and McMaster Universities Osteoarthritis Index scores and sub-scores

Treatment	Outcome	Baseline	3 mo	5 mo	Paired *t*-test			
					Baseline *vs* 3 mo		Baseline *vs* 5 mo	
					t value	*P* value	*t* value	*P* value
Arthroscopic debridement	WOMAC score	49.43 ± 10.33	28.57 ± 9.09	18.57 ± 7.12	5.143	0.002	8.712	0.000
	Pain score	12.43 ± 2.76	6.00 ± 2.65	4.14 ± 3.02	5.391	0.002	17.488	0.000
	Stiffness score	4.57 ± 2.15	3.00 ± 0.82	2.14 ± 2.12	2.008	0.091	2.232	0.067
	Function score	32.43 ± 8.89	19.57 ± 7.30	12.29 ± 3.64	3.658	0.011	6.134	0.001
Arthroscopic debridement + HA	WOMAC score	54.43 ± 14.55	24.86 ± 12.09	14.86 ± 5.58	4.975	0.003	7.254	0.000
	Pain score	12.57 ± 4.50	4.43 ± 2.44	2.14 ± 0.70	5.943	0.001	6.177	0.001
	Stiffness score	4.57 ± 2.82	2.43 ± 1.62	0.86 ± 1.21	1.605	0.160	2.931	0.026
	Function score	37.29 ± 9.66	18.00 ± 8.87	11.86 ± 4.22	4.559	0.004	7.0029	0.000
Arthroscopic debridement + PRP	WOMAC score	49.86 ± 7.22	19.71 ± 5.74	15.00 ± 8.45	7.827	0.000	8.105	0.000
	Pain score	13.14 ± 2.34	4.14 ± 1.86	1.71 ± 0.95	7.937	0.000	12.060	0.000
	Stiffness score	5.43 ± 3.16	1.71 ± 1.38	0.86 ± 1.07	3.176	0.019	3.600	0.011
	Function score	31.29 ± 6.26	13.86 ± 4.10	12.43 ± 6.80	6.397	0.001	5.781	0.001

HA: Hyaluronic acid; PRP: Platelet-rich plasma; WOMAC: Western Ontario and McMaster Universities Osteoarthritis Index.

respectively); the same was seen for the WOMAC sub-scores (Table 3). Upon post hoc analysis using the LSD test, pain score at the 5 mo follow-up was found to be significantly lower in the arthroscopic debridement with PRP group compared to the arthroscopic debridement group (P = 0.03) (Table 3).

DISCUSSION

OA was once considered a degenerative or "wear-and-tear" joint disease. However, it is now known to be a result of multifactorial interplay among mechanical factors, joint integrity, local inflammation, cellular, and biochemical processes[19]. To the best of our knowledge, our retrospective cohort study presented herein is the first to compare WOMAC score and WOMAC sub-score parameters between arthroscopic debridement treatments, alone and with postsurgical adjunctive PRP or HA, in KL grade 3

Table 3 Analysis of variance and least significance difference post hoc test for Western Ontario and McMaster Universities Osteoarthritis Index score and sub-scores

Score	Period	Arthroscopic debridement	Arthroscopic debridement + HA	Arthroscopic debridement + PRP	ANOVA *P* value	LSD post hoc test; *P* value		
						I *vs* II	I *vs* III	II *vs* III
WOMAC score	Baseline	49.43 ± 10.33	54.43 ± 14.55	49.86 ± 7.22	0.65	0.41	0.94	0.45
	3 mo	28.57 ± 9.09	24.86 ± 12.09	19.71 ± 5.74	0.23	0.47	0.09	0.32
	5 mo	18.57 ± 7.12	14.86 ± 5.58	15.00 ± 8.45	0.56	0.34	0.36	0.97
Pain score	Baseline	12.43 ± 2.76	12.57 ± 4.50	13.14 ± 2.34	0.91	0.94	0.69	0.75
	3 mo	6.00 ± 2.65	4.43 ± 2.44	4.14 ± 1.86	0.30	0.23	0.16	0.82
	5 mo	4.14 ± 3.02	2.14 ± 0.70	1.71 ± 0.95	0.06	0.06	0.03	0.67
Stiffness score	Baseline	4.57 ± 2.15	4.57 ± 2.82	5.43 ± 3.16	0.80	1.00	0.57	0.57
	3 mo	3.00 ± 0.82	2.43 ± 1.62	1.71 ± 1.38	0.22	0.43	0.08	0.32
	5 mo	2.14 ± 2.12	0.86 ± 1.21	0.86 ± 1.07	0.22	0.14	0.14	1.00
Function score	Baseline	32.43 ± 8.89	37.29 ± 9.66	31.29 ± 6.26	0.39	0.29	0.80	0.20
	3 mo	19.57 ± 7.30	18.00 ± 8.87	13.86 ± 4.10	0.32	0.68	0.15	0.29
	5 mo	12.29 ± 3.64	11.86 ± 4.22	12.43 ± 6.80	0.98	0.83	0.96	0.84

HA: Hyaluronic acid; PRP: Platelet-rich plasma; WOMAC: Western Ontario and McMaster Universities Osteoarthritis Index. I: Arthroscopic debridement; II: Arthroscopic debridement + HA; III: Arthroscopic debridement + PRP.

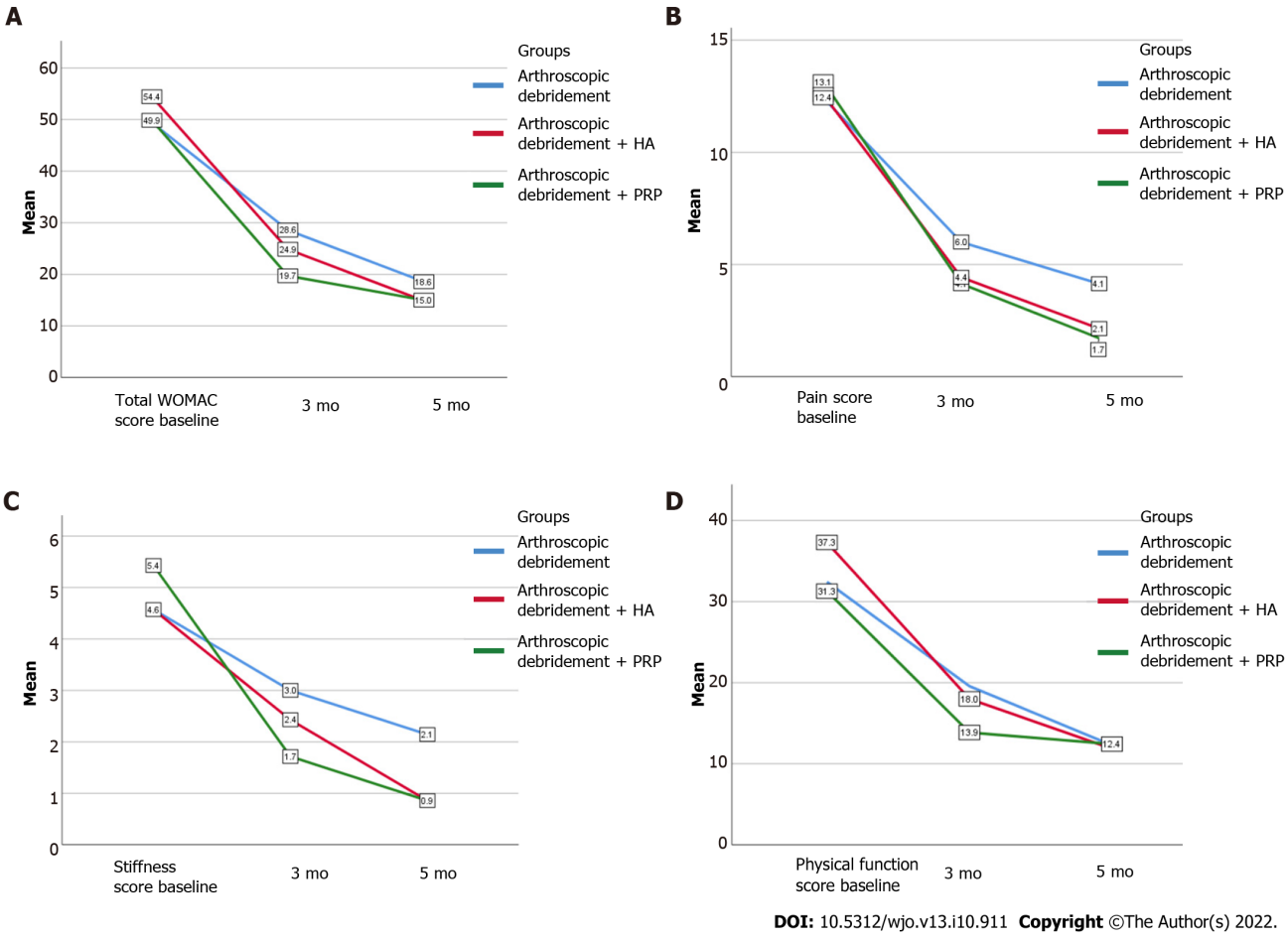
and 4 knee OA patients.

Arthroscopic debridement in knee OA is carried out when conservative treatment does not give satisfactory improvement in clinical symptoms but when joint replacement is not yet indicated[17]. Arthroscopy removes cartilage degradation products, mechanical irritants, and inflammatory cells from the joints, thus reducing pain and improving knee symptoms in KL grade 3 and 4 knee OA patients[20,21]. According to Kirkley *et al*[20], arthroscopy is able to delay total knee replacement in KL grade 3 knee OA patients aged ≥ 55 years. Steadman *et al*[22] further pinpointed that it was able to delay total knee replacement for 6.8 years. Despite the beneficial outcome, the use of arthroscopy in knee OA has remained controversial, with some studies reporting no significant difference being achieved through placebo arthroscopy, physical therapy, or medication[20,23]. However, adjunctive treatment with intraarticular HA or PRP injection after arthroscopic debridement has been expected to give better outcome than arthroscopic debridement alone.

Application of exogenous HA increases lubrication and reduces friction at the joint surface, thereby preventing chondrocyte degradation[13]. It also stimulates endogenous HA production[12] and produces anti-inflammatory effects by inhibiting tumor necrosis factor-alpha, interleukin (IL)-1 beta, and IL-8 expression[13]. The analgetic effects of HA treatment occur by its prompting a decrease in stress-activated ion channel sensitivity[12].

PRP is a small amount of plasma with concentrated platelets, giving it appreciable therapeutic anti-inflammatory, analgetic, and tissue regeneration properties. The anti-inflammatory effects occur through inhibition of the nuclear factor-kappa B (NF-κB) pathway and matrix metalloproteinases (MMPs)[24-27]. Upon application to the human system, it releases protease-activated receptor 4 peptide and anabolic chondral factors to provide analgetic effects[27,28]. PRP therapy also works in cartilage by releasing growth factors (specifically, platelet-derived growth factor and vascular endothelial growth factor, among various other growth factors), which are able to increase endogenous HA synthesis, re-epithelization, and tissue repair[29-32].

Our study showed significant reductions in WOMAC score and the sub-scores of pain and function for patients in the arthroscopic debridement group at their 3 mo and 5 mo follow-ups. These findings are in line with those from a study by Su *et al*[9], who showed that patients with KL grade 3 and 4 knee OA had significantly reduced WOMAC score at 1 year and 2 years after arthroscopic debridement, compared to conservative treatment. In another study, Bohnsack *et al*[21] performed arthroscopy in KL grade 3 and 4 knee OA patients and showed that Lysholm score (an 8-item knee scoring scale) was significantly improved, resulting in the improved ability to perform daily activities. In contrast, a study from Kirkley *et al*[20] showed that patients with KL grade 2-4 knee OA who underwent arthroscopic debridement and lavage experienced no significant improvement in WOMAC and SF-36 scores, compared to patients who received conservative treatment. Similarly, another study by Moseley *et al*[23] that compared arthroscopic debridement and placebo surgery (skin incision only) in knee OA patients



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Figure 1 Mean outcome scores at baseline and at 3 mo and 5 mo follow-ups. A: Mean Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) score; B: Mean pain score; C: Mean stiffness score; D: Mean physical function score. WOMAC: Western Ontario and McMaster Universities Osteoarthritis Index; HA: Hyaluronic acid; PRP: Platelet rich plasma.

yielded no significant difference in the groups' SF-36 and pain scale scores. Our study also showed that stiffness score did not significantly decrease in the arthroscopic debridement group. This could be due to the concept that application of the irrigation solution during arthroscopic debridement was not only meant to remove detritus but also synovial fluid and the HA-layer covering the cartilage; in this way, the shock absorbent layer and lubricating function would be affected[17].

We expected adjunctive treatment with HA intraarticular injection after arthroscopic debridement to overcome the limitation described directly above. And, indeed this was the case; our HA-treated arthroscopic debridement patients experienced significant improvement not only in WOMAC score, pain score, and function score at the 3 mo and 5 mo follow-ups but also in the stiffness score at the 5 mo follow-up. Similar improvements were shown in a study by Hempfling[17], which had compared knee arthroscopy with and without postprocedure HA injection. In that study, at the 12 mo follow-up, arthroscopy with HA was superior in clinical global impression, improved restricted ability to walk 100 m, pain on walking, and night pain. Atay *et al*[33] evaluated HA injections after arthroscopic debridement surgery in KL grade 2-3 knee OA and at 12 mo follow-up; there was a significant difference found in WOMAC score changes between the arthroscopy with HA group and the arthroscopy without HA group. Finally, a more recent meta-analysis by Shen *et al*[34] showed that HA after arthroscopy was able to reduce pain on motion, indicating that HA is significantly associated with increased physical function and WOMAC score.

Our search of the literature found no previous study on PRP injection following arthroscopic debridement in knee OA patients. In our study, this adjunctive treatment resulted in significantly lower WOMAC score and all WOMAC sub-scores at 3 mo and 5 mo follow-ups compared to baseline. Raeissadat *et al*[35] had evaluated WOMAC score in knee OA patients who received PRP injection; at the 6 mo follow-up, they found a significant improvement in WOMAC score and SF-36, compared to baseline. Another study by Patel *et al*[11] compared WOMAC score in knee OA patients who received one PRP injection, two PRP injections, or normal saline injection; a significant improvement in all WOMAC parameters occurred within 2 wk to 3 wk and lasted for 6 mo, whereas in the normal saline group, the WOMAC score worsened.

In our study, we compared WOMAC score and sub-scores between three treatment groups and there was no superiority between the groups. A pilot study by Trueba Vasavilbaso *et al*[16] comparing arthroscopic debridement, arthroscopic debridement with HA and arthroscopic debridement with PRP has shown that even though WOMAC score was significantly decreased at the 3 mo follow-up (*vs* baseline scores) in all groups, there was no significant difference in WOMAC score among them. A significant difference in WOMAC score was found at the 12 mo and 18 mo follow-ups, particularly between the group treated by arthroscopy alone and the group treated with arthroscopy and three HA injections. It is important to note that our relatively short follow-up time may have contributed to the non-significant differences in WOMAC score among the groups.

Post hoc analysis in our study showed a significant difference between the arthroscopic debridement and arthroscopic debridement with PRP groups in pain score at the 5 mo follow-up. This significant difference could have been due to the ability of PRP to inhibit pathways contributing to joint pain *via* its anti-inflammatory properties through inhibition of the NF-κB pathway and MMPs, decreasing IL-6 production, and releasing IL-10 anti-inflammatory cytokines[24-26].

According to Rajpoot *et al*[36], KL grade is positively correlated with WOMAC score, but to the best of our knowledge there has been no study specifically comparing WOMAC score in KL grade 3 and 4. In our study, the number of patients with KL grade 3 knees OA was significantly higher than those with KL grade 4, but we found no statistically significant difference either in WOMAC score or WOMAC sub-scores at baseline.

Lesions in knee OA not only affect the cartilage but also other structures, including the meniscus. A meniscal tear can contribute to progression of knee OA by its negative effects on load distribution, shock absorption, and stability of the knee joint. Individuals with meniscal tear frequently present with knee OA, which contributes to symptoms of the former. Reportedly, among KL grade 2-4 knee OA patients, 63% have meniscal tear[37,38]. Forty-seven percent of the patients in our study had meniscal tear discovered during the surgery. Even though a meniscal tear can contribute to knee OA symptoms, the occurrence of such was comparable at baseline in our patients, thus we did not do further statistical analysis or adjustment.

Limitations

The main limitation of this study was the small number of participants, as only 21 patients were enrolled. The short follow-up period precluded our ability to evaluate long-term outcomes of the three treatment groups. We suggest a prospective cohort and a longer follow-up period for future research and including imaging evaluation, such as with MRI.

CONCLUSION

Adjunctive PRP after arthroscopic debridement gave better improvement in pain symptom compared to arthroscopic debridement alone. However, neither treatment was superior regarding the ability to improve WOMAC score and other knee OA symptoms.

ARTICLE HIGHLIGHTS

Research background

The current management for knee osteoarthritis (OA) is not able to stop disease progression, particularly in Kellgren-Lawrence (KL) grade 3 and 4 OA. Thus, alternative therapeutic options are needed to prevent the progression of joint damage in OA and delay the need for knee arthroplasty.

Research motivation

Alternative therapies for knee OA are needed that can prevent disease progression. Such treatment is expected to increase quality of life and prevent or delay the need for arthroplasty.

Research objectives

To investigate whether adjunctive treatment with platelet-rich plasma (PRP) and hyaluronic acid (HA) after arthroscopic debridement provides better outcomes then arthroscopic debridement alone.

Research methods

This was a retrospective cohort study using medical record data. The Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) score and its sub-scores was used as the outcome parameter. The data were analyzed using the paired *t*-test, one-way analysis of variance, and post hoc least significant difference test.

Research results

Adjunctive PRP or HA after arthroscopic debridement was not superior to arthroscopic debridement alone in improving knee OA symptoms. However, adjunctive PRP resulted in improvement of pain symptoms. A longer evaluation period is needed to assess the long-term outcome.

Research conclusions

Adjunctive PRP or HA after arthroscopic debridement was not superior to arthroscopic debridement alone in improving knee OA symptoms. Adjunctive PRP after arthroscopic debridement was more beneficial in reducing pain.

Research perspectives

The results of this study are expected to provide clinicians with an alternative treatment for KL grade 3 and 4 knee OA. Future research with a prospective cohort and longer follow-up period is needed.

FOOTNOTES

Author contributions: Tirtosuharto H designed and conceived the study, collected the data, conducted the data analyses, and drafted the manuscript; Wiratnaya IGE and Astawa P designed and conceived the study, and revised the manuscript.

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REFERENCES

1 **Mobasheri A**, Batt M. An update on the pathophysiology of osteoarthritis. *Ann Phys Rehabil Med* 2016; **59**: 333-339 [PMID: 27546496 DOI: 10.1016/j.rehab.2016.07.004]
2 **Chen D**, Shen J, Zhao W, Wang T, Han L, Hamilton JL, Im HJ. Osteoarthritis: toward a comprehensive understanding of pathological mechanism. *Bone Res* 2017; **5**: 16044 [PMID: 28149655 DOI: 10.1038/boneres.2016.44]
3 **Li D**, Li S, Chen Q, Xie X. The Prevalence of Symptomatic Knee Osteoarthritis in Relation to Age, Sex, Area, Region, and Body Mass Index in China: A Systematic Review and Meta-Analysis. *Front Med (Lausanne)* 2020; **7**: 304 [PMID: 32766258 DOI: 10.3389/fmed.2020.00304]
4 **Arief A**, Budu, Usman MA, Sakti M, Lubis AMT, Bukhari A. Treatment of grade III knee osteoarthritis with bone marrow stimulation and intraarticular injection of triamcinolone and hyaluronic acid combination; three case report and literature review. *Int J Surg Case Rep* 2022; **95**: 107177 [PMID: 35623121 DOI: 10.1016/j.ijscr.2022.107177]

5 **Hawker GA**, Guan J, Croxford R, Coyte PC, Glazier RH, Harvey BJ, Wright JG, Williams JI, Badley EM. A prospective population-based study of the predictors of undergoing total joint arthroplasty. *Arthritis Rheum* 2006; **54**: 3212-3220 [PMID: 17009255 DOI: 10.1002/art.22146]

6 **Knop E**, Paula LE, Fuller R. Platelet-rich plasma for osteoarthritis treatment. *Rev Bras Reumatol Engl Ed* 2016; **56**: 152-164 [PMID: 27267529 DOI: 10.1016/j.rbre.2015.07.002]

7 **Moussa M**, Lajeunesse D, Hilal G, El Atat O, Haykal G, Serhal R, Chalhoub A, Khalil C, Alaaeddine N. Platelet rich plasma (PRP) induces chondroprotection *via* increasing autophagy, anti-inflammatory markers, and decreasing apoptosis in human osteoarthritic cartilage. *Exp Cell Res* 2017; **352**: 146-156 [PMID: 28202394 DOI: 10.1016/j.yexcr.2017.02.012]

8 **Li Z**, Long H, Liu Q, Lin J. Willingness to Have Total Knee Arthroplasty in Rural Areas of Northern China. *Orthop Surg* 2022; **14**: 587-594 [PMID: 35174639 DOI: 10.1111/os.13240]

9 **Su X**, Li C, Liao W, Liu J, Zhang H, Li J, Li Z. Comparison of Arthroscopic and Conservative Treatments for Knee Osteoarthritis: A 5-Year Retrospective Comparative Study. *Arthroscopy* 2018; **34**: 652-659 [PMID: 29229416 DOI: 10.1016/j.arthro.2017.09.023]

10 **Akan Ö**, Sarıkaya NÖ, Koçyiğit H. Efficacy of platelet-rich plasma administration in patients with severe knee osteoarthritis : can platelet-rich plasma administration delay arthroplasty in this patient population ? *Int J Clin Exp Med* 2018; **11(9)**: 9473-9483 [DOI: 10.21088/ijaa.2349.8471.7420.18]

11 **Patel S**, Dhillon MS, Aggarwal S, Marwaha N, Jain A. Treatment with platelet-rich plasma is more effective than placebo for knee osteoarthritis: a prospective, double-blind, randomized trial. *Am J Sports Med* 2013; **41**: 356-364 [PMID: 23299850 DOI: 10.1177/0363546512471299]

12 **Legré-Boyer V**. Viscosupplementation: techniques, indications, results. *Orthop Traumatol Surg Res* 2015; **101**: S101-S108 [PMID: 25596987 DOI: 10.1016/j.otsr.2014.07.027]

13 **Altman RD**, Manjoo A, Fierlinger A, Niazi F, Nicholls M. The mechanism of action for hyaluronic acid treatment in the osteoarthritic knee: a systematic review. *BMC Musculoskelet Disord* 2015; **16**: 321 [PMID: 26503103 DOI: 10.1186/s12891-015-0775-z]

14 **Zhang HF**, Wang CG, Li H, Huang YT, Li ZJ. Intra-articular platelet-rich plasma versus hyaluronic acid in the treatment of knee osteoarthritis: a meta-analysis. *Drug Des Devel Ther* 2018; **12**: 445-453 [PMID: 29551888 DOI: 10.2147/DDDT.S156724]

15 **Maheu E**, Rannou F, Reginster JY. Efficacy and safety of hyaluronic acid in the management of osteoarthritis: Evidence from real-life setting trials and surveys. *Semin Arthritis Rheum* 2016; **45**: S28-S33 [PMID: 26806183 DOI: 10.1016/j.semarthrit.2015.11.008]

16 **Trueba Vasavilbaso C**, Rosas Bello CD, Medina López E, Coronel Granado MP, Navarrete Álvarez JM, Trueba Davalillo CA, Gil Orbezo FI. Benefits of different postoperative treatments in patients undergoing knee arthroscopic debridement. *Open Access Rheumatol* 2017; **9**: 171-179 [PMID: 29026341 DOI: 10.2147/OARRR.S138353]

17 **Hempfling H**. Intra-articular hyaluronic acid after knee arthroscopy: a two-year study. *Knee Surg Sports Traumatol Arthrosc* 2007; **15**: 537-546 [PMID: 17187274 DOI: 10.1007/s00167-006-0260-1]

18 **White DK**, Master H. Patient-Reported Measures of Physical Function in Knee Osteoarthritis. *Rheum Dis Clin North Am* 2016; **42**: 239-252 [PMID: 27133487 DOI: 10.1016/j.rdc.2016.01.005]

19 **Lespasio MJ**, Piuzzi NS, Husni ME, Muschler GF, Guarino A, Mont MA. Knee Osteoarthritis: A Primer. *Perm J* 2017; **21**: 16-183 [PMID: 29035179 DOI: 10.7812/TPP/16-183]

20 **Kirkley A**, Birmingham TB, Litchfield RB, Giffin JR, Willits KR, Wong CJ, Feagan BG, Donner A, Griffin SH, D'Ascanio LM, Pope JE, Fowler PJ. A randomized trial of arthroscopic surgery for osteoarthritis of the knee. *N Engl J Med* 2008; **359**: 1097-1107 [PMID: 18784099 DOI: 10.1056/NEJMoa0708333]

21 **Bohnsack M**, Lipka W, Rühmann O, Peters G, Schmolke S, Wirth CJ. The value of knee arthroscopy in patients with severe radiological osteoarthritis. *Arch Orthop Trauma Surg* 2002; **122**: 451-453 [PMID: 12442182 DOI: 10.1007/s00402-002-0425-4]

22 **Steadman JR**, Briggs KK, Matheny LM, Ellis HB. Ten-year survivorship after knee arthroscopy in patients with Kellgren-Lawrence grade 3 and grade 4 osteoarthritis of the knee. *Arthroscopy* 2013; **29**: 220-225 [PMID: 23273893 DOI: 10.1016/j.arthro.2012.08.018]

23 **Moseley JB**, O'Malley K, Petersen NJ, Menke TJ, Brody BA, Kuykendall DH, Hollingsworth JC, Ashton CM, Wray NP. A controlled trial of arthroscopic surgery for osteoarthritis of the knee. *N Engl J Med* 2002; **347**: 81-88 [PMID: 12110735 DOI: 10.1056/NEJMoa013259]

24 **Fotouhi A**, Maleki A, Dolati S, Aghebati-Maleki A, Aghebati-Maleki L. Platelet rich plasma, stromal vascular fraction and autologous conditioned serum in treatment of knee osteoarthritis. *Biomed Pharmacother* 2018; **104**: 652-660 [PMID: 29803179 DOI: 10.1016/j.biopha.2018.05.019]

25 **McCarrel TM**, Mall NA, Lee AS, Cole BJ, Butty DC, Fortier LA. Considerations for the use of platelet-rich plasma in orthopedics. *Sports Med* 2014; **44**: 1025-1036 [PMID: 24760591 DOI: 10.1007/s40279-014-0195-5]

26 **Xie X**, Zhang C, Tuan RS. Biology of platelet-rich plasma and its clinical application in cartilage repair. *Arthritis Res Ther* 2014; **16**: 204 [PMID: 25164150 DOI: 10.1186/ar4493]

27 **Gobbi A**, Lad D, Karnatzikos G. The effects of repeated intra-articular PRP injections on clinical outcomes of early osteoarthritis of the knee. *Knee Surg Sports Traumatol Arthrosc* 2015; **23**: 2170-2177 [PMID: 24748286 DOI: 10.1007/s00167-014-2987-4]

28 **Chang KV**, Hung CY, Aliwarga F, Wang TG, Han DS, Chen WS. Comparative effectiveness of platelet-rich plasma injections for treating knee joint cartilage degenerative pathology: a systematic review and meta-analysis. *Arch Phys Med Rehabil* 2014; **95**: 562-575 [PMID: 24291594 DOI: 10.1016/j.apmr.2013.11.006]

29 **Dhillon MS**, Behera P, Patel S, Shetty V. Orthobiologics and platelet rich plasma. *Indian J Orthop* 2014; **48**: 1-9 [PMID: 24600055 DOI: 10.4103/0019-5413.125477]

30 **Jayabalan P**, Hagerty S, Cortazzo MH. The use of platelet-rich plasma for the treatment of osteoarthritis. *Phys Sportsmed* 2014; **42**: 53-62 [PMID: 25295767 DOI: 10.3810/psm.2014.09.2076]

31 **Lana JF**. Platelet Rich Plasma and Its Growth Factors: The State of the Art. In: Lana, J., Andrade Santana, M., Dias

Belangero, W., Malheiros Luzo, A. Platelet-Rich Plasma - Lecture Notes in Bioengineering. Berlin, Heidelberg: Springer, 2014: 1-59 [DOI: 10.1007/978-3-642-40117-6_1]

32 **Laver L**, Marom N, Dnyanesh L, Mei-Dan O, Espregueira-Mendes J, Gobbi A. PRP for Degenerative Cartilage Disease: A Systematic Review of Clinical Studies. *Cartilage* 2017; **8**: 341-364 [PMID: 28317389 DOI: 10.1177/1947603516670709]

33 **Atay T**, Aslan A, Baydar ML, Ceylan B, Baykal B, Kirdemir V. [The efficacy of low- and high-molecular-weight hyaluronic acid applications after arthroscopic debridement in patients with osteoarthritis of the knee]. *Acta Orthop Traumatol Turc* 2008; **42**: 228-233 [PMID: 19060515 DOI: 10.3944/aott.2008.228]

34 **Shen D**, Chen M, Chen K, Wang T, Lu L, Yang X. Efficacy of hyaluronic acid after knee arthroscopy: A systematic review and meta-analysis. *J Rehabil Med* 2018; **50**: 860-865 [PMID: 30299523 DOI: 10.2340/16501977-2366]

35 **Raeissadat SA**, Rayegani SM, Hassanabadi H, Fathi M, Ghorbani E, Babaee M, Azma K. Knee Osteoarthritis Injection Choices: Platelet- Rich Plasma (PRP) Versus Hyaluronic Acid (A one-year randomized clinical trial). *Clin Med Insights Arthritis Musculoskelet Disord* 2015; **8**: 1-8 [PMID: 25624776 DOI: 10.4137/CMAMD.S17894]

36 **Rajpoot M**, Peepra D, Pandey K, Varma H. Clinico-radiological correlation of osteoarthritis knee using Western Ontario and McMaster Universities score and Kellegren and Lawrance grading. *Int J Res Med Sci* 2016; **4**: 4873-4876 [DOI: 10.18203/2320-6012.ijrms20163783]

37 **McHugh CG**, Opare-Addo MB, Collins JE, Jones MH, Selzer F, Losina E, Katz JN. Treatment of the syndrome of knee pain and meniscal tear in middle-aged and older persons: A narrative review. *Osteoarthr Cartil Open* 2022; **4** [PMID: 35991623 DOI: 10.1016/j.ocarto.2022.100282]

38 **MacFarlane LA**, Yang H, Collins JE, Guermazi A, Jones MH, Teeple E, Xu L, Losina E, Katz JN. Associations among meniscal damage, meniscal symptoms and knee pain severity. *Osteoarthritis Cartilage* 2017; **25**: 850-857 [PMID: 28043939 DOI: 10.1016/j.joca.2016.12.023]

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ORIGINAL ARTICLE

Retrospective Study

Utilising the impact of COVID-19 on trauma throughput to adapt elective care models for more efficient trauma care

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Abstract

BACKGROUND

Coronavirus disease 2019 (COVID-19) has necessitated adaptations in local trauma services, with implementation of novel methods of practice, strategic adaptations, and shifting of resource management. Many of these may serve the driver for landmark changes to future healthcare provision.

AIM

To analyse the impact of COVID-19 on service provision by comparing throughput and productivity metrics with preceding years to identify differences in practice that were successful, cost-effective, and sustainable.

METHODS

We quantified orthopaedic trauma care provision at a single University Teaching Hospital over a three consecutive year period, from 1st January 2018 to 31st December 2020. Each year was split into four phases based on the 2020 national COVID-19 pandemic periods. We quantitatively analysed change in rates of inpatient trauma operative case load, sub-specialty variation, theatre throughput, and changes in management strategy. Qualitative analysis was based on multidisciplinary team interviews to highlight changes to care pathways.

RESULTS

Of 1704 cases were admitted in 2020, 11.9% and 12.4% fewer than 2019 and 2018, respectively. During phase 1, hip fractures encompassed the majority (48.8%) of trauma throughput, with all other subspecialties seeing a reduction. Mean length of stay was shorter during phase 1 (5.7 d); however, the time in theatre was longer (144.3 min). Both, Charlson (0.90) and Elixhauser (1.55) Comorbidity Indices indicated the most co-morbid admissions during 2020 phase 1.

CONCLUSION
COVID-19 has resulted in a paradigm shift in how care is accessed and delivered, with many evolving changes and adaptations likely to leave an impression upon healthcare provision in the future.

Key Words: COVID-19; Trauma; Surgery; Throughput; Care provision

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Core Tip: Based on our findings, we have made several recommendations that we will adopt locally going forward. We encourage other teams facing similar challenges to consider these factors to improve the care of trauma patients: (1) Dynamic elective approaches to care can reduce length of stay (LOS): The 'elective mindset' of the elective hospital nursing/physical therapy/occupational therapy teams yielded more expeditious post-operative rehabilitation our trauma patients, ensuring faster optimisation of a more co-morbid cohort of patients and reduced LOS; (2) Sustain the rising trend in safe non-operative management to reduce inpatient workload: This was a trend particularly observed in hand and wrist/foot and ankle trauma where the care pathways were altered in the face of rising coronavirus disease 2019 cases; and (3) Maintaining rapid re-education of skills: By rapidly adopting locally-relevant versions of national guidance and developing standardised algorithms and training pathways.

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INTRODUCTION

The coronavirus disease 2019 (COVID-19) pandemic has significantly impacted the provision of healthcare globally. Not only were elective planned care services largely paused, but ongoing essential services, such as trauma, had to adapt their ways of working to maintain safety for patients and healthcare professionals[1].

With the National Health Service (NHS) slow to effect change, these COVID-19 necessitated adaptations may serve the driver for landmark changes to the way healthcare is provided[2]. Should these changes prove successful, they may yield more sustained differences to the way we deliver care in the future. Hospitals across the United Kingdom have implemented strategic changes, with shifting of resource management and implementation of novel methods of practice (such as virtual consultations) [3-5]. These provided the ideal opportunity to drive much needed technological upgrades into the healthcare ecosystem. The post-pandemic environment is full of opportunities to improve the flexibility of care provision for the benefit of both, patients and providers, with the ultimate aim of creating enhanced and self-sustaining care models.

With this in mind, we sought to gain an in-depth view of the impact of COVID-19 on our local trauma service provision, by comparing our trauma throughput and other key productivity metrics with the preceding years to identify any key differences and adaptations that had occurred within the department to sustain clinical practice. By evaluating changes to practices implemented due to COVID-19 at our trauma unit, our goal was to evaluate those changes that were successful, cost-effective, easily adapted by clinicians, and deemed sustainable for the future, with a view to sharing our learnings more widely.

MATERIALS AND METHODS

Aims

We performed a comprehensive retrospective analysis of the objective impact of COVID-19 on our local trauma service provision, by comparing 2020 metrics with the equivalent 12-mo time periods in both 2019 and 2018. This study was formally registered and approved by our (KK1) Clinical Audit and Quality Improvement Team. The specific aspects of care provision we sought to evaluate included: (1) Change in rates of inpatient trauma case load; (2) Sub-specialty variation in trauma case load; (3) Theatre throughput (numbers of cases, duration, turnaround time); (4) Changes in trends in trauma

management (particularly rates of non-operative interventions); and (5) Changes to local strategy to care delivery.

Scope, population, timeline

Comparison of all trauma clinical activity at the Orthopaedic Trauma Unit of a single United Kingdom University Teaching Hospital over a three consecutive year period, from 1st January 2018 to 31st December 2020 (*i.e.*, 2018, 2019, 2020). For the purpose of this evaluation, each year was split into four phases based upon the main national COVID-19 pandemic periods in 2021 (Table 1).

Data sources

Data was obtained using the Hospital Information Support System (HISS) specifically coded for Trauma and Orthopaedics (HISS code 10). This data included information on patient co-morbidities [converted to Charlson Comorbidity Index (CCI)], patient demographic and mortality data. Operative data and timings were obtained using our Operating Theatre Software (ORMIS, code 10) and cross-referenced with a manually maintained Microsoft Excel (v16.46) encrypted spreadsheet of cases booked for theatre by our Trauma Coordinators. Descriptions of changes to patient care pathways were obtained through interviews of the multidisciplinary team (MDT), including senior management, Orthopaedic and Orthogeriatric clinicians, and ward teams (nursing and therapy).

Primary outcomes

Rates of all trauma caseload management across the three years, including a breakdown of: (1) Variation in total trauma throughput each year by phase; (2) Variation in specific subspecialty trauma by phase (subspecialties included: Hip, knee, foot and ankle, hand & wrist, shoulder, elbow, and complex multi-site); (3) CCI, Elixhauser Comorbidity Sum Index (ECI); (4) Inpatient length of stay (LOS); and (4) For operated cases, the time interval & delay to treatment (*i.e.*, from admission time to surgery start time).

Analysis

Descriptive statistics were presented as means ± SD. Qualitative analysis of interviews was performed to group the key changes to care pathways. The quantitative data was then analysed in the context of changes to practice, with a view to identifying sustainable interventions to maintain going forward.

RESULTS

A total of 1704 trauma cases were admitted to our trauma unit in 2020. This was 11.9% fewer than in 2019 (1934 cases) and 12.4% fewer than in 2018 (1945 cases) (Table 2). Figure 1A highlights the variation in total trauma throughput by phase.

Variation in subspecialty trauma

Table 2 highlight the variation in subspecialty trauma for phases 0-3 for each year investigated. During the 2020 lockdown (phase 1), hip fractures remained the bulk (48.4%) of the surgical workload. This was a slightly higher proportion than in 2019 (41.6%), and 2018 (37.9%). Absolute numbers for hip trauma remained equivalent (146 procedures). Figure 1B highlights the variation in trauma load during the lockdown period. Conversely, we noted a reduction in foot and ankle procedures during phase 1 in 2020 (26 procedures; 8.7% of overall workload) compared to 2019 (47 procedures; 13.4% of overall workload) and 2018 (60 procedures; 17.3% of overall workload). Similar reductions were noted for hand and wrist trauma in 2020 (44 procedures; 14.7% of overall workload) compared to 2019 (54 procedures; 15.4% of overall workload) and 2018 (53 procedures; 15.3% of overall workload). In 2020, surgical throughput during lockdown phase 1 was lower by 52 procedures than 2019 and by 47 in comparison to 2018. Additionally, all subspecialties, except for hips (146 procedures in both 2020 and 2019) and elbows (21 procedures in 2020, 19 in 2019), saw a reduction in absolute procedural numbers in comparison to 2019.

Patient demographics, LOS, comorbidities, and theatre parameters

Tables 3-5 highlight the variation in patient demographic, LOS, comorbidity indices, and theatre parameters from 2018 to 2020. More detailed breakdown of variation is presented in Supplementary Tables 1-3. The mean LOS was significantly shorter during the 2020 phase 1 (lockdown phase) (5.7 d) compared to 2019 (7.5 d) and 2018 (6.8 d). CCI[6], which encompasses 19 medical conditions and is the most widely used comorbidity risk adjustment model for Orthopaedic surgery, showed a higher mean index during the 2020 lockdown (0.90) compared to 2019 (0.84) and 2018 (0.65). These findings were replicated using the ECI[7], which utilises 31 conditions, highlighting more co-morbid patients during phase 1 in 2020 [1.55 *vs* 1.36 (2019) *vs* 1.09 (2018)].

The 'hours to surgery' metric was calculated from the decision to admit the patient to hospital to the time to surgery. There was no significant variation between the three years for both phase 0 (30.7 h *vs* 32.0 h *vs* 29.2 h) and phase 1 (30.8 h *vs* 32.1 h *vs* 31.5 h). However, the actual time in theatre (en-

Table 1 Timelines for each phase evaluated

Phase	Description	Dates	Days
Phase 0	Pre-lockdown	1st January - 22nd March	81
Phase 1	Lockdown	23rd March - 31st May	70
Phase 2	Post-lockdown	1st June - 30st September	122
Phase 3	To year end	1st October - 31st December	92

Table 2 Subspecialty trauma breakdown (2018-2020)

Subspecialty	Year	Phase 0	Phase 1	Phase 2	Phase 3	Total
		Pre-lockdown	Lockdown	Post-lockdown	To year end	
Hip	2018	183 (39.8%)	131 (37.9%)	311 (37.0%)	118 (39.6%)	743 (38.2%)
	2019	172 (39.3%)	146 (41.6%)	339 (40.4%)	139 (45.4%)	796 (41.2%)
	2020	163 (41.3%)	146 (48.8%)	291 (36.6%)	76 (35.3%)	676 (39.7%)
Knee	2018	26 (5.7%)	14 (4.0%)	47 (5.6%)	16 (5.4%)	103 (5.3%)
	2019	37 (8.4%)	24 (6.8%)	53 (6.3%)	27 (8.8%)	141 (7.3%)
	2020	36 (9.1%)	16 (5.4%)	55 (6.9%)	7 (3.3%)	114 (6.7%)
Foot & ankle	2018	69 (15.0%)	60 (17.3%)	120 (14.3%)	45 (15.1%)	294 (15.1%)
	2019	65 (14.8%)	47 (13.4%)	102 (12.2%)	39 (12.7%)	253 (13.1%)
	2020	45 (11.4%)	26 (8.7%)	98 (12.3%)	36 (16.7%)	205 (12.0%)
Hand & wrist	2018	70 (15.2%)	53 (15.3%)	148 (17.6%)	51 (17.1%)	322 (16.6%)
	2019	58 (13.2%)	54 (15.4%)	149 (17.8%)	33 (10.8%)	294 (15.2%)
	2020	60 (15.2%)	44 (14.7%)	147 (18.5%)	42 (19.5%)	293 (17.2%)
Shoulder	2018	27 (5.9%)	25 (7.2%)	45 (5.4%)	20 (6.7%)	117 (6.0%)
	2019	30 (6.8%)	22 (6.3%)	47 (5.6%)	21 (6.9%)	120 (6.2%)
	2020	27 (6.8%)	13 (4.3%)	52 (6.5%)	21 (9.8%)	113 (6.6%)
Elbow	2018	32 (7.0%)	32 (9.2%)	87 (10.3%)	16 (5.4%)	167 (8.6%)
	2019	29 (6.6%)	19 (5.4%)	62 (7.4%)	12 (3.9%)	122 (6.3%)
	2020	24 (6.1%)	21 (7.0%)	75 (9.4%)	15 (7.0%)	135 (7.9%)
Complex multi-site	2018	16 (3.5%)	8 (2.3%)	16 (1.9%)	7 (2.3%)	47 (2.4%)
	2019	4 (0.9%)	7 (2.0%)	14 (1.7%)	7 (2.3%)	32 (1.7%)
	2020	4 (1.0%)	1 (0.3%)	9 (1.1%)	3 (1.4%)	17 (1.0%)
Polytrauma	2018	37 (8.0%)	23 (6.6%)	67 (8.0%)	25 (8.4%)	152 (7.8%)
	2019	43 (9.8%)	32 (9.1%)	73 (8.7%)	28 (9.2%)	176 (9.1%)
	2020	36 (9.1%)	32 (10.7%)	68 (8.6%)	15 (7.0%)	151 (8.9%)

compasses both anaesthetic and operative surgical time) was notably longer during the 2020 lockdown phase 1 (144.3 min *vs* 96.3 min *vs* 92.9 min). This increased time can be accounted for by the COVID-19 related measures that were introduced into theatre practice during phase 1 for infection prevention and control (including donning and doffing, cleaning, theatre air changes), requiring strict adherence and understandably taking notably longer than standard processes. Therefore, while overall throughput and number of cases per day was lower in the 2020 lockdown phase, the time in theatre per case was greater, and consequently, the overall hours to get to surgery remained unchanged. Following the lockdown and the anticipated normalization of hospital practices (phase 2), we noted a reduction in the 'hours to surgery' in comparison to 2019 and 2018 (24.5 h *vs* 29.2 h *vs* 34.7 h). This timing was almost 21% less than phase 1 and phase 0 of the same year, suggestive of more effective pre-operative patient optimisation, or surgery being performed largely on fitter patients who required less pre-operative work-up during that time of year [2020 CCI - 0.68 (phase 2) *vs* 0.90 (phase 1)], as reflected in the 2020

Table 3 Patient demographics, length of stay, comorbidity indices and theatre parameters for 2018

	Phase 0 (*n* = 709)	Phase 1 (*n* = 571)	Phase 2 (*n* = 1363)	Phase 3 (*n* = 486)	Total (*n* = 3129)
	mean ± SD				
Age at injury	61.23 ± 22.40	56.40 ± 24.04	57.52 ± 24.36	59.06 ± 23.79	58.39 ± 23.83
Length of spell (d)	8.39 ± 10.31	6.84 ± 8.57	6.76 ± 10.19	7.02 ± 9.45	7.18 ± 9.84
Charlson Comorbidity Index	0.72 ± 1.31	0.65 ± 1.24	0.68 ± 1.26	0.60 ± 1.21	0.67 ± 1.26
Elixhauser Comorbidity Index	1.19 ± 1.39	1.09 ± 1.36	1.14 ± 1.38	1.06 ± 1.31	1.13 ± 1.37
Hours to surgery	29.24 ± 50.75	31.46 ± 48.29	34.72 ± 91.27	26.22 ± 52.95	31.54 ± 71.10
Time in theatre	98.59 ± 58.34	92.86 ± 48.23	94.33 ± 46.30	95.49 ± 48.66	95.23 ± 50.04
Time in theatre/recovery	61.23 ± 22.40	56.40 ± 24.04	57.52 ± 24.36	59.06 ± 23.79	58.39 ± 23.83
Sex: Female	383 ± 54.0%	296 ± 51.8%	726 ± 53.3%	249 ± 51.2%	1654 ± 52.9%
Sex: Male	326 ± 46.0%	275 ± 48.2%	637 ± 46.7%	237 ± 48.8%	1475 ± 47.1%

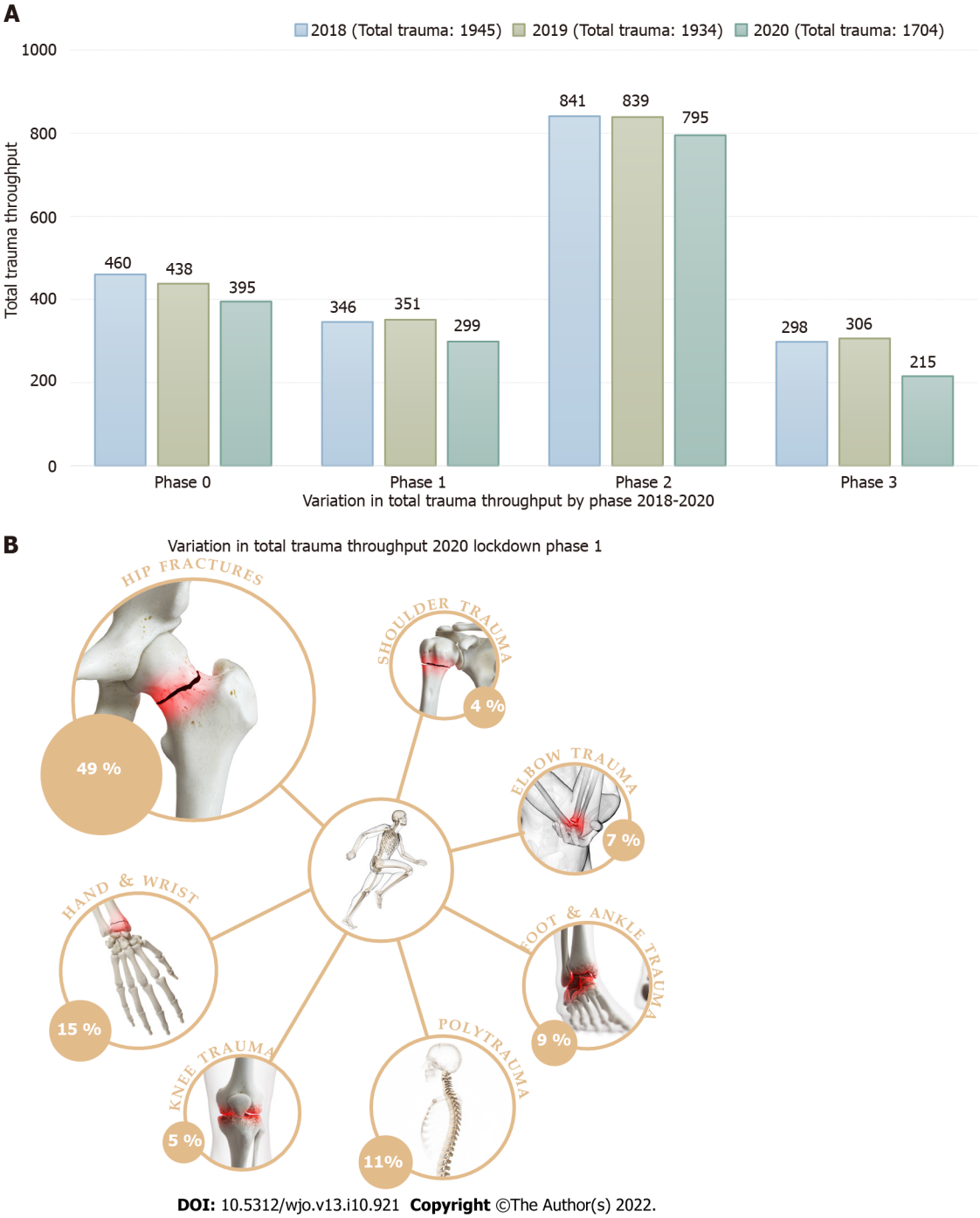
Table 4 Patient demographics, length of stay, comorbidity indices and theatre parameters for 2019

	Phase 0 (*n* = 664)	Phase 1 (*n* = 563)	Phase 2 (*n* = 1315)	Phase 3 (*n* = 471)	Total (*n* = 3013)
	mean ± SD				
Age at injury	58.89 ± 24.03	60.66 ± 23.17	58.66 ± 23.95	61.11 ± 22.98	59.47 ± 23.68
Length of spell (d)	7.30 ± 8.05	7.50 ± 9.90	6.67 ± 8.60	8.01 ± 10.88	7.18 ± 9.14
Charlson Comorbidity Index	0.71 ± 1.28	0.84 ± 1.49	0.78 ± 1.35	0.77 ± 1.30	0.77 ± 1.35
Elixhauser Comorbidity Index	1.20 ± 1.38	1.36 ± 1.55	1.39 ± 1.53	1.34 ± 1.42	1.33 ± 1.49
Hours to surgery	32.02 ± 57.64	32.13 ± 51.56	29.17 ± 47.03	31.96 ± 56.83	30.79 ± 51.99
Time in theatre	101.03 ± 49.49	96.30 ± 67.04	94.85 ± 57.61	95.95 ± 47.63	96.64 ± 56.36
Time in theatre/recovery	213.08 ± 110.23	208.29 ± 115.17	214.99 ± 141.51	228.39 ± 146.20	215.56 ± 131.70
Sex: Female	332 ± 50.0%	291 ± 51.7%	675 ± 51.3%	239 ± 50.7%	1537 ± 51.0%
Sex: Male	332 ± 50.0%	272 ± 48.3%	640 ± 48.7%	232 ± 49.3%	1476 ± 49.0%

Table 5 Patient demographics, length of stay, comorbidity indices and theatre parameters for 2020

	Phase 0 (*n* = 640)	Phase 1 (*n* = 425)	Phase 2 (*n* = 1210)	Phase 3 (*n* = 413)	Total (*n* = 2688)
	mean ± SD				
Age at injury	59.46 ± 23.95	62.16 ± 23.61	57.70 ± 24.07	60.97 ± 23.47	59.33 ± 23.93
Length of spell (d)	7.05 ± 7.87	5.69 ± 5.90	5.71 ± 7.54	7.53 ± 8.86	6.30 ± 7.64
Charlson Comorbidity Index	0.77 ± 1.23	0.90 ± 1.45	0.68 ± 1.19	0.68 ± 1.25	0.73 ± 1.26
Elixhauser Comorbidity Index	1.27 ± 1.46	1.55 ± 1.63	1.21 ± 1.37	1.19 ± 1.39	1.28 ± 1.44
Hours to surgery	30.71 ± 49.37	30.84 ± 34.56	24.50 ± 37.98	24.59 ± 37.14	26.97 ± 40.41
Time in theatre	95.62 ± 50.10	144.25 ± 64.24	127.98 ± 54.37	123.20 ± 54.48	122.11 ± 57.35
Time in theatre/recovery	215.97 ± 124.31	175.22 ± 117.92	195.23 ± 106.09	203.28 ± 132.37	199.65 ± 117.42
Sex: Female	347 ± 54.2%	237 ± 55.8%	649 ± 53.6%	234 ± 56.7%	1467 ± 54.6%
Sex: Male	293 ± 45.8%	188 ± 44.2%	561 ± 46.4%	179 ± 43.3%	1221 ± 45.4%

EIC. However, the absolute number of trauma admissions was also lower in phase 2 of 2020 compared to the equivalent timeframes in 2019 and 2018 (1210 *vs* 1315 *vs* 1363), which would contribute to the observed decrease in hours to surgery. The actual 'time in theatre' remained high (128.0 min) in the 2020 phase 2, but some improvement was noted over phase 1 (144.3 min). While theatre practices became more streamlined and efficient, the core aspects of COVID-19 measures remained vastly unchanged,



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Figure 1 Variation in total trauma throughput. A: By phase; B: During the 2020 lockdown phase 1, images obtained *via* www.shutterstock.com using standard image licence agreement. (SciePro/shutterstock). Complete image exclusively designed and created by the authors.

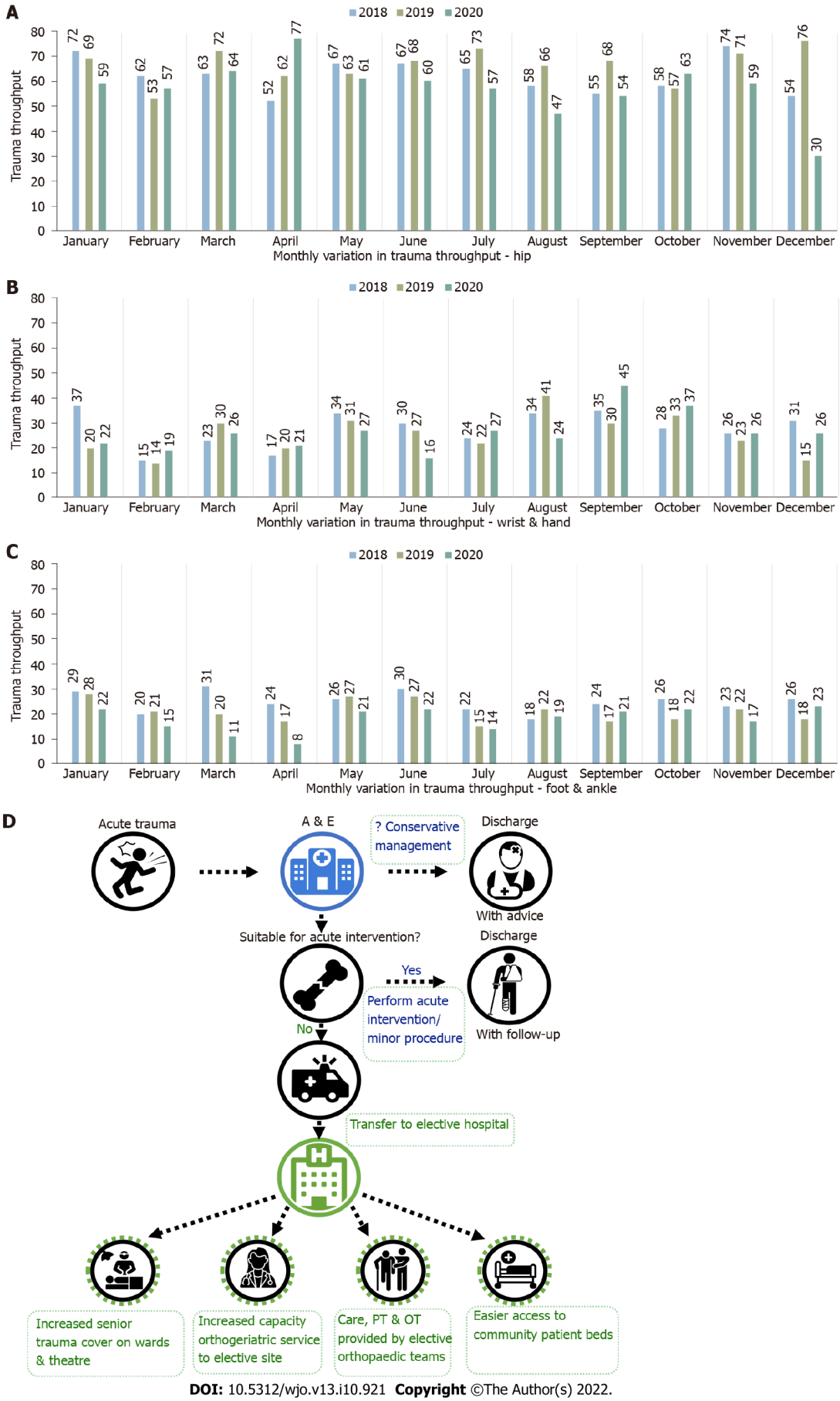
thus resulting in an overall increased time in theatre.

Number of trauma operations per month

Figures 2A-C highlight the monthly variation in the highest throughput trauma sub-specialties (hip, hand & wrist, and foot & ankle). Consistent with previous years, hip fracture surgery encompassed the bulk of monthly surgical trauma, including the period affected by the COVID-19 pandemic. Supplementary Figures 1-4 highlights monthly variation in the remainder of the sub-specialties.

Qualitative analysis of changes to trauma care delivery

The pandemic ushered in several significant changes to the way in which trauma care was delivered (Figure 2D). Alongside the key changes described below, other changes that impacted our department included partial redeployment of all Orthopaedic Specialty Registrars to the intensive care units, and cessation of all but selected urgent elective cases (*e.g.*, infected arthroplasty). Structured colleague



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Figure 2 Monthly variation in trauma throughput. A: Hip; B: Wrist & hand; C: Foot & ankle; D: Infographic, icons made by Freepik, icongeek26, iconmas and uniconlabs from www.flaticon.com and www.pngwing.com. Complete image exclusively designed and created by the authors.

interviews provided valuable MDT insight into what worked, and what was less successful.

Trauma care shift to our elective site: Patients requiring admission from the emergency department (ED) at our acute site were transferred by ambulance to our elective orthopaedic site to free capacity for COVID-19 admissions. Clinical staffing cover was accordingly adapted to ensure patient safety and prompt senior decision making. This transition was made swiftly and successfully as soon as elective activity was suspended, also lowering the exposure of our trauma patients to COVID-19.

Ward based nursing care and therapy provided by elective orthopaedic teams: The strategies adopted by these teams included similar protocols to the equivalent elective group (*e.g.*, early mobilisation regimes for total hip replacement patients applied following hip fracture surgery). Adopting more 'dynamic' approaches, with multiple therapy sessions per day, helped get patients safely mobilising sooner and facilitated discharge.

Transfer of increased capacity orthogeriatric service to elective site: Daily consultant-led ward-rounds facilitated rapid pre-operative stabilisation of patients with fragility femur fractures, alongside reduced surgical delay and LOS.

Easier access to community patient beds: Facilitated in conjunction with our community teams, a rapid electronic referral method was adopted during the pandemic, accelerating the request process for community beds and enabling more rapid discharge of patients that were 'medically' well but in need of rehabilitation prior to discharge home.

Increased senior trauma cover: Trauma care was led by a combination of our elective and trauma orthopaedic consultants and higher specialty trainees, working flexibly as required, with shadow rotas made to provide enhanced sickness cover. Whereas our usual trauma care is led by individual consultants' teams, supported by a supporting 'hot' floating consultant, the COVID-19 strategy involved a named consultant providing daily ward rounds of all admitted trauma patients, 7-d a week. This allowed issues to be identified and addressed early. In particular, weekend inpatient reviews facilitated on-day weekend discharges and preparation for anticipated Monday discharges.

Virtual clinics: While face-to-face elective clinics were significantly reduced, virtual telephone consultations were adopted. These were initially successfully applied to elective care, and thereafter to our trauma fracture clinics, enabling these acute services to reduce face-to-face contact, while maintaining overall throughput.

DISCUSSION

The COVID-19 pandemic has had a significant impact on both, our clinical ability to effectively manage trauma, as well as the way in which our patients have accessed trauma care. This has resulted in a paradigm shift in practice for the delivery of our trauma service, with many evolving changes and adaptations likely to leave their impression upon how healthcare will be provided in the future. Several centres across the United Kingdom.

This service evaluation project provided a quantitative and qualitative assessment of collective trauma throughput during four pre-determined phases, comparing throughput with the same periods in 2019 and 2018. Evaluation of phase 1 (*i.e.*, the 'lockdown' phase spanning 70 d) highlighted several important learning points. One of the expected key findings was that overall trauma throughput during phase 1 was reduced compared to 2019 and 2018 (299 procedures in *vs* 351 and 346, respectively). Despite this, hip fragility fracture numbers remained static at 146 procedures in both 2020 and 2019, still accounting for the bulk of the surgical workload during the lockdown phase (48.8% *vs* 41.6% *vs* 37.9%). There was a 45% reduction in the number of foot and ankle procedures between the 2020 phase 1 and its equivalent in 2019 as well as 2018 (26 procedures *vs* 47 *vs* 60). Similarly, hand procedures saw a 19% reduction compared to 2019 and 2018 (44 procedures *vs* 54 *vs* 53). There was no variation in polytrauma in phase 1 between 2020 and 2019 (32 cases).

Interpretation of these findings are suggestive of a reduction in overall emergency trauma presentations (which was anticipated in view of United Kingdom Government restrictions) and a shift towards more conservative measures for selective trauma, in keeping with updated national COVID-19 British Orthopaedic Association Standards for Trauma guidance[8]. For certain subspecialties (for example, foot and ankle, or hand and wrist), the nature of the trauma was conducive to more early interventions performed at presentation in the ED, without the need for admission and operative intervention.

A decrease was also observed in the overall mean LOS during phase 1 (5.69 d *vs* 7.50 *vs* 6.84). While successful approaches to determine (and reduce) the LOS through hospital are determined on mapping patient flow, replicating and understanding care models adopted by subspecialties during phase 1 to facilitate early discharge could have significant long-term benefits. Reducing the LOS has the potential to provide an effective means of containing and bridging the gap between service demand and resource constraints, particularly during the pandemic. Maintained orthogeriatric ward cover, daily consultant

ward presence, and improved availability of community beds played important roles in ensuring efficient management of hip fracture patients - the majority of the patient mix - and therefore those contributing most to LOS. Fewer outliers also facilitated more efficient patient management. Best Practice Tariffs for hip fragility fractures require prompt surgery and appropriate orthogeriatric involvement - both factors contributing to a shorter LOS[9]. Phase 1 in 2020 demonstrated a shorter LOS for these patients; if maintained in the post-COVID era, this could result in improved care and resource benefits for our trust.

Both the CCI and the ECI are useful tools to quantify the underlying comorbid disease status. Both indices were raised for the 2020 phase 1 cohort (CCI - 0.90 *vs* 0.84 *vs* 0.65; ECI - 1.55 *vs* 1.36 *vs* 1.09), suggesting that trauma service had more multi-morbid patients with non-communicable disease admitted and operated during the lockdown phase, whist the 'fitter' cohort stayed at home. This also correlates with the fact that hip fragility fracture surgery numbers remained static between 2019 and 2020. One theory to account for this is that the lockdown may have resulted in an overall reduction in the support system offered to vulnerable and multimorbid patients, who therefore had to manage in isolation, increasing their likelihood of sustaining a serious injury requiring operative intervention.

Limitations

We recognise that our study has several limitations. While every attempt was made to capture all trauma admissions, the total figures do not encompass all trauma presentations to the ED (for example, those patients who had interventions at presentation in ED and were subsequently discharged or followed up in clinic). However, we are confident that our figures do indeed represent the majority of inpatient trauma admissions. We were also potentially limited by the accuracy of coding of admitted patients and HISS data, which in turn would affect parameters such as the comorbidity indices. Finally, the local hospitals found themselves in an unusual position where partial restrictions were imposed for an extended period of time (54 d) due to the Leicestershire region being a higher risk area, which overlapped with phase 2, resulting in a lack of clear distinction between these phases.

Learning points

Based on our findings, we have made several recommendations that we will adopt locally going forward. We encourage other teams facing similar challenges to consider these factors to improve the care of trauma patients.

Dynamic elective approaches to care can reduce LOS: The 'elective mindset' of the LGH nursing/physical therapy/occupational therapy teams yielded more expeditious post-operative rehabilitation our trauma patients, ensuring more rapid optimisation of a more comorbid cohort of patients and reduced LOS during phases 1 and 2.

Sustain the rising trend in safe non-operative management to reduce inpatient workload: This was a trend particularly observed in hand and wrist/foot and ankle trauma where the care pathways were altered in the face of rising COVID-19 cases. We have since capitalised upon this opportunity to change our combined ED fracture management pathways for certain injuries to facilitate an increase the number of interventions and minor procedures performed at presentation at the front door under either ketamine or Penthrox® (Methoxyflurane), utilising our 24-h availability of fluoroscopic guidance for adult patients with our mobile C-arm X-ray in fracture clinic.

Maintaining rapid re-education of skills: By rapidly adopting local versions of national PPE guidance and developing standardised algorithms and training pathways, we maintained the hours to surgery and the improvements in time in theatre metrics. Redeploying these training pathways *via* designated trained senior staff will be integral to a rapid response in the face of future challenges, including from another COVID-19 wave.

CONCLUSION

The impact of the COVID-19 pandemic on healthcare systems globally cannot be underestimated. As the growing body of evidence and best-practice advice during the pandemic evolves, clinical practices will undoubtedly need to adapt accordingly. Our study allowed us to evaluate, analyse, and compare local trauma throughput variation during the pandemic, thus developing targeted interventions utilising an 'elective care model'. This culminated in a more streamlined trauma patient care pathway from admission to discharge. By incorporating these modifications to clinical practice into our 'new normal' of clinical practice, we hope to build on this opportunity from adversity to improve patient care going forward.

ARTICLE HIGHLIGHTS

Research background

Coronavirus disease 2019 (COVID-19) has necessitated adaptations in local trauma services, with implementation of novel methods of practice, strategic changes, and shifting of resource management. Many of these changes may serve the driver for landmark changes to future healthcare provision. The pandemic environment is full of opportunities to capitalise upon to improve the flexibility of care provision for the benefits of both, patients and providers, with the ultimate aim of creating a long-term self-sustaining care model.

Research motivation

We sought to compare throughput and productivity metrics with preceding years to identify differences in practice that were successful, cost-effective, and sustainable. Should these changes prove successful, they may yield more sustained differences to the way we deliver care in the future.

Research objectives

By evaluating changes to practices implemented due to COVID-19 at our trauma unit, our goal was to evaluate those changes that were successful, cost-effective, easily adapted by clinicians, and deemed sustainable for the future, with a view to sharing our learnings more widely.

Research methods

We performed a comprehensive retrospective analysis of the objective impact of COVID-19 on our local trauma service provision, by comparing 2020 metrics with the equivalent 12-mo time periods in both 2019 and 2018.

Research results

Of 1704 cases were admitted in 2020, 11.9% and 12.4% fewer than 2019 and 2018, respectively. Hip fractures remained the bulk of surgical workload at the height of the pandemic. Mean length of stay was shorter during phase 1 (5.7 d). The time in theatre was longer (144.3 min) as a consequence of COVID-19 related measures that were introduced into theatre practice. Only the most co-morbid patients were admitted into hospital during phase 1, indicated by higher Charlson (0.90) and Elixhauser Comorbidity Indices (1.55).

Research conclusions

By evaluating, analysing, and comparing local trauma throughput variation during the pandemic, we developed targeted interventions utilising an 'elective care model' for more efficient trauma care.

Research perspectives

COVID-19 has resulted in a paradigm shift in how care is accessed and delivered, with many evolving changes and adaptations likely to leave an impression upon healthcare provision in the future.

FOOTNOTES

Author contributions: All authors equally contributed to this paper with conception and design of the study, literature review and analysis, drafting, critical revision, editing and approval of the final manuscript.

Institutional review board statement: This study was formally registered and approved by our Clinical Audit and Quality Improvement Team.

Informed consent statement: No individual patient consent was required as this study utilised unidentifable and anonymised grouped datasets.

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REFERENCES

1 **Bevan Brittan**. Elective care in England. Assessing the impact of COVID-19 and where next. [cited 20 June 2022]. Available from: https://www.bevanbrittan.com/insights/articles/2020/elective-care-in-england-assessing-the-impact-of-covid-19-and-where-next/
2 **The Health Foundation**. Constructive comfort: accelerating change in the NHS. [cited 20 June 2022]. Available from: https://www.health.org.uk/research-projects/constructive-comfort-accelerating-change-in-the-nhs
3 **Murphy T**, Akehurst H, Mutimer J. Impact of the 2020 COVID-19 pandemic on the workload of the orthopaedic service in a busy UK district general hospital. *Injury* 2020; **51**: 2142-2147 [PMID: 32654849 DOI: 10.1016/j.injury.2020.07.001]
4 **Madanipour S**, Iranpour F, Goetz T, Khan S. COVID-19: lessons learnt and priorities in trauma and orthopaedic surgery. *Ann R Coll Surg Engl* 2021; **103**: 390-394 [PMID: 33974459 DOI: 10.1308/rcsann.2021.0028]
5 **Gibbons JP**, Forman S, Keogh P, Curtin P, Kiely R, O'Leary G, Skerritt C, O'Sullivan K, Synnott K, Cashman JP, O'Byrne JM. Crisis change management during COVID-19 in the elective orthopaedic hospital: Easing the trauma burden of acute hospitals. *Surgeon* 2021; **19**: e59-e66 [PMID: 32980258 DOI: 10.1016/j.surge.2020.08.008]
6 **Charlson ME**, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *J Chronic Dis* 1987; **40**: 373-383 [PMID: 3558716 DOI: 10.1016/0021-9681(87)90171-8]
7 **Elixhauser A**, Steiner C, Harris DR, Coffey RM. Comorbidity measures for use with administrative data. *Med Care* 1998; **36**: 8-27 [PMID: 9431328 DOI: 10.1097/00005650-199801000-00004]
8 **British Orthopaedic Association**. Specialty and subspecialty guidance and resources during the COVID-19 pandemic. [cited 20 June 2022]. Available from: https://www.boa.ac.uk/latest-news/specialty-and-subspecialty-guidance-and-resources.html
9 **British Geriatrics Society**. The Care of Patients with Fragility Fractures (Blue Book). [cited 20 June 2022]. Available from: https://www.bgs.org.uk/resources/care-of-patients-with-fragility-fracture-blue-book

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ORIGINAL ARTICLE

Clinical Trials Study

Traditional Chinese medicine ointment combined with tuina therapy in treatment of pain and swelling after total knee arthroplasty

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Abstract

BACKGROUND

The most effective treatment for knee joint pain is total knee arthroplasty (TKA), but the risk of pain and swelling in patients after surgery is high. Ice application, ankle pump exercise and non-steroidal anti-inflammatory painkillers are the primary clinical treatments after surgery. However, long-term use of non-steroidal anti-inflammatory pain relievers can easily cause gastrointestinal damage. Traditional Chinese medicine (TCM) ointments and tuina therapy integrate TCM and manipulation, which effectively promotes the penetration of TCM into the skin lesions, improves local blood circulation and inflammatory reaction and has good long-term effects on patients.

AIM

To evaluate the efficacy of TCM ointment combined with tuina therapy in the treatment of pain and swelling after TKA.

METHODS

The randomized controlled clinical trial enrolled 80 patients who underwent TKA *via* the same procedure. The patients were randomly divided among the treatment group (n = 40) and the control group (n = 40). The control group was given an analgesia pump in addition to oral painkillers as the postoperative intervention. The treatment group received TCM ointment with tuina therapy in addition to the analgesia pump and oral painkillers in the postoperative period. The following variables were recorded 3 d before surgery and 3 d, 7 d and 14 d after surgery: Visual analogue scale (VAS) score; skin temperature; circumferences at 15 cm above and below the patella; maximum active knee flexion angle; and the knee injury and Osteoarthritis Outcome score (KOOS).

RESULTS

After treatment, VAS was significantly lower in the treatment group than the control group at 7 d (t = 7.536, P < 0.001) and 14 d (t = 8.563, P < 0.001). The skin temperature of participants in the treatment group was significantly lower than that in the control group at 7 d (t = 2.968, P = 0.004) and 14 d (t = 4.423, P < 0.001). The circumference values of the two positions in the treatment group were lower than those in the control group at 7 d [t = 2.315, P = 0.023 (above); t = 2.121, P = 0.037 (below)] and 14 d [t = 2.374, P = 0.020 (above); t = 2.095, P = 0.039 (below)]. After 14 d of treatment, the maximum active knee flexion angle and KOOS of the two groups were significantly improved but were significantly higher in the treatment group (P < 0.05 for both).

CONCLUSION

TCM ointment and tuina therapy have significant advantages over standard care in the treatment of pain and swelling after TKA. This additional treatment may improve knee function but additional studies are needed to confirm our observations.

Key Words: Traditional Chinese medicine ointment; Tuina therapy; Total knee arthroplasty; Pain; Swelling

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Core Tip: Traditional Chinese medicine (TCM) ointments and tuina therapy integrate TCM and manipulation, which effectively promotes the penetration of TCM into skin lesions, improves local blood circulation and inflammatory reaction, and has a good long-term effect on patients. This study observed and compared several parameters after artificial knee arthroplasty in two groups. The control group received routine care, and the treatment group received routine care as well as a TCM ointment and tuina therapy. All parameters were significantly better in the treatment group, providing evidence that the integrated therapy may improve knee function in the long term.

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INTRODUCTION

Knee osteoarthritis, also known as senile knee arthritis and hypertrophic knee arthritis, is one of the most common types of senile orthopedic diseases[1]. Long-term bone and joint wear decrease a patient's ability to move, including running, squatting and even walking. Currently, the most effective treatment for severe knee osteoarthritis is total knee arthroplasty (TKA)[2]. However, pain and swelling of the knee after the operation may impact rehabilitation and patient quality of life.

Treatments for the pain and swelling of the knee include ice compresses, ankle pump exercises, and non-steroidal anti-inflammatory analgesics. However, non-steroidal anti-inflammatory analgesics are not suitable for long-term administration, due to possible induction of gastrointestinal damage[3]. Rehabilitation methods, such as ice compresses and ankle pump exercises, can promote vasoconstriction and lymphatic return in the short term. Unfortunately, most patients remain bedridden for an extended period after surgery and have poor clinical compliance[4].

Traditional Chinese medicine (TCM) ointment combined with tuina therapy can effectively promote the penetration of TCM into the skin, improve local blood circulation and inflammatory response, and has good long-term efficacy for patients[5]. The primary objective of this study was to gain insight into

the benefits of TCM ointment and tuina therapy to treat pain and swelling after TKA.

MATERIALS AND METHODS

Subjects

This study was a prospective study, and 80 patients (16 males and 64 females) were enrolled as research participants. All patients suffered from severe knee osteoarthritis and underwent TKA in the Fourth Department of Arthritis, Wangjing Hospital, China Academy of Chinese Medical Sciences between July 2021 and March 2022. Their age range was 56-82 years, with an average age of 68.18 ± 6.08 years. The average body mass index was 24.59 ± 2.69 kg/m^2. There were 47 cases with the left lower limb affected and 33 cases with the right lower limb affected. According to a random number table, the patients were divided into two equal groups of 40 patients, the treatment group and the control group. The general data of the patients in the two groups were not significantly different (Table 1). All patients signed an informed consent form, which was approved by the Ethics Committee of Wangjing Hospital, Chinese Academy of Chinese Medical Sciences.

Inclusion criteria were as follows: (1) Met the diagnostic criteria for knee osteoarthritis and TKA[6]; (2) Age from 60 years old to 80 years old; (3) Voluntarily participated in the study and signed the informed consent form; and (4) Postoperative limb pain and swelling were obvious with visual analogue scale (VAS) points ≥ 4.

Exclusion criteria were as follows: (1) Serious diseases, such as severe conditions of the cardiovascular, cerebrovascular or hematopoietic system, or mental disorders; (2) Severe dysfunction of the liver and kidney; (3) Autoimmune diseases, allergy diseases, and acute or chronic infectious diseases; (4) Postoperative complications; and (5) Skin damage, ulceration, allergy to TCM and skin diseases.

Patients were discontinued from the study if: (1) They had poor compliance or were not treated as prescribed; (2) They had incomplete data leading to the inability to evaluate the efficacy of the treatment; (3) They reported poor tolerance of the treatment; (4) They had deep vein thrombosis during the treatment; or (5) They showed drug allergy during treatment.

Study design

Both groups of patients received standard care after TKA. This consisted of patients being prescribed oral ibuprofen codeine sustained tablets, ice compress application continually for 72 h after the operation, and air pressure blood circulation apparatus utilization 20 min bid.

Patients in the treatment group received a TCM ointment and tuina therapy beginning on the 3rd d after the operation. The TCM ointment was applied to the acupoints of Zusanli (ST 36), Sanyinjiao (SP 6), Taichong (LR 3), Chengshan (BL 57), Shangjuxu (ST 37) and Futu (ST 32) on the affected side. Then, acupoint-tuina therapy was performed by pressing and rubbing each acupoint for 2 min. Next, local tuina therapy was performed by rubbing, kneading and scrubbing. The therapy was focused on the running parts of the meridians on the lower limbs, which includes the foot *yangming* stomach channel, the foot *taiyin* spleen channel and the foot *jueyin* liver channel. The treatment was applied for 20 min once a day for 14 d.

The TCM ointment was composed of Chuanxiong (*Rhizoma Chuanxiong*), Niuxi (*Radix Achyranthis Bidentatae*), Jixueteng (*Caulis Spatholobi*), Jinyinteng (*Caulis Lonicerae Japonicae*), Mangxiao (*Natrii Sulfas*), Moyao (*Myrrha*), Ruxiang (*Olibanum*), Huangqi (*Radix Astragali*), Shigao (*Gypsum Fibrosum*), Weilingxian (*Radix et Rhizoma Clematidis*) and Bingpian (*Borneolum Syntheticum*). These herbs were processed and mixed with paraffin oil petroleum jelly to make the ointment.

Observation factors

The following variables were measured on the third day before the operation and days 3, 7 and 14 after the operation, except for the knee range of motion and knee injury and Osteoarthritis Outcome score (KOOS), which were measured on the 3rd d before the operation and 14 d after the operation.

VAS score: Pain was evaluated by the VAS, with a total of 10 points (0-3 for mild pain, 4-6 for moderate pain, and 7-10 for severe pain).

Skin temperature[7]: The skin temperature of the patient's operation site [Zusanli (ST 36) acupoint] was measured.

Lower extremity swelling: The circumferences at 15 cm above and below the patella were measured with a tape measure. The measurement was repeated three times and averaged.

Range of motion and KOOS[8]: The knee range of motion and KOOS were used to evaluate the patient's pain, exercise, entertainment, quality of life and other items, with a total score of 100 points. The higher the score, the better the recovery of the patient's knee joint function.

Table 1 Comparison of general data between the treatment and control groups

Group	Sex, M/F	Age (yr)	BMI in kg/m²	Educational level, illiterate/primary school/senior high school/ junior college/college and university	Surgical limb, L/R
Treatment, n = 40	6/34	67.28 ± 5.51	24.44 ± 2.37	2/1/23/12/2/0	22/18
Control, n = 40	10/30	69.07 ± 6.54	24.92 ± 2.24	0/1/26/11/0/2	25/15
χ^2/t	1.250	1.332	1.020	6.227	0.464
P value	0.264	0.187	0.310	0.285	0.496

M: Male; F: Female; BMI: Body mass index; L: Left; R: Right.

Statistical analysis

All collected patient data were processed using SPSS 26.0 statistical software (IBM Corp., Armonk, NY, United States). Measurement data were expressed as mean ± SD ($\chi \pm s$), and qualitative data were expressed as frequencies. The measurement data were first analyzed for normality, followed by the t-test for those that conformed to the normal distribution and the rank-sum test for those that did not conform. Count data were compared using the χ^2 test. In the χ^2 test, if the sample size was ≥ 40 but the theoretical number of one of the grids was $1 \le T < 5$, then the continuity corrected χ^2 test was used. If the theoretical number $T < 1$ or the sample size was < 40, then Fisher's exact probability method was used. All statistical analyses were based on two-sided hypothesis testing, and the test level was $\alpha = 0.05$. Differences were considered statistically significant when $P < 0.05$.

RESULTS

VAS scores

There was no significant difference in the VAS scores between the two groups on the 3rd d before the operation and the 3rd d after the operation ($P > 0.05$). After the treatment, the VAS scores of the treatment group were significantly lower than those of the control group 7 d after the operation ($t = 7.536$, $P < 0.000$) and 14 d after the operation ($t = 8.563$, $P < 0.000$) (Table 2).

Skin temperature

There was no significant difference in skin temperature between the two groups at 3 d before or after the operation ($P > 0.05$). The skin temperature in the treatment group was significantly lower than in the control group on day 7 after the operation ($t = 2.968$, $P = 0.004$) and on day 14 after the operation ($t = 4.423$, $P = 0.000$) (Table 3).

Lower extremity swelling

There was no statistically significant difference between the upper and lower circumferences of the patients 3 d before and after the operation ($P > 0.05$). The circumference above and below the patella were significantly lower in the treatment group 7 d after the operation ($t = 2.315$, $P = 0.023$ and $t = 2.121$, $P = 0.037$, respectively) and 14 d after the operation ($t = 2.374$, $P = 0.020$ and $t = 2.095$, $P = 0.039$, respectively) (Table 4).

KOOS

There was no significant difference in the range of motion of the knee joint and the KOOS between the two groups before treatment ($P > 0.05$). Fourteen days after surgery, the range of motion of the knee joint and the KOOS of the two groups were significantly improved. The knee range of motion and KOOS of the treatment group were significantly higher than those of the control group ($P < 0.05$) (Table 5).

DISCUSSION

TKA is the primary treatment choice for patients with severe knee osteoarthritis as it can effectively relieve pain, improve knee function and improve quality of life[9]. However, the disadvantages of severe trauma due to the operation and many postoperative complications are a concern to patients[10]. Joint swelling and pain are the most reported complications caused by TKA. Ice is one of the most

Table 2 Comparison of visual analog scale scores between the two groups

Group	-3rd d	3rd d	7th d	14th d
Treatment, *n* = 40	6.75 ± 0.92	5.30 ± 0.79	2.57 ± 0.84	0.80 ± 0.93
Control, *n* = 40	6.60 ± 0.84	5.65 ± 0.80	4.00 ± 0.85	2.70 ± 1.04
t	0.758	1.965	7.536	8.563
P value	0.451	0.053	0.000	0.000

-3rd d: 3 d before the operation; 3rd d: 3 d after the operation; 7th d: 7 d after the operation; 14th d: 14 d after the operation.

Table 3 Comparison of skin temperature between the two groups (°C)

Group	-3rd d	3rd d	7th d	14th d
Treatment, *n* = 40	37.34 ± 0.28	37.21 ± 0.26	36.93 ± 0.21	36.63 ± 0.31
Control, *n* = 40	37.29 ± 0.34	37.24 ± 0.32	37.09 ± 0.27	36.94 ± 0.32
t	0.755	0.422	2.968	4.423
P value	0.452	0.674	0.004	0.000

-3rd d: 3 d before the operation; 3rd d: 3 d after the operation; 7th d: 7 d after the operation; 14th d: 14 d after the operation.

Table 4 Comparison of lower limb swelling between the two groups

	Group		*t*	*P* value
	Treatment, *n* = 40	Control, *n* = 40		
Upper circumference in cm				
-3 d	53.35 ± 4.94	51.83 ± 4.34	1.461	0.148
3 d	52.83 ± 4.91	51.51 ± 4.29	1.274	0.206
7 d	48.32 ± 4.57	50.53 ± 3.97	2.315	0.023
14 d	45.68 ± 4.69	47.96 ± 3.89	2.374	0.020
Lower circumference in cm				
-3 d	39.59 ± 3.58	38.16 ± 3.78	1.734	0.087
3 d	38.96 ± 3.55	37.50 ± 3.85	1.768	0.081
7 d	36.71 ± 2.95	39.21 ± 6.86	2.121	0.037
14 d	34.96 ± 2.96	36.70 ± 4.35	2.095	0.039

-3 d: 3 d before the operation; 3 d: 3 d after the operation; 7 d: 7 d after the operation; 14 d: 14 d after the operation.

popular interventions for these two complications. This method may ameliorate the inflammatory response, pain and edema because the permeability of blood vessels may decrease due to shrinking blood vessels at the surgical site[11]. However, in the process of icing, nurses must monitor the patient's blood supply, peripheral nerve sensation and skin temperature to avoid frostbite of the skin due to the low temperature[12,13]. Another widely adopted postoperative intervention is the ankle pump apparatus. It can significantly improve blood circulation and lymphatic return of the lower extremities to effectively prevent venous thrombosis. However, patient compliance can be unsatisfactory, or the patient may refuse the intervention due to postoperative pain[14,15].

In this study, the postoperative treatment was performed by applying a prepared TCM ointment and tuina therapy to the affected side. The pain, swelling and skin temperature of the patients in the treatment group were significantly better than those of the patients in the control group 7 d and 14 d after surgery. According to TCM, the association of ointment and tuina therapy can regulate qi and blood because they directly warm the meridians to unblock the congealing cold. This improves the function of the internal organs, reinforces healthy qi and eliminates pathogenic factors.

Table 5 Comparison of knee range of motion and knee injury and Osteoarthritis Outcome score between the two groups of patients

Group	Knee range of motion in degrees		KOOS score	
	-3rd d	14th d	-3rd d	14th d
Treatment, *n* = 40	95.23 ± 2.11	115.32 ± 2.12	65.83 ± 1.39	85.52 ± 0.82
Control, *n* = 40	95.14 ± 2.24	113.34 ± 2.16	65.73 ± 1.33	80.32 ± 1.13
t	0.185	4.138	0.329	23.556
P value	0.854	0.000	0.743	0.000

KOOS: Knee injury and Osteoarthritis Outcome score; -3rd d: 3 d before the operation; 14th d: 14 d after the operation.

The ointment was primarily composed of herbs that can activate blood and relieve stasis, such as Ruxiang (*Olibanum*) and Chuanxiong (*Rhizoma Chuanxiong*). The tuina therapy used in this study was an integration of various manipulation methods of traditional Chinese tuina, such as scrubbing manipulation, acupoint-pressing manipulation, rubbing manipulation and kneading manipulation. The application of these manipulations in a tender way can relax the tense muscles and release spasms. It can also promote the absorption of drugs, improve local blood circulation and accelerate the reduction of inflammatory reactions, thus achieving the purpose of eliminating swelling and relieving pain. At the same time, tuina therapy applied to local regions may bring the movement of the corresponding muscle tissue, resulting in the improvement of metabolism of inflammatory substances in local lesions. This action can induce the recovery of local capillary endothelial function and the enhancement of blood circulation in local lesions.

In this study, tuina therapy was applied to the acupoints on the patient's affected side. The acupoints were Zusanli (ST 36), Sanyinjiao (SP 6), Taichong (LV 3), Chengshan (BL 57), Shangjuxu (ST 37) and Futu (ST 32). Applying pressure to these acupoints can effectively improve muscle tension. Moreover, the manipulation of Zusanli (ST 36) and Sanyinjiao (SP 6) acupoints has a significant effect on the regulation of the liver, spleen and kidney and the alleviation of knee joint pain and lower extremity numbness[16]. The acupoint tuina therapy applied on the Taichong (LV 3), Chengshan (BL 57) and Shangjuxu (ST 37) acupoints can significantly improve atrophy and impediment (*bi*) of the lower extremities[17].

Tuina therapy conducted on a group of acupoints can promote the blood circulation of the lower extremities. Moreover, the therapy is conducted at a relatively quick frequency, which is adopted to reduce large-scale movements of the patient's bones and joints, and to reduce the damage caused by the manipulation. Treatment compliance is typically satisfactory because the scrubbing and kneading manipulation improves soft tissue relaxation of tendons and ligaments, which is soothing to the patient. Our results also indicated that edema was reduced in the treatment group 7 d and 14 d after surgery. Similarly, Tao *et al*[18] observed that the combination of ointment and massage manipulation had a positive effect on improving postoperative pain and edema.

CONCLUSION

TCM ointment combined with tuina therapy has significant advantages in treating pain, swelling, skin temperature and knee joint range of motion after artificial TKA. Additional studies with a longer follow-up time and larger sample size will confirm the benefits of adding this treatment to the postoperative care of TKA as well as determine the mechanism of action in reducing the inflammatory response.

ARTICLE HIGHLIGHTS

Research background

Total knee arthroplasty (TKA) is the preferred treatment for patients suffering from severe osteoarthritis. The pain and swelling of the knee after the operation may impact rehabilitation and patient quality of life. Routine care to treat these complications includes icing, ankle pump exercises and non-steroidal anti-inflammatory analgesics. However, there are drawbacks to these treatments.

Research motivation

The use of traditional Chinese medicine (TCM) ointments can warm meridians, regulate qi and blood, and improve viscera function. It can effectively relieve pain, significantly recover function, and significantly improve the quality of life. Tuina therapy has been shown to enhance the penetration of

ointments and has a good long-term effect on patients.

Research objectives

This study aimed to identify a benefit to adding a TCM ointment and tuina therapy to routine care for TKA.

Research methods

The randomized controlled clinical trial enrolled 80 patients who underwent TKA and were divided into two equal groups. All patients received routine care, with the treatment group also receiving TCM ointment with tuina therapy. The following variables were recorded 3 d before surgery and 3 d, 7 d and 14 d after surgery: Visual analog scale score; skin temperature; and circumferences at 15 cm above and below the patella. The maximum active knee flexion angle and the knee injury and Osteoarthritis Outcome score were recorded before surgery and 14 d after surgery.

Research results

All measured variables were significantly improved in the treatment group compared to the control group, who only received routine care during the postoperative period.

Research conclusions

Treatment with a TCM ointment and tuina therapy for knee arthroplasty patients effectively promoted the local lesion site metabolism and blood circulation, and had a significant inhibitory effect on the local inflammatory response and oxidative stress response.

Research perspectives

Additional studies with a longer follow-up time and larger sample size will confirm the benefits of adding this integrative treatment to the postoperative care of TKA as well as determine the mechanism of action in reducing the inflammatory response.

FOOTNOTES

Author contributions: Jiang B contributed to the conceptualization and data curation; Xu HR, Wang QL, Kong H, Zhang H, Tian J, Ding Y, Yang RX and Zhang L contributed to project administration; Xing L contributed to writing, including review and editing, and project administration; and all authors read and approved the final manuscript.

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REFERENCES

1 **Mahmoudian A**, Lohmander LS, Mobasheri A, Englund M, Luyten FP. Early-stage symptomatic osteoarthritis of the knee - time for action. *Nat Rev Rheumatol* 2021; **17**: 621-632 [PMID: 34465902 DOI: 10.1038/s41584-021-00673-4]

2 **Wu YL**, Chen RZ, Wang ML, Liu D, Liu JW. [Effect of warm needle moxibustion on morphological changes of cartilage and subchondral bone in knee osteoarthritis rabbits]. *Zhen Ci Yan Jiu* 2021; **46**: 123-128 [PMID: 33788433 DOI: 10.13702/j.1000-0607.200027]

3 **Zhang J**, Wei C, Wu Y, Lin H, Yin G, Chen H, Xie Z, Hou C. [Experimental study on crosslinked-chitosan in treatment of knee osteoarthritis in rabbits]. *Zhongguo Xiu Fu Chong Jian Wai Ke Za Zhi* 2019; **33**: 185-189 [PMID: 30739412 DOI: 10.7507/1002-1892.201804035]

4 **Liu JW**, Wu YL, Wei W, Zhang YL, Liu D, Ma XX, Li C, Ma YY. Effect of Warm Acupuncture Combined with Bone Marrow Mesenchymal Stem Cells Transplantation on Cartilage Tissue in Rabbit Knee Osteoarthritis. *Evid Based Complement Alternat Med* 2021; **2021**: 5523726 [PMID: 34422071 DOI: 10.1155/2021/5523726]

5 **Zhang W**, Gao Y, Guo C, Ibrahim Zeyad Ali K, Farid M. Effect of acupotomy versus electroacupuncture on ethology and morphology in a rabbit model of knee osteoarthritis. *J Tradit Chin Med* 2019; **39**: 229-236 [PMID: 32186046]

6 **Liu J**, Lin QX, Lu LM, Guo ZX, Liu H, Zhang LZ, Xiu ZB. [Effects of "knot-loosing" of acupotomy on motor function and morphological changes of knee joint in knee osteoarthritis rabbits]. *Zhen Ci Yan Jiu* 2021; **46**: 129-135 [PMID: 33788434 DOI: 10.13702/j.1000-0607.200347]

7 **Wang W**, Wang L, Xu Z, Yin Y, Su J, Niu X, Cao X. Effects of estradiol on reduction of osteoarthritis in rabbits through effect on matrix metalloproteinase proteins. *Iran J Basic Med Sci* 2016; **19**: 310-315 [PMID: 27114801]

8 **Wu G**, Zhang J, Chen W, Chen S, Huang Y, Lin R, Huang M, Li Z, Zheng L, Li X. Tougu Xiaotong capsule exerts a therapeutic effect on knee osteoarthritis by regulating subchondral bone remodeling. *Mol Med Rep* 2019; **19**: 1858-1866 [PMID: 30592265 DOI: 10.3892/mmr.2018.9778]

9 **Ruan A**, Wang Q, Ma Y, Zhang D, Yang L, Wang Z, Xie Q, Yin Y. Efficacy and Mechanism of Electroacupuncture Treatment of Rabbits With Different Degrees of Knee Osteoarthritis: A Study Based on Synovial Innate Immune Response. *Front Physiol* 2021; **12**: 642178 [PMID: 34421630 DOI: 10.3389/fphys.2021.642178]

10 **Wang XD**, Wan XC, Liu AF, Li R, Wei Q. Effects of umbilical cord mesenchymal stem cells loaded with graphene oxide granular lubrication on cytokine levels in animal models of knee osteoarthritis. *Int Orthop* 2021; **45**: 381-390 [PMID: 32556386 DOI: 10.1007/s00264-020-04584-z]

11 **Li M**, Li H, Ran X, Yin H, Luo X, Chen Z. Effects of adenovirus-mediated knockdown of IRAK4 on synovitis in the osteoarthritis rabbit model. *Arthritis Res Ther* 2021; **23**: 294 [PMID: 34863246 DOI: 10.1186/s13075-021-02684-8]

12 **Wang J**, Gao JS, Chen JW, Li F, Tian J. Effect of resveratrol on cartilage protection and apoptosis inhibition in experimental osteoarthritis of rabbit. *Rheumatol Int* 2012; **32**: 1541-1548 [PMID: 21327438 DOI: 10.1007/s00296-010-1720-y]

13 **An S**, Li J, Xie W, Yin N, Li Y, Hu Y. Extracorporeal shockwave treatment in knee osteoarthritis: therapeutic effects and possible mechanism. *Biosci Rep* 2020; **40** [PMID: 33074309 DOI: 10.1042/BSR20200926]

14 **Pape D**, Tischer T. [Osteoarthritis of the knee in young patients]. *Orthopade* 2021; **50**: 345 [PMID: 33909120 DOI: 10.1007/s00132-021-04095-8]

15 **Chen Z**, Wang C, You D, Zhao S, Zhu Z, Xu M. Platelet-rich plasma versus hyaluronic acid in the treatment of knee osteoarthritis: A meta-analysis. *Medicine (Baltimore)* 2020; **99**: e19388 [PMID: 32176063 DOI: 10.1097/MD.0000000000019388]

16 **Øiestad BE**, Juhl CB, Culvenor AG, Berg B, Thorlund JB. Knee extensor muscle weakness is a risk factor for the development of knee osteoarthritis: an updated systematic review and meta-analysis including 46 819 men and women. *Br J Sports Med* 2022; **56**: 349-355 [PMID: 34916210 DOI: 10.1136/bjsports-2021-104861]

17 **Zacharjasz J**, Mleczko AM, Bąkowski P, Piontek T, Bąkowska-Żywicka K. Small Noncoding RNAs in Knee Osteoarthritis: The Role of MicroRNAs and tRNA-Derived Fragments. *Int J Mol Sci* 2021; **22** [PMID: 34071929 DOI: 10.3390/ijms22115711]

18 **Tao JM**, Ma JY, Zhang H, Guo QJ, Tao Y. Observation on the clinical effect of ointment combined with joint loosening in the treatment of knee stiffness. *Shizhen Guoyi Guoyao* 2018; **29**: 1370-1371

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CASE REPORT

Derotational osteotomy and internal fixation of a 180° malrotated humerus: A case report

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Abstract

BACKGROUND

Humeral shaft fractures are relatively common in adults. Rotational malalignment is reported as one complication but severe rotational deformity of the humerus is extremely rare. To our knowledge, only three cases of symptomatic humeral malrotation have been reported. There are sparse literature reports of humeral reconstruction correction.

CASE SUMMARY

We present a case of extreme rotational deformity of the humerus (180°) after humeral shaft fracture. The patient complained of pain and difficulties with activities of daily living. In addition, she found the deformity cosmetically unacceptable. Therefore, she was searching for surgical correction. Neurolysis of the radial nerve followed by derotational osteotomy of the humerus and internal fixation were performed. Postoperatively, the patient demonstrated transient iatrogenic radial nerve palsy which recovered completely during postoperative follow-up. The Disabilities of the Arm, Shoulder, and Hand score improved from 55 preoperatively to 16 at the final 2-year follow-up.

CONCLUSION

Single-stage radial neurolysis, derotational osteotomy and stable fixation is a feasible option to improve anatomic and functional problems of severely malrotated humeral shaft fractures.

Key Words: Humerus; Malrotation; Corrective osteotomy; Plate osteosynthesis; Radial nerve palsy; Case report

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Core Tip: We present a case of extreme rotational deformity of the humerus (180°) after humeral shaft fracture. The patient complained about pain and difficulties with activities of daily living. A neurolysis of the radial nerve followed by derotational osteotomy of the humerus and internal fixation were performed. Postoperatively, the patient demonstrated transient iatrogenic radial nerve palsy which had complete recovery at 2 years postoperatively. The Disabilities of the Arm, Shoulder, and Hand score improved from a preoperative 55 to a final 16 at the final 2-year follow-up.

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INTRODUCTION

Humeral shaft fractures are relatively common, accounting for approximately 1%-5% of all fractures and 20% of humeral fractures in adults[1-2]. These fractures have been historically regarded as benign fractures; as such, most are managed nonoperatively with functional bracing. The assumption of benign nature is based on the robust blood supply of the humerus, its limited weight-bearing characteristics and the technical ease of splint application[3-4].

Upper extremity function is primarily dependent on the hand's ability to reach a desired point in space. Most studies of malalignment have focused on angulation[5-6]. Rotational malalignment has been reported as a possible complication of humeral shaft fractures, but considered normally tolerated and to not necessitate a surgical intervention. Nevertheless, extreme rotational deformity following humeral shaft fractures can occur and the recommended treatment for these entities has been rarely touched upon in the literature.

Herein, we describe a case of a 180° rotational deformity that developed after a midshaft humeral fracture that had been clinically addressed by nonoperative treatment which had resulted in shortening of the humerus, limited range of motion (ROM) of the shoulder, and flexion contracture of the elbow.

CASE PRESENTATION

Chief complaints

The patient complained of resting pain exacerbated with activities and severe limitations in activities of daily living. Furthermore, the cosmetic deformity was repulsive to her.

History of present illness

In 2009, the right-hand-dominant patient had sustained a traumatic left humeral shaft fracture which was treated nonoperatively. In 2019 at age 27, she was referred to our institution with severe malrotation of her left humerus associated with shortening of the upper arm and limited ROM of the shoulder and elbow. The patient complained about consistent pain which increases during activities and severe limitations of activities of daily living. Furthermore, the cosmetic deformity was repulsive to her.

History of past illness

There is no history of past illness.

Personal and family history

Personal and family history are not known.

Physical examination

Physical examination detected a rotational deformity of the left upper arm of 180°. In supine position, the palm of her left hand and her olecranon were facing up (Figure 1). The Patient's left arm was 5 cm shorter than her right (51 cm *vs* 56 cm). She complained of tenderness over the whole upper arm and movement-dependent pain in the shoulder region. No neurological deficits were diagnosed. Shoulder ROM was presented with only 80° of abduction (Table 1). The elbow demonstrated a flexion contracture of 85°. The patient's forearm was fixed in neutral with total loss of pronation and supination. Wrist ROM was about normal.

Table 1 Range of motion of the patient's left upper extremity

	Preoperative	Postoperative
Shoulder		
Flexion/anteversion	80°	140°
Extension/retroversion	20°	25°
External rotation	30°	30°
Internal rotation	60°	60°
Abduction	80°	80°
Adduction	10°	20°
Elbow		
Flexion	85°	90°
Extension	0°	0°
Pronation	0°	80°
Supination	0°	80°
Wrist		
Flexion	50°	50°
Extension	50°	50°
Radial deviation	20°	20°
Ulnar deviation	30°	30°



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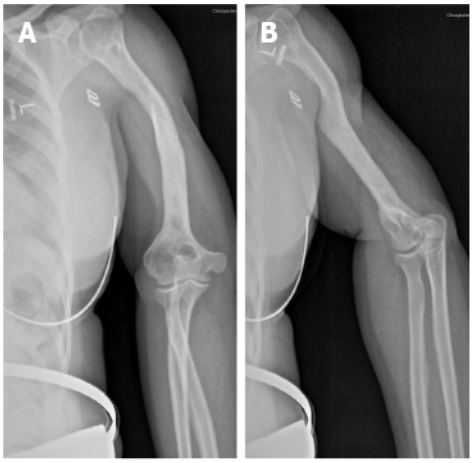
Figure 1 Severe malalignment of the patient's left arm. A: The patient in the operating room demonstrating the extreme deformity of the left upper extremity; B: In the supine position the palm of her hand and her olecranon (red narrow) were facing up.

Laboratory examinations

Laboratory examinations were unnecessary.

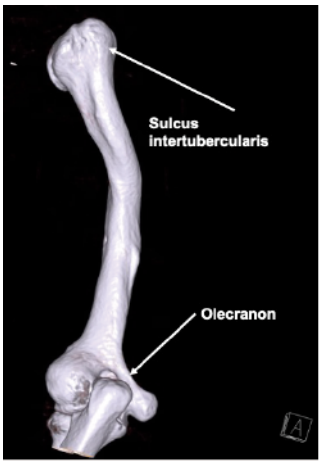
Imaging examinations

Radiographic imaging of the left shoulder and humerus demonstrated a malunited humeral shaft fracture with extensive remodeling and consolidated fracture site (Figure 2A). In addition, the shoulder displayed classic signs of post-traumatic osteoarthritis (Figure 2B). Preoperative three-dimensional computed tomography (3D CT) imaging confirmed a 180° malrotation of the humerus (Figure 3).



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Figure 2 Preoperative X-ray of the patient's left upper extremity. A: Preoperative X-rays of the left shoulder and upper arm of the patient revealed a deformed humerus and a complete consolidation; B: In addition, the X-ray displayed classic signs of post-traumatic osteoarthritis of the shoulder.



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Figure 3 Preoperative three-dimensional computed tomography of the patient's humerus. Extreme malrotation of 180° was detectable. The sulcus intertubercularis and olecranon served as landmarks.

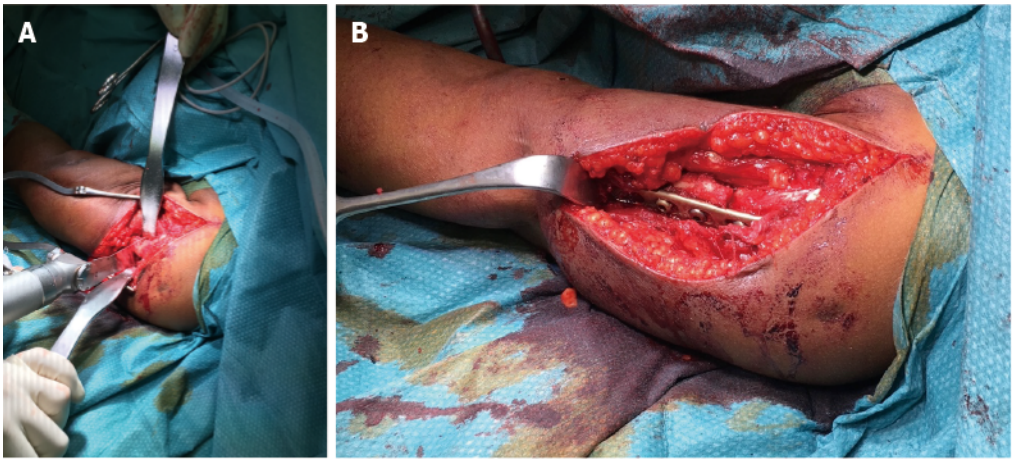
FINAL DIAGNOSIS

The patient demonstrated with rotational deformity of the left upper arm of 180°. Imaging of the left shoulder and upper arm revealed a malunited humeral fracture with extensive remodeling and fracture site consolidation.

TREATMENT

Preoperatively, different surgical options were discussed with the patient and her family. The patient gave informed consent for a single staged procedure with complete radial nerve neurolysis followed by corrective osteotomy and internal fixation *via* plate fixation.

Ten years after the initial injury, the patient finally underwent derotational osteotomy with internal fixation of the left humerus and radial nerve exploration. Surgery was performed in the supine position under brachial plexus blocking and general anesthesia. Proximal humerus and the humeral shaft were exposed through a deltopectoral approach with extension distally anteriorly, following the anatomic muscles of the upper arm. Through the same anterior extensile incision, the radial nerve was exposed and released from the posterior aspect of the deltoid, through the lateral intermuscular septum, to the distal the arm in order not to lessen tension during the humeral derotation. A transverse osteotomy at the level of the consolidated fracture was performed carefully with a micro-oscillating saw and using instruments to protect surrounding and posterior soft tissues (Figure 4A). Subsequently, the entire distal



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Figure 4 Intraoperative photographs. A: Transversal osteotomy of the humerus was performed at the level of the former fracture; B: Internal fixation was done with the use of an eight-hole dynamic compression plate (Limited Contact Dynamic Compression Plate System).

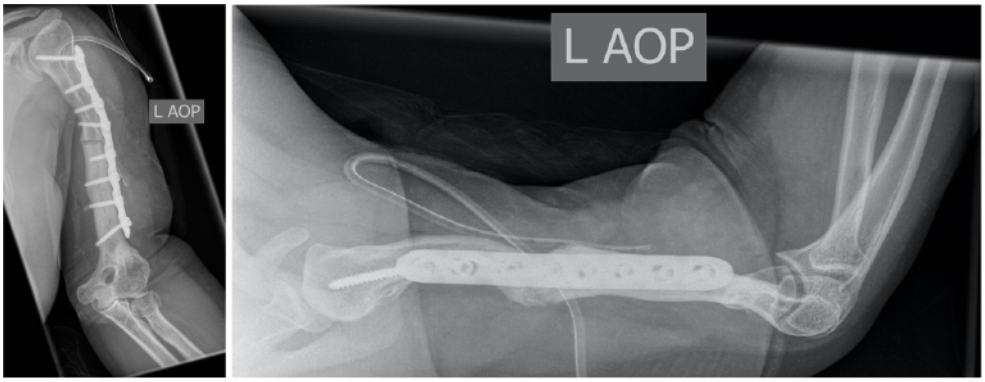
humerus was rotated 180° demonstrating no tension to the radial nerve under direct visualization. Finally, internal fixation was performed utilizing an (3.5 mm or 4.5 mm) eight-hole dynamic compression plate [Limited Contact Dynamic Compression Plate System (LC-DCP); DePuySynthes, Warsaw, IN, United States] (Figures 4B and 5). Postoperatively, normal vascularity was noted, and soft compartments were noted, but a secondary or iatrogenic partial radial nerve palsy with weak wrist and digit extension and decreased light touch sensation in the radial nerve distribution. This injury was related to devascularization from dissection and manipulation of the nerve and less likely from the preoperative brachial plexus regional block. Secondary to the known intact and not impinged radial nerve at the end of the procedure, the patient and surgeons agreed to treat this transient radial nerve palsy with observation and did not re-explore the dissection.

The osteotomy zone was immobilized utilizing a Gilchrist-bandage for 4 wk postoperatively. Physical therapy with shoulder mobilization was initiated immediately after surgery. Shoulder and elbow ROM gradually increased and full ROM was allowed after 6 wk. Additionally, the weakened wrist muscles were immobilized in a functional splint and daily passive exercises were performed to maintain full ROM and to avoid contractures.

Initially, the skin incision had healed uneventfully and no signs of superficial or deep surgical site infection were noted. However, approximately 4 mo postoperatively, the patient presented with a deep surgical site infection with involvement of the osteosynthesis material and a non-consolidated osteotomy zone (an infected nonunion with fixation failure). Since the patient was healthy without comorbidities, she wanted to continue with therapy and avoid recurrence of the deformity. Therefore, a single stage revision was reviewed with the patient. Operative treatment consisted of plate removal with thorough excisional debridement, recanalization of the humerus, followed by re-osteosynthesis as a single staged procedure. Aerococcus viridans bacteria were detected in the deep intraoperative tissue cultures. Therefore, an antimicrobial therapy with clindamycin was initiated and continued for 6 wk.

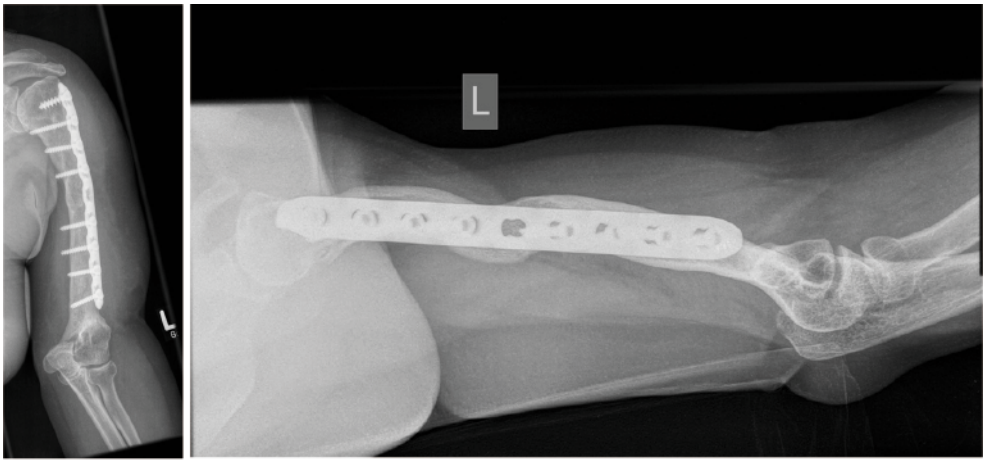
OUTCOME AND FOLLOW-UP

After revision surgery, the patient did not present for follow-up appointments. We assumed that she was satisfied with the operative outcome and had resolution of the infection and preoperative functional difficulties. Approximately 2 years after initial surgery, we contacted the patient and scheduled an appointment. She reported a high level of satisfaction, resolution of infection, diminishment of pain, and a complete return to daily activities and caring of her two toddlers. Physical exam demonstrated complete healing of the soft tissues and resolution of the infection and imaging demonstrated consolidation of the osteotomy zone (Figure 6). The patient only complained of pain in her left upper arm and shoulder when carrying heavy objects or after a strenuous day with constant use of her arm. She demonstrated increased shoulder ROM: flexion/extension 140-0-25°, abduction/adduction 80-0-20° and improved elbow ROM: flexion/extension 0-0-90°, with free supination and pronation. Compared to preoperative function, she demonstrated a marked improvement in all areas of arm motion. She did not have full shoulder ROM secondary to the preoperative, degenerative changes of her left shoulder (Figure 7). The patient described gradual improvement in the radial function within 3-4 mo of the initial surgery with complete recovery of the transient radial nerve palsy at the time of the follow-up examination. The patient completed the follow up Disabilities of the Arm, Shoulder, and



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Figure 5 Postoperative X-rays of the patient's left humerus after corrective osteotomy and internal fixation.



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Figure 6 X-rays at the patient's 2-year follow-up appointment. There was complete consolidation of the osteotomy zone.



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Figure 7 Postoperative cosmetic and functional outcome.

Hand (DASH) questionnaire comparing the pre- and post-operative scores. The DASH score improved from a preoperative score of 55 to 16 at the final follow-up.

DISCUSSION

Although rotational malalignment is recognized as a possible complication of humeral shaft fractures in adults, extreme rotational deformities are extremely rare. Accordingly, the literature regarding this topic is sparse. To our knowledge, only three cases have been reported[7,8] and there are only a few papers regarding upper limb correction in general, with most focusing on non-traumatic and pediatric indications[9,10]. In contrast, deformity correction and bone lengthening of the lower extremities are standard techniques with an increasing number of reports appearing in the literature. External fixators (unilateral, multiaxial, or circular) are utilized. Bulky techniques, like Ilizarov external fixation or Taylor-Spatial-Frame are still practiced and offered as reliable treatment options[11,12]. For upper limb treatment, circular fixation techniques like the Ilizarov external fixator and Taylor-Spatial-Frame pose problems of discomfort because of the limited distance to the thorax. Additionally, proximal or midshaft humeral fractures provide only limited bone stock for proximal fixation for all external fixation systems.

In our patient, the indications for operative intervention were the cosmetically unacceptable condition of a 180° malrotated arm as well as the inability to perform routine daily activities. She also reported limited ROM and severe pain of her left arm during shoulder movement. More extensive deformity corrections are usually performed as staged or continuous procedures utilizing external fixation to preserve neural structures and blood supply[13]. In our case, we decided against surgical correction by an external fixator for several reasons. On the one hand, the patient declined treatment with an Ilizarov fixator, citing the extensive follow-up care associated with it. Additionally, we needed a quick solution because it was unclear how long the patient would be in the area and available for follow-up and stepwise correction.

Although the patient's left arm already presented with a shorter length preoperatively, this condition did not bother our patient. Due to the decision just to perform a rotational correction and no lengthening of the arm, we chose derotational osteotomy, and exposure and release of the radial nerve by internal fixation. We assumed that exposing the nerve would reduce the risk for radial nerve injury. Nevertheless, the patient experienced radial nerve palsy postoperatively. Because of the good visualization of the radial nerve, we were able to rule out disruption or compression. There are reports of radial nerve injuries after deformity correction of the upper limb with different fixation systems[11,14] as well as after closed reduction of severe rotational deformity of the humerus[8]. Data on iatrogenic radial nerve injuries for open procedures vary between 6%-32%[15,16].

Regarding treatment, no clear consensus exists regarding if and when the nerve should be surgically explored[17]. Some authors recommend early exploration in cases of secondary nerve palsy[18], others advocate observation for a 4-to-6-mo period[19,20]. According to the literature, secondary radial nerve palsy has a good overall recovery rate of 93%[21]. In our case, the "wait and see" strategy was sufficient as the patient achieved complete neurological recovery. An increasing improvement in the radial nerve palsy was observed already after 4 mo. Two years after the initial surgery, the neurologic deficit had completely recovered, but the exact time point remains unclear because of the discontinued follow-up visits.

Different treatment options for surgical site infections and infected nonunions during a single or staged procedure have been discussed[22,23]. Due to the fact that our patient presented with infection 4 mo postoperatively, nonunion with secondary infection was assumed. Wu *et al*[24] reported a preference for single-stage treatment to address infected nonunions with Ilizarov fixation. Since our patient was healthy without comorbidities, we respected her request to continue with the initial therapy in order to avoid external fixation or recurrence of the deformity. Therefore, thorough debridement and hardware exchange were performed as a single-stage revision. Olszewski *et al*[22] reported their support of such an approach, based upon their data showing that 78% of patients healed after an index procedure and were able to avoid external fixation.

Bae *et al*[25] also described a case of severe malrotation of the humerus after humeral shaft fracture. Similar to our treatment, those authors described the performance of a derotation osteotomy of the left humerus with internal fixation and exposure of the radial nerve. They also reported a good postoperative result without neurological deficits.

In our case, the patient benefited greatly from the surgical procedure. Her preoperative DASH score was quite high (at 55) and had improved significantly after the deformity correction (to 16). Her 180° malrotated left upper arm represented a cosmetic problem, serving as a mental burden and significantly impairing her functional activities of daily living. Therefore, our treatment aimed for correction of the deformity, improvement of function, pain reduction, and achievement of the desired cosmetic result. These goals were achieved with very good results. The humeral malrotation has been entirely corrected and the overall deformity was reduced. Above all, shoulder ROM (especially shoulder flexion: 80° *vs* 140°) and pronation/supination of the elbow (0° *vs* 80°) increased significantly due to a more anatomic position of the humeral head articular surface. Some limitations persisted due to pre-existing degenerative changes. Furthermore, the flexion contracture of the elbow could not be resolved because of the long existing malalignment of the upper limb.

The patient noticed relevant pain relief from "severe" (preoperative) to "no" or "mild" pain postoperatively. At the 2-year follow-up appointment, she was very satisfied with the result of the operation. She indicated that she occasionally has pain in her left arm while carrying heavy objects. Ultimately, she

stated that she is now living a normal life with her children without limitations in her everyday activities.

Our case complements the sparse literature of extreme malrotation deformity of the humerus and illustrates that corrective osteotomy with internal fixation may be a feasible treatment approach to avoid uncomfortable circular external fixation and to reach good postoperative results. It is a valid method that improved outcomes following deformity correction. We admit that a stepwise procedure utilizing a fixator (*e.g.*, a Taylor-Spatial frame) would have offered the option of additional lengthening.

CONCLUSION

Malalignment after humeral shaft fractures often includes a malrotation component. Extensive rotational correction is rare and the literature is sparse. Common procedures for extensive alignment correction utilizing circular external fixations cause a great amount of discomfort, especially when utilized on the proximal or midshaft humerus. Acute rotational correction of 180° is feasible and can lead to good clinical results when performed carefully.

FOOTNOTES

Author contributions: Wenning KE helped with data collection, interpretation and writing the case report; Hoffmann MF contributed to study concept/design and data analysis; Jones CB, Schildhauer TA and Hoffmann MF helped with interpretation and contributed to the review of the final manuscript and final submission of the paper.

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Conflict-of-interest statement: All authors report no relevant conflict of interest for this article.

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REFERENCES

1 **Gallusser N**, Barimani B, Vauclair F. Humeral shaft fractures. *EFORT Open Rev* 2021; **6**: 24-34 [PMID: 33532084 DOI: 10.1302/2058-5241.6.200033]
2 **Brinker MR**, O'Connor DP. The incidence of fractures and dislocations referred for orthopaedic services in a capitated population. *J Bone Joint Surg Am* 2004; **86**: 290-297 [PMID: 14960673 DOI: 10.2106/00004623-200402000-00011]
3 **Rämö L**, Sumrein BO, Lepola V, Lähdeoja T, Ranstam J, Paavola M, Järvinen T, Taimela S; FISH Investigators. Effect of Surgery vs Functional Bracing on Functional Outcome Among Patients With Closed Displaced Humeral Shaft Fractures: The FISH Randomized Clinical Trial. *JAMA* 2020; **323**: 1792-1801 [PMID: 32396179 DOI: 10.1001/jama.2020.3182]
4 **Garnavos C**. Humeral Shaft Fractures. Rockwood Green's Fract Adults Philadelphia Wolters Kluwer. 2020; 1: 1231-1291
5 **Arora R**, Fichadia U, Hartwig E, Kannikeswaran N. Pediatric upper-extremity fractures. *Pediatr Ann* 2014; **43**: 196-204 [PMID: 24877490 DOI: 10.3928/00904481-20140417-12]
6 **Robinson CM**, Wylie JR, Ray AG, Dempster NJ, Olabi B, Seah KT, Akhtar MA. Proximal humeral fractures with a severe varus deformity treated by fixation with a locking plate. *J Bone Joint Surg Br* 2010; **92**: 672-678 [PMID: 20436005 DOI: 10.1302/0301-620X.92B5.22849]
7 **Hawi N**, Razaeian S, Krettek C, Meller R, Liodakis E. [Torsional malalignment of the humerus]. *Unfallchirurg* 2018; **121**:

199-205 [PMID: 29305619 DOI: 10.1007/s00113-017-0453-8]
8 **Chan D**, Petricciuolo F, Maffulli N. Fracture of the humeral diaphysis with extreme rotation. *Acta Orthop Belg* 1991; **57**: 427-429
9 **Farr S**, Mindler G, Ganger R, Girsch W. Bone Lengthening in the Pediatric Upper Extremity. *J Bone Joint Surg Am* 2016; **98**: 1490-1503 [PMID: 27605694 DOI: 10.2106/JBJS.16.00007]
10 **Tellisi N**, Ilizarov S, Fragomen AT, Rozbruch SR. Humeral lengthening and deformity correction in Ollier's disease: distraction osteogenesis with a multiaxial correction frame. *J Pediatr Orthop B* 2008; **17**: 152-157 [PMID: 18391816 DOI: 10.1097/BPB.0b013e3282f548dc]
11 **Hosny GA**. Humeral lengthening and deformity correction. *J Child Orthop* 2016; **10**: 585-592 [PMID: 27826910 DOI: 10.1007/s11832-016-0789-6]
12 **Malkova TA**, Borzunov DY. International recognition of the Ilizarov bone reconstruction techniques: Current practice and research (dedicated to 100th birthday of G. A. Ilizarov). *World J Orthop* 2021; **12**: 515-533 [PMID: 34485099 DOI: 10.5312/wjo.v12.i8.515]
13 **Goodier WD**, Calder PR. External fixation for the correction of adult post-traumatic deformities. *Injury* 2019; **50** Suppl 1: S36-S44 [PMID: 31054864 DOI: 10.1016/j.injury.2019.03.040]
14 **Malot R**, Park KW, Song SH, Kwon HN, Song HR. Role of hybrid monolateral fixators in managing humeral length and deformity correction. *Acta Orthop* 2013; **84**: 280-285 [PMID: 23506166 DOI: 10.3109/17453674.2013.786636]
15 **Hak DJ**. Radial nerve palsy associated with humeral shaft fractures. *Orthopedics* 2009; **32**: 111 [DOI: 10.3928/01477447-20090201-26]
16 **Bumbasirević M**, Lesić A, Bumbasirević V, Cobeljić G, Milosević I, Atkinson HD. The management of humeral shaft fractures with associated radial nerve palsy: a review of 117 cases. *Arch Orthop Trauma Surg* 2010; **130**: 519-522 [PMID: 19669771 DOI: 10.1007/s00402-009-0951-4]
17 **Schwab TR**, Stillhard PF, Schibli S, Furrer M, Sommer C. Radial nerve palsy in humeral shaft fractures with internal fixation: analysis of management and outcome. *Eur J Trauma Emerg Surg* 2018; **44**: 235-243 [PMID: 28280873 DOI: 10.1007/s00068-017-0775-9]
18 **Kwasny O**, Maier R, Kutscha-Lissberg F, Scharf W. [Treatment procedure in humeral shaft fractures with primary or secondary radial nerve damage]. *Unfallchirurgie* 1992; **18**: 168-173 [PMID: 1636222 DOI: 10.1007/BF02588269]
19 **Liu GY**, Zhang CY, Wu HW. Comparison of initial nonoperative and operative management of radial nerve palsy associated with acute humeral shaft fractures. *Orthopedics* 2012; **35**: 702-708 [PMID: 22868596 DOI: 10.3928/01477447-20120725-10]
20 **Wang JP**, Shen WJ, Chen WM, Huang CK, Shen YS, Chen TH. Iatrogenic radial nerve palsy after operative management of humeral shaft fractures. *J Trauma* 2009; **66**: 800-803 [PMID: 19276756 DOI: 10.1097/TA.0b013e31816142cf]
21 **Korompilias AV**, Lykissas MG, Kostas-Agnantis IP, Vekris MD, Soucacos PN, Beris AE. Approach to radial nerve palsy caused by humerus shaft fracture: is primary exploration necessary? *Injury* 2013; **44**: 323-326 [PMID: 23352153 DOI: 10.1016/j.injury.2013.01.004]
22 **Olszewski D**, Streubel PN, Stucken C, Ricci WM, Hoffmann MF, Jones CB, Sietsema DL, Tornetta P 3rd. Fate of Patients With a "Surprise" Positive Culture After Nonunion Surgery. *J Orthop Trauma* 2016; **30**: e19-e23 [PMID: 26270457 DOI: 10.1097/BOT.0000000000000417]
23 **Nasser AAH**, Fenton P, Bose D. Single stage versus two-stage orthoplastic management of bone infection. *Injury* 2022; **53**: 984-991 [PMID: 35063261 DOI: 10.1016/j.injury.2022.01.020]
24 **Wu CC**. Single-stage surgical treatment of infected nonunion of the distal tibia. *J Orthop Trauma* 2011; **25**: 156-161 [PMID: 21278604 DOI: 10.1097/BOT.0b013e3181eaaa35]
25 **Bae H**, Widmann RF, Hotchkiss RN. Extreme rotational malunion of the humerus. A case report. *J Bone Joint Surg Am* 2001; **83**: 424-427 [PMID: 11263648 DOI: 10.2106/00004623-200103000-00016]



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EDITORIAL

Genetics of congenital anomalies of the hand

Zisis Kyriazis, Panagoula Kollia, Ioanna Grivea, Sotirios Sotiriou, Zoe H Dailiana

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Abstract

Congenital anomalies of the hand are malformations occurring during the development of the human limb, and present as isolated disorders or as a part of a syndrome. During the last years, molecular analysis techniques have offered increasing knowledge about the molecular basis of hand malformations. Disturbances in the signaling pathways during the development of the upper limb result in malformations of the upper extremity. At present, several genes have been identified as responsible for hand anomalies and other have been recognized as suspect genes related to them. Different and new high throughput methods have been introduced for the identification of the gene mutations. In the current editorial, we summarize concisely the current molecular status of isolated hand genetic disorders and the recent progress in molecular genetics, including the genes related to the disorder. This progress improves the knowledge of these disorders and has implications on genetic counselling and prenatal diagnosis.

Key Words: Hand; Gene; Mutation; Molecular; Diagnosis; Disorders

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Core Tip: The genetic basis of hand disorders is elucidated by the expansion of knowledge and introduction of molecular analysis techniques which contribute to the identification of new genes responsible for them. New genes and mutations are being isolated and correlated with the disorder based on the advances in sequencing technology, such as next generation sequencing and genetic consultation, and future therapeutic developments are enhanced. There appears to be a gap in the literature concerning the knowledge about the genetic basis of all hand disorders. The current molecular status of them is discussed and a summary of different genes, already identified or suspected to be related with them, is presented.

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INTRODUCTION

Congenital anomalies of the hand very often have an autosomal dominant pattern of inheritance and most of them have a monogenic genetic basis with variable penetrance[1]. They are related with a disturbance of the normal procedure of the development of the limb, with diverse aetiology and variable clinical features, and their proposed classification system has changed throughout the years, incorporating a rather molecular than anatomic scope of the phenotypes[2]. Initially, the Swanson Classification of congenital anomalies of the hand, including nine categories of malformations, was used by the International Federation of Societies for Surgery of the Hand Committee on Congenital Conditions, as it was considered effective according to the knowledge at the time. Later on, as the awareness of pathogenetic routes and molecular basis of limb formation expanded, the object modeling technique classification was presented, dividing hand anomalies into four groups: Malformations (which include the majority of the disorders), deformations, dysplasias, and syndromes[3].

To date, several loci and disease-causing genes, including all four categories of hand disorders, have been identified in humans, and correlated to specific phenotypes.

Since these phenotype manifestations are indicators that the fetus or the newborn may suffer from a syndrome, the ability to identify the potential syndromes associated with these anomalies, is important for the clinician. Additionally, it is important to distinguish between syndromic and non-syndromic cases for reasons of genetic counselling. Therefore, we present a concise summary of the main genes that are responsible for the disorders, whose etiology is mainly based on known genetic and not external factors, and lead to hand disorder phenotypes when mutated.

POLYDACTYLY

Preaxial/Radial polydactyly

Preaxial polydactyly is a malformation described by an extra digit on the radial side of the hand with an incidence as high as 1 in 3000 births. It follows an autosomal dominant inheritance model with reduced penetrance[4]. Thumb polydactyly has been further subdivided into six subtypes by Wassel according to the level of (metacarpal, proximal, or distal phalange) and the extent of duplication (partial and complete)[5,6]. Next generation sequencing (NGS) analysis in a patient with Wassel III polydactyly identified three gene mutations as follows: (1) Substitution c.1639 G>T in *RPGRIP1* gene; (2) Insertion of adenine in *TMEM216* gene; and (3) A>G nucleotide substitution (c.490) in *FBN1* gene. In a patient with Wassel IV duplication, the following mutations were identified: (1) Adenine duplicated in exon 45 of *CEP290* gene; (2) Two substitutions in *RPGRIP1* gene, c.1639 G>T and c.685 G>A; (3) Adenine insertion in *TMEM216* gene, c.432-11 432-10 insA; (4) Substitution G>C c.8249 in *MEGF8* gene; and (5) Substitution T>A c.548 in *CEP164* gene. These mutations are suspected to be involved in the formation of thumb duplication phenotype[7]. Another suspected way of development of preaxial polydactyly is the overexpression of *HES1* gene. The produced protein is considered to intervene in SHH/GLI signaling axis and results in the manifestation of preaxial polydactyly[8]. The disease gene locus with triphalangeal thumb was identified in chromosome 7q36[9]. Point mutations (105C>G, 305A>T, 323T>C, 404G>A, 295T>C, 4909C>T, 297G>A, 334T>G, 402C>T, and 545G>A) have been identified, and a 739A>G transition near the 5-end of the zone of polarizing activity regulatory sequence (*ZRS*) and a 621C>G mutation in the *ZRS* of the *LMBR1* gene have also been mapped[10,11]. Two more novel mutations (ZRS131A>T and ZRS474C>G) correlated with preaxial polydactyly were identified in a recent study of a Chinese family[12]. No mutations have been identified for index finger polydactyly, which is inherited with an autosomal dominant trait[13].

Postaxial polydactyly

Postaxial polydactyly presents with extra digits on the ulnar side of the hands. Mutations in genes *ZNF141, GLI3, IQCE, GLI1, FAM92A1, KIAA0825*, and *DACH1* have been isolated and their involvement in this manifestation is identified[14].

Responsible gene loci have been mapped to 7pl5-q11.23, 13q21-q32, 19p13.2-p13.1, 7q21-q34, and 13q13.3- 13q21.2 regions using genome-wide scan[15]. Subsequently, two heterozygous mutations, p.A765PfsX14 and p.R539TfsX12 in *GLI3* gene, and P.T474I mutation in the *ZNF141* gene have been identified using exome sequencing[16-18]. Recently, a new suspected mutation in *GLI1* gene (c.1133 C>T) was isolated in an Indian family with the disorder and a mutation in *KIAA0825* gene has been isolated and suspected, although the role of the protein encoded by this gene in limb formation is still unclear[19,20].

Central polydactyly and complex types of polydactyly

Central polydactyly phenotype is characterized by duplication of the 2nd, 3rd, or 4th digit[21]. No disease causing locus or gene responsible for central polydactyly has been identified. Mirror image polydactyly is characterized by mirror-image duplication of fingers and toes[22]. A mutation of the *MIPOL1* gene at 14q13 and two heterozygous deletions including the *PITX1* gene were identified[23].

SPLIT-HAND MALFORMATION

Split-hand malformation may occur as an isolated trait or accompanied with other defects. It manifests as a clinically heterogeneous disorder characterized by absent central digital rays, which result in median clefts of the hand. Responsible mutations map to chromosome 7q21.3-q22.1, chromosome Xq26, and chromosome 10q25[24]. *LBX1, BTRC, POLL, FBXW4*, and *BTRC* gene mutations are reported as responsible for the disease[25]. Recent molecular studies have expanded the list of suspected gene mutations. A *TP63* gene translocation and *FGFR1, BHLHA9, LRP6, UBA2*, and *WNT10B* gene mutations have been recently identified[26-30].

RADIAL RAY DEFECTS

Radial ray defects occur as an isolated malformation or syndromic. They are characterized by partial or complete absence of radial ray structures. Radial defects comprise a large group of diseases. They are associated with *TBX3* gene, coding for a T-box transcriptional factor. *TBX3* is widely expressed in a variety of tissues including forelimbs and hindlimbs, epithelium of the mammary gland, the genital tubercle, and the uterus[31].

DEFECTS IN DORSO-VENTRAL PATTERNING

This disorder category involves nail-patella syndrome, which is autosomal dominant and is expressed with defects affecting the nails, skeleton, kidneys, and eyes. Loss of function mutations in the *LMXlB* gene lead to the syndrome[32,33]. *LMXlB* is involved in determination of dorso-ventral patterning of the limb. A mutation of *WIF1* gene has been isolated as a potential novel cause of the phenotype[34].

BRACHYDACTYLY

Brachydactyly phenotype may present as an isolated defect or in association with other malformations and refers to disproportionately short fingers and toes. Isolated brachydactylies usually occur as autosomal dominant traits and show a high degree of phenotypic variability. A locus on chromosome 5p13.3-p13.2 and the Indian hedgehog gene on chromosome 2q35-36 are involved in Type A1 brachydacty[35]. A mutation in the human bone morphogenetic protein receptor 1B gene (*BMPR1B*) on chromosome 4q can cause Type A2 brachydactyly. Mutations in growth/differentiation factor-5 gene (*GDF5*) alter the receptor binding affinities and can also cause symphalangism. No gene or locus for Type A3 brachydactyly has been identified. Type B Brachydactyly phenotype involves isolated mutations in the receptor kinase-like orphan receptor 2 gene (*ROR2*) on 9q22[36]. Type C Brachydactyly phenotype is considered to be caused by mutations in *GDF5*[37].

SYNDACTYLY

Syndactyly is characterized by the fusion of soft and/or bony tissue of the fingers of the hand and is the most common congenital malformation of the hand in North America and Europe. Syndactyly can occur as an isolated malformation or as part of a syndrome. *HOXD13, FBLN1, GJA1, LMBR1, LRP4, GREM, FGF16,* and *BHLHA9* genes are incriminated for the disorder, when mutated[38]. Syndactyly type I presents as fusion between the middle and ring fingers. It is an autosomal dominant malformation and the most common type of syndactyly. Mutations in human chromosome 2q34-q36 have been isolated. Syndactyly type II is a dominantly inherited malformation. Its phenotype contains soft tissue syndactyly between the middle and ring fingers and sometimes clinodactyly or camptodactyly of the little finger. *HOXDl3* gene mutations are involved in this disorder[39]. Syndactyly type III affects the ring and little fingers with the middle phalanx of the little finger being absent or rudimentary. Mutations in Connexin 43 are involved in this type of syndactyly. Syndactyly type IV manifests as syndactyly of all fingers, and syndactyly type V as metacarpal synostosis. The genetic background of the last two types is not yet investigated[40].

CONCLUSION

Genetic hand disorders and their genetic heterogeneity and allelic heterogeneity between families indicate more complex mechanisms besides simple Mendelian inheritance. These mechanisms include underlying genetic, epigenetic, and environmental factors[41]. With the advent of NGS technology, including exome sequencing and whole-genome sequencing, new mutations causing hand malformations are isolated and the molecular pathogenesis is exposed. Systematic bioinformatics analysis of the responsible genes, using high-throughput sequencing, is a valuable tool in establishing the precise genotype–phenotype correlations of hand genetic disorders. Diagnosis is still largely postbirth, although prenatal diagnosis *via* molecular and genetic methodologies exists. The expansion of our knowledge related to the mutations leading to different phenotypes, with the use of next generation sequencing analysis, will contribute to prenatal diagnosis, prediction of operative treatment strategy, and potential future applications in gene therapy.

FOOTNOTES

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REFERENCES

1 **Talamillo A**, Bastida MF, Fernandez-Teran M, Ros MA. The developing limb and the control of the number of digits. *Clin Genet* 2005; **67**: 143-153 [PMID: 15679824 DOI: 10.1111/j.1399-0004.2005.00404.x]
2 **Kornak U**, Mundlos S. Genetic disorders of the skeleton: a developmental approach. *Am J Hum Genet* 2003; **73**: 447-474 [PMID: 12900795 DOI: 10.1086/377110]

3 **Tonkin MA**, Oberg KC. The OMT Classification of Congenital Anomalies of the Hand and Upper Limb. *Hand Surg* 2015; **20**: 336-342 [PMID: 26387992 DOI: 10.1142/S0218810415400055]

4 **Wessel LE**, Daluiski A, Trehan SK. Polydactyly a review and update of a common congenital hand difference. *Curr Opin Pediatr* 2020; **32**: 120-124 [PMID: 31851054 DOI: 10.1097/MOP.0000000000000871]

5 **Manske MC**, Kennedy CD, Huang JI. Classifications in Brief: The Wassel Classification for Radial Polydactyly. *Clin Orthop Relat Res* 2017; **475**: 1740-1746 [PMID: 27613532 DOI: 10.1007/s11999-016-5068-9]

6 **Nguyen JL**, Ho CA. Congenital Disorders of the Pediatric Thumb. *JBJS Rev* 2022; **10** [PMID: 35230999 DOI: 10.2106/JBJS.RVW.21.00147]

7 **Kyriazis Z**, Kollia P, Grivea I, Varitimidis SE, Constantoulakis P, Dailiana ZH. Thumb duplication: molecular analysis of different clinical types. *Eur J Orthop Surg Traumatol* 2019; **29**: 421-426 [PMID: 30498907 DOI: 10.1007/s00590-018-2343-3]

8 **Sharma D**, Mirando AJ, Leinroth A, Long JT, Karner CM, Hilton MJ. HES1 is a novel downstream modifier of the SHH-GLI3 Axis in the development of preaxial polydactyly. *PLoS Genet* 2021; **17**: e1009982 [PMID: 34928956 DOI: 10.1371/journal.pgen.1009982]

9 **Heutink P**, Zguricas J, van Oosterhout L, Breedveld GJ, Testers L, Sandkuijl LA, Snijders PJ, Weissenbach J, Lindhout D, Hovius SE. The gene for triphalangeal thumb maps to the subtelomeric region of chromosome 7q. *Nat Genet* 1994; **6**: 287-292 [PMID: 8012392 DOI: 10.1038/ng0394-287]

10 **Balci S**, Demirtas M, Civelek B, Piskin M, Sensoz O, Akarsu AN. Phenotypic variability of triphalangeal thumb-polysyndactyly syndrome linked to chromosome 7q36. *Am J Med Genet* 1999; **87**: 399-406 [PMID: 10594878]

11 **Klopocki E**, Ott CE, Benatar N, Ullmann R, Mundlos S, Lehmann K. A microduplication of the long range SHH limb regulator (ZRS) is associated with triphalangeal thumb-polysyndactyly syndrome. *J Med Genet* 2008; **45**: 370-375 [PMID: 18178630 DOI: 10.1136/jmg.2007.055699]

12 **Zeng L**, Jin JY, Luo FM, Sheng Y, Wu PF, Xiang R. ZPA Regulatory Sequence Variants in Chinese Patients With Preaxial Polydactyly: Genetic and Clinical Characteristics. *Front Pediatr* 2022; **10**: 797978 [PMID: 35652055 DOI: 10.3389/fped.2022.797978]

13 **Atasu M**. Hereditary index finger polydactyly: phenotypic, radiological, dermatoglyphic, and genetic findings in a large family. *J Med Genet* 1976; **13**: 469-476 [PMID: 1018306 DOI: 10.1136/jmg.13.6.469]

14 **Ahmad Z**, Liaqat R, Palander O, Bilal M, Zeb S, Ahmad F, Jawad Khan M, Umair M. Genetic overview of postaxial polydactyly: Updated classification. *Clin Genet* 2022 [PMID: 36071556 DOI: 10.1111/cge.14224]

15 **Tsai LP**, Liao HM, Chen YJ, Fang JS, Chen CH. A novel microdeletion at chromosome 2q31.1-31.2 in a three-generation family presenting duplication of great toes with clinodactyly. *Clin Genet* 2009; **75**: 449-456 [PMID: 19459884 DOI: 10.1111/j.1399-0004.2008.01147.x]

16 **Radhakrishna U**, Blouin JL, Mehenni H, Patel UC, Patel MN, Solanki JV, Antonarakis SE. Mapping one form of autosomal dominant postaxial polydactyly type A to chromosome 7p15-q11.23 by linkage analysis. *Am J Hum Genet* 1997; **60**: 597-604 [PMID: 9042919]

17 **Schrauwen I**, Giese AP, Aziz A, Lafont DT, Chakchouk I, Santos-Cortez RLP, Lee K, Acharya A, Khan FS, Ullah A, Nickerson DA, Bamshad MJ, Ali G, Riazuddin S, Ansar M, Ahmad W, Ahmed ZM, Leal SM. FAM92A Underlies Nonsyndromic Postaxial Polydactyly in Humans and an Abnormal Limb and Digit Skeletal Phenotype in Mice. *J Bone Miner Res* 2019; **34**: 375-386 [PMID: 30395363 DOI: 10.1002/jbmr.3594]

18 **Umm-e-Kalsoom**, Basit S, Kamran-ul-Hassan Naqvi S, Ansar M, Ahmad W. Genetic mapping of an autosomal recessive postaxial polydactyly type A to chromosome 13q13.3-q21.2 and screening of the candidate genes. *Hum Genet* 2012; **131**: 415-422 [PMID: 21877132 DOI: 10.1007/s00439-011-1085-7]

19 **Bakar A**, Ullah A, Bibi N, Khan H, Rahman AU, Ahmad W, Khan B. A novel homozygous variant in the GLI1 underlies postaxial polydactyly in a large consanguineous family with intra familial variable phenotypes. *Eur J Med Genet* 2022; **65**: 104599 [PMID: 36067927 DOI: 10.1016/j.ejmg.2022.104599]

20 **Ullah I**, Kakar N, Schrauwen I, Hussain S, Chakchouk I, Liaqat K, Acharya A, Wasif N, Santos-Cortez RLP, Khan S, Aziz A, Lee K, Couthouis J, Horn D, Kragesteen BK, Spielmann M, Thiele H, Nickerson DA, Bamshad MJ, Gitler AD, Ahmad J, Ansar M, Borck G, Ahmad W, Leal SM. Variants in KIAA0825 underlie autosomal recessive postaxial polydactyly. *Hum Genet* 2019; **138**: 593-600 [PMID: 30982135 DOI: 10.1007/s00439-019-02000-0]

21 **Haber LL**, Adams HB, Thompson GH, Duncan LS, Didomenico LA, McCluskey WP. Unique case of polydactyly and a new classification system. *J Pediatr Orthop* 2007; **27**: 326-328 [PMID: 17414019 DOI: 10.1097/bpo.0b013e3180342ff5]

22 **Klopocki E**, Kähler C, Foulds N, Shah H, Joseph B, Vogel H, Lüttgen S, Bald R, Besoke R, Held K, Mundlos S, Kurth I. Deletions in PITX1 cause a spectrum of lower-limb malformations including mirror-image polydactyly. *Eur J Hum Genet* 2012; **20**: 705-708 [PMID: 22258522 DOI: 10.1038/ejhg.2011.264]

23 **Malik S**. Syndactyly: phenotypes, genetics and current classification. *Eur J Hum Genet* 2012; **20**: 817-824 [PMID: 22333904 DOI: 10.1038/ejhg.2012.14]

24 **Li QY**, Newbury-Ecob RA, Terrett JA, Wilson DI, Curtis AR, Yi CH, Gebuhr T, Bullen PJ, Robson SC, Strachan T, Bonnet D, Lyonnet S, Young ID, Raeburn JA, Buckler AJ, Law DJ, Brook JD. Holt-Oram syndrome is caused by mutations in TBX5, a member of the Brachyury (T) gene family. *Nat Genet* 1997; **15**: 21-29 [PMID: 8988164 DOI: 10.1038/ng0197-21]

25 **Qiu L**, Li C, Zheng G, Yang T, Yang F. Microduplication of BTRC detected in a Chinese family with split hand/foot malformation type 3. *Clin Genet* 2022; **102**: 451-456 [PMID: 35908152 DOI: 10.1111/cge.14204]

26 **Peng Y**, Yang S, Xi H, Hu J, Jia Z, Pang J, Liu J, Yu W, Tang C, Wang H. Whole genome sequencing reveals translocation breakpoints disrupting TP63 gene underlying split hand/foot malformation in a Chinese family. *Mol Genet Genomic Med* 2021; **9**: e1604 [PMID: 33471964 DOI: 10.1002/mgg3.1604]

27 **Papasozomenou P**, Papoulidis I, Mikos T, Zafrakas M. Split Hand Foot Malformation Syndrome: A Novel Heterozygous FGFR1 Mutation Detected by Next Generation Sequencing. *Curr Genomics* 2019; **20**: 226-230 [PMID: 31929729 DOI: 10.2174/1389202920666190530092856]

28 **Caylor R**, Fee T, Lay A, Skinner C, Everman D, Blue E, Bamshad M, Schwartz C, Friez M, Stevenson R. eP326: Genome

sequencing reveals BHLHA9 gene duplication as cause of multi-generational split-hand/foot malformation with long bone deficiency. *Genet Med* 2022; **24**: S204 [DOI: 10.1016/j.gim.2022.01.361]

29 **Yamoto K**, Saitsu H, Nishimura G, Kosaki R, Takayama S, Haga N, Tonoki H, Okumura A, Horii E, Okamoto N, Suzumura H, Ikegawa S, Kato F, Fujisawa Y, Nagata E, Takada S, Fukami M, Ogata T. Comprehensive clinical and molecular studies in split-hand/foot malformation: identification of two plausible candidate genes (LRP6 and UBA2). *Eur J Hum Genet* 2019; **27**: 1845-1857 [PMID: 31332306 DOI: 10.1038/s41431-019-0473-7]

30 **Kantaputra PN**, Kapoor S, Verma P, Intachai W, Ketudat Cairns JR. Split hand-foot malformation and a novel WNT10B mutation. *Eur J Med Genet* 2018; **61**: 372-375 [PMID: 29427788 DOI: 10.1016/j.ejmg.2018.02.001]

31 **Davenport TG**, Jerome-Majewska LA, Papaioannou VE. Mammary gland, limb and yolk sac defects in mice lacking Tbx3, the gene mu- tated in human ulnar mammary syndrome. *Development* 2003; **130**: 2263-2273 [PMID: 12668638 DOI: 10.1242/dev.00431]

32 **Dreyer S**, Zhou G, Baldini A, Winterpacht A, Zabel B, Cole W, Johnson R, Lee B. Mutations in LMX1 B cause abnormal skeletal patterning and renal dysplasia in nail patella syndrome. *Nat Genet* 1998; **19**: 47-50 [PMID: 9590287 DOI: 10.1038/ng0598-47]

33 **Lindelöf H**, Horemuzova E, Voss U, Nordgren A, Grigelioniene G, Hammarsjö A. Case Report: Inversion of *LMX1B* - A Novel Cause of Nail-Patella Syndrome in a Swedish Family and a Longtime Follow-Up. *Front Endocrinol (Lausanne)* 2022; **13**: 862908 [PMID: 35769074 DOI: 10.3389/fendo.2022.862908]

34 **Jones MC**, Topol SE, Rueda M, Oliveira G, Phillips T, Spencer EG, Torkamani A. Mutation of WIF1: a potential novel cause of a Nail-Patella-like disorder. *Genet Med* 2017; **19**: 1179-1183 [PMID: 28383544 DOI: 10.1038/gim.2017.20]

35 **Zeng F**, Liu H, Xia X, Shu Y, Cheng W, Xu H, Yin G, Xie Q. Case Report: Brachydactyly Type A1 Induced by a Novel Variant of in-Frame Insertion in the *IHH* Gene. *Front Genet* 2022; **13**: 814786 [PMID: 35669189 DOI: 10.3389/fgene.2022.814786]

36 **Shao J**, Liu Y, Zhao S, Sun W, Zhan J, Cao L. A novel variant in the ROR2 gene underlying brachydactyly type B: a case report. *BMC Pediatr* 2022; **22**: 528 [PMID: 36064339 DOI: 10.1186/s12887-022-03564-z]

37 **Dudley AT**, Ros MA, Tabin CJ. A re-examination of proximodistal pat- terning during vertebrate limb development. *Nature* 2002; **418**: 539-544 [PMID: 12152081 DOI: 10.1038/nature00945]

38 **Cassim A**, Hettiarachchi D, Dissanayake VHW. Genetic determinants of syndactyly: perspectives on pathogenesis and diagnosis. *Orphanet J Rare Dis* 2022; **17**: 198 [PMID: 35549993 DOI: 10.1186/s13023-022-02339-0]

39 **Patel R**, Singh SK, Bhattacharya V, Ali A. Novel HOXD13 variants in syndactyly type 1b and type 1c, and a new spectrum of TP63-related disorders. *J Hum Genet* 2022; **67**: 43-49 [PMID: 34321610 DOI: 10.1038/s10038-021-00963-5]

40 **Bell J**. On brachydactyly and symphalangism. In: Penrose LS, editor. The Treasury of Human Inheritance. Cambridge: Cambridge University Press, 1951: 1-31 [DOI: 10.1007/s12142-000-1047-2]

41 **Bosse K**, Betz RC, Lee YA, Wienker TF, Reis A, Kleen H, Propping P, Cichon S, Nöthen MM. Localization of a gene for syndactyly type 1 to chromosome 2q34-q36. *Am J Hum Genet* 2000; **67**: 492-497 [PMID: 10877983 DOI: 10.1086/303028]

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REVIEW

Changes in trends of orthopedic services due to the COVID-19 pandemic: A review

Eunice Obamiro, Radhika Trivedi, Nasim Ahmed

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Abstract

As of June 10, 2022, the World Health Organization has recorded over 532 million documented coronavirus disease 2019 (COVID-19) [(Coronavirus) SARS-CoV-2] cases and almost 6.3 million deaths worldwide, which has caused strain on medical specialties globally. The aim of this review is to explore the impact that COVID-19 has had on orthopedic practices. Providers observed a rapid decline in the number of orthopedic patients' admissions due to cancellation of elective procedures; however, emergent cases still required treatment. Various observational studies, case reports, and clinical trials were collected through a PubMed database search. Additional sources were found through Google. The search was refined to publications in English and between the years of 2019 and 2021. The keywords used were "COVID-19" and/or "Orthopedic Injuries". Thirty-seven studies were retained. The pandemic brought on significant changes to the mechanism of injury, number of admissions, type of injuries, and patient outcomes. Mortality rates significantly increased particularly amongst patients with hip fractures and COVID-19. Road traffic injuries remained a common cause of injury and domestic injuries became more prevalent with lockdown. Social isolation negatively affected mental health resulting in several orthopedic injuries. Telehealth services and separation for COVID-positive and COVID-negative patients benefited both patients and providers. While hospitals and medical facilities are still facing COVID-19 case surges, it is important to understand how this pandemic has impacted preparation, care, and opportunities for prevention education and ongoing care.

Key Words: Orthopedics; Surgery; Lockdown; Mental health; Telehealth; COVID-19

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Core Tip: Previous and impending surges of coronavirus disease 2019 have caused a disruption in orthopedic specialties in elective procedures and changed the causation and outcomes of emergent cases. The pandemic has also impacted patient care and short-term and long-term outcomes.

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INTRODUCTION

Now entering the third year of the coronavirus disease 2019 (COVID-19) [caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)] pandemic, the number of globally reported cases continues to increase at a rapid rate despite the introduction of authorized vaccines. As of June 10, 2022, there have been almost 532 million cases and over 6.3 million deaths worldwide[1]. Hospitals continue to be overwhelmed with positive cases as new variants emerge. Hospital protocols in patient care have been changing to keep health care workers and patients safe and to keep resources on hand[2]. Non-emergent procedures were delayed in stages to reduce the burden on healthcare services. The long-term effects of these delays have not yet been fully understood as the pandemic continues. These delays occurred across all specialties. In particular, many orthopedic surgeries were postponed, being one of the most common specialties to oversee elective procedures.

The lockdown brought on by the pandemic presented many challenges; routine procedures became more complex, patients were forced to seek medical care later than anticipated due to fear of contracting the disease or an overload in medical care facilities, and unavailability of rehabilitation centers postoperatively due to COVID-19 restrictions. Furthermore, limited mobility in certain age groups may have impacted bone and joint health. The focus of this review is to assess the overall impact that COVID-19 has had on patient care in the orthopedic service and evaluate new management methods for future implementation.

CLINICAL PRESENTATIONS

The PubMed database was searched for relevant studies. The search was refined to publications in English and between the years 2019 and 2021. The keywords used were "COVID-19" and/or "Orthopedic Injuries". Observational studies, clinical trials, and case reports were included in the selection process. Reviews, meta-analyses, and systematic reviews were excluded. Articles that were related to spinal injuries or oncology were also excluded due to the complex nature of these cases. This review was performed in accordance with Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. Additional resources were found using a Google web search (Figure 1). The Baishideng Publishing Group Reference Citation Analysis (RCA) tool was used to create and verify citations according to the journal's guidelines. The RCA tool also provided the Impact Index for articles. A total of 37 articles were identified and selected for the review (Table 1).

Lower extremity fractures

Campbell *et al*[3] utilized a prospective and retrospective study to compare the management of open lower limb fractures (oLLFs) in the pre- and peri-COVID pandemic periods. oLLFs comprised of open fractures of long bones, and hind or mid foot. A 64% reduction in ED attendances pre-COVID (25264) compared to that peri-COVID (9042) and 18% reduction in oLLFs have been observed. Despite a decrease of almost 50% in traffic, road traffic accidents (RTA) were still the most common cause of injury in this COVID period. There was a rise in incidents of oLLFs following a fall from a height, mostly seen in relatively young patients due to an increased incidence of suicide. Despite reassignments of junior surgical staff, some senior level surgical staff remained committed to provide emergency orthopedic surgery care that resulted in timely intervention of open long bone fractures.

Hip fractures & outcomes

Egol *et al*[4] researched the mortality and major complications in hip fracture care during the pandemic across seven musculoskeletal care centers across New York. The study focused on the health care

Table 1 Description of studies collected for the review

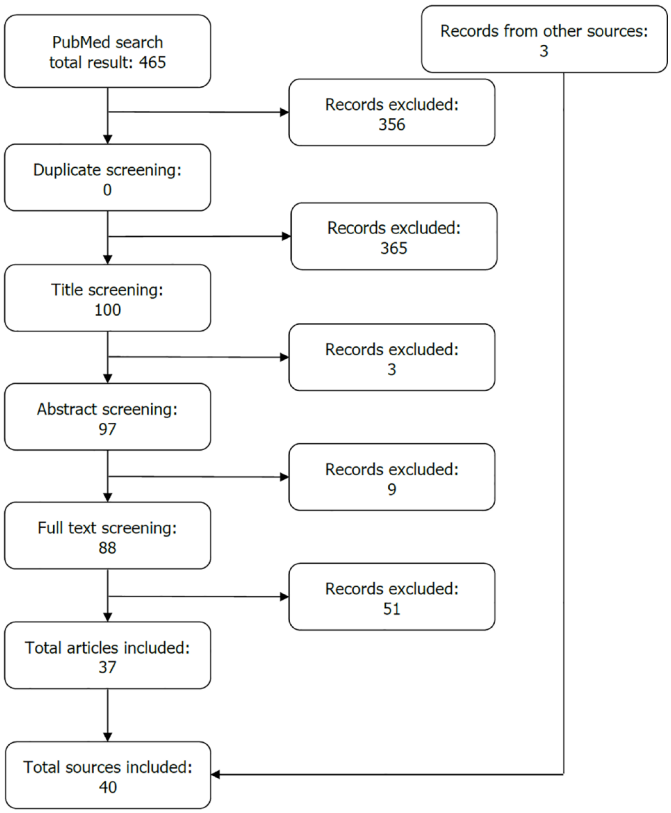
Title	Author	Country	Study during lockdown?	Extremity injured	Patient outcomes	Article impact index
Lower extremity fractures						
The COVID-19 Pandemic: The effect on open lower limb fractures in a London major trauma centre - a plastic surgery perspective	Campbell *et al*[3]	England	Yes	Lower extremity fractures	Despite a 64% reduction in ER attendance and 50% decrease in traffic, RTA were the most common mechanism of injury and oLLFs were reduced from 22 to 18; there was a rise in oLLFs in those with mental health diagnoses	1
Increased Mortality and Major Complications in Hip Fracture Care During the COVID-19 Pandemic: A New York City Perspective	Egol *et al*[4]	United States	Yes	Hip fractures	Rates of mortality in hip fracture patients in COVID-positive, suspected COVID, and COVID-negative groups were 35.3%, 7.1%, and 0.9%, respectively	28
Hip fracture care and mortality among patients treated in dedicated COVID-19 and non-COVID-19 circuits	Ojeda-Thies *et al*[5]	Spain	Yes	Hip fractures	COVID-negative patients were able to receive timely and adequate care; COVID-positive patients also received adequate care but there were delays in surgeries; separating COVID-positive and negative patients helped efficiently treat patients	1
Effect of Covid-19 on best practice care of hip fracture patients: An analysis from the National Hip Fracture Database (NHFD)	Tyas *et al*[6]	UK	Yes	Hip fractures	COVID-19 led to a significant reduction in best practice tariff with decreases in timely surgery, postoperative delirium, 20-d mortality, length of stay, and timely orthogeriatric review	0
Rehabilitation guidance for hip fracture patients during the COVID-19 pandemic using chat software: A new model	Gao *et al*[7]	China	Yes	Hip fractures	Complications and mortality were higher in the group that did not use WeChat; complications included UTIs, deep vein thrombosis, dislocation, and infections	1
Hip Fracture Outcomes During the COVID-19 Pandemic: Early Results From New York	Lebrun *et al*[8]	United States	Yes	Hip fractures	Mortality was 56% amongst COVID-19 patients and were at higher risk for pneumonia and hyperinflammation	19
IMPACT-Scot report on COVID-19 and hip fractures	Hall *et al*[9]	Scotland	Yes	Hip fractures	Low platelet count was an indicator for an increased risk of COVID-19 infection and COVID-19 was related with an increased risk of 30-d mortality	27.5
Hip fracture care during Covid-19: a regional trauma centre's experience	Crozier-Shaw *et al*[10]	Ireland	Yes	Hip fractures	Though there was a 20% reduction in hip fractures, the 30-d mortality rate increased from 2.2% to 8.3% and having COVID-19 also increased mortality rates	2
Clinical Characteristics and Perioperative Complication Profiles of COVID-19-Positive Patients Undergoing Hip Fracture Surgery	Galivanche *et al*[11]	United States	Yes	Hip fractures	COVID-positive patients presented with more comorbidities which resulted in a higher incidence of adverse events perioperatively	0
Treatment of Proximal Femoral Fragility Fractures in Patients with COVID-19 During the SARS-CoV-2 Outbreak in Northern Italy	Catellani *et al*[12]	Italy	Yes	Femur fractures	Surgery is required for positive outcomes, but respiratory stabilization is crucial to ensure survival, comfort, and stability	30
Influence of coronavirus disease 2019 pandemic state of emergency in orthopaedic fracture surgical treatment	Mitkovic *et al*[13]	Serbia	Yes	All	Overall number of fractures decreased, female patients were observed more for femoral neck fractures	2.5
The effect of COVID-19 pandemic on the care of fragility hip fracture patients in the United Kingdom	Orfanos *et al*[14]	United Kingdom	Yes	Hip fractures	Early intervention resulted in better outcomes, higher mortality rates amongst COVID-positive patients	0
How SARS-CoV-2 Pandemic Changed Traumatology and Hospital Setting: An Analysis of 498 Fractured Patients	Brayda-Bruno *et al*[15]	Italy	Yes	All	More femoral fractures during COVID era, average injury age increased to 69, separating COVID-negative and positive patients allowed patients to remain negative, faster diagnoses to discharge times	0
Do standards of care and early outcomes of periprosthetic fractures change during the	Zagra *et al*[16]	Italy	Yes	All	Delays in surgery, hip fractures were associated with higher mortality rates, 60% of orthopedic patients were at risk of developing	0

COVID-19 pandemic? A multicentre study					perioperative complications	
Perioperative management of patients with hip fractures and COVID-19: A single institution's early experiences	Muse *et al* [17]	United States	Yes	Femur fractures	Early intervention improved patient outcomes in COVID-positive patients; spinal anesthesia was used to prevent viral aerosolization; treatment plans should be altered based on severity of infection	1.5
Foot and ankle trauma management during the COVID-19 pandemic: Experiences from a major trauma unit	Shah *et al* [18]	England	Yes	Foot and ankle fractures	Telemedicine aided in reducing patient-provider contact and eased the burden of follow-up	1
Effect of the COVID-19 pandemic on foot surgeries	Kuliński *et al*[19]	Poland	Yes	Foot fractures	Total orthopedic surgeries declined by 55% and elective surgeries were not eliminated. The length of stay was decreased by 2.5 d for adults and 1.7 d for children	0
Outcomes of orthopaedic trauma surgery in COVID-19 positive patients	Al-Humadi *et al*[20]	United States	Yes	Lower Extremity	Operations in COVID-positive patients were accomplished with anticoagulation and hematologic and pulmonary management; complications and mortality still occurred	0
Upper extremity fractures						
Patient care modifications and hospital regulations during the COVID-19 crisis created inequality and functional hazard for patients with orthopaedic trauma	Dunkerley *et al*[21]	United Kingdom	Yes	Upper extremity fractures	The increase in use of telemedicine services resulted in 12% of patients discharged with potentially unstable fractures with a danger of mal-union	1.5
A Call to Arms: Emergency Hand and Upper-Extremity Operations During the COVID-19 Pandemic	Diamond *et al*[22]	United States	Yes	Hand and upper extremity	A 40% increase in volume injuries attributed to high risk behaviors such as lawlessness, assault, and high-speed auto accidents; lack of social and physical impacted and aggravated injuries	2
Upper extremity emergencies during SARS-COV-2 pandemic: Turnout trends	Fyllos *et al* [23]	Greece	Yes	Upper extremity fractures	The mechanisms for which emergency upper extremity and hand and wrist injuries occurred were mostly from domestic accidents such as new hobbies	0
The impact of COVID-19 on shoulder and elbow trauma in a skeletally immature population: an Italian survey	Gumina *et al* [24]	Italy	Yes	Shoulder and elbow	Pediatric cases decreased by 84.6%, shoulder and elbow traumas were caused by domestic accidents	1.5
Other fractures						
Outcomes of Orthopaedic Trauma Services at a UK Major Trauma Centre During a National Lockdown and Pandemic: The Need for Continuing the Provision of Services	Donovan *et al*[25]	United Kingdom	Yes	All	Theater time increased by 14 min due to new PPE requirements. Complication and mortality rates remained unchanged and there was not a higher risk of transmitting COVID-19 in the hospital	0.5
Proximal femur fractures in COVID-19 emergency: the experience of two Orthopedics and Traumatology Departments in the first eight weeks of the Italian epidemic	Maniscalco *et al*[26]	Italy	Yes	Femur fractures	There was a decrease of emergency ortho cases by 26.8%; femur fractures decreased, and other fracture types increased; school traumas were 0%, sports injuries decreased by 75.3%, work injuries decreased by 42.2%	0
Evaluation of containment measures' effect on orthopaedic trauma surgery during the COVID-19 pandemic: a retrospective comparison between 2019 and 2020	Druel *et al* [27]	France	Yes	Upper extremity, lower extremity, hand fractures	Work-related accidents, RTAs, and altercations decreased, but domestic accidents increased. Rates of infection decreased; overall there was a 28.7% decrease in trauma surgery patients	3
Impact of the COVID-19 pandemic on the trauma and orthopaedic department at level one Major Trauma Centre in the republic of Ireland	Elbardesy *et al*[28]	Ireland	Yes	All	Adult distal radius fractures increased by 88% and pediatric elbow fractures decreased by 13%. Fractures were mostly caused by independent outdoor activities	0
The impact of COVID-19 on orthopaedic trauma: A retrospective comparative study from a single university hospital in Italy	Andreozzi *et al*[29]	Italy	Yes	All	Average age of patients increased, 67% of injuries occurred in the home, and the most commonly injured body part was the hand	0

Effects of COVID-19 pandemic curfew on orthopedic trauma in a tertiary care hospital in Turkey	Kalem *et al* [30]	Turkey	Yes	All	Center saw a 65% decrease in upper extremity injuries. Overall human movement has decreased by about 40% which is correlated to the decrease in admissions	0
Elective surgeries						
COVID-19 consent and return to elective orthopaedic surgery: allowing a true patient choice?	Clough *et al* [31]	England	Yes	All	Rates of COVID-19 were lower at elective surgery compared to trauma sites	1
Practice patterns						
The Effect of COVID-19 on Orthopedic Practices and Surgeons in Louisiana	Kale *et al* [32]	United States	No	All	COVID-19 restructuring led to delays in care, injuries not properly healed, and increase in pain.	2
A clinical pathway for pre-operative screening of COVID-19 and its influence on clinical outcome in patients with traumatic fractures	Meng *et al* [33]	China	Yes	All	Average wait time to surgery increased by 4.1 d, resulting in complications such as pneumonia, fever, venous thromboembolism, and cardiovascular complications	7.5
Lessons Learnt from Managing Orthopaedic Trauma During the First Wave of the COVID-19 Pandemic at a UK District General Hospital	Patel *et al* [34]	United Kingdom	Yes	All	Delays to surgery were doubled and postoperative complications were more present but were not directly associated with COVID-19 status	1
Effect of COVID-19 on surgical management of open fractures and infection rates: A tertiary care experience in Indian set-up	Gupta *et al* [35]	India	Yes	All- open fractures	Even though this center saw a decrease of cases, there was a delay of patient presentation to the ER, delay in administering antibiotics, and an increase of emergency temporary fixations, infection rates, and readmissions	0.5
Pooling of neglected and delayed trauma patients - Consequences of 'lockdown' and 'Unlock' phases of COVID-19 pandemic- A retrospective cohort analysis from a tertiary centre	Saini *et al* [36]	India	Yes	Upper and lower extremity fractures	Complications (blood loss, requirement for bone grafts) rates increased, delays to surgery significantly increased from an average of 8.23 d to 21.38 d	0
Miscellaneous						
Mortality risk of surgically managing orthopaedic trauma during the COVID-19 pandemic	Balakumar *et al*[37]	United Kingdom	Yes	Femur fractures	The risk of contracting COVID-19 perioperatively was 11%, separating COVID-negative and -positive patients did not improve patient outcomes	0
Effect of COVID-19 on Ulnar Collateral Ligament Reconstruction in Major League Baseball Pitchers	Paul *et al* [38]	United States	No	Ulnar Collateral Ligament	Decreased movement had an impact on ulnar collateral ligament reconstruction rates when sporting practices resumed	0
The patterns and management of fracture patients under COVID-19 outbreak in China	Yu *et al*[39]	China	Yes	Upper and lower extremity fractures	Delays in surgery, decrease in total number of patients but increase in forearm, thigh, hand, and foot fractures. Hip fractures most prevalent	2

system's response to the essential care of its hip fracture patients and its effects on patient outcomes. This prospective study was employed from February 1, 2020 through April 15, 2020, to compare 138 recent and 115 pre-COVID hip fracture patients. Patients with recent hip fractures were grouped into three classes: COVID-positive, suspected COVID, and COVID-negative groups. The COVID-negative patients underwent surgery immediately whereas COVID-positive patients' surgery was delayed. The approach to surgery for hip fractures was the same regardless of COVID status. The majority of patients received general anesthesia and a proportion of patients underwent spinal anesthesia. As expected, higher mortality was found in COVID-positive patients compared to suspected or COVID-negative patients: 35.3%, 7.1%, and 0.9% respectively.

Ojeda-Thies *et al*[5] retrospectively studied patients treated for hip fractures during the COVID-19 pandemic from March 1, 2020 through May 1, 2020. This center divided 64 patients into three cohorts: pre-cohort of 17 patients, 14 COVID-positive patients, and 33 COVID-negative patients. More than 90% of patients received spinal anesthesia. There was a higher incidence of COVID positivity (23.5%) rate after the patients were discharged from the hospital following hip surgery and 50% of those patients died. That resulted in separating the anesthesia circuit for COVID-positive and COVID-negative patients. The study revealed that separate circuits for COVID-19 and non-COVID-19 patients allows adequate hip fracture care, despite delayed surgery in patients with severe respiratory illness from COVID. Separating patients that were not infected from those that were, helped with the efficiency of



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Figure 1 PRISMA Diagram for Literature Screening using the keywords "COVID-19" and/or "Orthopedic Injuries". Observational studies, clinical trials, and case reports were included in the selection process. Reviews, meta-analyses, and systematic reviews were excluded. Articles that were related to spinal injuries or oncology were also excluded. This review was performed in accordance with Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. Additional resources were found using a Google web search.

treating fractures amongst COVID-negative patients and significantly reduced the 30-day mortality and the conversion rates.

Tyas *et al*[6] studied the effect of COVID-19 on Best Practice Tariff for hip fractures in 40000 patients collected from the National Hip Fracture Database (NHFD) from England, Wales, and Northern Ireland. Best Practice Tariff was used to optimize care for patients, incentivize providers, and yield better outcome. Quality metrics such as timely surgery, postoperative delirium, 30-d mortality, hospital length of stay, and timely orthogeriatric review were assessed. Researchers concluded that COVID-19 led to a significant reduction in best practice tariff. Prompt geriatric review dropped over the review period. Significant changes in bone health assessments, reduction in falls assessments, and postoperative delirium were also observed. Mortality rates peaked at 13.7%. Therefore, it is important to maintain the quality care and assessment of geriatric hip fractures and management in next pandemic.

Gao *et al*[7] piloted a study at a hospital in China for tracking hip fracture patients postoperatively and providing rehabilitation guidance using a chat software called WeChat. The study selected 80 patients and divided them into two equal groups of observation and control. The control group was given traditional discharge instructions and the observation group received additional instructions that provided continuous instruction of physical therapy exercises through WeChat apps. This study was done at the peak season of COVID-19 between February 1, 2020 and April 30, 2020. Complications and mortality were significantly higher in the control group. Complications observed include urinary tract infections, deep vein thrombosis, dislocation or fracture around prosthesis, surgical site infection, and pneumonia. It was recommended that during the COVID-19 pandemic, it was helpful to use WeChat or another similar chat software to guide the rehabilitation of hip fractures to minimize postoperative complications.

LeBrun *et al*[8] studied 59 hip fracture patients in New York City over a 5-wk period, from March 20, 2020 to April 25, 2020 during the COVID-19 pandemic. Centralized care was established for emergency hip fracture management. Patients were separated into COVID-positive and COVID-negative groups based on infection status. The study showed that hospital mortality was significantly increased in the COVID-positive patients (56%) compared to COVID-negative patients (4%). All deaths in COVID-positive patients were related to COVID-19. COVID-positive patients were also at higher risk for complications such as pneumonia or hyperinflammation.

Hall *et al*[9] assessed the effects of COVID-19 on 30-d mortality for 317 patients with hip fractures in a multicenter retrospective study. The effects of social lockdown on the epidemiology of hip fractures were also assessed. Results showed that COVID-19 was independently related with an increased risk of 30-d mortality in hip fracture patients.

Crozier-Shaw *et al*[10] studied hip fracture care pre-COVID (45 hip fractures) and peri-COVID (36 hip fractures). A 20% reduction in hip fracture presentation was noted; however, the 30-day mortality was increased from 2.2% to 8.3%. Despite improved quality indicators that were observed in hip fracture management during the COVID-19 period, there was a 3-fold increase in mortality. Although four patients tested positive on swab test for COVID-19, two of them died. Therefore, COVID-19 was associated with increased mortality in hip fracture patients that were positive and undergoing surgery. Researchers found that these findings will be important to apply to orthogeriatric care during future COVID-19 waves.

Galivanche *et al*[11] collected 42002 patients through claims data that had undergone hip fracture surgical repair between April and December 2020. Of these, 678 were COVID-positive and while there were no significant differences in age, sex, or procedure type between the patients who were tested positive or negative for COVID-19, COVID-positive patients did present with a higher incidence of comorbidities. Propensity score matching was used to balance the two groups (COVID-positive *vs* COVID-negative). After matching, the COVID-19-positive group had a higher incidence of adverse events perioperatively such as venous thromboembolism (6.64% compared to 3.43%) and pneumonia (11.21% compared to 4.56%).

Catellani *et al*[12] studied 16 patients with femoral neck fractures that were COVID-positive with active infection and were receiving protocolized treatment for COVID-19 during the pandemic in northern Italy. Three patients died before surgery because of complications from COVID-19. After surgery, four patients died of respiratory failure. The overall mortality of hip fracture with active COVID-19 infection was 43.7%. Surgical mortality of hip fracture in patients with active COVID-19 infection was 30.77%. Patients who underwent surgery in the face of active infection had to pass strict criteria. Most patients received spinal anesthesia. A stabilization of respiratory parameters was observed in COVID-positive patients after the surgery. It was suggested that surgery may have contributed to the overall respiratory stability of patients, mobilization, comfort, and improvement in physiological ventilation in COVID-19-positive patients with proximal femoral fragility fractures.

Mitkovic *et al*[13] investigated the frequency and distribution of orthopedic fractures during the stay-at-home lockdown in Serbia. Researchers examined how the lockdown influenced the frequency of different fracture types. Staying at home for 54 d decreased the total number of fractures by 18.9% and females were more likely to suffer from femoral neck fractures during this time. However, femoral neck fractures occurred more frequently in the state of lockdown than during the same period in a non-emergency state in 2019. Mitkovic type method of external fixation was assumed to be an alternative method of tibial fracture fixation during the lockdown. That methodology presumed to be a reducing factor of intraoperative COVID-19 transmission among medical staff and hospitalization time.

Orfanos *et al*[14] performed a retrospective study on geriatric patients aged 60 years and above who sustained hip fracture after a fall in the United Kingdom. Of the 199 patients, 102 were included from the COVID-19 pandemic period and was compared to 97 patients from the same period in 2019. Approximately 11% of patients tested positive for COVID during the observation period. A higher proportion of female patients suffered hip fracture from a fall. However, mortality was found to be higher amongst males between the two groups (P = 0.005). There was no significant difference between the groups regarding 30-d all-cause mortality and morbidity. Early surgical intervention along with sufficient optimization prior to surgery in a COVID-positive patient was critical for his/her survival. Patients were also moved rapidly to rehabilitation facilities which aided in recovery.

Brayda-Bruno *et al*[15] studied 498 fracture patients in Italy during the COVID-19 pandemic to assess how the pandemic has changed traumatology and the hospital setting. It was assessed that unspecified femoral fractures were much more common in this time period than the previous time period (181/352 compared to 57/146). The average age of orthopedic patients prior to the pandemic was 61 years of age compared to during the pandemic which was 69 years of age. This institution required COVID-19 testing which expedited orthopedic services by separating COVID-negative and -positive patients. Patients that were admitted as COVID-negative remained COVID-negative during admission. Ten patients died in the pandemic group compared to zero deaths in the control group. Out of these ten patients, three died due to comorbidities and seven due to thromboembolic events related to COVID-19. Time between diagnoses and discharge was significantly lower (P = 0.03) despite an increase in orthopedic cases. The difference was attributed to early operative intervention in the pandemic group.

Zagra *et al*[16] conducted a retrospective multicenter study in patients with periprosthetic fractures (PPF) during COVID-19 pandemic in northern Italy. Out of 1390 patients, 38 were found to suffer from PPF. Most of the patients had femoral PPF. There was no difference in the incidence of PPF during the pandemic when compared with the earlier year prior to the pandemic. Routine screening for COVID-19 was performed and found around 10% or more with COVID-19 positivity because of positive test or the positive symptoms and imaging findings. Standard operative care was performed in PPF patients during the pandemic. Hip fracture was associated with increased 30-d mortality in COVID-positive patients compared to COVID-negative patients. Approximately 60% of PPF patients developed complic-

ations.

In a letter to the editor, Muse *et al*[17] used a retrospective case series of five COVID-19 orthopedic patients who sustained hip fractures, one femoral neck fracture and four intertrochanteric fracture, that underwent surgery at Montefiore Medical Center, New York. As per recommendation, hip fracture should be repaired within 48 h of admission to reduce mortality and morbidity, but only three out of the five patients underwent surgery within the 48 h timeframe and two had surgeries after 72 h of admission. While regional anesthesia is safe for COVID-positive patients, spinal anesthesia was used to prevent viral aerosolization in four patients. Only one patient received general anesthesia. None of the patients died. The most common complication was the need for packed red blood cell transfusion. Providers suggested that surgical treatment plans can be delayed if necessary.

Foot and ankle fractures

Shah *et al*[18] evaluated the impact of the pandemic on foot and ankle services in a single trauma center in the UK using a retrospective cohort study. A total of 206 patients were evaluated from admission to discharge to compare pre-lockdown and lockdown phases and stable and unstable fractures. Of 100 patients with stable ankle fractures, 35 (35%) were discharged from the emergency department without a planned follow-up. The majority of patients who presented unstable fractures required some form of interventions. Some of the patients were sent home with cast, advised elevation, non-weight bearing, and to follow up for definite treatment. In another group, partial fixations were employed to reduce intraoperative time and avert the need for invasive surgeries. Most of the operated patients were followed up within 2 wk for a wound check. Patients were advised on pain and plaster management to avoid face-to-face interactions with providers. Telemedicine reduced the patient-physician contact and reduced the burden of follow-up.

Kuliński *et al*[19] researched the effect of the COVID-19 pandemic on both elective and emergency foot surgeries on 145 orthopedic patients in Poland. The data showed a reduction in the total number of orthopedic admissions by 55% during the pandemic. Elective orthopedic interventions declined by 72% and emergency orthopedic interventions increased by 27% during the pandemic as compared to pre-pandemic era. Length of hospital stay decreased by 2.5 d in adults and 1.7 d in children. There was a decline of 32% in the number of patients coming to ED for injuries. The pandemic did not affect the average age of patients and the male to female ratio. It is suggested that the COVID-19 pandemic has affected the epidemiology and prevalence of foot surgeries in children and adults.

Al-Humadi *et al*[20] conducted a retrospective case series of 11 patients to investigate outcomes of lower extremity trauma surgery in COVID-19-positive patients. Most of the patients had hip fractures and the rest sustained femur and tibia and fibular fractures. Orthopedic operations in COVID-19-positive patients were successfully done with patient anticoagulation and hematologic and pulmonary management. These three were optimized prior to surgery to reduce venous thromboembolic events and avoid blood transfusion. Complications such as deep vein thrombosis, acute renal failure, and pneumonia still occurred and two patients died postoperatively. The patients who died were more than 50 years old and had a prior history of more than one comorbid condition.

Upper extremity fractures

Dunkerley *et al*[21] noted that the pandemic has decreased operative intervention of unspecified upper extremity fractures and increased the use of telemedicine clinics. In this prospective study which was performed at the peak of the COVID-19 outbreak from April 14 through April 28, 2020, of the 154 patients that were analyzed, 51% were managed as in a normal circumstance, whereas 49% of managements were impacted by the pandemic. Of those affected, 12% were discharged at diagnosis with potentially unstable upper extremities fractures, and this had the danger of mal-union. Additionally, 29% were discharged from the orthopedic virtual clinic as opposed to having in person clinical or radiological follow-up. Nurses in the trauma team would virtually request patient care instructions from physicians working remotely. Discharged patients were fixated with removable immobilization. Follow-up surveys given to patients who were treated by the virtual clinic showed a very high satisfaction rate of 4.8/5. While telemedicine played a vital role in orthopedic management and is economical and efficient to both patients and providers, there is a potential risk of poor outcomes such as mal-union, requiring corrective treatments in the future.

Diamond *et al*[22] conducted a multi-center study from two Level I trauma centers in Pennsylvania and California. Researchers studied the occurrence of emergency upper extremity operations during the COVID-19 pandemic specifically during shelter-on-place orders. Injuries included trauma to the forearm, hand, wrist, and finger. It was found that there was a 40% increase in volume attributed to high-risk behavior which was defined as lawlessness, assault, and high-speed auto accidents. Additionally, it was found that home improvement projects, lack of social and physical resources, and delay of treatment due to avoidance of treatment facilities are also impacting the high volume of upper extremity injuries.

Fyllos *et al*[23] compared the turnout of patients with orthopedic, upper extremity, and hand and wrist emergencies during pre-pandemic and peri-pandemic periods. During the pandemic, it was found that the numbers of patients with orthopedic, upper extremity, and hand and wrist problems (*e.g.*, arthritis and tendinopathy) were significantly reduced by 57.09%, 49.77%, and 49.95%, respectively,

compared to a patient population in 2019. However, upper extremity injury emergencies (*e.g.*, fractures and dislocations) increased from 37.17% to 43.32% and hand and wrist injury emergencies increased from 25.07% to 29.15%. Although other causes of injury have decreased, it is suggested that the increase of domestic accidents from new hobbies during the lockdown have been the probable cause of the surge.

Gumina *et al*[24] evaluated 404 patients under the age of 18 that were treated at the trauma center for shoulder and elbow injuries before and during the pandemic (from March 8, 2020 through April 8, 2020). Young people typically incur high-energy injuries from social activities, school activities, sports, parks, and clubs. Due to the prohibition of these events, injuries caused by these activities were almost eliminated. There were no cases of contusions, physeal fractures, other fractures, or dislocations of the elbow. The shoulder and elbow injuries seen at this center were mainly caused by falls in the home, offering an opportunity for education.

Other injuries

Donovan *et al*[25] performed a retrospective case-controlled study at a Level 1 trauma center in the UK. Factors such as anatomical area of injury, cause of injury, operative procedure, type of anesthesia, total operating time, complications, and 30-d mortality were analyzed against a dataset of 248 patients. The 248-patient dataset was comprised of 142 patients that required 165 operations pre-pandemic and 106 peri-pandemic patients that underwent 124 operations. During the COVID period, the results showed a 30% decrease in overall orthopedic injuries due to a reduced number of road traffic accidents and sporting injuries. Also, the number of hip fractures and low impact injuries remained the same. Operative time increased by 14 min due to the new personal protective equipment (PPE) requirements. During the COVID-19 pandemic, a higher number of patients received spinal anesthesia and fewer patients received general anesthesia. Complications and mortality rates did not change. The incidence of COVID-19 in the patients tested in the hospital and in the general population at the time of the study was the same at 8.5%.

Maniscalco *et al*[26] conducted a study on the impact of COVID-19 on orthopedic traumas presenting to the emergency orthopedic departments in Parma and Piacenza Hospital, Italy, evaluating patients admitted with proximal femur fractures. The study collected data for patients between February 22, 2020 and April 18, 2020 and was compared with 2019 data. The results showed a decrease in orthopedic cases at the ER by 26.8%. Regular mechanisms of injury vastly changed, where there was a 19.1% increase of the traumas occurring in the home, sports injuries decreased by 75.3%, work injuries decreased by 42.2%, and school traumas were reduced to 0%. A decrease in femur fractures from 38.9% to 33.5% was also observed during the pandemic. A higher mortality was reported during the pandemic in elderly patients with femur fracture due to COVID-19.

Druel *et al*[27] studied the effects of COVID-19 containment measures on 888 orthopedic trauma surgeries during the pandemic at a trauma center in France. Participants were divided into three cohorts: Reference, pre-containment, and containment groups. The occurrence of domestic accidents increased from 51.6% to 64.8% whereas work-related accidents, altercations, and RTA decreased. The decrease in the number of cases (from 6.7% to 4.0%) could be due to fear of going to medical facilities, fear of containment rules, or minimizing the seriousness of symptoms. Overall, the results showed a decrease of 28.7% in the number of patients undergoing trauma surgery services during the containment period.

Elbardesy *et al*[28] investigated the impact of COVID-19 pandemic on trauma and orthopedic center in Ireland among 505 patients. The study was conducted between March 1, 2020 and April 14, 2020 and compared patients from 2019 in the same time period. The total number of trauma and orthopedic surgeries performed decreased by 10.5%. Likewise, the number of pediatric orthopedic procedures decreased by 40.32%. Adult distal radius and pediatric elbow fractures increased by 88% and 13%, respectively, while hip fractures remained the most common trauma. Overall, the COVID-19 pandemic led to a decrease in the total number of trauma surgeries. Notably, injuries directly related to solo outdoor activities such as ankle, radius, elbow, and hand fractures increased.

Andreozzi *et al*[29] performed a retrospective comparative study of the impact of COVID-19 on orthopedic trauma in Italy. They analyzed the impact of the lockdown on acute orthopedic trauma. The overall number of admissions in the pre-COVID era was 995 as compared to 204 during COVID-19 outbreak. Average age of patients (51.9 years old) was significantly higher during the pandemic as compared to pre-pandemic (41.4 years old). Most injuries (65.7%) occurred at home during the pandemic as compared to 32.3% pre-pandemic. The most injured extremity during the pandemic was the hand (14.2%) compared to before the pandemic which was polytrauma (22.8%). While overall rates of acute traumas have decreased, the incidence of hip fractures remained high, indicating a need for focus on orthogeriatric care.

Kalem *et al*[30] studied the effect of COVID-19 pandemic on the prevalence and epidemiology in 361 orthopedic trauma patients in Turkey. The study examined the fractures distribution in three age categories (≤ 20 years, 21-64 years, and ≥ 65 years). The overall number of admissions decreased by 50.9% and upper extremity injuries decreased by 65%. The type of trauma and the mechanism of injury changed with a significant increase in low energy trauma and the upper extremities more affected during the pandemic (49.9% *vs* 30.5% peri-pandemic and pre-pandemic, respectively). However, there

was no difference in occurrence of fractures in geriatric patients. It is suggested that the decrease in admissions was parallel with a 40% decrease in overall human movement.

Elective surgeries

Clough *et al*[31] examined the risk of contracting COVID-19 in patients undergoing orthopedic surgery. The data was collected for March 2020 to June 2020. The 225 orthopedic trauma surgery patients were separated into three surgery sites to minimize the perioperative spread of COVID infection. At the acute site that had both COVID-positive and COVID-negative patients undergoing surgery for upper and lower limb fractures, the incidence of post-surgical COVID infection was 6.5% with a 50% mortality rate. Seven (8.3%) of the 84 patients who underwent surgeries for femoral neck fractures became positive, of whom five (71%) died. On the other hand, of the patients who had surgeries in the hospital that only performed elective cases, only 0.9% patients developed COVID-19 without any mortality.

Practice pattern

Kale *et al*[32] analyzed the effects of COVID-19 on orthopedic practices. A survey study was conducted with orthopedic surgeons by Louisiana Orthopaedic Association (LOA) at the peak of the pandemic. The response rate of the survey was 33%. The survey found that most surgeons delayed their elective surgeries. The decrease of patients in offices resulted in substantial loss of revenue. Furthermore, there was an increase in pain and deformities in patients due to the delay in elective procedures. Researchers found that many surgeons increased their revenue with the use of telehealth. This adaptation opens a new era of medicine.

Meng *et al*[33] performed a case series study at Beijing Chaoyang Hospital. Researchers aimed to analyze clinical outcomes of patients that were required to undergo orthopedic surgery. Fracture types included clavicle, scapular, vertebral compression, and upper and lower extremity fractures. Results showed an increase in average wait time from injury to surgery of 8.7 ± 3.4 d in March and April 2020 from 4.6 ± 2.6 d in the same period in 2019, almost doubling waiting time for surgeries in the pandemic. A higher percentage of patients in the pandemic developed complications such as pneumonia, fever, venous thromboembolism, and cardiovascular complications. This led to introduction of a novel clinical pathway for preoperative screening of COVID-19 in traumatic orthopedic patients, thereby reducing waiting time from injury to surgery.

Patel *et al*[34] conducted a retrospective study on orthopedic patients in the UK during in the pre-COVID-19 (328 patients) and peri-COVID-19 (178 patients) eras. The sample included patients with periprosthetic, pelvis, spine, upper and lower extremity, or multiple fractures. There was a reduction in orthopedic patients during the peri-COVID period and restructuring of orthopedic services in response to the COVID-19 pandemic was associated with a delay in surgery (4.91 d compared to 2.94 d) and increase in severity of postoperative complications such as nausea, vomiting, and superficial phlebitis. Complications, however, were not associated with COVID-19 status. Fast-track emergency operative orthopedic services during the pandemic were recommended.

Gupta *et al*[35] performed a retrospective study to compare the surgical management of upper and lower extremity open fractures during the pre-COVID (89 patients) and peri-COVID (52 patients) eras. The results showed that despite the decrease in total trauma cases, there were delays in presentation to the ED. Due to this interruption, there was a delay in administration of first dose of antibiotics; however, there was no significant delay in presentation to surgery. There was a trend of higher infection rate perhaps due to delay in antibiotics administration.

Saini *et al*[36] performed a retrospective study on 488 upper and lower limb fracture patients in India to explore the consequences of neglected and delayed care during and after the lockdown. It was discovered that the average delay in surgical time and hospital stay was significantly increased during each period. During lockdown, the average delay was 8.23 ± 6.1 d and after lockdown the average delay was 21.38 ± 26.14 d. Complications such as blood loss, stay in the ICU, surgical time, and requirement for bone grafts were greatly increased after the lockdown period was over though not statistically significant. Out of 45 patients who developed non-union or malunion, 42 required corrective procedures.

Miscellaneous

Balakumar *et al*[37] researched the risk of operating on a variety of urgent orthopedic cases during the COVID-19 pandemic first lockdown, between March 26, 2020 and May 20, 2020, for clinical decision making and efficiency of medical resource utilization. Researchers included 433 patients in the study. The average age of the patients was 65 years and the majority were involved in low energy mechanism, with femoral neck fracture being the dominant orthopedic injury. Of all patients, 72% were treated at an elective surgery site (ESS) and 23% were treated at major trauma centers (MTC). The overall mortality in femoral neck fracture was identified at 15.9%. Higher mortality was observed at the ESS (13.7%) compared to the MTC (7.7%). The higher mortality at the ESS was observed in patients who were tested positive for COVID (40.1% *vs* 20%). The main outcome was mortality risk considering that orthopedic patients were being treated at the MTC which admitted both COVID-positive and COVID-negative patients. It was suggested that there was an 11% rate of contracting COVID-19 peri-operatively due to

being admitted to the hospital. However, using a site not designated for treating COVID-19 patients for orthopedic surgery and performing surgery at an ESS did not improve the outcome of mortality, risk of infection, or length of stay.

Paul *et al*[38] studied the effect of COVID-19 on ulnar collateral ligament repair (UCLR) in 106 major league baseball (MLB) players. The study observed at all pitchers of the MLB who underwent UCLR repair and found no difference in overall UCLR repair from baseball seasons 2017 through 2020 (n = 16, 20, 16, and 18). However, when the repair was examined with the number of games played pre-pandemic compared to pandemic season, it was found that pitchers were about three times more likely to undergo UCLR repair after the COVID-19 lockdown. The higher rate of UCLR was most likely due to the lack of preseason activity during lockdown periods.

Yu *et al*[39] compared patterns and management of fracture patients in the pre-COVID and peri-COVID eras (January 24, 2020 through March 9, 2020) in China. Fracture types included upper and lower extremities and vertebra. Researchers found a 42% decrease in the number of orthopedic patients during the COVID-19 pandemic. Time of injury to hospitalization of the patients did not change; however, time of injury to operation significantly increased during the pandemic (4.5 ± 4.1 d *vs* 2.0 ± 1.5 d, P < 0.001) when compared with 2019 data. Similarly, length of stay of patients after surgery was longer in the pandemic when compared to 2019 data. Mandatory screenings delayed surgery by more than 48 h. It was recommended that screening of emergency patients should be a priority to minimize risk of infection among other patients and hospital staff.

CONCLUSION

The presentation of coronavirus, while not entirely mysterious, was bound to have unprecedented effects on healthcare workers, regulations in medical specialties, and patients. Orthopedic specialties globally observed numerous changes over the evolution of the pandemic. Orthopedic cases varied in severity. Medical facilities were forced to create alternative treatment plans for emergent and elective orthopedic procedures, and the data presented showed the impact of COVID-19 on orthopedic injury. Some of the changes implemented during this time showed to be beneficial and could be potential long-term solutions for optimizing medical orthopedic management.

Hip replacements are generally the most common elective procedure, but elective procedures were halted and therefore most institutions did not perform them. Hip fractures have still been very common during this time[4,25,28]; however, the pandemic has increased the mortality and complication rate particularly amongst COVID-positive patients[5,8,11,16,38]. The importance of early treatment and proper rehabilitation was strongly emphasized in order to ensure prompt recovery[14].

Mechanism of injury also changed during the pandemic. COVID-19 impacted the number of RTAs significantly as well as sporting injuries due to lockdowns and cancellation of group gatherings[3,25,27]. Work injuries also decreased significantly due to lockdowns and remote work[26,28]. School traumas were reduced as students were engaged in online learning[24,26]. With the vast population sheltering at home, there was a dramatic increase in domestic injuries that included home improvement projects, running, and cycling[22,28,29]. There was also a rise from 18% to 35% in oLLFs in patients with mental health conditions, implying that social isolation even if necessary, negatively impacts mental health[3,22]. A 40% increase in upper extremity injuries due to high-risk behaviors was observed during this time which could also be a consequence of social isolation[22].

The use of telehealth services was introduced in several facilities to alleviate the burden on healthcare facilities as well as limit exposure of both patients and providers to COVID-19. Virtual patient care proved to have a positive impact on the rehabilitation of patients postoperatively, lowering the rate of complications[7]. The use of telehealth services, while beneficial, did have adverse effects in patients that required more hands-on treatment[21]. These patients will be required to seek care or corrective treatment for the injury in the future[21]. To take full advantage of the benefits of telehealth, the screening for the patients that can be seen virtually should be stringent in order to ensure quality care.

From the management changes that were seen during this period, there were some takeaways that should be emphasized in current standards of practice. Early intervention was and should be a priority. This is essential for patients with hip fractures or other severe fractures to minimize the risk of mal-union. Telehealth was a service to bridge the gap in healthcare for those that were COVID-positive and needed treatment or even for facilities that were not allowing any patients to be seen in person[7]. This is a service that in the future would be valuable to patients that are immobile, are ill, or have transportation issues[40]. Since appropriate PPE allows healthcare providers to treat COVID-19 patients with minimal exposure, separating COVID-positive and COVID-negative patients allowed for timely injury management and COVID management. Knowing that COVID-19 will continue to be prevalent, separating COVID-positive and negative patients can help expedite treatment for both groups of patients. This literature review emphasized the necessity of being prepared to perform routine but emergent procedures even in unprecedented crises.

There were some limitations in this study. The previous and current literature does not allow us to explore how new approaches in orthopedic management would impact patient care in the long term.

Also, as we are still facing COVID-19 surges, the data to support an outcomes study is not yet available. Further research should be conducted to examine how orthopedic injury management has changed when COVID-19 is at its nadir.

To summarize, while hospitals and medical facilities are still facing COVID-19 case surges, it is important to understand how this pandemic has impacted the various specialties of healthcare. Significant changes were noted in orthopedic practices since the start of the COVID-19 pandemic including different mechanisms of injury, higher mortality rates, and injury to different areas of the body. Changes that positively impacted patient outcomes should be made standards of practice and practices that negatively impacted patient outcomes should be actively evaluated to not only be avoided in regular care but also in times of crises.

FOOTNOTES

Author contributions: Obamiro E conducted the initial screening of sources and wrote the manuscript; Trivedi R acquired additional sources, and wrote and edited the manuscript; Ahmed N developed the research question, acquired additional sources, and wrote and edited the manuscript.

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REFERENCES

1 **WHO**. World Health Organization. COVID-19 Dashboard. Feb/03/2022. Available from: https://covid19.who.int/
2 **Guy**, DK, Bosco, JA, Savoie, FH. AAOS Guidelines for Elective Surgery During the COVID-19 Pandemic. American Academy of Orthopedic Surgeons. April 2, 2020. Online Publication. Available from: https://www.aaos.org/about/covid-19-information-for-our-members/aaos-guidelines-for-elective-surgery/
3 **Campbell E**, Zahoor U, Payne A, Popova D, Welman T, Pahal GS, Sadigh P. The COVID-19 Pandemic: The effect on open lower limb fractures in a London major trauma centre - a plastic surgery perspective. *Injury* 2021; **52**: 402-406 [PMID: 33341244 DOI: 10.1016/j.injury.2020.11.047]
4 **Egol KA**, Konda SR, Bird ML, Dedhia N, Landes EK, Ranson RA, Solasz SJ, Aggarwal VK, Bosco JA 3rd, Furgiuele DL, Ganta A, Gould J, Lyon TR, McLaurin TM, Tejwani NC, Zuckerman JD, Leucht P; NYU COVID Hip Fracture Research Group. Increased Mortality and Major Complications in Hip Fracture Care During the COVID-19 Pandemic: A New York City Perspective. *J Orthop Trauma* 2020; **34**: 395-402 [PMID: 32482976 DOI: 10.1097/BOT.0000000000001845]
5 **Ojeda-Thies C**, Cuarental-García J, García-Gómez E, Salazar-Zamorano CH, Alberti-Maroño J, Ramos-Pascua LR. Hip fracture care and mortality among patients treated in dedicated COVID-19 and non-COVID-19 circuits. *Eur Geriatr Med* 2021; **12**: 749-757 [PMID: 33550563 DOI: 10.1007/s41999-021-00455-x]
6 **Tyas B**, Wilkinson M, Singisetti K. Effect of Covid-19 on best practice care of hip fracture patients: An analysis from the National Hip Fracture Database (NHFD). *Surgeon* 2021; **19**: e298-e303 [PMID: 33589398 DOI: 10.1016/j.surge.2021.01.003]
7 **Gao SS**, Wang YJ, Zhang GX, Zhang WT. Rehabilitation guidance for hip fracture patients during the COVID-19 pandemic using chat software: A new model. *J Back Musculoskelet Rehabil* 2021; **34**: 337-342 [PMID: 33896813 DOI: 10.3233/BMR-200324]
8 **LeBrun DG**, Konnaris MA, Ghahramani GC, Premkumar A, DeFrancesco CJ, Gruskay JA, Dvorzhinskiy A, Sandhu MS, Goldwyn EM, Mendias CL, Ricci WM. Hip Fracture Outcomes During the COVID-19 Pandemic: Early Results From New York. *J Orthop Trauma* 2020; **34**: 403-410 [PMID: 32482977 DOI: 10.1097/BOT.0000000000001849]
9 **Hall AJ**, Clement ND, Farrow L, MacLullich AMJ, Dall GF, Scott CEH, Jenkins PJ, White TO, Duckworth AD; IMPACT-Scot Study Group. IMPACT-Scot report on COVID-19 and hip fractures. *Bone Joint J* 2020; **102-B**: 1219-1228 [PMID: 32634029 DOI: 10.1302/0301-620X.102B9.BJJ-2020-1100.R1]
10 **Crozier-Shaw G**, Hughes AJ, Conlon B, Sheehan E, Merghani K. Hip fracture care during Covid-19: a regional trauma

centre's experience. *Ir J Med Sci* 2021; **190**: 1275-1280 [PMID: 33392978 DOI: 10.1007/s11845-020-02476-0]

11 **Galivanche AR**, Mercier MR, Schneble CA, Brand J, Pathak N, Varthi AG, Rubin LE, Grauer JN. Clinical Characteristics and Perioperative Complication Profiles of COVID-19-Positive Patients Undergoing Hip Fracture Surgery. *J Am Acad Orthop Surg Glob Res Rev* 2021; **5** [PMID: 34653097 DOI: 10.5435/JAAOSGlobal-D-21-00104]

12 **Catellani F**, Coscione A, D'Ambrosi R, Usai L, Roscitano C, Fiorentino G. Treatment of Proximal Femoral Fragility Fractures in Patients with COVID-19 During the SARS-CoV-2 Outbreak in Northern Italy. *J Bone Joint Surg Am* 2020; **102**: e58 [PMID: 32345864 DOI: 10.2106/JBJS.20.00617]

13 **Mitkovic MM**, Bumbasirevic M, Milenkovic S, Gajdobranski D, Bumbasirevic V, Mitkovic MB. Influence of coronavirus disease 2019 pandemic state of emergency in orthopaedic fracture surgical treatment. *Int Orthop* 2021; **45**: 815-820 [PMID: 32728928 DOI: 10.1007/s00264-020-04750-3]

14 **Orfanos G**, Al Kaisi K, Jaiswal A, Lim J, Youssef B. The effect of COVID-19 pandemic on the care of fragility hip fracture patients in the United Kingdom. A case control study in a major trauma centre. *Surgeon* 2021; **19**: e440-e445 [PMID: 33648854 DOI: 10.1016/j.surge.2021.01.008]

15 **Brayda-Bruno M**, Giorgino R, Gallazzi E, Morelli I, Manfroni F, Briguglio M, Accetta R, Mangiavini L, Peretti GM. How SARS-CoV-2 Pandemic Changed Traumatology and Hospital Setting: An Analysis of 498 Fractured Patients. *J Clin Med* 2021; **10** [PMID: 34208115 DOI: 10.3390/jcm10122585]

16 **Zagra L**, D'Apolito R, Guindani N, Zatti G, Rivera F, Ravasi F, Mosconi M, Momoli A, Massè A, Franceschini M, D'Angelo F, Dallari D, Catani F, Casiraghi A, Bove F, Castelli CC. Do standards of care and early outcomes of periprosthetic fractures change during the COVID-19 pandemic? *J Orthop Traumatol* 2021; **22**: 22 [PMID: 34128114 DOI: 10.1186/s10195-021-00584-w]

17 **Muse IO**, Montilla E, Gruson KI, Berger J. Perioperative management of patients with hip fractures and COVID-19: A single institution's early experiences. *J Clin Anesth* 2020; **67**: 110017 [PMID: 32836189 DOI: 10.1016/j.jclinane.2020.110017]

18 **Shah R**, Ahad A, Faizi M, Mangwani J. Foot and ankle trauma management during the COVID-19 pandemic: Experiences from a major trauma unit. *J Clin Orthop Trauma* 2021; **16**: 285-291 [PMID: 33613010 DOI: 10.1016/j.jcot.2021.01.014]

19 **Kuliński P**, Tomczyk Ł, Morasiewicz P. Effect of the COVID-19 pandemic on foot surgeries. *Adv Clin Exp Med* 2021; **30**: 1249-1253 [PMID: 34610226 DOI: 10.17219/acem/140610]

20 **Al-Humadi SM**, Tantone R, Nazemi AK, Hays T, Pawlak A, Komatsu DE, Namm JD. Outcomes of orthopaedic trauma surgery in COVID-19 positive patients. *OTA Int* 2021; **4**: e129 [PMID: 34746661 DOI: 10.1097/OI9.0000000000000129]

21 **Dunkerley S**, Thelwall C, Omiawele J, Smith A, Deo S, Lowdon I. Patient care modifications and hospital regulations during the COVID-19 crisis created inequality and functional hazard for patients with orthopaedic trauma. *Int Orthop* 2020; **44**: 2481-2485 [PMID: 32767088 DOI: 10.1007/s00264-020-04764-x]

22 **Diamond S**, Lundy JB, Weber EL, Lalezari S, Rafijah G, Leis A, Gray BL, Lin IC, Gupta R. A Call to Arms: Emergency Hand and Upper-Extremity Operations During the COVID-19 Pandemic. *J Hand Surg Glob Online* 2020; **2**: 175-181 [PMID: 32835183 DOI: 10.1016/j.jhsg.2020.05.004]

23 **Fyllos A**, Varitimidis S, Papageorgiou F, Karamanis N, Alexiou K, Veloni A, Malizos K, Dailiana Z. Upper extremity emergencies during SARS-COV-2 pandemic: Turnout trends. *Injury* 2021; **52**: 387-394 [PMID: 33246643 DOI: 10.1016/j.injury.2020.11.045]

24 **Gumina S**, Proietti R, Villani C, Carbone S, Candela V. The impact of COVID-19 on shoulder and elbow trauma in a skeletally immature population: an Italian survey. *JSES Int* 2021; **5**: 3-8 [PMID: 32984859 DOI: 10.1016/j.jseint.2020.08.003]

25 **Donovan RL**, Tilston T, Frostick R, Chesser T. Outcomes of Orthopaedic Trauma Services at a UK Major Trauma Centre During a National Lockdown and Pandemic: The Need for Continuing the Provision of Services. *Cureus* 2020; **12**: e11056 [PMID: 33224652 DOI: 10.7759/cureus.11056]

26 **Maniscalco P**, Poggiali E, Quattrini F, Ciatti C, Magnacavallo A, Vercelli A, Domenichini M, Vaienti E, Pogliacomi F, Ceccarelli F. Proximal femur fractures in COVID-19 emergency: the experience of two Orthopedics and Traumatology Departments in the first eight weeks of the Italian epidemic. *Acta Biomed* 2020; **91**: 89-96 [PMID: 32420932 DOI: 10.23750/abm.v91i2.9636]

27 **Druel T**, Andeol Q, Rongieras F, Bertani A, Bordes M, Alvernhe A. Evaluation of containment measures' effect on orthopaedic trauma surgery during the COVID-19 pandemic: a retrospective comparison between 2019 and 2020. *Int Orthop* 2020; **44**: 2229-2234 [PMID: 32696333 DOI: 10.1007/s00264-020-04712-9]

28 **Elbardesy H**, Meagher E, Guerin S. Impact of the COVID-19 pandemic on the trauma and orthopaedic department at level one Major Trauma Centre in the republic of Ireland. *Acta Orthop Belg* 2021; **87**: 571-578 [PMID: 34808735 DOI: 10.52628/87.3.26]

29 **Andreozzi V**, Marzilli F, Muselli M, Previ L, Cantagalli MR, Princi G, Ferretti A. The impact of COVID-19 on orthopaedic trauma: A retrospective comparative study from a single university hospital in Italy. *Orthop Rev (Pavia)* 2020; **12**: 8941 [PMID: 33585026 DOI: 10.4081/or.2020.8941]

30 **Kalem M**, Kocaoğlu H, Merter A, Karaca MO, Özbek EA, Kınık HH. Effects of COVID-19 pandemic curfew on orthopedic trauma in a tertiary care hospital in Turkey. *Acta Orthop Traumatol Turc* 2021; **55**: 191-195 [PMID: 34100357 DOI: 10.5152/j.aott.2021.20263]

31 **Clough TM**, Shah N, Divecha H, Talwalkar S. COVID-19 consent and return to elective orthopaedic surgery: allowing a true patient choice? *Bone Jt Open* 2020; **1**: 556-561 [PMID: 33215154 DOI: 10.1302/2633-1462.19.BJO-2020-0125.R1]

32 **Kale NN**, Patel AH, Leddy MJ 3rd, Savoie FH 3rd, Sherman WF. The Effect of COVID-19 on Orthopedic Practices and Surgeons in Louisiana. *Orthopedics* 2020; **43**: 351-355 [PMID: 33211903 DOI: 10.3928/01477447-20201023-01]

33 **Meng Y**, Leng K, Shan L, Guo M, Zhou J, Tian Q, Hai Y. A clinical pathway for pre-operative screening of COVID-19 and its influence on clinical outcome in patients with traumatic fractures. *Int Orthop* 2020; **44**: 1549-1555 [PMID: 32468202 DOI: 10.1007/s00264-020-04645-3]

34 **Patel BA**, Green SF, Henessy C, Adamu-Biu F, Davda K, Chennagiri R, Kankate R, Ghani Y. Lessons Learnt from Managing Orthopaedic Trauma During the First Wave of the COVID-19 Pandemic at a UK District General Hospital.

Indian J Orthop 2021; 1-9 [PMID: 34024932 DOI: 10.1007/s43465-021-00419-0]

35 **Gupta R**, Singhal A, Kapoor A, Dhillon M, Masih GD. Effect of COVID-19 on surgical management of open fractures and infection rates: A tertiary care experience in Indian set-up. *J Clin Orthop Trauma* 2021; **12**: 16-21 [PMID: 33132629 DOI: 10.1016/j.jcot.2020.10.050]

36 **Saini N**, Ranjan R, Jain VK, Shukla A. Pooling of neglected and delayed trauma patients - Consequences of 'lockdown' and 'Unlock' phases of COVID-19 pandemic- A retrospective cohort analysis from a tertiary centre. *J Clin Orthop Trauma* 2021; **21**: 101533 [PMID: 34334981 DOI: 10.1016/j.jcot.2021.101533]

37 **Balakumar B**, Nandra RS, Woffenden H, Atkin B, Mahmood A, Cooper G, Cooper J, Hindle P. Mortality risk of surgically managing orthopaedic trauma during the COVID-19 pandemic. *Bone Jt Open* 2021; **2**: 330-336 [PMID: 34027674 DOI: 10.1302/2633-1462.25.BJO-2020-0189.R1]

38 **Paul RW**, Omari A, Fliegel B, Bishop ME, Erickson BJ, Alberta FG. Effect of COVID-19 on Ulnar Collateral Ligament Reconstruction in Major League Baseball Pitchers. *Orthop J Sports Med* 2021; **9**: 23259671211041359 [PMID: 34497864 DOI: 10.1177/23259671211041359]

39 **Yu P**, Wu C, Zhuang C, Ye T, Zhang Y, Liu J, Wang L. The patterns and management of fracture patients under COVID-19 outbreak in China. *Ann Transl Med* 2020; **8**: 932 [PMID: 32953732 DOI: 10.21037/atm-20-4174]

40 **McMaster T**, Wright T, Mori K, Stelmach W, To H. Current and future use of telemedicine in surgical clinics during and beyond COVID-19: A narrative review. *Ann Med Surg (Lond)* 2021; **66**: 102378 [PMID: 33996071 DOI: 10.1016/j.amsu.2021.102378]

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ORIGINAL ARTICLE

Basic Study

Role of the posterior deep deltoid ligament in ankle fracture stability: A biomechanical cadaver study

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Abstract

BACKGROUND

The deltoid ligament is a key component of ankle fracture stability. Clinical tests to assess deltoid ligament injury have low specificity. In supination external-rotation (SER) type-IV ankle fractures, there is either a medial malleolus fracture or deltoid ligament injury. These injuries are often considered unstable, requiring surgical stabilisation. We look to identify the anatomical basis for this instability. This study investigates the anatomical basis for such instability by re-creating SER type ankle fractures in a standardised cadaveric study model, investigating the anatomical basis for such instability.

AIM

To investigate the anatomical basis for fracture instability in SER type ankle fractures.

METHODS

Four matched pairs of cadaveric limbs were tested for stability both when axially loaded and under external rotation stress. Four matched pairs of cadaveric limbs (8 specimens) were tested for stability when axially loaded to 750 N with a custom rig. Specimens were tested through increasing stages of SER injury in a stepwise fashion before restoring the lateral side with open reduction and internal fixation (ORIF). Clinical photographs and radiographs were recorded at each step. We

defined instability in accordance with well accepted radiological parameters: > 4 mm medial clear space opening on a mortise-view radiograph or > 7 degrees of talar tilt.

RESULTS

All specimens with an intact posterior deep deltoid ligament were stable. Once the posterior deep deltoid ligament was sectioned there was instability in all specimens. Stabilisation of the lateral side prevented talar shift, but not talar tilt.

CONCLUSION

If the posterior deep deltoid ligament is intact then SER fractures can be managed without surgery. If the posterior deep deltoid is incompetent, ORIF and cautious rehabilitation is recommended because the talus can still tilt in the mortise.

Key Words: Trauma; Fracture stability; Biomechanics; Cadaveric study; Basic science

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Core Tip: The deltoid ligament is a key component of ankle fracture stability. No fracture with an intact posterior deep deltoid ligament demonstrated instability on axial loading or rotational stress. This study suggests the instability can only occur in the presence of posterior deep deltoid ligament deficiency, supporting the non-operative treatment of many ankle fractures. If the posterior deep deltoid ligament is intact then supination external-rotation fractures can be managed without surgery. If the posterior deep deltoid is incompetent, open reduction and internal fixation and cautious rehabilitation is recommended because the talus can still tilt in the mortise.

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INTRODUCTION

Ankle fractures are common and yet there is wide variation in how they are managed[1]. The concept of ankle fracture stability has long been used to guide whether an ankle fracture can be managed non-operatively or whether operative stabilisation is required[2]. In practice, the criteria used to define a stable ankle fracture have been open to interpretation. Understanding of this issue has progressed over recent years. Many stable fractures are still treated operatively. This leads to increased costs both in terms of surgical admission for treatment and in dealing with complications in fractures which may have been safely managed without surgery[3,4].

To determine whether operative stabilisation is required or not, a precise understanding of the injured parts of the ankle is required. The widely used Danis-Weber Classification, which forms the basis of the AO Classification, is not adequate for distinguishing between stable Weber B fibula fractures and unstable Weber B fibula fractures[5]. The Lauge-Hansen classification offers a better understanding of which bony and ligamentous structures are injured[6].

The Lauge-Hansen Classification was introduced over 70 years ago[6]. The structures that are injured progress in an orderly fashion, depending upon the position of the foot at the time of injury and the type of force applied. The foot is either Supinated or Pronated. The applied force is either rotational (external or internal) or translational (abduction or adduction). Supination external-rotation (SER) injuries are the most common type of ankle fracture. In SER injury, supination of the foot means that the lateral structures are tight and so these are the first to fail. Next to fail, as rotation continues, is the posterior part of the ankle and finally the medial side.

Lauge-Hansen[6] described 4 stages to SER injury. SER-I is injury to the anterior inferior tibio-fibular ligament. With further force, an oblique fibula fracture will occur (SER-II). The next structure to fail is either the posterior malleolus or the posterior inferior tibiofibular ligament (SER-III). In the final stage, deltoid ligament injury or medial malleolar fracture occurs (SER-IV). Lauge-Hansen[6] based his classification upon laboratory simulation with cadaveric specimens. In clinical practice there is variation in both the foot position and force applied. Injury patterns therefore vary from patient to patient.

SER injuries account for 80% of ankle fractures[1]. Diagnostic difficulty arises in cases where there is a fibula fracture (Weber B) but no posterior malleolus fracture or medial malleolus fracture. Where there is a fracture of the medial malleolus then the diagnosis of SER-IV (and instability) is generally considered straightforward. If the medial side of the joint has no fracture, then determining whether the injury is a stable SER-II (with no deltoid ligament injury) or an unstable SER-IV (with injury to the deltoid ligament) is challenging.

Defining the presence of ligamentous medial injury is not straightforward. Traditionally, medial tenderness and ecchymosis have been used as clinical signs of deltoid ligament injury. Studies have demonstrated, however, no correlation between medial tenderness and deltoid ligament incompetence. DeAngelis *et al*[7] examined 55 patients with SER injuries and found that only 25% of patients who were tender medially had a positive external rotation stress radiograph. Twenty-five percent of patients without medial tenderness also had a positive external rotation stress radiograph. This, along with the earlier studies by McConnell *et al*[8] and Egol *et al*[9], demonstrate that clinical findings are of little value in determining ankle fracture stability. Clinical assessment alone is unreliable. Radiological studies with ultrasound and magnetic resonance imaging have also proven of little use in clinical practice[10-15].

It has been argued that a formal examination under anaesthesia (EUA) of the injured ankle will demonstrate instability in "ligamentous bi-malleolar" fractures. Whilst this strategy would reliably discriminate between SER-II and SER-IV, such an approach is impractical given the large number of patients. The Gravity Stress View was introduced to demonstrate, without formal EUA, whether the deltoid ligament complex is competent (no talar shift) or not (talar shift demonstrated)[16,17]. However, this technique has subsequently been shown to have a high rate of false positives[18]. Ankles may appear unstable because of ankle plantarflexion which gives the false impression of a wide medial clear space[19].

Weightbearing radiographs are now considered to be the best means of demonstrating whether a Weber B ankle fracture is stable (SER-II) or unstable (SER-IV)[18]. Properly conducted weightbearing radiographs show whether the ankle is stable under physiological load. The implication of this is that the deltoid ligament is sufficiently competent to maintain the position of the talus in the mortise when the ankle is held at 90 degrees. This study did not address the question of partial deltoid ligament injury and whether that affects stability.

The anatomy of the deltoid ligament has been described in various levels of detail[20]. For the purposes of understanding ankle fractures, the deltoid ligament can be usefully considered to have three components: Superficial; deep anterior tibio-talar and deep posterior tibio-talar. Michelson *et al*[21], in a cadaveric study, investigated stability when both the superficial and deep deltoid ligaments were sectioned, using a gravity stress-view. They showed increased medial clear space in all 8 specimens. This study did not investigate which components of the deltoid ligament complex gave the ankle mortice stability. In particular, the authors did not distinguish between the roles of the two components of the deep deltoid ligament. The superficial ligament is not crucial to the maintenance of the talus in the mortice. The deep deltoid ligament is. It has been shown that the posterior deep deltoid (tibio-talar) ligament is the thickest component[22], that it is tight when the ankle is plantigrade and that the anterior component is tight in plantarflexion[23]. We designed our protocol to investigate the contributors to ankle fracture stability in SER type injuries, including the posterior and anterior portions of the deep deltoid ligaments.

MATERIALS AND METHODS

Thawed fresh-frozen cadaveric specimens from the tibial plateau to the foot were used. The tissues were used in accordance with the Human Tissue Act 2004, with all investigators undergoing appropriate training prior to study commencement. Four matched pairs of specimens were tested using the protocol (8 specimens in total). A bespoke jig was used, capable of axially loading and simultaneously applying torque through a cadaveric specimen. The jig was designed to load the specimens with 750 N and to permit mortise-view and lateral view radiographs to be taken using an image intensifier. 750 N was selected to recreate the single leg standing force of a 75 kg individual. The image intensifier was operated by a radiographer. In this study we re-created a fracture of the lateral malleolus with a subsequent injury to the deltoid ligament in line with Lauge Hansen SER type IV injury. We did not specifically investigate bony medial malleolus fractures.

With the intact specimen in the jig and axially loaded to 750 N, a baseline mortise-view radiograph was taken. This radiographic view was repeated using the image intensifier at each step in a systematic reproduction of SER injury. Structures were divided in the order in which they fail during a Lauge-Hansen SER type injury. The osteotomy was performed using an oscillating saw from the level of the distal most aspect of the syndesmosis posteriorly, to its most proximal aspect anteriorly, completely dividing the fibula. The osteotomy was fixed using a standard AO technique. A single cortical lag screw across the fracture site and a 1/3 tubular stainless steel plate, with 2 uni-cortical cancellous screws and 3 bi-cortical cortical screws fixing the neutralisation plate either side of the fracture. A tri-cortical screw was placed across the syndesmosis. The anterior deep deltoid and posterior deep deltoid were divided

sequentially - firstly the anterior 50% of the ligament, and secondarily the posterior 50% to allow for subtle variations in anatomy and maintain reproducibility between specimens. At each step the specimen was axially loaded with 750 N and radiographs were obtained. Each radiograph was investigated for signs of instability, defined in our study as > 4 mm medial clear space and/or 7 degrees of talar tilt (Figure 1A, Table 1).

RESULTS

None of the 8 specimens showed any evidence of instability either with axial loading or with rotational force until division of the posterior deep deltoid ligament. Apparent stability under axial loading was still evident in all 8 specimens through every step of the experiment, even when the posterior deep deltoid ligament was divided (Figure 1B). When the specimens were subjected to external rotation force, all 8 specimens were stable at steps A to E of the experiment (up to and including division of the anterior deep deltoid ligament). However, instability was demonstrated in all 8 specimens after division of the posterior deep deltoid ligament. Talar tilt and talar shift were both demonstrated (Figure 1C). All specimens demonstrated > 4 mm medial clear space and > 7 degrees of talar tilt.

After fixation of the osteotomy, external rotation stress views and continuous screening showed < 4 mm medial clear space. All 8 specimens demonstrated talar tilt > 7 degrees (Figure 1D). All ankles were stable until we divided the posterior deep deltoid ligament. At this point instability was only reproduced on external rotation stress testing. Even with the posterior deep deltoid ligament divided, specimens showed no talar shift on axial loading with 750 N.

DISCUSSION

Ankle injuries follow patterns that are well understood and these patterns form the basis of the Lauge-Hansen classification[6]. The introduction of a more simple classification, relying solely upon description of the fibula fracture, led to indiscriminate fixation of fibula fractures. The presence of a Weber B fracture was considered an indication for surgery, since the fibula was felt to be the primary stabiliser of the ankle[24]. More recently, demonstrable instability of the talus within the mortise has become the indication for surgery. Interest is currently focused on how best to identify this instability[1-3,25].

This study reproducibly demonstrates that with an intact posterior deep deltoid ligament the talus remains stable beneath the tibial plafond when loaded axially and when subject to external rotation stress testing. Anatomical studies have highlighted different components of the deltoid ligament[22,24,26]. Imaging studies have confirmed that a partial deep deltoid ligament injury can occur and this means that the SER-IV injury is a heterogeneous group[10].

In SER-IV injuries the medial side may have a fracture or ligament injury. The medial malleolus fracture fragment may be large or small. Small fracture fragments may affect the anterior colliculus and this represents the attachment of the anterior deep deltoid ligament[27]. A large fracture fragment of the medial malleolus includes the whole deep deltoid attachment - the anterior colliculus with the anterior deep deltoid ligament and the posterior colliculus with the posterior deep deltoid[28]. After fixation of a large medial malleolus fracture the joint is stable. This highlights the primary importance of the posterior deep deltoid ligament. Medial side integrity determines ankle stability, and the key structure is the posterior deep deltoid ligament. This concept can be extended from medial side fractures to medial side ligamentous injuries. If the deep deltoid is partially injured and the posterior component is intact, then the ankle is stable. However, such stability is only conferred by the posterior deep deltoid ligament when it is tight, with the ankle in a plantigrade position.

Gougoulias *et al*[1] proposed that SER-IV injuries be subdivided into types a and b. They recommended management strategies based on assessment of stability with weightbearing X-rays (Table 2). According to their recommendations, in SER-IVa injuries the posterior deep deltoid is intact (IVa) so the ankle fracture can be immobilized and treated without surgery. The foot should be maintained at 90 degrees to the leg. This is best achieved in a formal below-knee walking cast and not with a removable boot. If the plantigrade position is lost then there is potential for a poor result, with late deltoid ligament insufficiency[29-31]. In SER-IVb injuries, where the posterior deep deltoid ligament is also injured, the ankle is unstable and operative stabilisation of the fibula fracture should be considered.

Our study highlights the importance of the posterior deep deltoid ligament in SER injuries. Only once the posterior deep deltoid ligament was divided did the specimens become unstable. When the posterior deep deltoid ligament is intact (SER-IVa) the injury can be treated non-operatively but, like Gougoulias *et al*[1], we recommend that a formal plantigrade below knee walking cast is used. All SER-IVb injuries were unstable in our study. Gougoulias *et al*[1] recommended open reduction and internal fixation (ORIF) of the fibula for these injuries. In our study, axially loaded specimens still appeared stable, with no talar shift. The bony anatomy and soft tissue envelope are likely factors conferring this

Table 1 Study protocol

Experimental step	Specimen
A	Intact
B	AITFL divided
C	Fibula osteotomy at the level of syndesmosis
D	PITFL divided
E	Superficial and anterior deep deltoid ligament divided
F	Posterior deep deltoid ligament divided
G	Fracture & syndesmosis fixation

AITFL: Anterior inferior tibiofibular ligament; PITFL: Posterior inferior tibiofibular ligament.

Table 2 Management recommendations based on weight-bearing X-rays as suggested by Gougoulias *et al*[1]

Fracture type	NWB XR	WB Xray	Deep deltoid ligament	Management
SER-II	Stable	Stable	Intact (PTTL & ATTL)	Boot & WB
SER-IVa	Unstable	Stable	Partial tear (ATTL only)	WB Cast 6/52
SER-IVb	Unstable	Unstable	Ruptured (PTTL & ATTL)	ORIF

SER: Supination external-rotation; AITFL: Anterior inferior tibiofibular ligament; PITFL: Posterior inferior tibiofibular ligament; ORIF: Open reduction and internal fixation; NWB: Non weight bearing; WB: Weight-bearing.

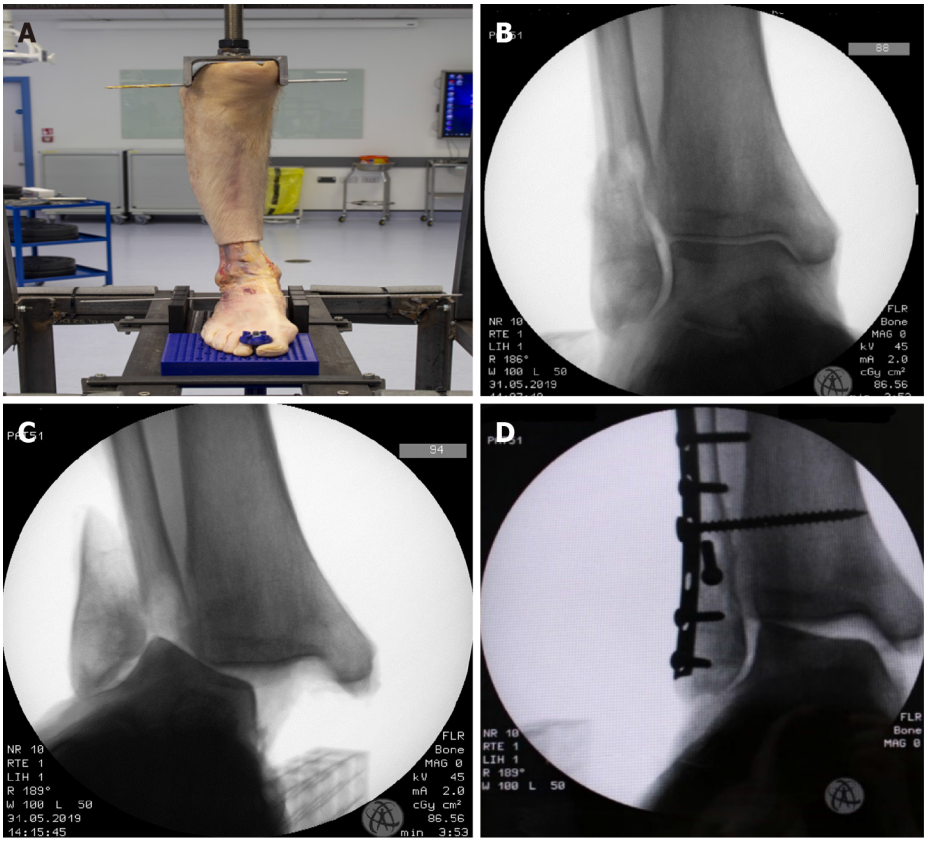
stability. The experimental setup only tested the axially loaded specimens in a plantigrade position. Radiological determinants of instability vary with the position of the ankle[19]. When rotational force was applied the SER-IVb specimens, all were markedly unstable (Figure 1B). This supports the recommendation that ORIF of the fibula should be used to restore stability. When we tested SER-IVb specimens after fibula ORIF, talar tilt was still demonstrable. We would go further than Gougoulias *et al* [3] and recommend that, postoperatively, SER-IVb injuries should be immobilized in a plantigrade position to allow proper healing of the deltoid ligament. Physiotherapy protocols should also be modified to avoid late deltoid insufficiency. Deltoid ligament repair has been suggested as a potential supplementary treatment for SER-IVb injuries, however at this stage, deltoid repair appears to have no effect on functional outcome scores[32].

This study has limitations. Eight specimens is a small sample size, but the uniformity of our results make it highly improbable that the conclusions would differ if further specimens were tested. A syndesmosis screw is not routinely used in the fixation of SER-IV fractures. Some authors advocate a "hook test" after fibula fixation but randomized controlled studies have found no benefit with the addition of a position screw, even when talar shift was observed after fibula ORIF in the short or medium term[33,34]. We added the syndesmosis screw so that the controversial role of mild syndesmosis instablilty after ORIF could be excluded as a reason for talar displacement.

The results of this study show that if the posterior deep deltoid ligament is intact, the ankle is stable. We did not investigate specifically whether an intact anterior deep deltoid ligament would also afford stability if the posterior deep deltoid is torn. However, Tornetta[27] have already demonstrated the prime importance of the posterior deep deltoid ligament.

The results of our study provide further evidence that the majority of SER injuries can be treated non-operatively. Injury to the posterior deep deltoid ligament is the watershed. Clinicians choosing non-operative treatment for SER-IV fractures - both types a and b - should carefully consider immobilisation and rehabilitation protocols. This is because of our finding that that talar tilt occurs even after fibula ORIF when the posterior deep deltoid ligament is divided.

Operative stabilisation of SER-IVb fractures should be followed by cautious postoperative care, holding the ankle in a plantigrade position to allow the posterior deep deltoid ligament to heal. SER-IVa fractures can be successfully managed non-operatively but, since stability depends upon the posterior deep deltoid, immobilisation of the ankle at 90 degrees is indicated. For this reason, a cast rather than a removable boot is suggested. Operative fixation of the fibula might permit more rapid rehabilitation. The merits of surgery, and the potential complications, should be discussed with patients on an individual basis.



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Figure 1 Experiment set-up. A: Experiment set-up; B: Specimen under load at stage E showing no talar tilt or shift; C: Same specimen under dynamic stress testing demonstrating shift and tilt at stage F; D: Specimen after fixation under stress testing demonstrating talar tilt - step G.

This cadaver study demonstrates the critical importance of the posterior deep deltoid ligament in ankle stability after SER-IV fracture. The results increase the body of evidence supporting the non-operative management of ankle fractures, even those injuries that initially appear to be potentially unstable. Our results also suggest that even when treated with ORIF, an SER-IVb fracture may demonstrate talar tilt on external rotation. Whether this leads to detrimental outcomes in patients remains unclear. Deltoid ligament repair is an area of current interest with recent research suggesting although repairing the deltoid ligament may improve radiological parameters, it has yet to demonstrate improved patient reported outcome measures[32].

It is generally accepted that more severe ankle injuries perform worse long term, particularly giving a greater risk of ankle arthrosis or reflex sympathetic dystrophy[35]. Clinical studies are required to further evaluate these recommendations. One area of interest, lies within the fact that all axially loaded specimens with an intact posterior deep deltoid appeared stable until external rotation stress was applied. Further studies could demonstrate whether some of these injuries, apparently stable in a weight bearing cast, are in fact unstable. If held appropriately in cast it is as yet unknown whether this finding is clinically significant. We believe that these findings should stimulate debate regarding the management of SER-IV fractures. Non-operative treatment of SER-IVa injuries relies upon an intact posterior deep deltoid ligament, and this only affords stability when the ankle is plantigrade.

CONCLUSION

If the posterior deep deltoid ligament is intact then SER fractures can be managed without surgery. If the posterior deep deltoid is incompetent, ORIF and cautious rehabilitation is recommended because the talus can still tilt in the mortise.

ARTICLE HIGHLIGHTS

Research background

Ankle fractures are common injuries, with supination external-rotation (SER) type injuries being the most common sub-group. Operative intervention in the form of open reduction and internal fixation (ORIF) should be reserved for patients with unstable fractures. There is debate within the literature as to which ankle fractures should be fixed and why, with some of this controversy relating to the degree of deltoid ligament injury required to create such instability and necessitate operative intervention.

Research motivation

We feel that many SER type ankle fractures are stable injuries which can be treated non-operatively. Reducing the incidence of unnecessary operations will reduce potential morbidity for patients and reduce healthcare costs. Through the authors' previous experience in cadaveric dissection, it was felt the posterior portion of the deep deltoid ligament was usually thick and strong, which may afford an ankle fracture stability. We created our protocol to investigate the anatomical basis for ankle fracture instability.

Research objectives

To identify the anatomical basis for instability in SER type ankle fractures.

Research methods

A bespoke jig was created to load a thawed cadaveric ankle specimen both with axial load and rotational torque. The 8 sepecimens were loaded both axially and with external rotation during each stage of a SER type ankle fracture, with AP radiographs recorded at each stage. The radiographs were investigated for evidence of ankle fracture instability in terms of talar shift and talar tilt. A detailed description of the study method is included in the research paper. To our knowledge, our study design is unique answering a question which has never previously been anss in a cadaveric basic science study.

Research results

We determined no evidence of radiological instability in any specimen with an intact posterior deep deltoid ligament. Only on disruption of the posterior deep deltoid ligament instability possible under our test conditions.

Research conclusions

Only ankle fractures with a damaged posterior deep deltoid ligament should require operative intervention. With an intact posterior deep deltoid ligament, the ankle can be held in a neutral position, with the ligament reducing the talus within the ankle mortise.

Research perspectives

Clinical studies to investigate the functional outcomes between SER injuries treated operatively and non-operatively may provide further evidence to support the non-operative treatment of ankle fractures with an intact deep deltoid ligament. Further clinical studies are also needed to investigate the functional outcomes of patients following a SER-IVb type injury. It is unclear whether subtle rotational instability may continue following fibular ORIF. Our cadaveric study suggests rotational instability can occur following ORIF of the fibular in these injuries due to the disrupted posterior deep deltoid ligament. It is unknown whether this remains *in vivo* after appropriate immobilisation in a plaster cast. If instability remains, further investigation into the role of deltoid ligament repair is needed.

FOOTNOTES

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REFERENCES

1 **Gougoulias N**, Sakellariou A. When is a simple fracture of the lateral malleolus not so simple? *Bone Joint J* 2017; **99-B**: 851-855 [PMID: 28663388 DOI: 10.1302/0301-620X.99B7.BJJ-2016-1087.R1]
2 **Lampridis V**, Gougoulias N, Sakellariou A. Stability in ankle fractures: Diagnosis and treatment. *EFORT Open Rev* 2018; **3**: 294-303 [PMID: 29951269 DOI: 10.1302/2058-5241.3.170057]
3 **Gougoulias N**, Khanna A, Sakellariou A, Maffulli N. Supination-external rotation ankle fractures: stability a key issue. *Clin Orthop Relat Res* 2010; **468**: 243-251 [PMID: 19618247 DOI: 10.1007/s11999-009-0988-2]
4 **Pakarinen H**. Stability-based classification for ankle fracture management and the syndesmosis injury in ankle fractures due to a supination external rotation mechanism of injury. *Acta Orthop Suppl* 2012; **83**: 1-26 [PMID: 23205893 DOI: 10.3109/17453674.2012.745657]
5 **Kennedy JG**, Johnson SM, Collins AL, DalloVedova P, McManus WF, Hynes DM, Walsh MG, Stephens MM. An evaluation of the Weber classification of ankle fractures. *Injury* 1998; **29**: 577-580 [PMID: 10209586 DOI: 10.1016/s0020-1383(98)00116-8]
6 **Lauge-Hansen N**. Fractures of the ankle. II. Combined experimental-surgical and experimental-roentgenologic investigations. *Arch Surg (1920)* 1950; **60**: 957-985 [PMID: 15411319]
7 **DeAngelis NA**, Eskander MS, French BG. Does medial tenderness predict deep deltoid ligament incompetence in supination-external rotation type ankle fractures? *J Orthop Trauma* 2007; **21**: 244-247 [PMID: 17414551 DOI: 10.1097/BOT.0b013e3180413835]
8 **McConnell T**, Creevy W, Tornetta P 3rd. Stress examination of supination external rotation-type fibular fractures. *J Bone Joint Surg Am* 2004; **86**: 2171-2178 [PMID: 15466725 DOI: 10.2106/00004623-200410000-00007]
9 **Egol KA**, Amirtharajah M, Tejwani NC, Capla EL, Koval KJ. Ankle stress test for predicting the need for surgical fixation of isolated fibular fractures. *J Bone Joint Surg Am* 2004; **86**: 2393-2398 [PMID: 15523008 DOI: 10.2106/00004623-200411000-00005]
10 **Bäcker HC**, Vosseller JT, Bonel H, Cullmann-Bastian J, Krause F, Attinger MC. Weightbearing Radiography and MRI Findings in Ankle Fractures. *Foot Ankle Spec* 2021; **14**: 489-495 [PMID: 32484366 DOI: 10.1177/1938640020921571]
11 **Crim J**, Longenecker LG. MRI and surgical findings in deltoid ligament tears. *AJR Am J Roentgenol* 2015; **204**: W63-W69 [PMID: 25539277 DOI: 10.2214/AJR.13.11702]
12 **Jeong MS**, Choi YS, Kim YJ, Kim JS, Young KW, Jung YY. Deltoid ligament in acute ankle injury: MR imaging analysis. *Skeletal Radiol* 2014; **43**: 655-663 [PMID: 24599341 DOI: 10.1007/s00256-014-1842-5]
13 **Nortunen S**, Lepojärvi S, Savola O, Niinimäki J, Ohtonen P, Flinkkilä T, Lantto I, Kortekangas T, Pakarinen H. Stability assessment of the ankle mortise in supination-external rotation-type ankle fractures: lack of additional diagnostic value of MRI. *J Bone Joint Surg Am* 2014; **96**: 1855-1862 [PMID: 25410502 DOI: 10.2106/JBJS.M.01533]
14 **Rosa I**, Rodeia J, Fernandes PX, Teixeira R, Saldanha T, Consciência JG. Ultrasonographic Assessment of Deltoid Ligament Integrity in Ankle Fractures. *Foot Ankle Int* 2020; **41**: 147-153 [PMID: 31597464 DOI: 10.1177/1071100719882679]
15 **Won HJ**, Won HS, Oh CS, Han SH, Chung IH, Suh JS, Lee WC. Posterior tibiotalar ligament: an anatomic study correlated with MRI. *Clin Anat* 2014; **27**: 798-803 [PMID: 24038173 DOI: 10.1002/ca.22302]
16 **Gill JB**, Risko T, Raducan V, Grimes JS, Schutt RC Jr. Comparison of manual and gravity stress radiographs for the evaluation of supination-external rotation fibular fractures. *J Bone Joint Surg Am* 2007; **89**: 994-999 [PMID: 17473136 DOI: 10.2106/JBJS.F.01002]
17 **Schock HJ**, Pinzur M, Manion L, Stover M. The use of gravity or manual-stress radiographs in the assessment of supination-external rotation fractures of the ankle. *J Bone Joint Surg Br* 2007; **89**: 1055-1059 [PMID: 17785745 DOI: 10.1302/0301-620X.89B8.19134]
18 **Weber M**, Burmeister H, Flueckiger G, Krause FG. The use of weightbearing radiographs to assess the stability of supination-external rotation fractures of the ankle. *Arch Orthop Trauma Surg* 2010; **130**: 693-698 [PMID: 20082083 DOI: 10.1007/s00402-010-1051-1]
19 **Ashraf A**, Murphree J, Wait E, Winston T, Wooldridge A, Meriwether M, Wilson J, Grimes JS. Gravity Stress Radiographs and the Effect of Ankle Position on Deltoid Ligament Integrity and Medial Clear Space Measurements. *J Orthop Trauma* 2017; **31**: 270-274 [PMID: 28431410 DOI: 10.1097/BOT.0000000000000817]
20 **Savage-Elliott I**, Murawski CD, Smyth NA, Golanó P, Kennedy JG. The deltoid ligament: an in-depth review of anatomy, function, and treatment strategies. *Knee Surg Sports Traumatol Arthrosc* 2013; **21**: 1316-1327 [PMID: 22878436 DOI:

10.1007/s00167-012-2159-3]
21 **Michelson JD**, Varner KE, Checcone M. Diagnosing deltoid injury in ankle fractures: the gravity stress view. *Clin Orthop Relat Res* 2001; 178-182 [PMID: 11400880 DOI: 10.1097/00003086-200106000-00024]
22 **Won HJ**, Koh IJ, Won HS. Morphological variations of the deltoid ligament of the medial ankle. *Clin Anat* 2016; **29**: 1059-1065 [PMID: 27618430 DOI: 10.1002/ca.22793]
23 **Boss AP**, Hintermann B. Anatomical study of the medial ankle ligament complex. *Foot Ankle Int* 2002; **23**: 547-553 [PMID: 12095124 DOI: 10.1177/107110070202300612]
24 **Harper MC**. Deltoid ligament: an anatomical evaluation of function. *Foot Ankle* 1987; **8**: 19-22 [PMID: 3623356 DOI: 10.1177/107110078700800104]
25 **Seidel A**, Krause F, Weber M. Weightbearing vs Gravity Stress Radiographs for Stability Evaluation of Supination-External Rotation Fractures of the Ankle. *Foot Ankle Int* 2017; **38**: 736-744 [PMID: 28511569 DOI: 10.1177/1071100717702589]
26 **Campbell KJ**, Michalski MP, Wilson KJ, Goldsmith MT, Wijdicks CA, LaPrade RF, Clanton TO. The ligament anatomy of the deltoid complex of the ankle: a qualitative and quantitative anatomical study. *J Bone Joint Surg Am* 2014; **96**: e62 [PMID: 24740670 DOI: 10.2106/JBJS.M.00870]
27 **Tornetta P 3rd**. Competence of the deltoid ligament in bimalleolar ankle fractures after medial malleolar fixation. *J Bone Joint Surg Am* 2000; **82**: 843-848 [PMID: 10859104 DOI: 10.2106/00004623-200006000-00011]
28 **Pankovich AM**, Shivaram MS. Anatomical basis of variability in injuries of the medial malleolus and the deltoid ligament. II. Clinical studies. *Acta Orthop Scand* 1979; **50**: 225-236 [PMID: 107720 DOI: 10.3109/17453677908989760]
29 **Alshalawi S**, Galhoum AE, Alrashidi Y, Wiewiorski M, Herrera M, Barg A, Valderrabano V. Medial Ankle Instability: The Deltoid Dilemma. *Foot Ankle Clin* 2018; **23**: 639-657 [PMID: 30414658 DOI: 10.1016/j.fcl.2018.07.008]
30 **Hintermann B**, Knupp M, Pagenstert GI. Deltoid ligament injuries: diagnosis and management. *Foot Ankle Clin* 2006; **11**: 625-637 [PMID: 16971253 DOI: 10.1016/j.fcl.2006.08.001]
31 **Pellegrini MJ**, Torres N, Cuchacovich NR, Huertas P, Muñoz G, Carcuro GM. Chronic deltoid ligament insufficiency repair with Internal Brace™ augmentation. *Foot Ankle Surg* 2019; **25**: 812-818 [PMID: 30478015 DOI: 10.1016/j.fas.2018.10.004]
32 **Salameh M**, Alhammoud A, Alkhatib N, Attia AK, Mekhaimar MM, D'Hooghe P, Mahmoud K. Outcome of primary deltoid ligament repair in acute ankle fractures: a meta-analysis of comparative studies. *Int Orthop* 2020; **44**: 341-347 [PMID: 31776609 DOI: 10.1007/s00264-019-04416-9]
33 **Kortekangas TH**, Pakarinen HJ, Savola O, Niinimäki J, Lepojärvi S, Ohtonen P, Flinkkilä T, Ristiniemi J. Syndesmotic fixation in supination-external rotation ankle fractures: a prospective randomized study. *Foot Ankle Int* 2014; **35**: 988-995 [PMID: 24962527 DOI: 10.1177/1071100714540894]
34 **Pakarinen HJ**, Flinkkilä TE, Ohtonen PP, Hyvönen PH, Lakovaara MT, Leppilahti JI, Ristiniemi JY. Syndesmotic fixation in supination-external rotation ankle fractures: a prospective randomized study. *Foot Ankle Int* 2011; **32**: 1103-1109 [PMID: 22381193 DOI: 10.3113/FAI.2011.1103]
35 **Yaradilmis YU**, Öğük C, Okkaoglu MC, Ateş A, Demirkale İ, Altay M. Injury mechanisms of ankle fractures with dislocation and analysis of differences on functional outcome. *Ulus Travma Acil Cerrahi Derg* 2020; **26**: 818-825 [PMID: 32946097 DOI: 10.14744/tjtes.2020.57034]

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ORIGINAL ARTICLE

Basic Study

Anatomic relationship of extensor indicis propius and extensor digitorum communis: Implications for tendon transfer

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Abstract

BACKGROUND

The extensor indicis proprius (EIP) tendon is a frequently used donor for a variety of tendon transfers, most commonly for reconstruction of the extensor pollicis longus (EPL). EIP is known to have frequent anatomic variants including split tendons and variations in tendon arrangement.

AIM

To characterize the anatomy of the EIP at the level of the extensor retinaculum, where tendon harvest is often performed, and share our preferred technique for EIP to EPL transfer.

METHODS

Twenty-nine fresh-frozen cadaveric forearms without history of forearm or hand injury or surgery were dissected. Tendon circumference and relationship of the EIP and extensor digitorum communis to the index (EDCI) at the metacarpophalangeal (MCP) joint and the distal extensor retinaculum were recorded. Distance from the distal extensor retinaculum to the EIP myotendinous junction was measured.

RESULTS

EIP was ulnar to the EDCI in 96.5% of specimens (28/29) at the distal edge of the extensor retinaculum. In the remaining specimen, EIP was volar to EDCI. Tendon circumference at the distal extensor retinaculum averaged (9.3 mm ± 1.7 mm) for EDCI and 11.1 mm (± 2.7 mm) for EIP (P = 0.0010). The tendon circumference at the index MCP joint averaged 11.0 mm (± 1.7 mm) for EDCI and 10.6 mm (± 2.1 mm) for EIP (P = 0.33). EIP had a greater circumference in 76% (22/29) of specimens at the distal extensor retinaculum whereas EIP had a greater circumference in only 31% (9/29) of specimens at the MCP joint.

CONCLUSION
The EIP tendon is frequently ulnar to and greater in circumference than the EDCI at the distal extensor retinaculum, which can be taken into consideration for tendon transfers involving EIP.

Key Words: Surgical anatomy; Tendon transfer; Extensor digitorum communis; Extensor indicis proprius; Tendon harvest; Cadaveric Dissection

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Core Tip: We found that extensor indicis proprius (EIP) was consistently ulnar to extensor digitorum communis to the index in 96.5% of specimens at the distal extensor retinaculum. The EIP had a greater circumference in 76% (22/29) of specimens at the distal extensor retinaculum. This research contributes to the body of knowledge on extensor tendon anatomy and facilitates the smaller incisions and dissection of EIP needed for tendon transfers.

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INTRODUCTION

The extensor indicis proprius (EIP) is a redundant extrinsic extensor of the index finger. It is present in 96.5% of the population and is commonly used for tendon transfers[1]. To correctly harvest the EIP and plan procedural incisions, a thorough understanding of the arrangement of the extensor tendons and their junctural connections is required.

Understanding the variability in anatomic relationships is important when harvesting EIP through a small incision. These variations have been documented in clinical and anatomic studies[2]. The EIP originates from the dorsal aspect of the ulna, the interosseus membrane, and the extensor pollicis longus (EPL) septum[3]. It has the most distal muscle belly of all the extensor tendons, and is the only muscle belly that enters the fourth compartment, under the extensor retinaculum and deep to the extensor digitorum communis (EDC) tendons[1]. Multiple studies have noted that anatomic variants are frequent (10%)[4-7] with regards to arrangement and number of slips. Defining each slip as the presence of independent fascial sheaths at the metacarpal level, the EIP has been cited to have double slips in 16% and triple slips in 7% of cadaveric studies[5]. Gonzalez *et al*[6] classified the arrangement of EIP and extensor digitorum communis to the index (EDCI) at the metacarpophalangeal (MCP) joint into six types: (1) Single EIP ulnar to a single EDCI; (2) Single EDCI between two slips of EIP; (3) Two slips of EIP ulnar to a single EDCI; (4) Single EIP ulnar to two slips of EDCI; (5) Single EIP radial to a single EDCI; and (6) Single EIP volar to a single EDCI. The most common arrangement is a single EIP inserting ulnar to a single EDCI on the extensor hood in 81%-98.3% of specimens[1,4,6], volar to the EDCI in 10% to 11%[4,5,7], and radial to EDCI in 3%-8%[5]. In other tendon transfers, tendon circumference may also be used as a distinguishing characteristic. Celik *et al*[8] examined the width and thickness of EDCI and EIP tendons at the level of mid-diaphyseal metacarpal bones and found similar thickness for EDCI and EIP (1.5 mm ± 0.4 mm and 1.47 mm ± 0.38 mm respectively). To our knowledge, no studies have examined the relationship and anatomy of the EIP and EDCI at the level of tendon harvest.

Clinical relevance

EPL ruptures occur in 0.7% of non-displaced distal radius fractures and 3% of dorsally displaced distal radius fractures[9,10]. Tendon attrition is attributed to friction and compression in the poorly vascularized third compartment between the extensor retinaculum and displaced bone fragments of the dorsal radial tubercle[11]. EIP to EPL transfer is one of the most common tendon transfers in the upper extremity. In addition to anatomic proximity and its redundancy for index finger extension, EIP is synergistic to EPL: The motion of extending the index finger and the thumb interphalangeal (IP) joint is commonly performed together during tasks, allowing patients to recover thumb extension after transfer without extensive relearning. Many techniques exist for harvesting and performing this tendon transfer. The incision for harvest can be made longitudinally or transversely, at the level of the distal or proximal extensor retinaculum, and transfer can occur with two incisions or three with a pulvertaft distal to the retinaculum[12]. Classically described, this tendon transfer has been performed through three incisions: A transverse incision over the MCP joint to transect the ulnar EIP, a longitudinal incision over the thumb metacarpal to dissect out the ruptured tendon and carry out the transfer, and a longitudinal

incision at the extensor retinaculum to identify EIP and perform tendon harvest. However, technique adaptations may be considered that use the anatomic relationship of these tendons. We performed a cadaveric study to evaluate the relationship between EDCI and EIP and share our preferred surgical technique for EIP to EPL tendon transfer. We sought to characterize the circumference and relationship of the EIP and EDCI tendons at the distal extensor retinaculum, which is relevant for tendon identification when performing an EPL transfer.

MATERIALS AND METHODS

Specimens

Twenty-nine skeletally mature fresh frozen cadaveric forearms ages 19 to 52 were obtained. Clinical histories confirmed no previous trauma or surgery to the donor. Tendons were defined as independent bands originating from muscle. Tendons were occasionally divided into one or more separable smaller slips at the retinaculum. Individual slips were defined distal to the muscle belly with independent fascial sheaths.

Dissection

All specimens were dissected with a single dorsal longitudinal incision made just ulnar to Lister's tubercle extending from the index MCP joint to proximal to the extensor retinaculum. Subcutaneous fat and superficial nerves and veins were elevated in a single flap and tenosynovium was dissected off the EDCI and EIP. The extensor retinaculum was identified as oblique transverse fibers with roughly parallel proximal and distal edges. A 4-0 Prolene suture was used to measure the circumference of the two tendons at the distal edge of extensor retinaculum and the MCP joint (Figure 1) with a single simple knot, and dissection scissors were used to cut the knot at the intersection. The remaining Prolene suture was then measured with a ruler to derive circumference of the tendon. Prolene was chosen for its high intrinsic memory and thus decreased risk for error in measurement of small caliber circumference tendons[13]. The distance in millimeters between the distal edge of the extensor retinaculum and the myotendinous junction of EIP was measured as well. All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2008.

Statistics

To assess our sample with a statistical two-tailed significance of 0.05, power of 80%, and effect size r = 0.6, our a priori power analysis yielded a sample size of 25 was required. Paired t-tests were applied to compare the values obtained from the EIP and EDCI tendon measurements at the distal extensor retinaculum and MCP joint. $P < 0.05$ was considered to be significant.

RESULTS

Twenty-nine fresh frozen human cadaver forearms were dissected. They were from 20 men and 9 women. The right forearm was dissected in 16 cases and the left in 13 cases. None of the specimens had vascular or nerve variations that were apparent upon dissection. None had evidence of prior surgery to the hand, forearm, or wrist, and clinical histories of the specimens confirmed no history of trauma to the area.

In all but one specimen, the EIP tendon was ulnar to the EDCI tendon (96.5%, 28/29); in the remaining specimen, the EIP was volar to the EDCI. The tendon circumference at the distal edge of the extensor retinaculum averaged 9.3 mm (± 1.7 mm) for the EDCI and 11.1 mm (± 2.7 mm) for the EIP (P = 0.001). The tendon circumference at the index MCP joint was measured to be 11.0 mm (± 1.7 mm) for the EDCI and 10.6 mm (± 2.1 mm) for the EIP (P = 0.331). The EIP had a greater circumference in 76% (22/29) of specimens at the distal extensor retinaculum whereas the EIP had a greater circumference in 31% (9/29) of specimens at the MCP joint. The distance from the distal extensor retinaculum to the myotendinous junction of EIP varied widely but averaged 16.2 mm (± 11.1 mm), which is similar to findings in other studies[11] (Table 1). We did not find significant differences in tendon circumference between specimens of different sex, but overall the tendon circumferences were lower for females as compared to male specimens (Table 2). In addition, the distance between the distal extensor retinaculum to myotendinous junction was lower in female specimens compared to that of males (Table 2); this was also not statistically significant.

In one specimen, the EIP tendon was split at the extensor retinaculum, with the radial branch joining the EDCI tendon at the MCP. However, both slips of the EIP were still found to be ulnar to the EDCI tendon at the distal extensor retinaculum (Figure 2).

Table 1 Specimen demographics and measurements

Laterality	Age (yr)	Sex	Circumference at dER (mm)		Circumference at MCP (mm)		EIP distance from dER to myotendinous junction (mm)	Relationship of EIP to EDCI
			cEDCI	cEIP	cEDCI	cEIP	EIP	
Left	52	M	8	15	12	14	29	EIP ulnar
Left	54	F	9	10	13	10	15	EIP ulnar
Right	38	M	12	13	12	12	16	EIP ulnar
Left	48	M	12	15	14	13	15	EIP ulnar
Right	54	F	11	11	13	9	14	EIP ulnar
Right	30	M	7	8	11	8	20	EIP ulnar
Left	24	M	11	12	9	10	18	EIP ulnar
Right	44	M	9	14	11	14	23	EIP ulnar
Left	38	F	9	8	10	9	27	EIP ulnar
Right	57	F	9	12	11	13	18	EIP ulnar
Right	19	M	8	9	10	10	2	EIP ulnar
Right	44	M	11	13	11	11	37	EIP ulnar
Left	30	M	7	5	14	9	22	EIP ulnar
Left	49	F	9	13	10	10	4	EIP ulnar
Left	19	M	9	9	8.5	11	2	EIP ulnar
Right	48	M	9	8	9	9	48	EIP ulnar
Right	48	M	8	14	12	14	25	EIP ulnar
Left	44	M	11	13	12	8	17	EIP ulnar
Right	24	M	10	14	13	12	13	EIP ulnar
Left	35	M	14	10	14	10	10	EIP ulnar
Left	20	M	9	11	10	8	2	EIP ulnar
Right	20	M	9	13	8	11	3	EIP volar
Left	20	F	10	7	11	8	10	EIP ulnar
Right	21	F	9	10	10	9	3	EIP ulnar
Left	40	M	7	11	10	8	24	2 slips of EIP ulnar
Right	49	F	7	8	11	11	4	EIP ulnar
Right	33	M	9	12	9.5	12	18	EIP ulnar
Right	20	F	9	10	9	8	6	EIP ulnar
Left	33	M	9	15	11	15	24	EIP ulnar
Average	36.4		9.3	11.1	11.0	10.6	16.2	
Standard deviation	12.7		1.7	2.7	1.7	2.1	11.1	

dER: Distal extensor retinaculum; MCP: Metacarpophalangeal; EIP: Extensor indicis proprius; EDCI: Extensor digitorum communis to the index; M: Male; F: Female.

DISCUSSION

Although EIP has a role in index finger extension, it also possesses utility in tendon transfers. It is most often used in cases of EPL rupture, and many anatomic studies have been performed on extensor tendon variations[1,4,8,14]. The causes of these differences remain obscure, although differences in racial grouping have been suggested. South Asian populations have the highest rate of single-slip EIP and the lowest rate of double-slip EIP when compared to Japanese, Europeans and North Americans[1].

Table 2 Measurements of extensor indicis proprius and extensor digitorum communis to the index tendons, segregated by gender

Sex	Age (yr) ± Std	Circumference at dER (mm) ± Std		Circumference at MCP (mm) ± Std		EIP distance from dER to myotendinous junction (mm) ± Std
		cEDCI	cEIP	cEDCI	cEIP	EIP
M	34.7 ± 11.1	9.5 ± 1.9	11.7±2.8	11.1 ± 1.8	11.0 ± 2.3	18.4 ± 11.8
F	40.2 ±1 5.8	9.1 ± 1.1	9.9 ± 2.0	10.9 ± 1.4	9.7 ± 1.6	11.2 ± 8.0
P value	0.28	0.56	0.09	0.77	0.14	0.11

Std: Standard deviation; dER: Distal extensor retinaculum; MCP: Metacarpophalangeal; EIP: Extensor indicis proprius; EDCI: Extensor digitorum communis to the index; M: Male; F: Female.



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Figure 1 Tendon circumference measurement. Tendon circumference was measured utilizing 4-0 prolene at distal extensor retinaculum and at the metacarpophalangeal joint for both the extensor indicis proprius and extensor digitorum communis to the index tendons. Prolene was used to obtain accurate circumference measurements. The distal extensor retinaculum was marked prior to measurements to ensure repeatability and consistent measurement to the myotendinous junction.



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Figure 2 Interesting case of a split extensor indicis proprius tendon that joined the extensor digitorum communis to the index tendon. A specimen in which the EIP consisted of two slips, one of which arose from the extensor indicis proprius and joined the extensor digitorum communis to the index just proximal to the metacarpophalangeal joint.

We chose to measure EIP and EDCI circumference at the distal edge of the extensor retinaculum because this is where EIP is typically harvested to attain sufficient tendon length for transfer. Given that the EIP has the most distal muscle belly, often in the extensor retinaculum, we hypothesized that the EIP would have a greater circumference than the EDCI at the distal extensor retinaculum. Although the EIP circumference 11.1 mm (± 2.7 mm) was statistically greater than EDCI circumference 9.3 mm (± 1.7 mm) (P = 0.001), this was found to be true in only in 76% (22/29) of specimens. Perhaps this could be attributed to the wide variety in distance between the distal edge of the extensor retinaculum and the muscle belly of EIP, which averaged 16.2 mm (± 11.1 mm), similar to findings in other studies[11].

Although we hypothesized that a smaller distance between the myotendinous junction of EIP and the distal edge of the extensor retinaculum would be associated with a greater difference in circumference between EIP and EDCI, this was not found to be statistically significant (P = 0.510).

In 28/29 specimens with a single insertion for EIP, the EIP was located ulnar to the EDCI at the extensor retinaculum. It was located directly volar in the other specimen. The specimen with a split EIP had both branches ulnar to EDCI. These findings are consistent with the known literature where the vast majority (approximately 99%) of single slip EIP tendons are ulnar to EDCI[15], even when 7% of EIPs had two slips and of these, half had both tendons ulnar[1]. These findings are useful when identifying tendons for transfer with small transverse incisions at the distal extensor retinaculum. Although there are other reports of minimally invasive single incision EIP to EPL transfer[15] with a 3 cm incision placed midway between the course of the EIP and EPL at the level of mid-diaphyseal metacarpal, we believe the frequent anatomic variations in the EDCI and EIP relationship warrant additional incisions for EIP harvest and identification.

Preferred surgical technique

Given the finding of the frequently more ulnar EIP to EDCI tendon at the level of the distal extensor retinaculum, we recommend performing a small transverse as opposed to a longitudinal incision at the extensor retinaculum, allowing for a more cosmetic scar. Here, we share our preferred technique using wide awake local EIP to EPL tendon transfer[16].

Begin by injecting 30 mL of 1% lidocaine with 1 : 100000 epinephrine 2 cm beyond the distal extent of the planned incisions. For incisions, we recommend a small 1 cm transverse incision just ulnar to Lister's tubercle at the distal aspect of the extensor retinaculum over the EIP tendon, a 1cm transverse incision over the index metacarpophalangeal joint, and a 2 cm longitudinal incision over the thumb carpometacarpal joint, where the distal stump of the EPL is often located for transfer. At the distal extensor retinaculum, fully flex the wrist and identify the ulnar EIP tendon. Perform a small 1cm transverse incision at the index MCP joint to transect the more ulnar EIP tendon. The extensor indicis is consistently "free" from junctura tendinae[3,8], and after dissecting the EIP tendon from EDCI, a small Ragnell retractor may be used to harvest the EIP tendon through the 1 cm incision at the distal extensor retinaculum. A transverse incision acknowledging the frequent relationship of the EIP being more ulnar or volar to EDCI at the distal extensor retinaculum avoids the longitudinal incision previously used by the authors for dissection to the myotendinous junction, improving cosmesis with an incision hidden along Langer's lines. Use a single 4-0 Fiberwire (Arthrex, Naples, FL) suture to secure any remaining distal EIP tendon stump to EDCI at the MCP joint to prevent the tendon stump from interfering with range of motion of the MCP joint. Transfer the harvested tendon subcutaneously into the longitudinal thumb incision (underneath dorsal radial branch of radial nerve), leaving the tendon in the extensor retinaculum. Use a tendon weaver to make 3 Pulvertaft weaves at 90 degree angles to each other and set the appropriate tension for the tendon to allow full extension of MCP and IP joints, or just shy of full extension to accommodate for loosening of the transfer. Place a single 4-0 Fiberwire suture before asking the patient to move the thumb. Check full flexion and full extension to ensure appropriate range of motion. Place a 4-0 Fiberwire horizontal mattress suture through each subsequent weave. Splint in thumb spica with thumb fully extended for 4 wk and start the retraining process with a hand therapist. In cases of suspected abnormal anatomy, we recommend following the EIP tendon proximally with an additional incision at the myotendinous junction to evaluate for the most distal muscle belly in order to isolate the correct slip(s) for tendon transfer. Should there be a split tendon, consider using a single slip for the tendon transfer.

Limitations

Although a power analysis was implemented to detect significance for an effect size of 0.6 with 2 mm difference in tendon circumference, it is inadequately powered to capture all variations due to the relatively low incidence of these tendon variations. We performed our dissections from a random selection of cadaveric specimens but there is a chance that it is not representative of the population as a whole. Lastly, there is a chance of measurement error given the small values being analyzed. To counteract this, Prolene, a synthetic monofilament composed of isostatic crystalline stereoisomer of polypropylene was chosen for its intrinsic high memory characteristics and thus decreased risk for error in measurement with small caliber tendons[13]. Considering these limitations, we believe that our study is well designed to accurately depict the relationship between the EIP and EDCI at the distal retinaculum and builds on the existing literature characterizing the complex relationship of dorsal hand tendons.

CONCLUSION

We found that EIP was consistently ulnar to EDCI in 96.5% of specimens at the distal extensor retinaculum. The EIP had a greater circumference in 76% (22/29) of specimens at the distal extensor retinaculum. This research contributes to the body of knowledge on extensor tendon anatomy and

facilitates the smaller incisions and dissection of EIP needed for tendon transfers.

ARTICLE HIGHLIGHTS

Research objectives

We sought to characterize the arrangement and circumference of the extensor indicis proprius (EIP) tendon with respect to the extensor digitorum communis tendon to the index finger (EDCI) at the level of the extensor retinaculum, where tendon harvest is often performed, and share our preferred technique for EIP to extensor pollicis longus (EPL) transfer.

Research methods

Twenty-nine fresh-frozen cadaveric forearms were dissected. Tendon circumference and relationship of the EIP and EDCI at the metacarpophalangeal (MCP) joint and the distal extensor retinaculum were recorded. Distance from the distal extensor retinaculum to the EIP myotendinous junction was measured.

Research results

EIP was ulnar to the EDCI in 96.5% of specimens (28/29) at the distal edge of the extensor retinaculum. In the remaining specimen, EIP was volar to EDCI. Tendon circumference at the distal extensor retinaculum averaged (9.3 mm ± 1.7 mm) for EDCI and 11.1 mm (± 2.7 mm) for EIP (P = 0.0010). The tendon circumference at the index MCP joint averaged 11.0 mm (± 1.7 mm) for EDCI and 10.6 mm (± 2.1 mm) for EIP (P = 0.33). EIP had a greater circumference in 76% (22/29) of specimens at the distal extensor retinaculum whereas EIP had a greater circumference in only 31% (9/29) of specimens at the MCP joint.

Research conclusions

The EIP tendon is frequently ulnar to and greater in circumference than the EDCI at the distal extensor retinaculum, suggesting a minimally invasive approach to tendon transfer using transverse incisions hidden in Langer's lines would be effective and safe.

Research perspectives

This research contributes to the body of knowledge on extensor tendon anatomy and facilitates the smaller incisions and dissection of EIP needed for tendon transfers.

Research motivation

Understanding the variability in anatomic relationships is important when harvesting EIP through a small incision. To our knowledge, no studies have examined the relationship and anatomy of the EIP and EDCI at the level of tendon harvest at the distal extensor retinaculum.

Research background

The EIP is a redundant extrinsic extensor of the index finger, commonly used in tendon transfer for EPL ruptures. Many variations of the course and arrangement of the tendons have been previously described. It is important to understand the arrangement and anatomy of the EIP tendon at the level of tendon harvest.

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FOOTNOTES

Author contributions: Zhou J contributed to study design, dissections, statistical analysis, and writing the manuscript; Frey C contributed to study design, dissections, statistical analysis, and writing the manuscript; Segovia N carried out statistical analyses and assisted with manuscript revisions; Yao J contributed to study design and manuscript revisions.

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REFERENCES

1 **Yammine K**. The prevalence of the extensor indicis tendon and its variants: a systematic review and meta-analysis. *Surg Radiol Anat* 2015; **37**: 247-254 [PMID: 25096501 DOI: 10.1007/s00276-014-1352-0]
2 **Hirai Y**, Yoshida K, Yamanaka K, Inoue A, Yamaki K, Yoshizuka M. An anatomic study of the extensor tendons of the human hand. *J Hand Surg Am* 2001; **26**: 1009-1015 [PMID: 11721244 DOI: 10.1016/S0363-5023(01)70045-7]
3 **Zilber S**, Oberlin C. Anatomical variations of the extensor tendons to the fingers over the dorsum of the hand: a study of 50 hands and a review of the literature. *Plast Reconstr Surg* 2004; **113**: 214-221 [PMID: 14707639 DOI: 10.1097/01.PRS.0000091163.86851.9C]
4 **von Schroeder HP**, Botte MJ. Anatomy of the extensor tendons of the fingers: variations and multiplicity. *J Hand Surg Am* 1995; **20**: 27-34 [PMID: 7722260 DOI: 10.1016/S0363-5023(05)80053-X]
5 **von Schroeder HP**, Botte MJ. Anatomy and functional significance of the long extensors to the fingers and thumb. *Clin Orthop Relat Res* 2001; 74-83 [PMID: 11210972 DOI: 10.1097/00003086-200102000-00010]
6 **Gonzalez MH**, Weinzweig N, Kay T, Grindel S. Anatomy of the extensor tendons to the index finger. *J Hand Surg Am* 1996; **21**: 988-991 [PMID: 8969421 DOI: 10.1016/S0363-5023(96)80305-4]
7 **Mestdagh H**, Bailleul JP, Vilette B, Bocquet F, Depreux R. Organization of the extensor complex of the digits. *Anat Clin* 1985; **7**: 49-53 [PMID: 3994853 DOI: 10.1007/BF01654629]
8 **Celik S**, Bilge O, Pinar Y, Govsa F. The anatomical variations of the extensor tendons to the dorsum of the hand. *Clin Anat* 2008; **21**: 652-659 [PMID: 18792963 DOI: 10.1002/ca.20710]
9 **Skoff HD**. Postfracture extensor pollicis longus tenosynovitis and tendon rupture: a scientific study and personal series. *Am J Orthop (Belle Mead NJ)* 2003; **32**: 245-247 [PMID: 12772876]
10 **Heidemann J**, Gausepohl T, Pennig D. [Narrowing of the third extensor tendon compartment in minimal displaced distal radius fractures with impending rupture of the EPL tendon]. *Handchir Mikrochir Plast Chir* 2002; **34**: 324-327 [PMID: 12494385 DOI: 10.1055/s-2002-36303]
11 **Lepage D**, Tatu L, Loisel F, Vuillier F, Parratte B. Cadaver study of the topography of the musculotendinous junction of the finger extensor muscles: applicability to tendon rupture following closed wrist trauma. *Surg Radiol Anat* 2015; **37**: 853-858 [PMID: 25577541 DOI: 10.1007/s00276-015-1417-8]
12 **Schneider LH**, Rosenstein RG. Restoration of extensor pollicis longus function by tendon transfer. *Plast Reconstr Surg* 1983; **71**: 533-537 [PMID: 6828587 DOI: 10.1097/00006534-198304000-00015]
13 **Swanson NA**, Tromovitch TA. Suture materials, 1980s: properties, uses, and abuses. *Int J Dermatol* 1982; **21**: 373-378 [PMID: 6752052 DOI: 10.1111/j.1365-4362.1982.tb03154.x]
14 **Ozturk K**, Kastamoni Y, Dursun A, Albay S. Prevalence of the extensor digitorum, extensor digiti minimi and extensor indicis tendons and their variations. *Hand Surg Rehabil* 2020; **39**: 320-327 [PMID: 32259596 DOI: 10.1016/j.hansur.2020.02.010]
15 **Lahiri A**. A Simple and Quick Tendon Transfer Technique to Restore Thumb Function OPEN ACCESS Surgical Technique. *World J Surg Surg Res* 2020; **3**: 1208
16 **Lalonde DH**. Wide-awake extensor indicis proprius to extensor pollicis longus tendon transfer. *J Hand Surg Am* 2014; **39**: 2297-2299 [PMID: 25283490 DOI: 10.1016/j.jhsa.2014.08.024]

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ORIGINAL ARTICLE

Retrospective Cohort Study

Can immediate postoperative radiographs predict outcomes in pediatric clubfoot?

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Abstract

BACKGROUND

The goal of treatment for pediatric idiopathic clubfoot is to enable the patient to comfortably walk on his or her soles without pain. However, currently accepted treatment protocols are not always successful. Based on the abnormal bone alignment reported in this disease, some studies have noted a correlation between radiographic characteristics and outcome, but this correlation remains debated.

AIM

To assess the correlation between immediately postoperative radiographic parameters and functional outcomes and to identify which best predicts functional outcome.

METHODS

To predict the outcome and prevent early failure of the Ponseti's method, we used a simple radiographic method to predict outcome. Our study included newborns with idiopathic clubfoot treated with Ponseti's protocol from November 2018 to August 2022. After Achilles tenotomy and a long leg cast were applied, the surgeon obtained a single lateral radiograph. Radiographic parameters included the tibiocalcaneal angle (TiCal), talocalcaneal angle (TaCal), talofirst metatarsal angle (Ta1st) and tibiotalar angle (TiTa). During the follow-up period, the Dimeglio score and functional score were examined 1 year after surgery. Additionally, recurring events were reported. The correlation between functional score and radiographic characteristics was analyzed using sample and multiple logistic regression, and the optimal predictor was also identified.

RESULTS

In total, 54 feet received approximately 8 manipulations of casting and Achilles tenotomy at a mean age of 149 days. The average TiCal, TaCal, Ta1st, and TiTa angles were 75.24, 28.96, 7.61, and 107.31 degrees, respectively. After 12 mo of follow up, we found 66% excellent-to-good and 33.3% fair-to-poor functional

outcomes. The Dimeglio score significantly worsened in the poor outcome group (P value < 0.001). Tical and TaCal showed significant differences between each functional outcome (P value < 0.05), and the TiCal strongly correlated with outcome, with a smaller angle indicating a better outcome, each 1 degree decrease improved the functional outcome by 10 percent. The diagnostic test revealed that a TiCal angle of 70 degrees predicts an inferior functional outcome.

CONCLUSION

The TiCal, derived from lateral radiographs immediately after Achilles tenotomy, can predict functional outcome at 1 year postoperatively, justifying its use for screening patients who need very close follow-up.

Key Words: Idiopathic clubfoot; Radiograph; Functional outcome; Tenotomy; Prognostic; Tibiocalcaneal angle

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Core Tip: Idiopathic clubfoot is an abnormality of bone alignment. Current treatment strategies are associated with recurrence, which results in pain and poor quality of life. Radiography-assisted outcome prediction must be harmless in young children. The lateral tibiocalcaneal angle was directly related to functional outcomes, as a smaller angle was associated with a better outcome. A lateral tibiocalcaneal angle exceeding 70 degrees immediately after Achilles tenotomy predicted an inferior outcome.

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INTRODUCTION

Talipes equinovarus, known as idiopathic clubfoot, is a complexity inside the bone of the foot, with a birth prevalence of approximately 1-3 cases per thousand born[1,2]. The treatment goals are painlessness and a plantigrade walk. Currently, Ponseti's technique, which includes casting, Achilles tenotomy and bracing, is the accepted treatment strategy, but up to 11%-48% recurrence has been found [3-7].

However, Ponseti noted that radiography cannot predict prognosis because it is not associated with clinical appearance[8]. Nevertheless, some reports identified a significant relationship between preoperative radiographs and treatment decisions. For example, a lateral tibiocalcaneal angle > 80 degrees indicates a need for Achilles tenotomy[9]. In 2015, a retrospective study found that a preoperative dorsiflex angle > 16.6 degrees did not require reoperation and was related to recurrence [10]. Furthermore, a lateral tibiocalcaneal angle > 77 degrees and lateral talocalcaneal angle < 29 degrees at the time of brace withdrawal predicts reoperation[11].

The purposes of this study were as follows: To demonstrate the correlation between immediately postoperative radiographic parameters and functional outcome. To identify the radiographic parameter that best predicts functional outcome.

MATERIALS AND METHODS

Population

This work was a retrospective cohort study conducted from November 2018 to August 2022. Any newborn patient who was diagnosed with idiopathic clubfoot was included. Exclusion criteria included syndromic clubfoot, recurrent cases and patients who had received previous treatment. All patients underwent weekly manipulation of their feet according to the Ponseti technique, followed by Achilles tendon tenotomy and long leg cast application. Immediately after this procedure, the surgeon took one radiograph of the lateral foot and ankle.

Radiography and clinical parameters

In an attempt to predict the outcome and prevent early failure of the Ponseti's method, we used a simple radiographic method to predict outcome because radiographic postoperative studies are lacking

and radiographic assessment is not associated with disadvantages[12].

Radiographic parameters included the tibiocalcaneal angle (TiCal), talocalcaneal angle (TaCal), talofirst metatarsal angle (Ta1st) and tibiotalar angle (TiTa) (Figure 1). Foot characteristics were evaluated according to the Dimeglio classification, and functional scores were assessed 1 year after surgery, as described by Ponseti, and interpreted as follows: A total score < 70, 70-79, 80-89, and 90-100 represents poor, fair, good, and excellent outcomes, respectively[13]. Additionally, recurring events were reported if further surgery was needed. Data were analyzed by 2 observers, a fourth-year resident orthopedic training and pediatric orthopedic surgeon, and interrater reliability was confirmed using the kappa statistic.

Statistical analysis

All statistical analyses were performed using STATA 11 statistical software (Stata Corp., College Station, TX, United States). The chi-squared test and Fisher's exact test were used to assess independence between two dichotomous variables. The chi-squared test was applied under the assumption that the sample was large. When more than 20 percent of cells had expected frequencies < 5, the Fisher's exact test was run for small-sized samples. The two-sample *t*-test was used to compare the mean of continuous variables, and the Mann-Whitney U test was used when the variable did not have a normal distribution. Logistic regression by using a penalized maximum likelihood estimation method was used to determine factors associated with functional scores, *P* value < 0.05 was considered statistically significant and the magnitude of association was shown as crude odds ratios (OR), adjusted OR, and 95% confidence intervals (CI).

RESULTS

The study included 54 feet from 35 newborn patients with clubfoot. All feet received manipulation, and a long leg cast was applied approximately 8 times on average. Then, the Achilles tenotomy procedure was performed at an average age of 149 days. Immediately after surgery and cast application, we obtained radiographs and found that the average TiCal, TaCal, Ta1st, and TiTa angles were 75.24, 28.96, 7.61, and 107.31 degrees, respectively. After the last cast was removed, the brace protocol was utilized as usual, and the Dimeglio score significantly worsened in the poor outcome group (*P* value < 0.001), which was clearly evident 6 mo postoperatively. After 12 mo of follow up, 24% of cases required further surgery, 66% of cases had an excellent-to-good functional outcome and 33.3% of cases had a fair-to-poor functional outcomes. Demographic data did not significantly differ between groups, as shown in Table 1.

Table 2 presents the significant differences in the Tical and TaCal angles between each functional outcome (*P* value < 0.05), and the TiCal angle was strongly predictive of outcome, as shown in Table 3. Furthermore, the study shows that a lower TiCal angle corresponded to a better outcome, with an adjusted odds ratio of 0.90 (0.83-0.99). Specifically, each 1 degree decrease improved the functional outcome by 10 percent. The diagnostic test revealed that a TiCal angle of 70 degrees predicts an inferior functional outcome, with 88.9% sensitivity, 41.7% specificity, and 0.56 ROC area (95%CI: 0.42-0.70).

DISCUSSION

Idiopathic clubfoot is the most common multifactorial irreducible foot problem in newborns[2,14]. To date, the Ponseti protocol is widely utilized to treat this condition, in which the deformity is corrected sequentially by Achilles tenotomy and a brace is applied. However, a previous study showed a 33%-41% rate of recurrence[15,16]. Clubfoot is pathogenically characterized by abnormal bone alignment and abnormal radiographic features compared with normal feet, including bony abnormalities from incorrect treatment, whereas radiographic features from correct treatment are obviously better than pre-treatment[17,18].

This study found a correlation between radiographic data, lateral tibiocalcaneal and talocalcaneal angles derived immediately postoperation, and functional outcomes at the 12 mo follow-up. This finding is in agreement with a previous report that supports the use of radiographs for treatment guidance, especially in residual deformity correction, such as complete subtalar release or postero-medial release procedures[19-21].

The tibiocalcaneal angle was the most reliable feature for predicting outcome in the present study, as a smaller angle predicted a better outcome based on the plantigrade ability. We found that a cutoff point of > 70 degrees could predict fair-to-poor functional outcome at walking age with 88.9% sensitivity, similar to the equinus position, which results in a poor quality of life. Similarly, previous studies recommended using this angle to predict risk of relapse and decide the surgical type, such as Achilles tenotomy, soft tissue release, and even reconstructive procedures for recurrent clubfoot, to improve functional outcome, but these studies investigated older children[8,10,11,22,23]. Additionally, a close relationship of clinical and talocalcaneal and talo-1st metatarsal angles was found in some studies[17,24,

Table 1 Demographic data for the excellent/good and fair/poor functional groups

Demographic data	Excellent and good group (*n* = 36)	Fair and poor group (*n* = 18)	Mean different (95%CI)	*P* value
Male, *n* (%)	26 (72.22)	11 (61.11)	-	0.407[b]
Number of casts	8.69 (3.05)	8.33 (3.39)	-0.36 (-2.19, 1.47)	0.6950[a]
Age at tenotomy (d), mean (SD)	144 (53.52)	161.55 (69.11)	17.55 (-16.66, 51.77)	0.3081[a]
Brace compliance, *n* (%)	29 (80.56)	17 (94.44)	-	0.245[c]

[a]Independent samples *t* test.
[b]Pearson chi square test.
[c]Fisher's exact test. SD: Standard error.

Table 2 Mean range of each radiographic angle in clubfeet patients after surgery in lateral view

Angle	Excellent and good group, mean (SD)	Fair and poor group, mean (SD)	Mean different (95%CI)	*P* value[a]
Tibiocalcaneal angle	72.55 (10.36)	80.61 (7.76)	8.05 (2.49, 13.61)	0.0053
Talocalcaneal angle	31.66 (11.92)	23.55 (12.00)	-8.11 (-15.03, -1.18)	0.0225
Talofirst metatarsal angle	7.72 (7.83)	7.38 (5.23)	-0.33 (-4.44, 3.77)	0.8713
Tibiotalar angle	107.72 (11.73)	106.50 (15.53)	-1.22 (-8.80, 6.36)	0.7478

[a]Independent samples *t* test.

Table 3 Correlation of radiographic parameters and functional outcomes

Angle	Functional score, excellent and good group (*n* = 36), fair and poor group (*n* = 18)		
	Crude odds ratio (95%CI)[a]	Adjusted odds ratio (95%CI)	*P* value[b]
Tibiocalcaneal angle	0.90 (0.84-0.97)	0.90 (0.83-0.99)	0.031
Talocalcaneal angle	1.06 (1.00-1.12)	1.04 (0.97-1.11)	0.199
Talofirst metatarsal angle	1.00 (0.92-1.09)	0.99 (0.89-1.10)	0.916
Tibiotalar angle	1.00 (0.96-1.05)	1.01 (0.95-1.07)	0.707

[a]Simple logistic regression.
[b]Multiple logistic regression. CI: Confidence interval.

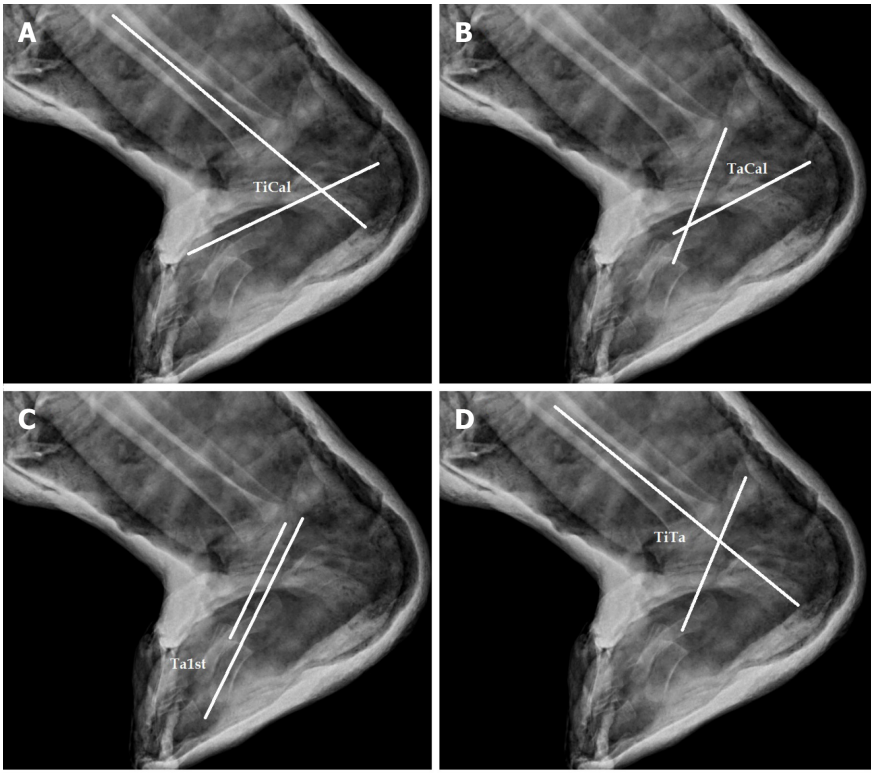
25].

Although a later study from 2017 discovered that radiographic abnormalities are not indicative of clinical abnormalities and that the Ponseti method can improve foot shape but cannot correct bone deformities, the treatment protocol needs to be based on various data sources[8,26]. Radiography is a criterion to screen patients who need very close follow-up.

This study has the following strengths: (1) We used functional outcome as the end result instead of recurrence because recurrence is a subjective assessment that the surgeon utilizes to determine whether to perform additional interventions; (2) We analyzed only ossified bone to provide more accurate results; and (3) We based our analysis on one lateral view radiograph, which is harmless to patients, as shown in a previous study[12].

Limitations of the study

The small sample analyzed in this study precludes large effect sizes between groups. Furthermore, we calculated the angle based on only ossified bone in a small child for accuracy reasons. Consequently, we may lack information from other nonossified bone.



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Figure 1 Radiographic angles. A: The tibiocalcaneal angle was defined as the angle between the axis of the tibia and the axis of the calcaneus; B: The talocalcaneal angle was defined as the angle between the talus axis and the calcaneus axis'; C: Talofirst metatarsal angle was defined as the angle between the axis of the talus and the axis of the 1st metatarsal bone; D: The tibiotalar angle was defined as the angle between the axis of the tibia and the axis of the talus.

CONCLUSION

The tibiocalcaneal angle, derived from lateral radiographs immediately after Achilles tenotomy and casting, can predict functional outcome at 1 year postoperatively and provide a sufficient rationale for screening patients who need very close follow-up.

ARTICLE HIGHLIGHTS

Research background

Idiopathic clubfoot is an abnormal bone alignment and there are currently failure cases resulting from the currently acceptable treatment protocol. Postoperative radiographs are expected to predict outcomes beginning at the prewalking age.

Research motivation

To predict the outcome and early prevention in cases that may fail with Ponseti's method, considering the lack of radiographic postoperative studies and almost none of the disadvantages of radiation taken once, we decided to use the simple radiographic method for outcome prediction.

Research objectives

To assess the correlation between immediately postoperative radiographic parameters and functional outcomes.

Research methods

Patients with idiopathic clubfoot were assessed for radiographic parameters immediately postoperatively, and functional scores were assessed at follow-up.

Research results

The tibiocalcaneal and talocalcaneal angles showed significant differences between each functional outcome, and the tibiocalcaneal angle had a strong effect, with a smaller angle seeming better.

Research conclusions

The tibiocalcaneal angle, derived from lateral radiographs immediately after Achilles tenotomy and cast, can predict functional outcome at 1 year postoperatively.

Research perspectives

A larger population and long-term follow-up of 5 to 10 years would provide a better correlation of the radiographic parameters and functional outcomes.

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FOOTNOTES

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REFERENCES

1 **Pavone V**, Bianca S, Grosso G, Pavone P, Mistretta A, Longo MR, Marino S, Sessa G. Congenital talipes equinovarus: an epidemiological study in Sicily. *Acta Orthop* 2012; **83**: 294-298 [PMID: 22489891 DOI: 10.3109/17453674.2012.678797]
2 **Society for Maternal-Fetal Medicine**, McKinney J, Rac MWF, Gandhi M. Congenital talipes equinovarus (clubfoot). *Am J Obstet Gynecol* 2019; **221**: B10-B12 [PMID: 31787157 DOI: 10.1016/j.ajog.2019.09.022]
3 **Morcuende JA**, Abbasi D, Dolan LA, Ponseti IV. Results of an accelerated Ponseti protocol for clubfoot. *J Pediatr Orthop* 2005; **25**: 623-626 [PMID: 16199943 DOI: 10.1097/01.bpo.0000162015.44865.5e]
4 **Ponseti IV**, Smoley EN. Congenital club foot: the results of treatment. *Iowa Orthop J* 1984; **4**: 24-33
5 **Ponseti IV**. Relapsing clubfoot: causes, prevention, and treatment. *Iowa Orthop J* 2002; **22**: 55-56 [PMID: 12180612]
6 **Morcuende JA**, Dolan LA, Dietz FR, Ponseti IV. Radical reduction in the rate of extensive corrective surgery for clubfoot using the Ponseti method. *Pediatrics* 2004; **113**: 376-380 [PMID: 14754952 DOI: 10.1542/peds.113.2.376]
7 **Hosseinzadeh P**, Kiebzak GM, Dolan L, Zionts LE, Morcuende J. Management of Clubfoot Relapses With the Ponseti Method: Results of a Survey of the POSNA Members. *J Pediatr Orthop* 2019; **39**: 38-41 [PMID: 28178093 DOI: 10.1097/bpo.0000000000000953]
8 **Baghdadi T**, Bagheri N, Najafi A, Mansouri P, Farzan M. Ponseti Casting Method in Idiopathic Congenital Clubfoot and Its Correlation with Radiographic Features Abstract. *Arch Bone Jt Surg* 2017; **5**: 168-173 [PMID: 28656164]
9 **Kang S**, Park SS. Lateral tibiocalcaneal angle as a determinant for percutaneous achilles tenotomy for idiopathic clubfeet. *J Bone Joint Surg Am* 2015; **97**: 1246-1254 [PMID: 26246259 DOI: 10.2106/jbjs.o.00076]

10 **O'Halloran CP**, Halanski MA, Nemeth BA, Zimmermann CC, Noonan KJ. Can Radiographs Predict Outcome in Patients With Idiopathic Clubfeet Treated With the Ponseti Method? *J Pediatr Orthop* 2015; **35**: 734-738 [PMID: 25393569 DOI: 10.1097/bpo.0000000000000354]

11 **Shabtai L**, Hemo Y, Yavor A, Gigi R, Wientroub S, Segev E. Radiographic Indicators of Surgery and Functional Outcome in Ponseti-Treated Clubfeet. *Foot Ankle Int* 2016; **37**: 542-547 [PMID: 26704175 DOI: 10.1177/1071100715623036]

12 **Radler C**, Manner HM, Suda R, Burghardt R, Herzenberg JE, Ganger R, Grill F. Radiographic evaluation of idiopathic clubfeet undergoing Ponseti treatment. *J Bone Joint Surg Am* 2007; **89**: 1177-1183 [PMID: 17545419 DOI: 10.2106/jbjs.f.00438]

13 **Laaveg SJ**, Ponseti IV. Long-term results of treatment of congenital club foot. *J Bone Joint Surg Am* 1980; **62**: 23-31 [PMID: 7351412 DOI: 10.2106/00004623-198062010-00004]

14 **Pavone V**, Chisari E, Vescio A, Lucenti L, Sessa G, Testa G. The etiology of idiopathic congenital talipes equinovarus: a systematic review. *J Orthop Surg Res* 2018; **13**: 206 [PMID: 30134936 DOI: 10.1186/s13018-018-0913-z]

15 **Haft GF**, Walker CG, Crawford HA. Early clubfoot recurrence after use of the Ponseti method in a New Zealand population. *J Bone Joint Surg Am* 2007; **89**: 487-493 [PMID: 17332096 DOI: 10.2106/jbjs.f.00169]

16 **Ramírez N**, Flynn JM, Fernández S, Seda W, Macchiavelli RE. Orthosis noncompliance after the Ponseti method for the treatment of idiopathic clubfeet: a relevant problem that needs reevaluation. *J Pediatr Orthop* 2011; **31**: 710-715 [PMID: 21841450 DOI: 10.1097/BPO.0b013e318221eaa1]

17 **Prasad P**, Sen RK, Gill SS, Wardak E, Saini R. Clinico-radiological assessment and their correlation in clubfeet treated with postero-medial soft-tissue release. *Int Orthop* 2009; **33**: 225-229 [PMID: 17768623 DOI: 10.1007/s00264-007-0448-0]

18 **Addosooki A**, Tammam H, Morsy AF, Marzouq A, Ahmed EH, Ahmed AM, Said E. Correlation of radiographic parameters with clinical correction in idiopathic congenital talipes equinovarus undergoing Ponseti treatment. *Int Orthop* 2021; **45**: 3139-3146 [PMID: 34313808 DOI: 10.1007/s00264-021-05138-7]

19 **Tarraf YN**, Carroll NC. Analysis of the components of residual deformity in clubfeet presenting for reoperation. *J Pediatr Orthop* 1992; **12**: 207-216 [PMID: 1552024 DOI: 10.1097/01241398-199203000-00011]

20 **Yamamoto H**, Furuya K. One-stage posteromedial release of congenital clubfoot. *J Pediatr Orthop* 1988; **8**: 590-595 [PMID: 3170741 DOI: 10.1097/01241398-198809000-00018]

21 **Thometz J**, Manz R, Liu XC, Klein J, Manz-Friesth B. Reproducibility of radiographic measurements in assessment of congenital talipes equinovarus. *Am J Orthop (Belle Mead NJ)* 2009; **38**: 617-620 [PMID: 20145787]

22 **Moerman S**, Zijlstra-Koenrades N, Reijman M, Kempink DRJ, Bessems JHJM, de Vos-Jakobs S. The Predictive Value of Radiographs and the Pirani Score for Later Additional Surgery in Ponseti-Treated Idiopathic Clubfeet, an Observational Cohort Study. *Children (Basel)* 2022; **9** [PMID: 35740802 DOI: 10.3390/children9060865]

23 **Li J**, Xu C, Li Y, Liu Y, Xu H, Canavese F. Are early antero-posterior and lateral radiographs predictive of clubfoot relapse requiring surgical intervention in children treated by Ponseti method? *J Child Orthop* 2022; **16**: 35-45 [PMID: 35615392 DOI: 10.1177/18632521221080478]

24 **Ponseti IV**, El-Khoury GY, Ippolito E, Weinstein SL. A radiographic study of skeletal deformities in treated clubfeet. *Clin Orthop Relat Res* 1981; 30-42 [PMID: 7285433 DOI: 10.1097/00003086-198110000-00003]

25 **Uglow MG**, Clarke NM. The functional outcome of staged surgery for the correction of talipes equinovarus. *J Pediatr Orthop* 2000; **20**: 517-523 [PMID: 10912611 DOI: 10.1097/01241398-200007000-00018]

26 **Cohen-Sobel E**, Caselli M, Giorgini R, Giorgini T, Stummer S. Long-term follow-up of clubfoot surgery: analysis of 44 patients. *J Foot Ankle Surg* 1993; **32**: 411-423 [PMID: 8251997]

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ORIGINAL ARTICLE

Retrospective Study

Septic arthritis of the hand: From etiopathogenesis to surgical treatment

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Abstract

BACKGROUND

Septic arthritis of the hand, which is the second most common after damage of the knee joint, remains one of the leading causes of temporary disability. An inflammation can cause dysfunction of the joint, and in the most severe cases, the need for amputation of the finger may arise. The results of their treatment today, especially from a functional point of view, cannot be considered satisfactory. Urgent surgical treatment is extremely important in septic arthritis of the hand, as it helps to prevent cartilage destruction and the development of osteomyelitis.

AIM

To explore the features of the course of septic arthritis of the hand as well as approaches to surgical treatment and its results, depending on the nature of the damage to the articular structures.

METHODS

The results of the treatment of 170 patients with septic arthritis of the hand, which were treated in the period of 2020-2021, were analyzed. Inflammation of the

interphalangeal and metacarpophalangeal joints (MCP) of fingers 1, 2, and 3 was more often noted in 147 (81.6%) joints. The most common cause of arthritis was a penetrating injury as a result of household trauma (101, 59.4%), animal bite (30, 17.6%), and clenched fist injury (15, 8.8%). Septic arthritis with contiguous osteomyelitis was observed in 98 (54.4%) cases. Surgical treatment was completed with drainage and irrigation of the joint. Early mobilization was used to restore function. In patients with osteomyelitis, it was aimed at the formation of neoarthrosis. Arthrodesis was not applied. Long-term results of treatment were assessed in 142 (83.5%) patients within 1 mo to 12 mo after discharge from the hospital [the median was 7 mo (IQR: 4-9)].

RESULTS

The most commonly isolated organism was *Staphylococcus aureus* (35.3%). The median treatment delay in patients without osteomyelitis was 5 d (IQR: 4-7); for septic arthritis with contiguous osteomyelitis, it was 14 d (IQR: 5-21). Radiography for osteomyelitis within 2 wk was uninformative: 41.2% of diagnoses. A single surgical treatment was required in 138 (81.2%) patients, two treatments in 22 (12.9%), and three or more in 10 (5.9%). Total elimination of the infection was achieved in 163 (95.9%) patients. The best functional results of treatment were noted in patients without osteomyelitis. After septic arthritis, Total Active Motion (TAM) for the MCP was 96.2% (IQR: 85.1-98.0), for the proximal interphalangeal joint (PIP) 82.4% (IQR: 54.5-98.5), and for the distal interphalangeal joint (DIP) 69.4% (IQR: 65.4-74.1). In cases with osteomyelitis, it was possible to achieve the formation of neoarthrosis with TAM for MCP-64.2% (IQR: 45.3-90.1), for PIP-62.5% (IQR: 41.8-68.9), and for DIP-59.4% (IQR: 50-62.1). Additionally, the severity of pain during movements did not exceed 1 point.

CONCLUSION

The delay in treatment of patients with septic arthritis of the hand was accompanied by a high incidence of osteomyelitis, especially in the presence of diabetes mellitus. Urgent surgical treatment, along with continued irrigation of the joint and antibiotic therapy, made it possible to eliminate the infection, and early rehabilitation restored the range of motion. The best results were noted in patients without osteomyelitis. With the development of osteomyelitis, a complex of early rehabilitation measures also made it possible to partially restore the range of motion due to the formation of neoarthrosis, without resorting to arthrodesis.

Key Words: Septic arthritis; Osteomyelitis; Hand; Surgical treatment; Neoarthrosis

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Core Tip: The timing of surgical treatment initiation is extremely important in septic arthritis of the hand. Prompt and timely surgical intervention can prevent the destruction of cartilage and the development of osteomyelitis. In the presence of osteomyelitis, surgical debridement followed by early rehabilitation aimed at developing neoarthrosis may be an alternative to traditional treatment using arthrodesis. This conception makes it possible to largely preserve the range of active motions in the affected joint.

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INTRODUCTION

It is difficult to overestimate the importance of the hand as a unique anatomical and physiological formation. The hand is important not only from the point of view of aesthetics but is also often decisive in the performance of professional activities. Therefore, any disease or traumatic injury can cause irreparable damage[1,2]. Septic diseases of the hand are characterized by a high prevalence and remain one of the leading causes of temporary disability. Among the pathologies of the hand, septic arthritis of the metacarpophalangeal and interphalangeal joints is characterized by particular severity. An inflammation can cause dysfunction of the joint, and in the most severe cases, the need for amputation of the finger[1,3,4] may arise. The incidence of septic arthritis of the hand differs significantly by region and ranges from 2 to 12 cases per 100000 population per year[5]. Among septic arthritis, septic arthritis of

the hand takes second place in prevalence (15%-20%) after lesions of the knee joint, and among hand infections it occurs in 5%-18% cases[3,6]. Pathogenesis, clinical manifestations, and approaches to the treatment of septic arthritis of the hand have quite significant differences from inflammation of large joints. The causes of their occurrence are most often the direct penetration of the infection as a result of traumatic injury or the spread of infection from the surrounding soft tissues during felon, tenosynovitis, *etc*. In the absence of timely and complete treatment, cartilage destruction and osteomyelitis will develop in a short time[7-9]. A diagnosis of septic arthritis of the hand is based on clinical data, as well as the results of instrumental and laboratory research. Such clinical manifestations as pain, edema, hyperemia, and limitation of range of motion (ROM) are typical but do not allow us to establish the stage of the inflammatory process, including cartilage destruction and osteomyelitis[10]. The most commonly used radiography is also uninformative in the early stages. All these substantiate the expediency of using computed tomography and magnetic resonance imaging, which have high diagnostic value[1,3,11]. The microbial landscape in septic arthritis of the hand is not well understood. The leading role of *Staphylococcus aureus* (*S. aureus*) in this pathology has been reported. At the same time, data regarding the frequency of isolation of methicillin-resistant *S. aureus* (MRSA) differ significantly (from 0% to 73%)[10,12-14].

Treatment of septic arthritis of the hand is based on a combination of surgical methods and antibiotic therapy[10,15,16]. A number of authors note that persistent inflammation after surgical debridement determines the need to perform repeated surgical intervention within 24-48 h[2,17,18]. Articular cartilage destruction and osteomyelitis are considered by most experts as indications for arthrodesis[4, 10,17,19]. The possibility of neoarthrosis formation after resection of the destroyed joint is not considered. Some authors, characterizing their own observations, testify that arthrodesis was not performed in patients with osteochondral destruction. However, they do not report long-term functional results of the treatment [15].

The duration of antibiotic therapy remains a subject of discussion. A significant number of authors are supporters of long-term (at least 1 mo) administration of antibiotics[20-22]. However, in a study performed by Gjika *et al*[23], it was shown that a shorter 2-wk course of antibiotic therapy was as effective as a 4-wk course. The most important moment in the treatment of septic arthritis of the hand is the beginning of rehabilitation as a factor contributing to the restoration of movements and a decrease in joint stiffness. Some authors refer to supporters of early rehabilitation (1 d after surgery), while others consider it necessary to ensure peace for 7-14 d[5,16,18,24].

Thus, although septic arthritis of the hand is a common pathology, many questions regarding its etiology, pathogenesis, and treatment approaches remain insufficiently explored. There is still no answer to the question of whether there is a real alternative to arthrodesis in the presence of osteochondral destruction of the joint.

MATERIALS AND METHODS

Population

The results of the examination and treatment of 170 patients (180 joints) who were hospitalized with a diagnosis of septic arthritis of the hand from 2020 to 2021 were retrospectively analyzed. The average age of the patients was 49 years (IQR: 34-65). There were 116 men (68.2%) and 54 women (31.8%). Damage to the joints of the right hand was observed in 103 (60.6%) patients, and damage to the left hand was observed in 67 (39.4%). Most often, inflammation of the joints of 1, 2, and 3 fingers was diagnosed (detected: 147 (81.6%) joints). Septic arthritis of the metacarpophalangeal joint (MCP) was noted in 55 (30.6%) cases, proximal interphalangeal joint (PIP) in 54 (30%), distal interphalangeal joint (DIP) in 45 (25%), and interphalangeal joint of the first finger (IP of the thumb) in 26 (14.4%) (Figure 1).

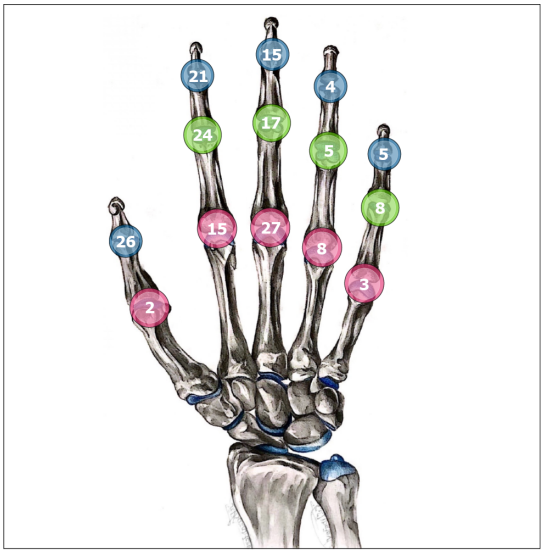
Exogenous infection was detected in 164 (96.5%) patients, and endogenous (the source of infection was not found) was detected in 6 (3.5%). Among the causes of septic arthritis, various types of household trauma were most often noted-101 (59.4%), animal bites-30 (17.6%), and clenched fist injury-15 (8.8%) (Figure 2).

The nature of the clinical course of arthritis was assessed based on the duration of symptoms: Acute-less than 3 wk and chronic-3 wk or more[25]. An acute course was observed in 156 (91.8%) patients, and a chronic course was observed in 14 (8.2%).

While a specialized classification of septic arthritis of the hand needs further specification, the classification of septic arthritis of large joints worked out by Tan *et al*[26] is widely used in surgery. Isolated septic arthritis was noted in 11 (6.1%) cases, septic arthritis with soft-tissue extension but no osteomyelitis in 71 (39.4%), and septic arthritis with contiguous osteomyelitis in 98 (54.4%).

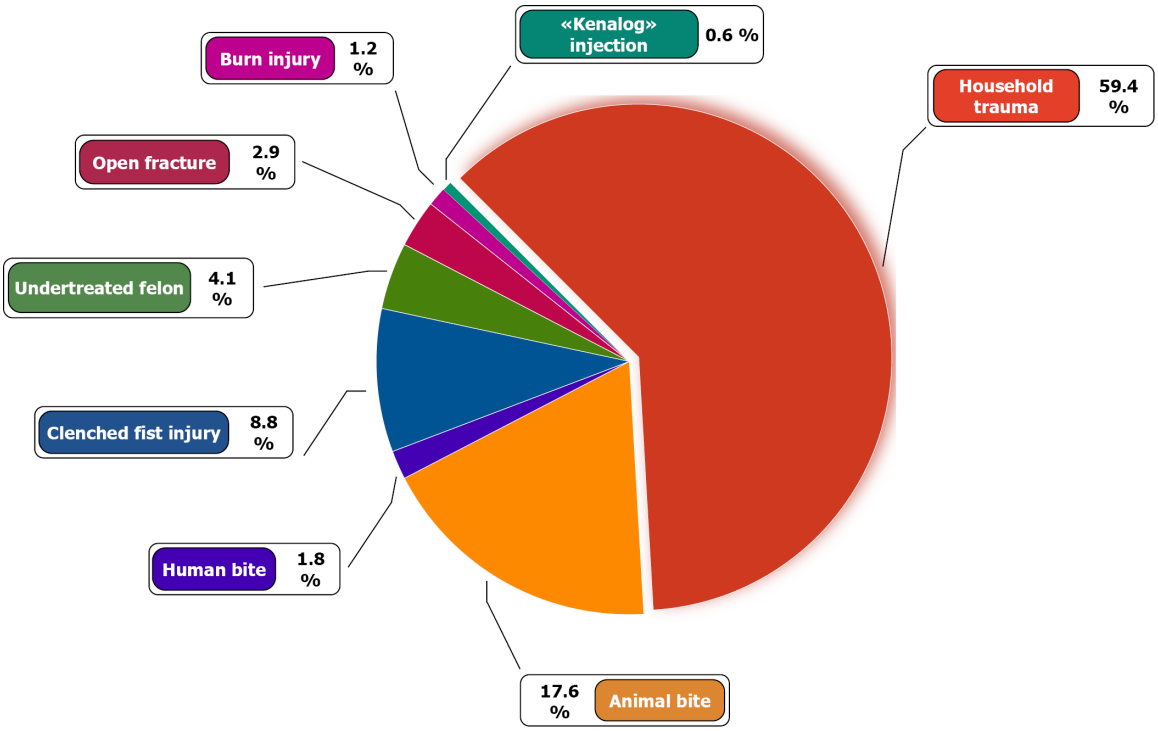
Among comorbidities, arterial hypertension was most often observed (36 patients; 21.2%), followed by diabetes mellitus (16 patients; 9.4%) and postinfarction cardiosclerosis (7 patients; 4.1%).

All patients underwent surgical treatment during the first day after hospitalization. It included the excision of all nonviable tissues (soft tissues, and in the case of osteomyelitis, both bone and cartilage structures) and ended with drainage and irrigation of the joint cavity. The drains were removed after the inflammation subsided, usually after 3-5 d. Persistent inflammation served as the basis for repeated



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Figure 1 Distribution of 180 small joints involved in 170 episodes of septic arthritis.



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Figure 2 Causative factors of septic arthritis of the hand.

surgical treatment within 24-48 h. Although the conventional surgical approach for septic arthritis with contiguous osteomyelitis is the need for arthrodesis (either primary or delayed), a different approach was used in these observations. The concept of the formation of neoarthrosis was fundamental, and was achieved through early mobilization, starting 5-7 d after the removal of the affected bone and cartilage structures.

Immobilization of the hand was carried out for 3-5 d using a developed design that allows axial extension of the affected finger (Figure 3). Subsequently, rehabilitation activities began.

Antibacterial therapy at the inpatient stage included intravenous administration of antibiotics such as amoxicillin/clavulanate, ceftriaxone, ciprofloxacin, and clindamycin. The results of microbiological research were taken into account. Patients who developed osteomyelitis after discharge continued to receive oral antibiotic therapy for 2 wk.



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Figure 3 Immobilization of the hand using a developed design that allows axial extension of the affected finger.

The long-term results of the performed treatment were evaluated in 142 (83.5%) patients within 1 mo to 12 mo after discharge from the hospital [the median was 7 mo (IQR: 4-9)]. The evaluation parameters included totalelimination of the infection as well as the volume of active movements of the affected joint (ROM). For this, the Total Active Motion (TAM) system was used. TAM is described by the American Society for Surgery of the Hand as the sum of active MCP, PIP, and DIP arc of motion in degrees of an individual digit. This calculation can then be compared to the TAM of the contralateral hand[27]. If necessary, control radiography or computed tomography was performed.

The severity of chronic pain during movement was assessed using a 10-cm visual analog scale (VAS), where 0 is no pain, and 10 cm is pain that is as bad as it could possibly be. In the analysis, centimeters were converted into points, where 1 cm equaled 1 point on the pain scale.

When examining patients, along with general clinical methods, radiography, computed tomography, microbiological examination with identification of microbial flora and determination of its sensitivity to antibiotics, as well as morphological examination of tissues removed during surgical treatment were used.

Statistical analysis

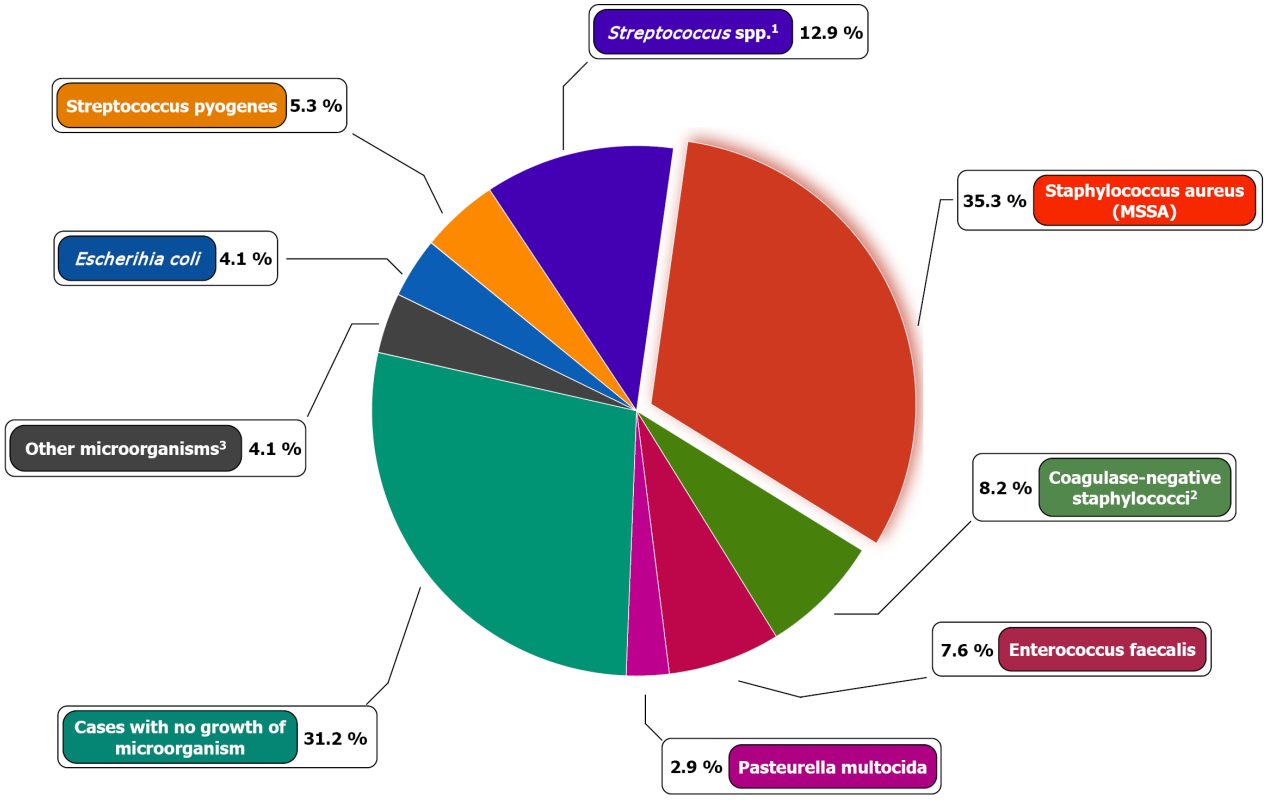
Statistical processing was carried out by methods of collecting and grouping factual material, calculating the median (Me) and IQR. The normality of the distribution was determined using the Shapiro-Wilk normality test. The significance of difference for nonparametric indicators was determined using the Mann-Whitney *U* test. Differences in indicators at $P < 0.05$ were considered significant. The study was reviewed by our biostatistic expert

RESULTS

Men predominated among the sick (68.2% *vs* 31.8% of women). The most common inflammation was MCP of the middle finger (15%), IP of the thumb (14.4%), PIP of the index finger (13.3%), and DIP of the index finger (11.7%). Septic arthritis of the MCP of the middle finger in all cases was the result of a clenched fist injury. At the same time, damage to the joint capsule and the extensor tendon of the finger was observed. Defects in the treatment of felon as a cause of septic arthritis DIP were identified in 7 (4.1%) patients.

The clinical course of septic arthritis in most patients (91.8%) was regarded as acute. However, local inflammation prevailed. An increase in body temperature was noted only in 55 (32.4%) patients; the median was 37.2 °C (IQR: 37.2-37.6). An increase in the number of leukocytes in the peripheral blood was observed in 82 (48.2%) patients; the median was 11.1 × 10^9/L (IQR: 10.2-13.6).

As a result of microbiological analysis, the bacterial flora was identified in 117 (68.8%) cases (Figure 4). In other plates the growth of microflora was absent. Among the isolated microorganisms, *S. aureus* was the most common (35.3%). A feature of the observations was that *MRSA* was not detected in any case. Monoinfection was noted in 98 (57.6%) cases, and polymicrobial infection was detected in 19



[1]*Streptococcus* spp. consisted of *Streptococcus mitis*, *Streptococcus anginosus*, and *Streptococcus agalactiae*.

[2]Coagulase-negative staphylococci consisted of *Staphylococcus epidermidis* and *Staphylococcus haemolyticus*.

[3]Other microorganisms consisted of *Klebsiella pneumoniae*, *Bacillus cereus*, *Proteus mirabilis*, *Acinetobacter baumannii*, *and Enterobacter aerogenes*.

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Figure 4 Microorganisms cultured from patients with septic arthritis of the hand.

(11.2%).

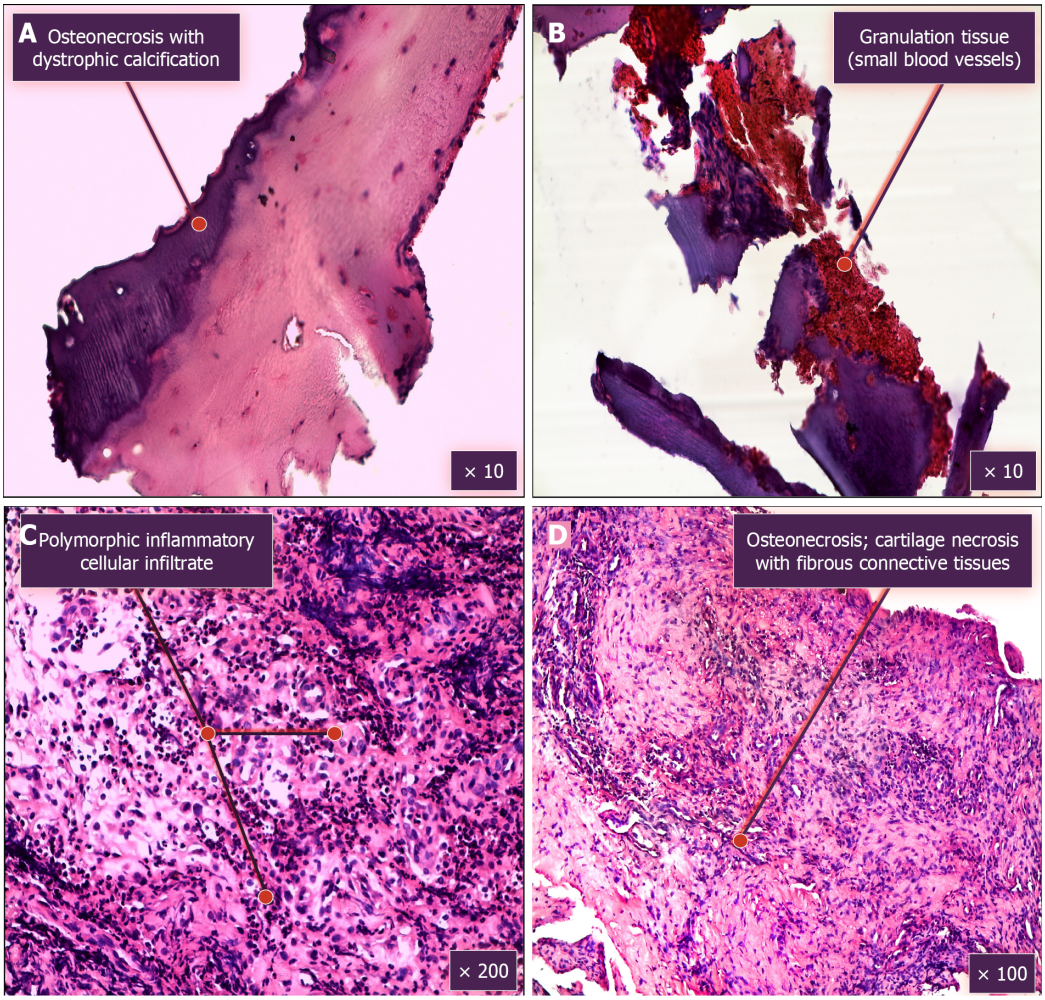
Another feature of the presented observations was a large number of cases of septic arthritis with contiguous osteomyelitis: 98 (54.4%) cases. To explain this fact, the duration of the delay in the start of treatment in various anatomical types of septic arthritis was analyzed. The median treatment delay in patients with septic arthritis without osteomyelitis was 5 d (IQR: 4-7). Septic arthritis with contiguous osteomyelitis was significantly longer and lasted for 14 d (IQR: 5-21). The diagnosis of osteomyelitis was confirmed by the results of intraoperative revision, morphological examination, and radiography (Figure 5). At the same time, radiographic data did not always make it possible to diagnose osteomyelitis in a timely manner. Among all cases with proven osteomyelitis (n = 98) with a treatment delay of up to 14 d (n = 51), it was detected on radiographs only in 21 (41.2%) cases. If the delay in treatment exceeded 14 d (n = 47), then radiographic signs of osteomyelitis were much more common and were reported in 39 (83%) cases. In 8 (17%) observations, even in these terms, radiographs did not allow a correct diagnosis.

The course of septic arthritis in patients with diabetes mellitus (n = 16) was characterized by particular severity. Fourteen (87.5%) of them developed osteomyelitis. The median treatment delay was 6 d (IQR: 4-28).

Surgical treatment has become a fundamental moment in the treatment of septic arthritis. A single surgical treatment was performed in 138 (81.2%) patients. The need for two surgical treatments was noted in 22 (12.9%) patients. Three or more treatments were required in 10 (5.9%) patients. Thus, repeated operations were performed in 32 (18.8%) patients. There was a certain relationship between the cause of septic arthritis and the need to perform repeated surgical treatment. The highest frequency of repeated surgical interventions was noted in patients with diabetes mellitus: 56.3%.

The duration of antibiotic therapy depended on the anatomical form of arthritis and the effectiveness of the treatment. In septic arthritis without osteomyelitis, the duration of antibiotic therapy averaged 7 d (IQR: 5-7). Septic arthritis with contiguous osteomyelitis was longer and lasted for 23 d (IQR: 21-25). This included inpatient and subsequent outpatient antibiotics.

In the majority of patients (163, 95.9%), it was possible to achieve elimination of infection and healing the wounds. However, 7 (4.1%) patients required rehospitalization for surgical treatment due to the ongoing septic process. Among them, there were 3 patients initially hospitalized with a diagnosis of septic arthritis of the hand without osteomyelitis and 4 with a diagnosis of septic arthritis with



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Figure 5 Morphological examination of tissues removed during surgical treatment (hematoxylin and eosin staining). A: Osteonecrosis with dystrophic calcification; B: Granulation tissue (small blood vessels); C: Polymorphic inflammatory cellular infiltrate; D: Osteonecrosis; cartilage necrosis with fibrous connective tissues.

contiguous osteomyelitis.

The best functional results were noted in the treatment of septic arthritis without osteomyelitis. The TAM assessment showed that the range of active movements of the finger was maximal after suffering septic arthritis of the MCP, and its median was 96.2% (IQR: 85.1-98.0) on the ROM of the contralateral finger. Slightly worse rates were reported for lesions of the proximal interphalangeal [median, 82.4% (IQR: 54.5-98.5)] and distal interphalangeal [median, 69.4% (IQR: 65.4-74.1)] joints. If we consider the recovery of ROM in a particular joint, then it was significantly better in the MCP [median, 97.6% (IQR: 84.6-100.0)] ($P < 0.05$). The worst indicators were characterized by the DIP [median, 62.1% (53.6-67.9)]. The median ROM of PIP was 84% (IQR: 68.2-98.5). The severity of pain during movement (according to the VAS scale) was minimal and did not exceed 1 point on a ten-point scale.

In cases of septic arthritis with contiguous osteomyelitis, the formation of neoarthrosis allowed only partial restoration of the range of active movements. The median TAM with MCP destruction was 62.7% (IQR: 48.1-87.5), with destruction of PIP was 60.5% (IQR: 51.8-71.8), and with DIP destruction was 63.2% (IQR: 61.5-71.7). The ROM in these joints was as follows: MCP-64.2% (IQR: 45.3-90.1), PIP-62.5% (41.8-68.9), and DIP-59.4% (50.0-62.1) (Figures 6-8). The severity of pain during movement was insignificant, although it was statistically significantly higher than pain in patients with septic arthritis without osteomyelitis. It was 0.86 points (IQR: 0.72-1.45) for MCP, 1.05 points (IQR: 0.71-1.55) for PIP, and 0.4 points (IQR: 0.3-0.55) for DIP (Table 1, Supplementary material).

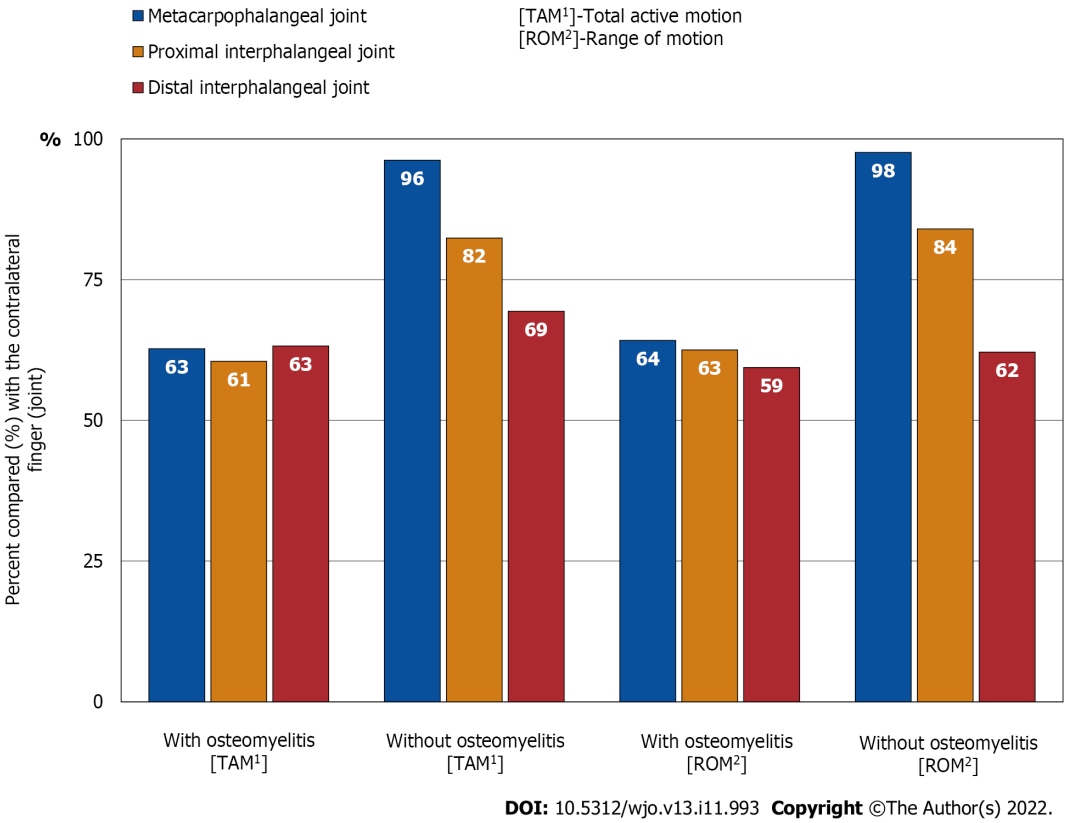
DISCUSSION

The occurrence of septic arthritis of the hand, as a rule, was the result of a penetrating injury to the joint. The predominance of men with septic arthritis was explained by their frequent traumatization. The

Table 1 Summary of total active motion and range of motion

Outcome	Patients without osteomyelitis, median (IQR)	Patients with osteomyelitis, median (IQR)	*P* value
TAM, %			
MCP	96.2 (85.1-98.0)	62.7 (48.1-87.5)	0.01072
PIP	82.4 (54.5-98.5)	60.5 (51.8-71.8)	0.00695
DIP	69.4 (65.4-74.1)	63.2 (61.5-71.7)	0.03662
ROM, %			
MCP	97.6 (84.6-100.0)	64.20 (45.30-95.05)	0.03362
PIP	84.0 (68.2-98.5)	62.5 (41.8-68.9)	0.01017
DIP	62.1 (53.6-67.9)	59.4 (50.0-62.1)	0.00960
Pain, VAS, cm			
MCP	0.40 (0.20-0.55)	0.86 (0.72-1.45)	< 0.00100
PIP	0.98 (0.75-1.50)	1.05 (0.71-1.55)	< 0.00100
DIP	0.20 (0.10-0.45)	0.40 (0.30-0.55)	< 0.00100

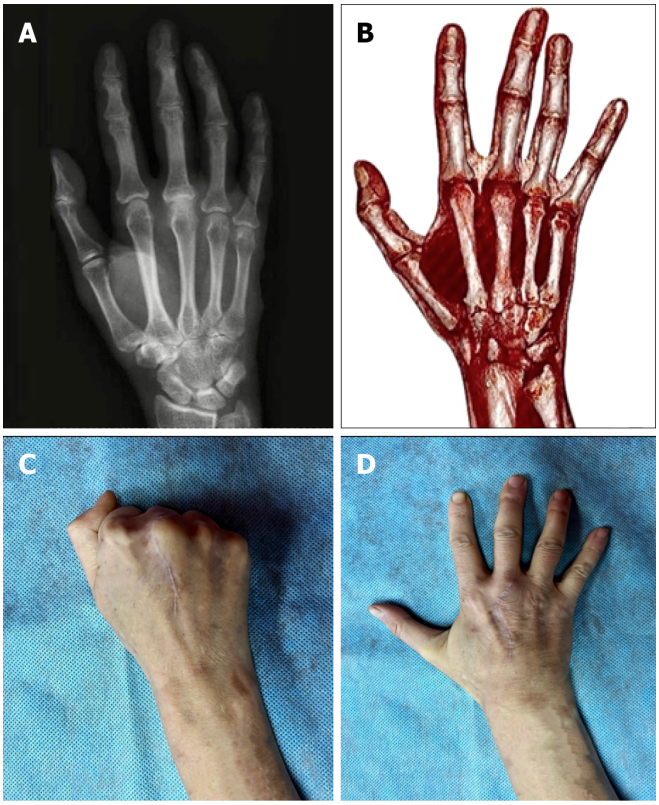
The values are given as the median and IQR. TAM: Total active motion; ROM: Range of motion; MCP: Metacarpophalangeal joint; PIP: Proximal interphalangeal joint; DIP: Distal interphalangeal joint; VAS: Visual analogue scale.



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Figure 6 Summary of total active motion and range of motion.

frequency of lesions of different joints of the hand was different. The most frequent involvement in the inflammatory process of MCP of the middle finger (15%), IP of the thumb (14.4%), and PIP (13.3%) and DIP (11.7%) of the index finger can be explained by the high frequency of damage. *S. aureus* has become a characteristic causative agent of joint infection. A feature of these observations was the fact that its polyantibiotic-resistant form, *MRSA,* was not isolated. The clinical course of septic arthritis of the hand in most cases was characterized as acute with a predominance of local inflammation.



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Figure 7 Outcomes of septic arthritis with osteomyelitis of the metacarpophalangeal joint, third finger (right hand). A: Preoperative radiography; B: 3D-reconstruction (CT) 5 mo after operative intervention; C and D: Long-term outcomes of the function recovery of the metacarpophalangeal joint.

Patients with septic arthritis with contiguous osteomyelitis were characterized by a significant delay in the start of treatment associated with late seeking medical help. The radiography performed during the first 14 d after the onset of the disease was uninformative, and must be taken into account in clinical practice. The course of septic arthritis of the hand in patients with diabetes mellitus was characterized by the greatest severity. This was evidenced by the high incidence of osteomyelitis in these patients (87.5%) with a relatively small delay in the start of treatment (the median was 6 d). Thus, timely treatment of septic arthritis of the hand is one of the most important factors in the prevention of osteomyelitis.

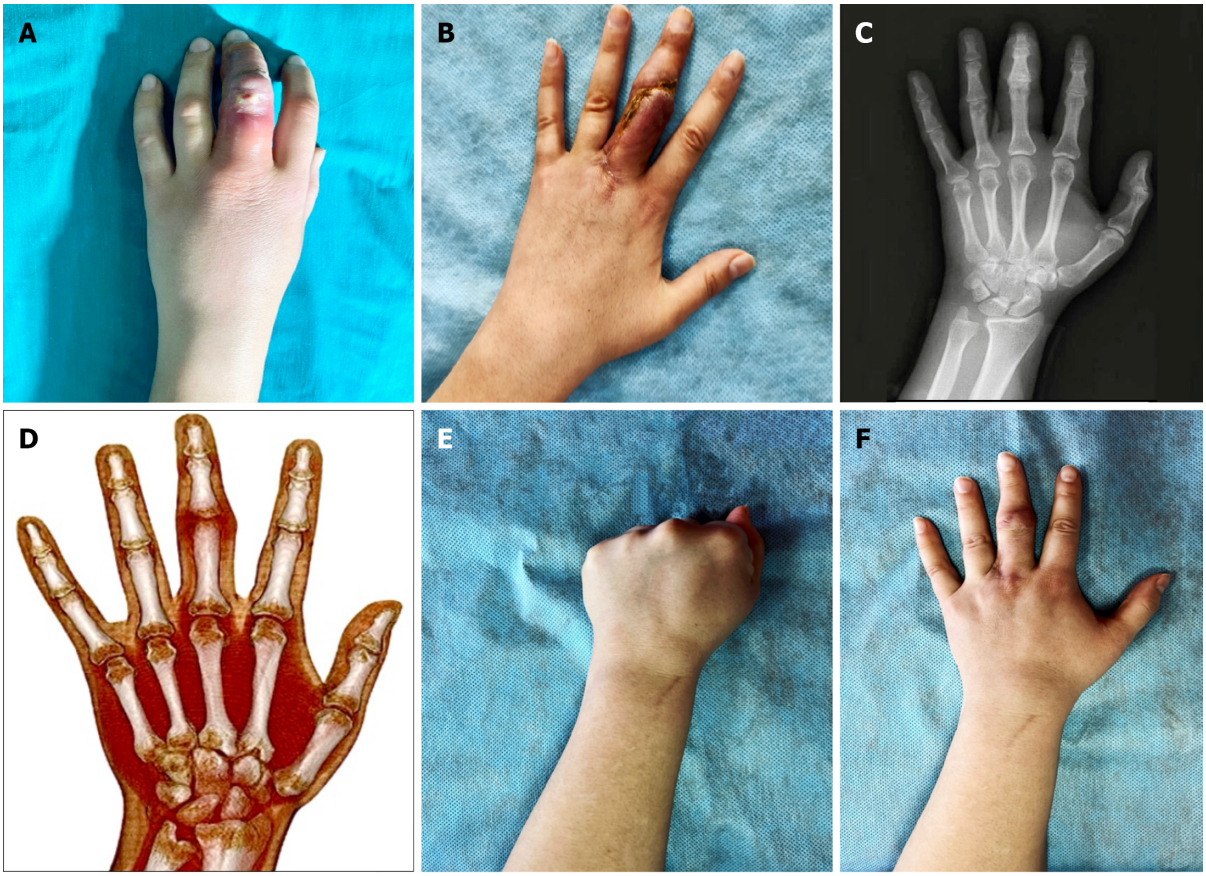
Surgical treatment, which ended with drainage and irrigation of the joint supplemented by antibiotic therapy, eliminated the inflammatory process. Some patients (18.8%) had a need for repeated surgical treatments. Most often, this concerned patients with diabetes mellitus, as well as victims of human and animal bites. In these cases, highly virulent microflora from the oral cavity entered the tissues.

Antibacterial therapy for septic arthritis without osteomyelitis was characterized by a short course (the median was 7 d), differing from the longer duration in osteomyelitis (the median was 23 d).

In 7 (4.1%) patients, after discharge from the hospital, a recurrence of the septic process was noted, which required readmission for surgical treatment. In 3 of them, septic arthritis with soft-tissue extension but no osteomyelitis was initially diagnosed, and signs of osteomyelitis were revealed during rehospitalization. Perhaps this situation was associated with an underestimation of objective data during the initial hospitalization, or with defects in subsequent outpatient treatment. Another 4 patients were initially diagnosed with osteomyelitis, and in all cases there was a severe lesion of the soft tissue of the finger. Of these, 2 patients had to undergo finger amputation as a result, including a patient with severe diabetes mellitus (Supplementary Table 1).

The key to success in restoring joint function was early rehabilitation. Arthrodesis was not used in patients with osteomyelitis after surgical debridement with removal of affected bone and cartilage structures. A complex of early rehabilitation measures contributed to the formation of neoarthrosis with a significant restoration of the volume of active movements. Painful arthrosis as one of the grounds for arthrodesis was not observed in any case. The functional results of the treatment of septic arthritis of the hand with osteomyelitis were slightly worse than those in cases without osteomyelitis. However, they also testified to the possibility of restoring more than 50% of the ROM in the joint without significant pain.

Contraindications to the start of early rehabilitation were related to patients who had damage to the flexor/extensor tendons that did not allow recovery of joint function. In these cases, arthrodesis was achieved using prolonged immobilization of the finger in a functionally advantageous position. Patients



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Figure 8 Treatment of septic arthritis with osteomyelitis of the proximal interphalangeal joint, third finger (left hand). A: Clinical presentation at admission; B: Short-term outcomes after operative intervention; C: Preoperative radiography; D: 3D-reconstruction (CT) 4 mo after operative intervention; E and F: Long-term outcomes of the function recovery of the proximal interphalangeal joint.

who violated the prescribed rehabilitation regime and systematically failed to follow the recommendations of a specialist were excluded from the research.

The main limitations are related to the fact that the research is retrospective. Not in all cases was it possible to estimate the extent of damage to paraarticular soft tissues, if any. Also, insufficient information was received on the condition of the flexor/extensor tendons of the finger, the presence and extent of their possible damage. And this is of fundamental importance in predicting the possibility of restoring the function, and choosing the nature and extent of rehabilitation measures. With an overall significant number of patients included in the research, the number of patients with concomitant diabetes mellitus is relatively small. Therefore, the data concerning this category of patients need to be clarified. A retrospective research also created significant difficulties in assessing the quality of rehabilitation after discharge of patients from the hospital. While rehabilitation, as you know, is the most important factor in restoring the function of the hand after septic arthritis.

CONCLUSION

To sum up, the duration of delay in treatment of patients significantly correlated with the incidence of osteomyelitis. In patients with diabetes mellitus, osteomyelitis developed much faster, which must be taken into account in clinical practice. Timely surgical treatment, along with continued irrigation of the joint and antibiotic therapy, made it possible to eliminate the infection, and early rehabilitation allowed restoring the ROM. The best results were noted in patients without osteomyelitis. With the development of osteomyelitis, a complex of early rehabilitation measures also made it possible to partially restore the ROM due to the formation of neoarthrosis, without resorting to arthrodesis.

ARTICLE HIGHLIGHTS

Research background

Septic arthritis of the hand, which is the second most common after damage of the knee joint, remains one of the leading causes of temporary disability. The results of their treatment today, especially from a functional point of view, cannot be considered satisfactory.

Research motivation

Dissatisfaction with the results of the treatment of septic arthritis of the hand, including a significant number of cases of joint stiffness and even amputations of the fingers, followed by the loss of the ability of patients to engage in their usual work activities, which is a severe psychological trauma, motivated us to find ways to solve this problem.

Research objectives

To explore the etiology and clinical course of septic arthritis of the hand; to analyze the timing of the development of osteomyelitis with a delay in the treatment of patients; and to compare approaches to surgical treatment and rehabilitation depending on the nature of the pathological process.

Research methods

The results of treatment of 170 patients with septic arthritis of the hand were retrospectively analyzed. The causes of the disease and the nature of the microbial flora were explored. The frequency of various forms of septic arthritis of the hand and approaches to surgical treatment were analyzed.

Research results

The most common pathogen was *S. aureus*. The form of septic arthritis was largely determined by the duration of treatment delay. In the presence of osteomyelitis, it was maximal. In patients with diabetes mellitus, osteomyelitis developed much earlier. Comprehensive treatment made it possible to eliminate the infection. Functional outcomes were better in patients without osteomyelitis. With the development of osteomyelitis, surgical debridement and early rehabilitation made it possible to partially restore the range of motion without resorting to arthrodesis.

Research conclusions

Timely surgical treatment of septic arthritis of the hand allows reducing the number of cases of osteomyelitis. Early rehabilitation is the key to success in restoring hand function after surgery. The development of osteochondral destruction does not exclude the possibility of partial restoration of function due to the formation of neoarthrosis.

Research perspectives

To optimize approaches to the surgical treatment of septic arthritis of the hand and postoperative rehabilitation, it is necessary to develop a specialized classification of this disease, taking into account the involvement in the pathological process of not only the elements of the joint, but also the paraarticular soft tissues and flexor/extensor tendons of the finger.

FOOTNOTES

Author contributions: Lipatov KV performed conceptualization and manuscript writing, review, and editing; Asatryan A and Melkonyan G performed methodology and writing of the original draft; Kazantcev AD performed visualization and manuscript writing, review, and editing; Solov'eva EI and Gorbacheva IV performed investigation and writing of the original draft; Vorotyntsev AS and Emelyanov AY performed formal analysis and supervision.

Institutional review board statement: The study was reviewed and approved by the I.M. Sechenov First Moscow State Medical University Institutional Review Board (Approval No. 03-22).

Informed consent statement: All study participants, or their legal guardian, provided informed written consent prior to study enrollment.

Conflict-of-interest statement: All the authors have no conflict of interest related to the manuscript.

Data sharing statement: The original anonymous dataset is available on request from the corresponding author at lipatov_k_v@staff.sechenov.ru.

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REFERENCES

1 **McKay P**, Formby PM, Dickens J, Gibson M. Osteomyelitis and septic arthritis of the hand and wrist. *Curr Orthop Pract* 2010; **21**: 542-550 [DOI: 10.1097/bco.0b013e3181f1f2c1]
2 **Meier R**, Wirth T, Hahn F, Vögelin E, Sendi P. Pyogenic Arthritis of the Fingers and the Wrist: Can We Shorten Antimicrobial Treatment Duration? *Open Forum Infect Dis* 2017; **4**: ofx058 [PMID: 28491895 DOI: 10.1093/ofid/ofx058]
3 **Sendi P**, Kaempfen A, Uçkay I, Meier R. Bone and joint infections of the hand. *Clin Microbiol Infect* 2020; **26**: 848-856 [PMID: 31917233 DOI: 10.1016/j.cmi.2019.12.007]
4 **Chenoweth B**. Septic Joints: Finger and Wrist. *Hand Clin* 2020; **36**: 331-338 [PMID: 32586459 DOI: 10.1016/j.hcl.2020.03.006]
5 **Lamou HJ**, Kim S, Kuchenbuch C, Thelen S, Eisenschenk A, Hakimi M. Septic Arthritis of the Hand and Wrist. *Handchir Mikrochir Plast Chir* 2021; **53**: 290-295 [PMID: 34134161 DOI: 10.1055/a-1512-0321]
6 **Angly B**, Steiger R, Zimmerli W. Septic arthritis of finger joints. *Handchir Mikrochir Plast Chir* 2007; **39**: 118-123 [PMID: 17497608 DOI: 10.1055/s-2007-965137]
7 **Nair R**, Schweizer ML, Singh N. Septic Arthritis and Prosthetic Joint Infections in Older Adults. *Infect Dis Clin North Am* 2017; **31**: 715-729 [PMID: 29079156 DOI: 10.1016/j.idc.2017.07.013]
8 **Ross K**, Mehr J, Carothers B, Greeley R, Benowitz I, McHugh L, Henry D, DiFedele L, Adler E, Naqvi S, Lifshitz E, Tan C, Montana B. Outbreak of Septic Arthritis Associated with Intra-Articular Injections at an Outpatient Practice - New Jersey, 2017. *MMWR Morb Mortal Wkly Rep* 2017; **66**: 777-779 [PMID: 28749922 DOI: 10.15585/mmwr.mm6629a3]
9 **Sultana S**, Dey R, Bishayi B. Dual neutralization of TNFR-2 and MMP-2 regulates the severity of S. aureus induced septic arthritis correlating alteration in the level of interferon gamma and interleukin-10 in terms of TNFR2 blocking. *Immunol Res* 2018; **66**: 97-119 [PMID: 29218573 DOI: 10.1007/s12026-017-8979-y]
10 **Giuffre JL**, Jacobson NA, Rizzo M, Shin AY. Pyarthrosis of the small joints of the hand resulting in arthrodesis or amputation. *J Hand Surg Am* 2011; **36**: 1273-1281 [PMID: 21705153 DOI: 10.1016/j.jhsa.2011.05.022]
11 **Barbieri RA**, Freeland AE. Osteomyelitis of the hand. *Hand Clin* 1998; **14**: 589-603, ix [PMID: 9884897]
12 **Kowalski TJ**, Thompson LA, Gundrum JD. Antimicrobial management of septic arthritis of the hand and wrist. *Infection* 2014; **42**: 379-384 [PMID: 24307329 DOI: 10.1007/s15010-013-0566-0]
13 **Bach HG**, Steffin B, Chhadia AM, Kovachevich R, Gonzalez MH. Community-associated methicillin-resistant Staphylococcus aureus hand infections in an urban setting. *J Hand Surg Am* 2007; **32**: 380-383 [PMID: 17336847 DOI: 10.1016/j.jhsa.2007.01.006]
14 **Kistler JM**, Thoder JJ, Ilyas AM. MRSA Incidence and Antibiotic Trends in Urban Hand Infections: A 10-Year Longitudinal Study. *Hand (N Y)* 2019; **14**: 449-454 [PMID: 29322874 DOI: 10.1177/1558944717750921]
15 **Kwak SH**, Bae JY, Oh Y, Jang HS, Ahn TY, Lee SH. Primarily treated patients versus referred patients in the treatment of native septic arthritis of digits: a retrospective comparative study. *BMC Musculoskelet Disord* 2020; **21**: 780 [PMID: 33246444 DOI: 10.1186/s12891-020-03770-9]
16 **Chung SR**, Kang YC, McGrouther DA. Techniques for Continuous Irrigation of Septic Joints of the Hand. *Tech Hand Up Extrem Surg* 2019; **23**: 133-137 [PMID: 30973488 DOI: 10.1097/BTH.0000000000000241]
17 **McBride S**, Mowbray J, Caughey W, Wong E, Luey C, Siddiqui A, Alexander Z, Playle V, Askelund T, Hopkins C, Quek N, Ross K, Orec R, Mistry D, Coomarasamy C, Holland D. Epidemiology, Management, and Outcomes of Large and Small Native Joint Septic Arthritis in Adults. *Clin Infect Dis* 2020; **70**: 271-279 [PMID: 30941403 DOI: 10.1093/cid/ciz265]
18 **Vorderwinkler KP**, Mühldorfer M, Pillukat T, van Schoonhoven J. Treatment of bacterial infection in the interphalangeal joints of the hand. *Oper Orthop Traumatol* 2011; **23**: 192-203 [PMID: 21735254 DOI: 10.1007/s00064-011-0024-z]
19 **Allieu Y**, Chammas M, Hixson ML. External fixation for treatment of hand infections. *Hand Clin* 1993; **9**: 675-682 [PMID: 8300736]
20 **Clerc O**, Prod'hom G, Greub G, Zanetti G, Senn L. Adult native septic arthritis: a review of 10 years of experience and lessons for empirical antibiotic therapy. *J Antimicrob Chemother* 2011; **66**: 1168-1173 [PMID: 21393124 DOI: 10.1093/jac/dkr047]
21 **Türker T**, Capdarest-Arest N, Bertoch ST, Bakken EC, Hoover SE, Zou J. Hand infections: a retrospective analysis. *PeerJ* 2014; **2**: e513 [PMID: 25210653 DOI: 10.7717/peerj.513]
22 **Stengel D**, Bauwens K, Sehouli J, Ekkernkamp A, Porzsolt F. Systematic review and meta-analysis of antibiotic therapy for bone and joint infections. *Lancet Infect Dis* 2001; **1**: 175-188 [PMID: 11871494 DOI: 10.1016/S1473-3099(01)00094-9]

23 **Gjika E**, Beaulieu JY, Vakalopoulos K, Gauthier M, Bouvet C, Gonzalez A, Morello V, Steiger C, Hirsiger S, Lipsky BA, Uçkay I. Two weeks versus four weeks of antibiotic therapy after surgical drainage for native joint bacterial arthritis: a prospective, randomised, non-inferiority trial. *Ann Rheum Dis* 2019; **78**: 1114-1121 [PMID: 30992295 DOI: 10.1136/annrheumdis-2019-215116]

24 **Sinha M**, Jain S, Woods DA. Septic arthritis of the small joints of the hand. *J Hand Surg Br* 2006; **31**: 665-672 [PMID: 17046120 DOI: 10.1016/j.jhsb.2006.08.011]

25 **Osmon DR**, Berbari EF, Berendt AR, Lew D, Zimmerli W, Steckelberg JM, Rao N, Hanssen A, Wilson WR; Infectious Diseases Society of America. Diagnosis and management of prosthetic joint infection: clinical practice guidelines by the Infectious Diseases Society of America. *Clin Infect Dis* 2013; **56**: e1-e25 [PMID: 23223583 DOI: 10.1093/cid/cis803]

26 **Tan V**, Pepe MD, Esterhai JL. Sepsis of the shoulder girdle. In: Disoders of the shoulder: diagnosis and management. Iannotti J, Williams GR, editors. Philadelphia, Baltimore, New York, London, Buenos Aires, Hong Kong, Sydney, Tokyo: Lippincott Williams and Wilkins, 1998: 951-976 [DOI: 10.1111/ene.12281]

27 **American Society for Surgery of the Hand**. Clinical Assessment Committee Report. IL, United States: Rosemont, 1976 [DOI: 10.1016/s0363-5023(76)80027-5]

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ORIGINAL ARTICLE

Observational Study

Patient preference for trigger finger treatment

Christian Blough, Jawad Najdawi, Stuart Kuschner

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Abstract

BACKGROUND

Trigger finger is a common disorder of the hand that can cause disabling symptoms. Treatment options range from conservative management with observation and splinting, to surgical release, but there is currently not a consensus on a treatment algorithm.

AIM

To determine patient preference for the treatment of trigger finger using an online survey.

METHODS

An online crowdsourcing platform, Amazon Mechanical Turk, was used to recruit participants for this study. Participants were led through a scenario in which they were diagnosed with trigger finger. They were then asked to rank their preference of treatment options from the following: Observation, splinting, corticosteroid injection, surgery. The results of the surveys were then analyzed using R software.

RESULTS

Of 323 participants completed the survey. 7 participants were excluded because they failed to correctly answer the attention question, leaving 316 participants whose results were included. As a first choice for treatment 117 (37%) of the included participants chose observation, 86 (27%) chose splinting, 61 (19%) chose corticosteroid injection, and 52 (16%) chose surgery. The mean rank for observation was 2.26, for splinting was 2.30, for corticosteroid injection was 2.53, and for surgery was 2.91. The ranking of each treatment option was statistically different (P value < 0.05) from the others except for observation and splinting.

CONCLUSION

The practice of shared decision making with patients is imperative to providing the best care possible. The results from this study, especially the preference for less invasive treatment, may help providers better frame discussion around treatment options of trigger fingers. This in turn, may increase patient satisfaction

in the treatment of trigger finger.

Key Words: Trigger finger; Trigger digit; Hand surgery; Shared decision making

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Core Tip: Given the lack of current consensus on ideal management of trigger fingers, it is imperative for providers to pursue shared decision making with their patients. The results from this study may help providers better frame discussion around treatment options of trigger fingers. This, in turn, should lead to increased patient satisfaction.

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INTRODUCTION

Trigger finger, or stenosing flexor tenosynovitis, is a disorder of the hand which causes catching, or 'triggering', of the finger with extension of a flexed digit. This in turn can lead to difficulties with activities of daily living and interfere with patient's work. It is one of the most common causes of hand disability, effecting between 2%-3% of the worldwide population[1]. The variability of symptoms is large, with mild symptoms being pain, and more severe symptoms including flexion contractures of the involved digit(s). The specific etiology of trigger finger has yet to be determined but multiple theories exist[1]. Treatment options range from conservative management with observation or splinting, to one of the most common options, corticosteroid injection, to surgical intervention with percutaneous or open release, with no clear guidelines on an algorithm[2]. The choice of treatment depends on patient and surgeon preference. There is currently a plethora of research indicating that patients seek to be more actively involved in their care with the use of a shared decision-making framework[3-5]. The goal of this study was to determine patient preferences regarding trigger finger in an effort to better prepare providers for shared decision-making conversations with their patients.

MATERIALS AND METHODS

An online, survey based, descriptive study was performed through the use of a crowdsourcing website, Amazon Mechanical Turk (AMT). Participants for this study were randomly recruited through AMT. Studies have shown that AMT produces results similar to conventional surveying techniques and the population surveyed is representative of the United States internet population[6-8].

AMT workers must be older than 18 years of age to participate on the platform. Survey participants are screened through AMT to ensure that the same individual cannot complete multiple responses. AMT screens participants to ensure quality responses. Additionally, an attention check question was included to verify the quality of the responses. If a survey participant failed the attention check, their response was excluded.

If a participant completed the survey and adequately responded to the attention check, they were compensated ($0.20 *per* unique response) through the AMT platform for their time.

Attention check question

In an effort to ensure that participants were paying close attention to the prompts, questions, and giving meaningful opinions about the prior, an attention check question was inserted into the survey as follows.

"Attention check. Please select answer 3 if you are paying attention".

Respondents who did not answer this question correctly were excluded from the study.

Survey questions

The authors devised the survey in an effort to simulate a real clinical scenario. The participants were presented with the following scenario and questions. It begins as follows:

Scenario I: Trigger finger is a common problem affecting the hand. Patient's report pain and a clicking sensation with motion of the finger. The affected finger can catch or lock when trying to make a fist. Symptoms can limit the ability to grasp or hold objects. (A short 8 s video was made available to the respondents *via* a hyperlink that showcased an example of a trigger finger). Assume that your doctor has diagnosed you as having trigger finger.

Your doctor discusses the following options for treatment: (1) Observation: 50% of patients with trigger finger will get better without any treatment, most within one year[9]; (2) Splint: A restrictive splint keeping the finger straight will be worn on the involved finger. You are told this treatment option resolves symptoms 55% of the time[10]; (3) Cortisone injection: A very small steroid injection will be administered in the office. Some patients experience temporary pain from the injection. Symptoms resolved after one injection for 45% of patients, after two injections 60% of patients, and after three injections 76% of patients[11,12]; and (4) Surgery: Open release of the structure that causes the trigger resolves symptoms > 90% of the time[2].

Question 1: Which treatment option would you initially choose?

Observation

Splinting

Cortisone injection

Surgery

Participants were then asked to rank the remaining treatment options based on how they would prefer to be treated for their trigger finger.

Data analysis

Results from the survey were pooled and mean ranking was calculated using Microsoft Excel Online (Redmond, WA). The statistical review was then completed by a biomedical statistician. To assess the variance of mean ranking of each treatment type a Friedman Rank Sum Test was run. Additionally, a pairwise Wilcoxon Rank Sum tests with a Bonferroni adjustment for multiple comparisons was run to allow analysis of the difference in rankings between treatment types. This analysis was completed using R software (Boston, MA).

RESULTS

A total of 323 participants completed the survey *via* AMT. 7 participants were excluded because they failed the attention check question, leaving 316 participants who were included in the study, as seen in Figure 1.

Following the prompt asking which treatment option they would initially choose, 117 (37%) participants opted for observation as their first preferred method of treatment *vs* 86 (27%), 61 (19%), and 52 (16%) participants who responded with splinting, a cortisone injection, and surgery, respectively, as their first preferred method of treatment. Participants were then asked to rank what their second, third, and fourth preferred methods of treatment would be.

These results can collectively be seen in Table 1.

The mean ranking for observation was 2.26, for splint 2.30, for cortisone injection 2.53, and for surgery 2.91. The Friedman Rank Sum of this data was then calculated and the Chi-Squared was 50.5 with a P value less than 0.00001. These results can be seen in Table 2.

A pairwise comparison using Wilcoxon Rank Sum Tests was then performed revealing significant differences (P value < 0.05) in all treatment choices relative to one another, except for observation *vs* splint. These results can be seen in Table 3.

DISCUSSION

Epidemiology

As previously noted, trigger finger has an estimated lifetime incidence in 2%-3% of the population[1]. It most often affects middle-aged women (2-6 times as likely as men) in their dominant hand[13,14]. The ring finger is the most commonly affected digit, followed by the middle finger, index finger, and little finger (excluding the thumb)[15]. The constellation of diseases that constitute metabolic syndrome, specifically diabetes, hypertension, and dyslipidemia, have all been shown to be risk factors[15]. The incidence is also increased in patients with other hand conditions, including carpal tunnel syndrome, de Quervain's tenosynovitis, and Dupuytren's contracture[16]. Diabetes mellitus puts patients at elevated risk of developing trigger finger, with lifetime incidence in this subset of the population estimated at 10%[17]. The risk of developing trigger finger, as well as the severity of symptoms, is positively correlated with elevated glycosylated hemoglobin levels, specifically HbA1c levels greater than 7%[18].

The diagnosis of trigger finger is relatively straightforward. Patients report a locking or catching sensation with active range of motion of a digit. There may be pain with motion and motion of the digit

Table 1 Patient preference for treatment of trigger finger

	Observation	Splint	Cortisone injection	Surgery
1st Choice	117 (37%)	86 (27%)	61 (19%)	52 (16%)
2nd Choice	69 (22%)	96 (30%)	93 (29%)	58 (18%)
3rd Choice	61 (19%)	86 (27%)	97 (31%)	72 (23%)
4th Choice	69 (22%)	48 (15%)	65 (21%)	134 (42%)
Sum	316	316	316	316

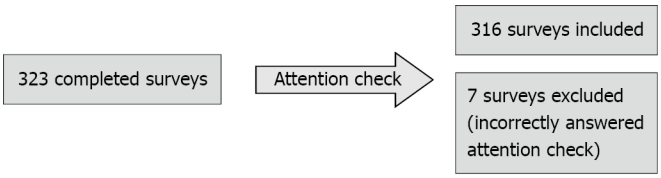
Table 2 Descriptives of rank for each treatment option

	N	Mean ranking	Standard deviation
Cortisone injection	316	2.53	1.02
Splint	316	2.30	1.03
Surgery	316	2.91	1.12
Observation	316	2.26	1.17

Table 3 Pairwise comparison using Wilcoxon Rank Sum Tests (*P* value)

	Cortisone injection	Splint	Surgery	Observation
Cortisone injection				
Splint	0.0426[a]			
Surgery	< 0.00001[a]	< 0.00001[a]		
Observation	0.0093[a]	1.0000	< 0.00001[a]	

[a]$P < 0.05$.



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Figure 1 Study participants. A total of 323 participants completed the survey *via* Amazon Mechanical Turk. 7 participants were excluded because they failed the attention check question, leaving 316 participants who were included in the study.

may be diminished[19]. The physician can observe the phenomena described by the patient or feel the catching at the level of the A1 pulley or detect crepitus at this level. The patient often reports pain with palpation at the A1 pulley. Subluxation of the extensor tendon at the dorsal aspect of the metacarpophalangeal (MCP) joint secondary to a sagittal band rupture and a locked metacarpal phalangeal joint are rare but are occasionally confused with trigger finger. The pathophysiology of trigger finger is felt to be the result of thickening and narrowing of the tendon sheath–and not in the tendon itself or tenosynovium[19,20]. This size mismatch occurs at the level of the A1 pulley. Thickening at the A1 pulley restricts motion of the flexor tendon.

No standard protocol exists for treatment of trigger finger[21,22]. Treatment options include splinting, corticosteroid injection and surgery[23]. In addition to these interventions, observation (no treatment) is an option. The reported success rates for each option vary considerably. There are only a few reports on the natural history of untreated trigger finger. McKee *et al*[9], in 2018, reported the results of 343 patients with a diagnosis of trigger finger who received no treatment, 178 patients (52%) had complete spontaneous resolution. Of the 178 patients who had complete spontaneous resolution, 50% did so within 8 mo of initial consultation and 90% had complete resolution within one year[9]. The

authors hypothesized that improvement resulted from "some remodeling over time of the pulley" and decreased inflammation from rest and lifestyle modification. Schofield and Citron reported on the natural history of adult trigger thumb in 30 patients enrolled in a prospective study[24]. (According to the authors) five patients insisted on treatment, triggering resolved in the remaining patients without treatment after an average of 6-8 mo, within a range of 2-15 mo.

Not all patients are willing to wait but would like to "do something." For those who want to do something but are not ready for surgery, splinting and cortisone injections are options. Several splinting designs and techniques have been described[25-29]. Colbourn *et al*[28] reported improvement in 28 patients who wore a custom-made thermoplastic splint which limited motion at the MCP joint for 6 wk [28]. Rodgers *et al*[25] reported the results of splinting the distal interphalangeal (DIP) joint in meat packing plant laborers, some of whom also were given a cortisone injection. At a mean one year follow up 81% were treated successfully[25]. Tarbhai *et al*[27] compared splinting of the MCP joint *vs* splinting of the DIP joint in a prospective randomized study of 30 subjects[27]. Success was defined as complete or partial relief of triggering. Success rate with splinting of the DIP joint was 47%, a lower success rate than reported by Rodgers *et al*[25]. Success rate with blocking splint of the MCP joint was 77%. Teo *et al* [26] compared splinting of the MCP joint with splinting of the proximal interphalangeal (PIP) joint. Both splints were effective in reducing pain and disability and improving triggering symptoms, but the PIP splint was more effective[26]. Collectively, splinting of the affected digit, in various forms, appears to be a viable treatment option.

Corticosteroid injection into the flexor tendon sheath was first described by Howard *et al*[30] in 1953. Reported success rates vary[2]. Wojahn *et al*[11] investigated the long-term effectiveness of a single corticosteroid injection for trigger finger in 366 patients with a minimum 5 year follow up[11]. 45% of patients had long term success following one injection. Most failures (84%) occurred within the first two years following injection. Dala-Ali *et al*[31] reported results in patients who received up to 3 cortisone injections[31]. Studying 90 trigger digits in 61 patients the reported a 34% success rate with one injection, 63% success rate with 2 injections and 66% success rate with 3 injections. Dardas *et al*[12] investigated the effectiveness of repeat cortisone injections for trigger fingers[12]. Second injections provided long term success in 39% of trigger fingers and third injections provided a similar 39% success rate. The authors reported a hypothetical success rate of 82% after 3 injections. Rozental *et al*[20] looked at prognostic indicators of recurrence following cortisone injection[20]. Insulin dependent diabetes, younger age and involvement of multiple digits were associated with higher rate of treatment failure. Grandizio *et al*[32] also noted that younger age was a risk factor for persistent triggering after a cortisone injection[32]. However, in their study diabetes was not a risk factor for failure.

Many patients, when given the option of cortisone injection, want to know how soon they might see improvement. Seigerman *et al*[33] investigated time to improvement after cortisone injection in a study involving 452 patients and found that most patients experience relief of pain and triggering at 3 wk following cortisone injection[33]. They reported that the majority of patients had some pain relief within the first week after cortisone injection. Improvement in trigger lagged behind pain relief.

When non-operative modalities fail, surgery is an option. While percutaneous procedures and endoscopic surgery are options, the most common surgical intervention is release of the A1 pulley *via* an open incision. The success rate is high, with success rates reported at > 95%, and the procedure is considered low risk but complications can and do occur[34]. Everding *et al*[23] in a retrospective review of 795 digits release in 543 patients reported complications in 12%[23]. Most common complications were persistent pain, swelling, persistent or recurrent triggering. Reoperation rate was 2.4% including revision release and investigation and debridement. The rate of infection following trigger finger release is low but increased rate of infection is reported if surgery is performed within 90 d of cortisone injection[35,36].

Percutaneous release of the first annular pulley is a procedure that has been increasing in popularity. The biggest advantage of this procedure is its less invasive nature and lower cost compared to open release. The biggest disadvantage is the lower success rate, reported at around 94%, often due to incomplete release of the annular pulley[37].

Augmentation of percutaneous release with sonographic guidance is a recent technique that has increases the success rate of percutaneous release. One factor limiting wider acceptance of sonographic guidance is the high cost[37]. More research is needed to assess the cost effectiveness of sonographic guidance.

Recommendations for a treatment algorithm are reported in the literature, but consensus lacks. Amirfeyz *et al*[38] stated that there was weak evidence to support use of a splint and that a single cortisone injection may be offered as initial treatment, but surgery should be next if injection fails[38].

Cost of treatment can affect recommendations that a provider makes. Zhuang *et al*[39] evaluated cost effectiveness of cortisone injections *vs* open trigger finger release and reported that, from a healthcare payer perspective, offering 3 cortisone injections before surgery is a cost-effective strategy[39]. Kerrigan and Stanwix examined cost of treatment and concluded that the least costly treatment would be 2 injections before surgery[40].

The published papers that review results of various treatment options, and studies that examine costs associated with treatment for trigger finger, often fail to consider the patient's perspective. In our investigation participants were asked to assume they were diagnosed as having a trigger finger. They were

given a hyperlink that allowed them to see an 8 s video which demonstrated a trigger finger. They were then presented with 4 options for treatment: Observation, use of a splint, cortisone injection and surgery. A plurality (37%) chose observation as their first method of treatment and 27% chose splinting as their choice. Thus, more than half selected a non-invasive modality as their first choice. Analysis revealed that patients do have a preference between treatment options, except when choosing between observation and splinting.

This contrasts most current recommendations on treatment which recommend corticosteroid injection as a first line treatment. This information can inform physicians when seeing a patient who presents with a trigger finger that there may be a reluctance by the patient to undergo an invasive intervention (cortisone injection or surgery). The job of the treating physician is not to persuade the patient to pursue a particular treatment modality but rather to educate, to explain, to discuss, to answer questions, and to listen and respond. The results of this study provide the treating physician with a very general idea of what patients may want when learning they have a trigger finger.

Limitations

The use of an online survey inherently limits patient knowledge on treatment options, including duration of treatment, success rates, and complications. All of these factors are likely to affect a patient's selection of treatment.

No demographics were collected from the participants. It has previously been shown that the AMT worker population is representative of the general United States internet population is similar studies[6-8,41,42]. However, the internet population may not be the same as the population treated for trigger finger.

It was unknown if any study participants previously had trigger finger. They were given a prompt and information to review as well as a video of a trigger finger. An individual's perspective on treatment may change if they experience the symptoms of a disorder, as opposed to simply reading about it.

The severity of trigger finger symptoms varies widely. Our survey did not indicate to participants the severity of their symptoms which may affect the treatment they chose to pursue.

The inclusion of a pay-per-response model could lead to a selection bias as individuals may have not viewed our particular pay as high enough to proceed with the survey.

Participants were not offered an option for percutaneous A1 pulley release. Given the less invasive nature of this procedure compared to open release, patients may be more likely to choose this option.

CONCLUSION

The practice of shared decision making with patients is imperative to providing the best care possible. The results from this study, especially the preference for less invasive treatment, may help providers better frame discussion around treatment options of trigger fingers. This in turn, may increase patient satisfaction in the treatment of trigger finger.

ARTICLE HIGHLIGHTS

Research background

Trigger finger is one of the most common hand disorders that can lead to debilitating symptoms.

Research motivation

To provide increased insight to providers treating patients with trigger finger to better allow shared decision making.

Research objectives

To determine patient preference for the treatment of trigger finger.

Research methods

An online survey was perfomed using a crowdsourcing website. Participants were led through scenarios regarding the symptoms of trigger finger and treatment options. They were then asked questions regarding their preferred treatment.

Research results

Of 316 participants results were included. 37% of the participants chose observation as their first choice, 27% splinting, 19% corticosteroid injection, and 16% surgery. The mean rank of each treatment option was statistically different from the others, except for observation and splinting.

Research conclusions

Patients may have more of a preference for less invasive treatment of trigger finger. This information can help providers better frame discussions around shared decision making with patients.

Research perspectives

Further research is needed to better understand patient factors that effect treatment choice.

FOOTNOTES

Author contributions: Blough C and Kuschner S designed the research study; Blough C and Najdawi J performed the research study and analyzed the data; Blough C and Kuschner S prepared the manuscript; all authors have read and approve the final manuscript.

Institutional review board statement: This study was exempt from IRB review as described in 45 CFR part 46. Participants were made aware of the voluntary nature of this survey and the data was collected in a way that the subjects' identity could not be ascertained by the researches.

Informed consent statement: An online, survey based, descriptive study was performed through the use of a crowdsourcing website, Amazon Mechanical Turk (AMT). Participants for this study were randomly recruited through AMT.

Conflict-of-interest statement: All the authors report no relevant conflicts of interest for this article.

Data sharing statement: No additional data are available.

STROBE statement: The authors have read the STROBE guidelines, and the manuscript was prepared and revised according to the STROBE guidelines.

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REFERENCES

1 **Lunsford D**, Valdes K, Hengy S. Conservative management of trigger finger: A systematic review. *J Hand Ther* 2019; **32**: 212-221 [PMID: 29290504 DOI: 10.1016/j.jht.2017.10.016]
2 **Gil JA**, Hresko AM, Weiss AC. Current Concepts in the Management of Trigger Finger in Adults. *J Am Acad Orthop Surg* 2020; **28**: e642-e650 [PMID: 32732655 DOI: 10.5435/JAAOS-D-19-00614]
3 **Dardas AZ**, Stockburger C, Boone S, An T, Calfee RP. Preferences for Shared Decision Making in Older Adult Patients With Orthopedic Hand Conditions. *J Hand Surg Am* 2016; **41**: 978-987 [PMID: 27524694 DOI: 10.1016/j.jhsa.2016.07.096]
4 **Huetteman HE**, Shauver MJ, Nasser JS, Chung KC. The Desired Role of Health Care Providers in Guiding Older Patients With Distal Radius Fractures: A Qualitative Analysis. *J Hand Surg Am* 2018; **43**: 312-320.e4 [PMID: 29338893 DOI: 10.1016/j.jhsa.2017.11.005]
5 **Bozic KJ**, Belkora J, Chan V, Youm J, Zhou T, Dupaix J, Bye AN, Braddock CH 3rd, Chenok KE, Huddleston JI 3rd. Shared decision making in patients with osteoarthritis of the hip and knee: results of a randomized controlled trial. *J Bone Joint Surg Am* 2013; **95**: 1633-1639 [PMID: 24048550 DOI: 10.2106/JBJS.M.00004]
6 **Bartneck C**, Duenser A, Moltchanova E, Zawieska K. Comparing the similarity of responses received from studies in Amazon's Mechanical Turk to studies conducted online and with direct recruitment. *PLoS One* 2015; **10**: e0121595 [PMID: 25876027 DOI: 10.1371/journal.pone.0121595]
7 **Buhrmester M**, Kwang T, Gosling SD. Amazon's Mechanical Turk: A New Source of Inexpensive, Yet High-Quality, Data? *Perspect Psychol Sci* 2011; **6**: 3-5 [PMID: 26162106 DOI: 10.1177/1745691610393980]
8 **Amiri MM**, Ring D, Fatehi A. People Prefer to Continue with Painful Activities Even if They Lead to Earlier Surgery. *Clin*

Orthop Relat Res 2021; **479**: 1927-1935 [PMID: 33760765 DOI: 10.1097/CORR.0000000000001730]
9 **McKee D**, Lalonde J, Lalonde D. How Many Trigger Fingers Resolve Spontaneously Without Any Treatment? *Plast Surg (Oakv)* 2018; **26**: 52-54 [PMID: 29619360 DOI: 10.1177/2292550317740691]
10 **Drijkoningen T**, van Berckel M, Becker SJE, Ring DC, Mudgal CS. Night Splinting for Idiopathic Trigger Digits. *Hand (N Y)* 2018; **13**: 558-562 [PMID: 28825334 DOI: 10.1177/1558944717725374]
11 **Wojahn RD**, Foeger NC, Gelberman RH, Calfee RP. Long-term outcomes following a single corticosteroid injection for trigger finger. *J Bone Joint Surg Am* 2014; **96**: 1849-1854 [PMID: 25410501 DOI: 10.2106/JBJS.N.00004]
12 **Dardas AZ**, VandenBerg J, Shen T, Gelberman RH, Calfee RP. Long-Term Effectiveness of Repeat Corticosteroid Injections for Trigger Finger. *J Hand Surg Am* 2017; **42**: 227-235 [PMID: 28372638 DOI: 10.1016/j.jhsa.2017.02.001]
13 **Nimigan AS**, Ross DC, Gan BS. Steroid injections in the management of trigger fingers. *Am J Phys Med Rehabil* 2006; **85**: 36-43 [PMID: 16357547 DOI: 10.1097/01.phm.0000184236.81774.b5]
14 **Langer D**, Maeir A, Michailevich M, Luria S. Evaluating Hand Function in Clients with Trigger Finger. *Occup Ther Int* 2017; **2017**: 9539206 [PMID: 29097982 DOI: 10.1155/2017/9539206]
15 **N JHS**, L AHAF, R GVG, da Silveira DCEC, B PN, Almeida SF. Epidemiology of Trigger Finger: Metabolic Syndrome as a New Perspective of Associated Disease. *Hand (N Y)* 2021; **16**: 542-545 [PMID: 31456430 DOI: 10.1177/1558944719867135]
16 **Chammas M**, Bousquet P, Renard E, Poirier JL, Jaffiol C, Allieu Y. Dupuytren's disease, carpal tunnel syndrome, trigger finger, and diabetes mellitus. *J Hand Surg Am* 1995; **20**: 109-114 [PMID: 7722249 DOI: 10.1016/s0363-5023(05)80068-1]
17 **Zyluk A**, Puchalski P. Hand disorders associated with diabetes: a review. *Acta Orthop Belg* 2015; **81**: 191-196 [PMID: 26280955 DOI: 10.1016/s0363-5023(03)80421-5]
18 **Mustafa KN**, Khader YS, Bsoul AK, Ajlouni K. Musculoskeletal disorders of the hand in type 2 diabetes mellitus: prevalence and its associated factors. *Int J Rheum Dis* 2016; **19**: 730-735 [PMID: 26259148 DOI: 10.1111/1756-185X.12617]
19 **Makkouk AH**, Oetgen ME, Swigart CR, Dodds SD. Trigger finger: etiology, evaluation, and treatment. *Curr Rev Musculoskelet Med* 2008; **1**: 92-96 [PMID: 19468879 DOI: 10.1007/s12178-007-9012-1]
20 **Rozental TD**, Zurakowski D, Blazar PE. Trigger finger: prognostic indicators of recurrence following corticosteroid injection. *J Bone Joint Surg Am* 2008; **90**: 1665-1672 [PMID: 18676896 DOI: 10.2106/JBJS.G.00693]
21 **Shapiro LM**, Eppler SL, Kamal RN. The Feasibility and Usability of a Ranking Tool to Elicit Patient Preferences for the Treatment of Trigger Finger. *J Hand Surg Am* 2019; **44**: 480-486.e1 [PMID: 30797655 DOI: 10.1016/j.jhsa.2019.01.005]
22 **Brozovich N**, Agrawal D, Reddy G. A Critical Appraisal of Adult Trigger Finger: Pathophysiology, Treatment, and Future Outlook. *Plast Reconstr Surg Glob Open* 2019; **7**: e2360 [PMID: 31592381 DOI: 10.1097/GOX.0000000000002360]
23 **Everding NG**, Bishop GB, Belyea CM, Soong MC. Risk factors for complications of open trigger finger release. *Hand (N Y)* 2015; **10**: 297-300 [PMID: 26034447 DOI: 10.1007/s11552-014-9716-9]
24 **Schofield CB**, Citron ND. The natural history of adult trigger thumb. *J Hand Surg Br* 1993; **18**: 247-248 [PMID: 8501386 DOI: 10.1016/0266-7681(93)90120-5]
25 **Rodgers JA**, McCarthy JA, Tiedeman JJ. Functional distal interphalangeal joint splinting for trigger finger in laborers: a review and cadaver investigation. *Orthopedics* 1998; **21**: 305-9; discussion 309 [PMID: 9547815 DOI: 10.3928/0147-7447-19980301-13]
26 **Teo SH**, Ng DCL, Wong YKY. Effectiveness of proximal interphalangeal joint-blocking orthosis vs metacarpophalangeal joint-blocking orthosis in trigger digit management: A randomized clinical trial. *J Hand Ther* 2019; **32**: 444-451 [PMID: 30030005 DOI: 10.1016/j.jht.2018.02.007]
27 **Tarbhai K**, Hannah S, von Schroeder HP. Trigger finger treatment: a comparison of 2 splint designs. *J Hand Surg Am* 2012; **37**: 243-249, 249.e1 [PMID: 22189188 DOI: 10.1016/j.jhsa.2011.10.038]
28 **Colbourn J**, Heath N, Manary S, Pacifico D. Effectiveness of splinting for the treatment of trigger finger. *J Hand Ther* 2008; **21**: 336-343 [PMID: 19006759 DOI: 10.1197/j.jht.2008.05.001]
29 **Kamath J**, Jain M, Madegowda A. A Simple Splint for Trigger Finger. *J Hand Microsurg* 2022; **14**: 109-110 [PMID: 35256836 DOI: 10.1055/s-0040-1709220]
30 **Howard LD Jr**, Pratt DR, Bunnell S. The use of compound F (hydrocortone) in operative and non-operative conditions of the hand. *J Bone Joint Surg Am* 1953; **35-A**: 994-1002 [PMID: 13108902 DOI: 10.2106/00004623-195335040-00019]
31 **Dala-Ali BM**, Nakhdjevani A, Lloyd MA, Schreuder FB. The efficacy of steroid injection in the treatment of trigger finger. *Clin Orthop Surg* 2012; **4**: 263-268 [PMID: 23205235 DOI: 10.4055/cios.2012.4.4.263]
32 **Grandizio LC**, Speeckaert A, Brothers J, Graham J, Klena JC. Predictors of Recurrence After Corticosteroid Injection for Trigger Digits. *Hand (N Y)* 2017; **12**: 352-356 [PMID: 28644937 DOI: 10.1177/1558944716668862]
33 **Seigerman D**, McEntee RM, Matzon J, Lutsky K, Fletcher D, Rivlin M, Vialonga M, Beredjiklian P. Time to Improvement After Corticosteroid Injection for Trigger Finger. *Cureus* 2021; **13**: e16856 [PMID: 34522494 DOI: 10.7759/cureus.16856]
34 **Turowski GA**, Zdankiewicz PD, Thomson JG. The results of surgical treatment of trigger finger. *J Hand Surg Am* 1997; **22**: 145-149 [PMID: 9018628 DOI: 10.1016/s0363-5023(05)80195-9]
35 **Matzon JL**, Lebowitz C, Graham JG, Lucenti L, Lutsky KF, Beredjiklian PK. Risk of Infection in Trigger Finger Release Surgery Following Corticosteroid Injection. *J Hand Surg Am* 2020; **45**: 310-316 [PMID: 32113702 DOI: 10.1016/j.jhsa.2020.01.007]
36 **Ng WKY**, Olmscheid N, Worhacz K, Sietsema D, Edwards S. Steroid Injection and Open Trigger Finger Release Outcomes: A Retrospective Review of 999 Digits. *Hand (N Y)* 2020; **15**: 399-406 [PMID: 30239211 DOI: 10.1177/1558944718796559]
37 **Zhao JG**, Kan SL, Zhao L, Wang ZL, Long L, Wang J, Liang CC. Percutaneous first annular pulley release for trigger digits: a systematic review and meta-analysis of current evidence. *J Hand Surg Am* 2014; **39**: 2192-2202 [PMID: 25227600 DOI: 10.1016/j.jhsa.2014.07.044]
38 **Amirfeyz R**, McNinch R, Watts A, Rodrigues J, Davis TRC, Glassey N, Bullock J. Evidence-based management of adult trigger digits. *J Hand Surg Eur Vol* 2017; **42**: 473-480 [PMID: 28488453 DOI: 10.1177/1753193416682917]

39 **Zhuang T**, Wong S, Aoki R, Zeng E, Ku S, Kamal RN. A Cost-Effectiveness Analysis of Corticosteroid Injections and Open Surgical Release for Trigger Finger. *J Hand Surg Am* 2020; **45**: 597-609.e7 [PMID: 32471754 DOI: 10.1016/j.jhsa.2020.04.008]

40 **Kerrigan CL**, Stanwix MG. Using evidence to minimize the cost of trigger finger care. *J Hand Surg Am* 2009; **34**: 997-1005 [PMID: 19643287 DOI: 10.1016/j.jhsa.2009.02.029]

41 **Shauly O**, Gould D, Patel K. Crowdsourcing the public's perception of microsurgical and nonsurgical interventions for erectile dysfunction. *Eur J Plast Surg* 2020; **43**: 443-452 [DOI: 10.1007/s00238-020-01639-7]

42 **Mayfield CK**, Thomas I, Shauly O, Gould DJ, Seruya M. Validating Grading of Aesthetic Outcomes of Web Space Reconstruction for Finger Syndactyly: Crowdsourcing Public Perceptions Using Amazon Mechanical Turk. *Aesthet Surg J Open Forum* 2021; **3**: ojaa046 [PMID: 33791667 DOI: 10.1093/asjof/ojaa046]

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SYSTEMATIC REVIEWS

Viral infections in orthopedics: A systematic review and classification proposal

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Abstract

BACKGROUND

Although the impact of microbial infections on orthopedic clinical outcomes is well recognized, the influence of viral infections on the musculoskeletal system might have been underestimated.

AIM

To systematically review the available evidence on risk factors and musculoskeletal manifestations following viral infections and to propose a pertinent classification scheme.

METHODS

We searched MEDLINE, Cochrane Central Register of Controlled Trials (CENTRAL), the Reference Citation Analysis (RCA), and Scopus for completed studies published before January 30, 2021, to evaluate risk factors and bone and joint manifestations of viral infection in animal models and patient registries. Quality assessment was performed using SYRCLE's risk of bias tool for animal studies, Moga score for case series, Wylde score for registry studies, and Newcastle-Ottawa Scale for case-control studies.

RESULTS

Six human and four animal studies were eligible for inclusion in the qualitative synthesis. Hepatitis C virus was implicated in several peri- and post-operative complications in patients without cirrhosis after major orthopedic surgery. Herpes virus may affect the integrity of lumbar discs, whereas Ross River and Chikungunya viruses provoke viral arthritis and bone loss.

CONCLUSION

Evidence of moderate strength suggested that viruses can cause moderate to severe arthritis and osteitis. Risk factors such as pre-existing rheumatologic disease contributed to higher disease severity and duration of symptoms. Therefore, based on our literature search, the proposed clinical and pathogenetic classification scheme is as follows: (1) Viral infections of bone or joint; (2) Active bone and joint inflammatory diseases secondary to viral infections in other organs or tissues; and (3) Viral infection as a risk factor for post-surgical bacterial infection.

Key Words: Viral infection; Musculoskeletal system; Bone and joint manifestations; Chikungunya; Zika; Hepatitis C virus; Herpesviridae; Ross River virus; Cross-reactivity; Classification

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Core Tip: Viral infections can include multiple orthopedic manifestations, thus resulting in significant distress. In addition, the outcome of orthopedic surgeries may be influenced by certain chronic viral infections such as hepatitis C virus. There is evidence of autoimmune-mediated mechanisms, immunosuppression, and perhaps direct viral infection provoking this, although the precise mechanisms have yet to be fully understood. In this review, a classification scheme was proposed. However, further research is needed to unveil the relative contributions of the identified mechanisms and develop novel preventative and treatment strategies.

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INTRODUCTION

Fracture-related and periprosthetic joint infections (PJIs) represent dreadful complications of orthopedic surgery[1]. Although the impact of microbial infections has been well documented, the influence of viral infections on orthopedics might have been underestimated[2]. The first investigation into the probable cause of bone reactions brought on by viral infections was conducted in 1962 by Marcowa[3], who examined the tick-borne encephalitis virus's ability to cause mice to develop tibial osteitis histologically and radiographically. The potential cause of bone reaction due to viral infections was firstly studied in 1962 by Marcowa[3], who histologically and radiographically evaluated tick-borne encephalitis virus, which induced tibial osteitis in mice. Since then, evidence has suggested that viral agents, such as parvovirus B19, hepatitis B, C virus, Human immunodeficiency virus (HIV), and alphavirus, cause viral arthritis with an estimated incidence of 1% of all acute arthritides[4].

Furthermore, an elevated risk of total hip arthroplasty (THA) revision has been documented in HIV patients 90 days post-procedure[5]; whereas sepsis, pneumonia, microbial joint infection, and revision surgery are more ubiquitous in hepatitis C virus (HCV)/hepatitis B virus (HBV) patients after total joint arthroplasty[5]. In addition, orthopedic manifestations of Alphaviridae have been observed[6], with Chikungunya virus (CHIKV), Ross River virus (RRV), and Sindbis virus being implicated and with viral ribonucleic acid (RNA) being present in joints for months post-infection[6]. Flaviviridae are also relevant as arthralgia occurs in 23%-80% of Zika virus infections[7]. In addition, a decrease in Alkaline

Phosphatase (ALP) production by osteoblasts post-infection tends to delay their maturation[8].

Arthritis is a significant pain generator in HIV patients and is mediated by the premature degenerative joint disease through non-specific chronic synovitis and thickening of the 'vessels' wall/tubuloreticular structures[9]. HIV further accelerates bone degeneration by altering the sealing zone and increasing osteoclast-mediated bone resorption[10]. Finally, Parvovirus B19, a deoxyribonucleic acid (DNA) virus, can cause mono- or polyarthropathy with a preponderance in adult female patients (80%)[11] and with a duration of symptoms varying from 2 months to 4 years[11].

Additionally, it would be reasonable to broadly categorize the orthopedic signs and symptoms of viral infections into three somewhat similar groups. More precisely, manifestations can be provoked by the inflammatory response or direct infection during the acute phase of the illness. This could be the case in Flaviviridae members, such as the Zika virus and Alphaviridae member RRV[7,8]. In addition, the Chikungunya virus (CHIKV) causes orthopedic manifestations mainly *via* autoimmune mechanisms such as cross-reactivity[6]. Lastly, certain viral infections could predispose to microbial infections due to immunosuppression. Examples would be HIV and HCV/HBV[5]. Of note, in the case of HIV, this was more commonly documented in the pre-highly active antiretroviral therapy (HAART) era[5].

In this present systematic review, we sought to systematically evaluate the risk factors for developing persistent arthritis after a viral infection and the impact of viral infections on musculoskeletal clinical outcomes. Lastly, we sought to categorize the musculoskeletal manifestations of viral infections according to their causative mechanism and offer insight into novel treatment strategies.

MATERIALS AND METHODS

This review included human and animal model studies exploring bone and joint manifestations secondary to human viral infections. Observational studies, papers that did not report clinical outcomes, rheumatological articles, and papers that assessed patients under 18 years of age were excluded. Moreover, case series with less than ten subjects were discarded to increase the validity and credibility of our reporting. We searched MEDLINE, Cochrane Central Register of Controlled Trials (CENTRAL), the Reference Citation Analysis, and Scopus for completed studies published before January 30, 2021. We also considered the trial registries of ClinicalTrials.gov, the EU clinical trial register, and the Australian New Zealand Clinical Trials Registry to search for completed yet unpublished studies. The search terms for MEDLINE were 'clinical trials', 'case series,' 'viral infection,' and 'bone'/joint'. KT and KS conducted the literature search independently without any language restrictions. Articles were deduplicated and examined for eligibility using title and article screening. Subsequently, a full-text evaluation of the remainder of the articles was performed. Any discrepancies between authors in the study selection procedure were resolved through discussion. KT and KS independently extracted relevant information from the included full-text articles, including any risk factors for persistent musculoskeletal manifestations.

Quality assessment

Two reviewers (KT and DK) assessed the quality of the included studies using SYRCLE's risk of bias tool[12] for animal studies, Newcastle-Ottawa Scale for case-control studies[13], Wylde score for Registry Studies[14], and Moga score for case series[15]. For the included animal studies, the following domains were considered: sequence generation, baseline characteristics (*i.e.*, sex, age, weight), allocation concealment, random housing, identical housing conditions, blinding of caregivers, random outcome assessment, blinding of outcome assessors, incomplete outcome data, selective outcome reporting, other bias (*i.e.*, contamination, pooling drugs, the influence of funders, units of analysis errors, design risk, new animals added for dropouts). Regarding case-control studies, we assessed the adequacy of case definition, representativeness, control selection and definition, comparability of cases and controls based on design analysis, ascertainment of exposure on the same method for both cases and controls, and non-response rates. For registry studies, we evaluated the following domains: consecutive patients, representativeness, percentage of follow-up, and minimization of potential confounding. In addition, we checked the quality of the included case studies against the 18-criteria checklist included in the Moga score[15].

Outcome assessment

The primary outcome measure of the present systematic review was bone and joint manifestations after direct viral infections other than those associated with abnormal autoimmune responses. The secondary outcomes included the general impact of viruses on clinical features and the study of any risk factors for developing persistent musculoskeletal manifestations following viral infections.

RESULTS

The literature search yielded 995 potentially relevant records. After removing duplicates, the remaining 985 articles were screened for eligibility. Following title and abstract evaluation, 84 articles were eligible for inclusion. The full texts were assessed, and ten articles were included for systematic review (Figure 1). Of these papers, two addressed treatment strategies, and three dealt with arthroplasties in patients with HCV. In addition, six papers involved humans looking at Chikungunya, HCV, and RRV [16-25].

Quality assessment

For the included animal studies, the domains of follow-up, minimization of potential confounding, representativeness, baseline characteristics (*i.e.*, sex and age), other bias (*i.e.*, contamination, pooling drugs, influence of funders, unit of analysis errors, design risk, new animals added for dropouts) and adequate definitions of cases, selection and definition of controls, ascertainment of the same exposure to control and cases, and comparability of cases and controls were considered to be at low risk of bias (Supplementary Table 1). Moreover, the following domains were judged to be at unclear risk of bias: sequence generation, allocation concealment, random housing, blinding of caregivers, random outcome assessment, blinding of outcome assessors, incomplete outcome data, and selective outcome reporting (Supplementary Table 1). Furthermore, the domains of identical housing conditions were found to be at an unclear risk of bias (Supplementary Table 1). Regarding the case-control studies, the Newcastle-Ottawa score was used, and the only domain found to have an unclear risk of bias was the non-response rate for both included papers (Supplementary Table 2). On the contrary, the adequacy and representativeness of cases and the selection and definition of controls had a low risk of bias (Supplementary Table 2). Lastly, the comparability of cases and controls based on design, and the ascertainment of exposure, were deemed to be at low risk of bias (Supplementary Table 2). Furthermore, following an appraisal of the two included registry studies, representativeness was deemed adequate because the articles were multicenter with sufficient follow-up (Supplementary Table 3). Lastly, the case series of Alpantaki *et al* [25] and Soden *et al*[22] were evaluated utilizing the Moga score (Supplementary Table 4), with the former study reaching a sum of 13 and the latter achieving a sum of 10 (Supplementary Table 4).

Arthroplasties and major orthopedic surgeries in patients with HCV infection

Three studies related to HCV infection were identified[18-20]. In particular, Best *et al*[18] published a retrospective cohort study in 2015 looking at non-cirrhotic HCV patients subjected to total hip and knee arthroplasty. Half of the included cases were subjected to total hip arthroplasty (THA) (approximately 50% males), and the rest to total knee arthroplasty (TKA) (40% males) (Table 1). Likewise, Chowdhury *et al*[19] published a retrospective study in 2017 to assess the effect of HCV infection 90 days after TKA, THA, and spine surgery. This study included 2262 patients, half HCV positive (Table 1). Moreover, Pour *et al*[20] investigated HCV-positive patients relative to matched controls with a 1:2 ratio in 2011 and included individuals who underwent THA and TKA from 1995-2006 in the US (Table 1). Risk factors in the article published by Best *et al*[18] included length of hospital stay (LOHS), age, gender, comorbidities, post-operative bleeding, thrombocytopenia, transfusion reaction, cardiac complications, respiratory and renal complications, as well as osteomyelitis, and infection. In the study of Chowdhury *et al*[19], age, race, readmission, and death within 30 or 90 days post-operatively were identified as outcome measures/risk factors (Table 1). Lastly, those identified by Pour *et al*[20] were age, gender, BMI, preoperative platelets, complication rate, and LOHS (Table 1). Best *et al*[18] noted that patients from the HCV-positive group presented fewer comorbidities such as diabetes mellitus, hypertension, cardiovascular disease, and osteoporosis as well as a shorter LOHS (5.3 ± 3.4 compared with 5.4 ± 5.1 days in the non-HCV group, $P < 0.001$)[18]. In the above study, the overall complication rate was higher in the HCV group with prosthetic joint infection (OR was 9.5 [95%CI 8.3 to 10.8], $P < 0.001$)[18]. More specifically, acute renal failure and peripheral vascular complications showed an OR of 8 (95%CI 7.4 to 8.6, $P < 0.001$) and 4.8 (95%CI 4.3 to 5.4, $P < 0.001$), respectively[18]. It is underlined that stratification of the 'patients' cohort into THA and TKA revealed a significant difference in the comorbidities of these patients[18]. Other complications noted in the HCV group were deep venous thrombosis and pulmonary embolism, pneumonia, post-operative bleeding, and a higher blood transfusion rate[18]. Similar results were presented by Pour *et al*[20], who noted a statistically significant difference when the complications of revision hip or knee arthroplasty were compared between the two study groups ($P < 0.05$)[20]. When comparing the results of Best and Pour's studies, the only difference was the LOHS [18, 20]. Furthermore, Chowdhury *et al*[19]; reported higher readmission and mortality rates in the HCV group after THA, TKA, lumbar interbody fusion, decompression, and discectomy.

Orthopaedic manifestations induced by low-grade viruses

The role of a Herpes virus infection in intervertebral disc degeneration was studied by Alpantaki *et al* [25]. More precisely, 16 consecutive patients (8 males) with a mean age of 40 years undergoing discectomy within six months of lumbar disc herniation were included. Those individuals constituted the study group, while two patients with thoracolumbar burst fractures formed the control group[25].

Table 1 Study characteristics of articles dealing with hepatitis C virus patients undergoing total knee arthroplasty/total hip arthroplasty or other major orthopedic surgery

Author (year)	Study design	Inoculated groups and number of subjects	Risk factors/outcome measures	Outcomes	Follow-up
Best (2014)	Retrospective cohort study of non-cirrhotic HCV positive individuals and HCV negative patients who underwent TKA/THA in the USA from 1990-2007	Group 1: 26444 HCV patients, 14452 subjected to THA (51.2% males) and 11992, to TKA (36.5% males); Group 2: 8336822 HCV negative patients, 2968679 subjected to THA (42.6% males), and 5370202 subjected to TKA (36.2% males)	Gender, Age, LOHS, Comorbidities, post-operative bleeding, thrombocytopenia, transfusion reaction, cardiac complications, peripheral vascular complications, urinary complications, acute renal failure, myocardial infarction, pulmonary embolism, pneumonia, deep venous thrombosis, blood transfusion, osteomyelitis, and infection	LOHS, age, rates of total complications, and post-operative bleeding	Not specified
Chowdhury (2017)	Retrospective registry study with a propensity-matched cohort including HCV patients and uninfected participants who have undergone TKA, THA, and spine procedures in the USA between 2006-2014	Group 1: 1131 (52% males) with HCV; Group 2: 95161 (56% males) non-HCV individuals, and after propensity score matching, 1131 non-HCV patients were matched to the HCV group, and the cohort consisted of 2262 patients	Mortality within 30- or 90-d, readmission, and complications within 30 and 90 d	Mortality assessment, complication, and readmission rate evaluation	Up to 30 and 90 d post-operatively or upon complication
Pour (2011)	Retrospective case-control study with a control group matched at a 2:1 ratio with asymptomatic HCV patients subjected to THA and TKA from 1995-2006 in the USA	Group 1: n = 39 (29 males) HCV patients who have undergone THA; Group 2: n = 80 (60 males) patients who have undergone THA (control group); Group 3: n = 32 (15 males) HCV patients subjected to TKAGroup 4: 64 (30 males) patients subjected to TKA (control group)	Age, gender, BMI, need for transfusion, preoperative PLTS, LOHS, and the complication rate	Complication assessment (wound, mechanical, fracture, reoperation, revision); Length of hospital stay	101 mo (range 66-140) for the HCV patients subjected to THA; 94 mo (range 45-131 mo) for the control group subjected to THA, 117 months (range 67-150 mo) for the HCV patients subjected to TKA; 98 mo (range 49-133 mo) for the control group subjected to TKA

TKA: Total knee arthroplasty; THA: Total hip arthroplasty; HCV: Hepatitis C virus; LOHS: Length of hospital stay; PLTS: Platelets; BMI: Body mass index.

Moreover, material from the herniated or fractured disc and peripheral blood samples were sampled intraoperatively. Polymerase chain reaction (PCR) detected Herpesviridae DNA in 13 study group subjects[25].

Regarding blood samples, seropositivity of patients was assessed with IgM and IgG assays for HSV-1 and Cytomegalovirus (CMV)[25]. Moreover, the surrounding tissues of the herniated disc were tested by qRT-PCR for mRNA levels of TNF-α and IL-6[25]. Herpes simplex virus type-1 (HSV-1) DNA was detected in 9/16 subjects, and CMV DNA was found in 6 subjects, while 2/16 subjects had a co-infection with both species[25]. On the contrary, DNA from HSV-2, Varicella-Zoster Virus, Epstein-Barr Virus, Human Herpes Virus 6, 7, and 8 were not found in any participants, and the control group tested negative for Herpesviridae DNA[25]. In addition, the IgG serological tests were positive in 13/16 subjects with PCR positivity for viral DNA, whereas all subjects were negative for IgM antibodies, indicating the absence of an acute reaction at the time of surgical excision[25]. Furthermore, IL-6, TNF-a, and viral mRNA in the study group were two to three times higher than in the control group[25]. This is the only indication that the Herpesviridae evoke disc herniation in individuals, regardless of age or sex [25].

Ross River Virus infection causes viral arthritis

We note that almost all Alphaviruses can cause joint manifestations. For instance, the RRV is detectable in the serum within 7-10 days after the initial symptoms, with synovial fluid infiltration by mononuclear cells being a common phenomenon throughout the disease. Soden *et al*[22] assessed synovial membrane biopsies of inflamed knees weeks after the initial symptoms of RRV infection (Table 2), whereas Chen *et al*[16] studied the effects of the RRV on human osteoblasts, bone loss in an established murine model, and viral arthralgia. Soden *et al*[22] also used RT-PCR to detect viral RNA from synovial membrane biopsy samples that were histologically evaluated with standard H&E staining, immunohistochemistry, and TRIzol treatment[22]. Chen *et al*[16] included 21-d-old male and female C57BL/6 WT mice inoculated with 10^4 PFU RRV T48 strain (Table 2). This study replicated bone infection and implemented μCT to assess bone loss in WT mice (Table 2). In addition, it compared the RANKL/osteoprotegerin

Table 2 Study characteristics of the included articles dealing with the Ross River Virus

Author (year)	Study design	Inoculated groups and number of subjects	Outcomes	Follow-up
Chen (2014)	*In vitro* and *in vivo* animal interventional study	For the *in vitro* experiment: 21-day-old male and female C57BL/6 WT mice were inoculated in the thorax with 10^4 PFU of RRV. Those mice received 500 μg of anti-IL-6 antibody injections on days 0 and 2, 4, 6, 8 post-infection. For the *in vivo* investigation: Serum samples from 14 Ross River virus patients (7M and 7F) were obtained, and serum from 13 healthy individuals (7M). Synovial fluid samples from 12 RRV-induced polyarthritis patients (6M) were retrieved and from 6 healthy individuals (3M).	The animal part of the study investigated whether RRV replicates in the bone (murine model) and viral titers were measured. μCT imaging was used to assess the impact of the infection on bone architecture and loss. The role of IL-6 on bone loss was evaluated. The human part of the study looked at OPG, RANKL, and TRAP5b levels in RRV-positive patients.	Not specified
Soden (2000)	Prospective observational study involving humans	Biopsy tissue from inflamed knees from 12 patients was retrieved.	Histological examination of the synovial membrane. RT-PCRto look for the presence of viral RNA	The follow-up was performed at 3-mo intervals until 6 m following symptom resolution

RANKL: Receptor activator of nuclear factor kappa beta (NF-kB ligand); TRAP5b: Tartrate-resistant acid phosphatase serum band 5 (TRAP5b); WT: Wild type; RT-PCR: Reverse transcription-polymerase chain reaction; μCT: Micro-computed tomography; RRV: Ross River virus; M: Male; F: Female; IL-6: interleukin 6.

(OPG) levels in the serum of healthy and RRV-infected individuals (Table 2). Soden *et al*[22] detected RRV RNA in the synovial membrane in 2 subjects 5 weeks after the onset of symptoms, with almost all subjects presenting with detectable histological abnormalities, including minor lining layer hyperplasia, vascular proliferation, and mononuclear cell infiltration[22]. This study proved that RRV affects the joints by directly triggering an inflammatory reaction and is also detectable weeks after the initial symptoms[22]. Chen *et al*[16] detected high viral titers in the femur, tibia, patella, and foot, mainly in osteoblastic bone cells. Notably, high viral levels were detected until day 21 post-infection[16]. By day 15, post-infection μCT imaging showed an evident bone loss in the tibial epiphysis, metatarsal joints, and vertebrae, accompanied by a decrease in trabecular thickness and a reduction in the growth plate [16]. By contrast, these findings were not noticed in the control group[16]. Lower OPG and higher RANKL levels were observed in the study group, while serum TRAP5b levels were also higher[16]. These findings indicate increased osteoclastogenesis in humans, similar to that observed in a murine model[16]. It is worth noting that the RRV also has a tropism for osteocytes[16].

Chikungunya evokes bone and joint manifestations

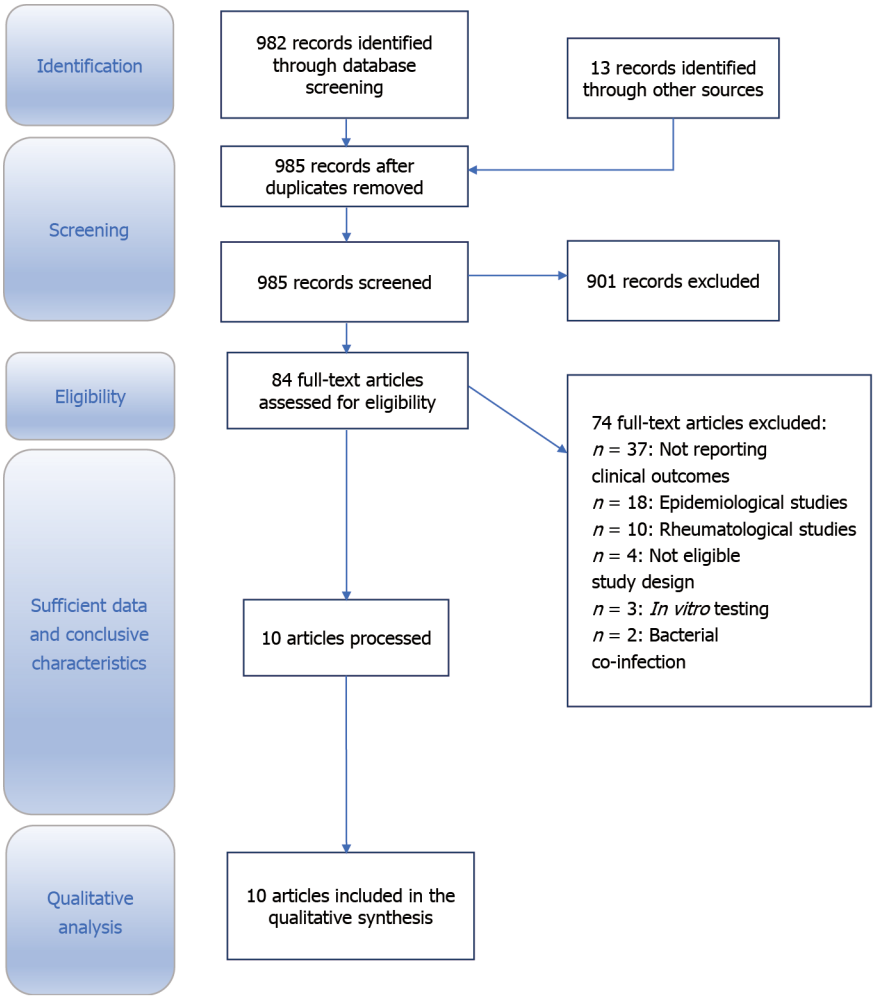
Four studies looking at CHIKV alphavirus joint manifestations fulfilled our eligibility criteria (Table 3). Chang *et al*[23] recruited 907 clinically and laboratory-confirmed CHIKV-infected patients. Of these, 38 presented with chronic knee arthritis and were deemed eligible for selection. Furthermore, a control group with ten location-matched individuals was considered (Table 3). Chen *et al*[21] studied bone loss after CHIKV infection by recruiting 14 CHIKV patients (6 males) and a control group consisting of 7 healthy individuals (3 males) (Table 3). The second part of the experiment included 25 day-old C57BL/6 mice infected with CHIKV-mCherry (Table 3). Goupil *et al*[24] studied bone and cartilage loss during CHIKV infection by employing two groups of mice featuring IRF 3/7 with deficient type 1 interferon response and adult wild-type C57BL/6. The study group consisted of 11 IRF mice and the control group of 9 C57BL/6 mice[24]. Hawman *et al*[17] studied the persistence of the viral RNA and its role in 'joint pathology. Two groups of 3-wk-old C57BL/6J WT mice and $Rag1^{-/-}$ with a lack of T and B cells were formed, and a control group was also included. Chang *et al*[23] collected synovial fluid samples for viral culture and performed qRT-PCR and mass spectrometry for the detection/quantification of viral genome and proteins, respectively (Table 3). Moreover, serum samples were analyzed for CRP, IgM, IgM-RF, anti-cyclic citrullinated peptide (anti-CCP), and selected cytokine and chemokine levels[23]. Chen *et al*[21] collected serum from the 3rd to the 22nd post-infection week and compared the RANKL/OPG of the 14 CHIKV patients and the seven healthy participants. In the second part of the study, 25 d old C57BL/6 mice were infected with CHIKV-mCherry (20 μL of 10^5 PFU at the ventral side of the foot), and a control group was injected with saline (Table 3)[21]. They were followed up on the 1st, 3rd, 7th, and 15th days post-infection[21]. Goupil *et al*[24] injected IRF 3/7 mice with IFN-1 deficiency, and C56BL/6 WT mice, with 2 × 10^4 PFU CHIKV SVO 476-96 at the caudoventral aspect of the hindfoot[24]. In addition, intact hindlimbs were collected from both groups and scanned *via* μCT to evaluate differences in the morphology of joints and the trabecular bones post-infection[24]. Furthermore, histopathological analysis was performed using hematoxylin, eosin, and Mason's Trichrome staining [24]. Hawman *et al*[17] utilized CHIKV patients' serum to inoculate $Rag1^{-/-}$ mice which lacked T and B cells, and WT mice with CHIKV SL 15649 in the left rear footpad[17]. Viral titers were measured, and

Table 3 Study characteristics of the included articles dealing with Chikungunya virus infection

Author (year)	Virus information	Study design	Inoculated groups and number of subjects	Outcome measures	Follow-up
Chang (2017)	Colombian patients infected by CHIKV	Case-control study of 38 participants with CHIVK and chronic arthritis and 10 location-matched controls without CHIKV or arthritis	Group 1: Out of 907 patients who were clinically (424) and laboratory (483) confirmed for CHIKV, 38 individuals with chronic arthritis post-infection were selected; Group 2: 10 matched controls without CHIKV/arthritis were considered	Synovial fluid samples were analyzed by PCR, and mass spectrometry for viral proteins. No virus could be detected.	Not specified
Chen (2015)	Chikungunya virus from infected patients' serum. CHIKV-mCherry strain was also used	*In vitro* study utilizing serum from 14 CHIK patients and 7 healthy individuals; *In vivo* animal study utilizing 25 d-old C57BL/6 mice infected with CHIKV/mCherry	Group 1: Serum from 14 CHIKV patients (8F 6M) was collected between the 3rd and 22nd week post-infection; Group 2: Serum from 7 (4F and 3M) healthy individuals was also used; Group 1: 25 d-old mice were infected with 20 μL 10^5 PFU CHIKV-mCherry in the ventral side of the foot. Group 2: Consisted of the control group of mice.	For the *in vitro* study: Serum RANKL/OPG ratio was measured; For the *in vivo* study: Day 3 post-infection peak swelling was measured until day 10. Levels of RANKL and OPG were measured inside the joint during days 1, 3, 7 and 15 post-infection.	Days 1, 3, 7, and 15 post-infection
Goupil (2016)	Chikungunya virus SVO 476-96	*In vivo* animal study featuring IRF 3/7 C57BL/6 mice (M and F > 8 wk old) and C57BL/6J mice (> 8 wk old only F)	Group 1: 11 IRF mice were intradermally injected with 2×10^4 PFU; Group 2: 9 control C57BL/6j mice were injected with 2×10^4 PFU	Intact hindlimbs were collected and scanned μCT to evaluate the difference between the morphology of two types of mice (joint, trabecular bone). Histopathological evaluation was also performed. On day 5, post-infection 4 mice were euthanized due to being lethargic, and 6 mice died due to rapid progression of the illness	For the IRF mice 1, 2, 3, 5, 6, 7th day post-infection;For the C57BL/6J mice 7, 14, 21st day post-infection
Hawman (2013)	Chikungunya SL15649 from serum sample	*In vivo* animal study featuring 3-week-old C57BL/6J mice and congenial rag_/- mice	Group 1: 55 mice were inoculated in the left rear footpad with 10^3 PFU (10 μL). MAbs (200 μg each of CHK-152 and CHK-166) were administered intraperitoneally on days -1 and 3 for prophylaxis studies. For therapeutic studies, MAbs were administered on days 21 and 25 post-infection; Group 2: Control mice were subject to mock-infection	Duration of CHIKV infection in tissues was assessed, and associated histopathological changes were evaluated	Day 3 and weeks 1, 2, 4, 6, 12, 16

CHIKV: Chikungunya virus; PCR: Polymerase chain reaction; WT: Wild type; RT-PCR: Reverse transcription polymerase chain reaction; μCT: Micro-computed tomography; M: Male; F: Female; IL-6: Interleukin 6; PFU: Plaque-forming unit; MAbs: Monoclonal antibodies.

histopathological analysis was performed[17]. Chang *et al*[23] found no evidence of viral infection, and therefore it was concluded that either CHIKV is exclusively found in synovial tissue cells or it provokes arthritis through autoimmune mechanisms. Chen *et al*[21] found higher RANKL levels in the CHIKV patients and almost the same OPG levels (Table 3) in the CHIKV and control groups. This finding indicated an osteoclastic condition during the infection. From a clinical point of view, edema was greatest on the third day of CHIKV-mCherry mice follow-up, which was eventually resolved by day 10 [21]. Moreover, the pro-osteoclastic microenvironment was created early after the acute infection as RANKL/OPG was elevated from day one and remained high thereafter[21]. In addition, CHIKV was replicated in a murine bone and induced bone loss of 25% relative to uninfected mice[21]. The immune response resulted in arthritis on the 3rd post-infection day, featuring elevated MCP-2/CCL8 and increased cellularity[21]. Goupil *et al*[24] found that C57BL/6J mice on the 7th post-infection day suffered from moderate dermatitis/dermal edema, extensive degeneration/necrosis of skeletal muscles, minimal periostitis, mononuclear/neutrophilic synovitis, and equivocal cartilage necrosis. On day 14 post-inoculation, mild to moderate dermatitis was observed, as well as extensive skeletal muscle degeneration/necrosis with early evidence of regeneration, extensive periostitis, and persistent synovitis with distal joint involvement[24]. On day 21 post-infection, the following findings were documented: minimal/mild dermatitis, resolving necrosis/inflammation of muscles (immature fibrosis), extensive periostitis with periosteal bone proliferation, subacute lymphoplasmacytic synovitis, synovial hypertrophy/fibrosis, and cartilage necrosis[24]. The tendons showed variable mild peritendonitis from day seven and minimal myocyte necrosis in the contralateral feet[24]. When the IRF type mice were assessed by Goupil *et al*[24], the following findings were observed by the fourth day post-infection: multifocal mild to moderate epidermic necrosis, mild neutrophilic dermatitis/edema, rare vascular necrosis, mild myofiber degeneration, periosteal necrosis, and minimal inflammation of



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Figure 1 The flow diagram.

tendons and cartilage. At the same time, the synovium presented with multifocal degeneration/necrosis affecting a few joints. Subsequently, extensive synovitis in multiple joints was documented[24]. By day 7, these findings worsened with extensive epidermal necrosis, extensive vascular necrosis, moderate myofiber degeneration/necrosis, bone marrow and periosteum necrosis, articular cartilage necrosis, and fibrinosuppurative synovitis in the majority of joints[24]. The tendons only presented mild inflammation[24]. It was concluded that the bone and joint manifestations resulted from acute viral infection rather than autoimmune-mediated mechanisms[24]. Hawman *et al*[17] documented that viral inoculation of Rag1$^{-/-}$ mice that lacked T and B cells resulted in higher virus titers. In addition, the histopathological analysis presented more intense synovitis, arthritis, and tendonitis[17]. These findings support the notion that joint manifestations of CHIKV infection directly result from the infection rather than the host's immune system[17]. It should be noted that the authors of the included studies proposed possible treatment strategies for CHIKV infection. In particular, Chen *et al*[21] used an inhibitor of monocyte chemoattractant protein (MCP) (*i.e.*, Bindarit) twice daily intraperitoneally (100 mg/kg) in mice which reduced joint swelling and bone loss but not viral titers[21]. Hawman *et al*[17], on the other hand, proved that tissue-specific administration of monoclonal antibodies reduced the viral RNA in these tissues.

DISCUSSION

It is undeniable that viral infections pose a substantial yet unclear impact on the musculoskeletal system. Most aspects have not yet been studied sufficiently, mainly due to the lack of technological advancements until the 21st century. In light of the above, a systematic review was designed to delineate the risk factors and orthopedic clinical outcomes secondary to viral infections. More specifically, the effects of chronic HCV infection on TKA and THA, as well as the role of Herpesviridae on lumbar disc degeneration, were addressed. Moreover, the musculoskeletal effects of the Chikungunya virus and

RRV-mediated chronic arthritis were examined.

The impact of viruses on clinical musculoskeletal outcomes

HCV is a significant cause of orthopedic complications such as an oligoarthritis of large and middle joints or rarely a rheumatoid arthritis-like illness[26]. A higher level of post-operative complications and a higher mortality rate were noted in the HCV group despite the patients being younger and having fewer medical comorbidities[18]. Nevertheless, the hospitalization of HCV patients was shorter, perhaps due to them being transferred to different units to have their complications addressed[18]. A possible explanation would be the circulating autoantibodies leading to decreased lymphoproliferation. As a result of lymphoproliferation, predisposition to infection, leukocytoclastic vasculitis[27], and glomerulonephritis[27,28] develop. In addition to the above features of HCV patients, a hypercoagulability profile was observed[18].

It should be noted that HCV has been shown to induce thrombocytopenia and impaired platelet function[29,30,31], predisposing to higher rates of bleeding[18]. Pour *et al*[20] also documented increased reoperation rates, higher mechanical complications, and hospital stays in the HCV group. To be more precise, complications included periprosthetic femoral fractures, femoral implant loosening, and hip dislocation secondary to migration of acetabular implant that required a revision of the THA [20]. On the other hand, chronic HCV disease was associated with multiple extrahepatic manifestations such as diabetes mellitus and thyroiditis, thrombocytopenia, glomerulonephritis, inflammatory myositis, arthralgia, mixed connective tissue disease, leukocytoclastic vasculitis, and lymphadenopathy. These can be attributed to circulating autoantibodies that could alter the physiological process of healing[20]. In addition, low-key inflammation can alter the function of platelets, further compounding the pathophysiologic mechanism[20]. Another aspect worth mentioning is the potential difference in the socio-economic level of HCV-infected individuals and that of healthy participants[20]. Furthermore, ancillary liver effects were investigated by Chowdhury *et al*[19], and it was thought that they were implicated in immunosuppression and impaired wound healing. These findings confirm the significance of HCV infection in post-operative outcomes and highlight the importance of including HCV testing in the preoperative workup.

Regarding the potential of Herpesviridae being a possible cause of disc degeneration, Alpantaki *et al* [25] studied 16 patients undergoing discectomy six months after lumbar disc herniation subjected to Herpesviridae DNA testing[25]. Positivity for at least one species (most commonly HSV) was found in 13[25]. Possible mechanisms implicated in disc degeneration could be the vascular channels formed during fetal development that remain patent until the 4th-6th year of life, as well as migrating macrophages and retrograde axoplasmic transport[25]. However, it remains unclear whether degeneration is solely secondary to the upregulation of inflammatory cytokines or whether viral-induced cell death could also contribute[32]. In addition, it has been postulated that Herpesvirus 6 could cause Langerhans' Histiocytosis[33]. This rare disease affecting children of 1 to 4 years of age has predominantly bone involvement, and, more often than not, the first presentation of the disease is a pathological fracture[33].

Furthermore, CHIKV has a cyclical pattern of epidemics from 7 to 20 years and affects countries neighboring the Indian Ocean, Central Africa, China, Italy, and France. After transmission *via* a mosquito bite, the virus multiplies locally and is then transferred to the whole host body *via* lymphoid organs and the bloodstream. Mononuclear cell infiltration and viral replication in muscles and joints cause severe pain and arthritis. Although CHIKV infection is self-limiting, arthritis/arthralgia occurs for a particular amount of time due to the immune response or an active viral reservoir in joints[34]. In 2018, a systematic review and meta-analysis of 2415 individuals suffering from CHIKV infection in the US revealed that 52% of the patients appeared to have persistent arthritis 10 to 72 weeks after the primary infection[35]. It has been thought that arthritis may develop due to epigenetic modifications of macrophages which present a more aggressive cell behavior[36]. Another possible cause could be the concomitant presence of seronegative rheumatoid arthritis, although this has been doubted by Chen *et al* [21]. Moreover, Chen *et al*[21] noted that Alfaviridae, such as RRV, could infect primary human osteoblasts and cause the production of inflammatory cytokines, thus promoting osteoclastogenesis[37-39]. In addition, when analyzed with μCT, it was clear that Alfaviridae could also lead to bone loss. Interestingly, after treatment with IL-6 inhibitors, bone loss was blocked, thus highlighting the central role of inflammation in pathogenesis[16]. Finally, it is essential to stress the impact of CHIVK-mediated arthritis as 82% of chronically infected patients present with arthritis that substantially impacts their quality of life[23].

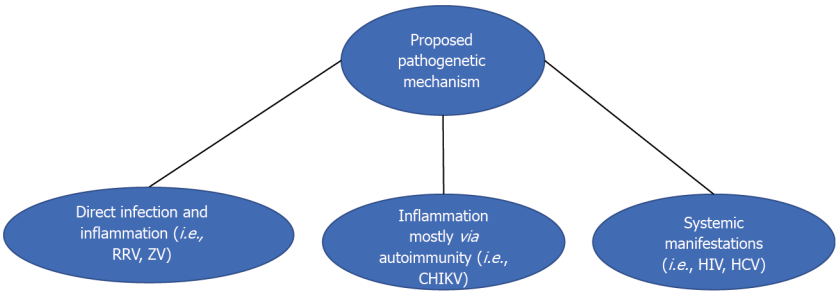
The proposed clinical and pathogenetic viral infection classification system

In the current review, we have proposed a classification system for the pathogenesis of viral infection (Table 4 and Figure 2). Regarding the first proposed category addressing the viral infections of bones and joints, we noted that the Alphavirdae member RRV replicated in murine bones[16]. To address this proposed mechanism further, we note that human osteoblasts could be infected with RRV and produce inflammatory cytokines such as IL-6. In addition, in the inflamed knees of affected patients, RRV RNA was present five weeks after the onset of symptoms[22]. However, some patients presented symptoms in the absence of detectable viruses[22], and this finding is partially congruent with the initial

Table 4 Proposed viral classification scheme

Proposed pathogenetic mechanism	Viruses involved	Evidence supporting the proposed mechanism
Direct infection and subsequent inflammation	Ross Rover and Zika viruses	RRV causes arthritis with its RNA coinciding with the appearance of symptoms; Evidence of human osteoblasts being primarily infected
Inflammation primarily through autoimmune mechanisms such as cross-reactivity	CHIKV	CHIKV causes arthritis in the absence of evident infection. Other supporting information includes rheumatoid factor negative RA and exclusive presence in the synoviocytes. Animal studies implicate a potential role of primary infection
Systemic manifestations resulting in immunosuppression	HCV and HIV	Greater rates of microbial infections in HCV patients post-surgery. Greater rates of infections post-surgery pre-HAART. High rates of mechanical and medical comorbidities

RRV: Ross River virus; HCV: Hepatitis C virus; HIV: Human immunodeficiency virus; CHIKV: Chikungunya virus; HAART: Highly active antiretroviral therapy; RA: Rheumatoid arthritis; hOBs: Human osteoblasts.



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Figure 2 Graphical demonstration of the proposed viral pathogenetic mechanism. RRV: Ross River virus; CHIKV: Chikungunya virus; HIV: Human immunodeficiency virus; HCV: Hepatitis C virus; ZV: Zika virus.

hypothesis that RRV provokes orthopedic manifestations through primary infection and inflammation [22].

Regarding the second proposed category, active bone and joint inflammatory diseases occur secondary to viral infections in other organs or tissues. CHIKV indeed causes arthralgia/arthritis without being directly detectable[23]. No evidence of it was found *via* RT-PCR, mass spectrometry, and culture of synovial fluid, thus agreeing with the initial hypothesis of it causing arthritis principally *via* cross-reactivity and suggesting immunomodulatory agents in its treatment[23]. Although, productive infection of musculoskeletal cells was reported by Chen *et al*[21]. In addition, Hawman *et al*[17] presented animal evidence revealed persistent viral infection, but safe extrapolations to human biology cannot be made based on this finding.

Lastly, the third proposed category included viral infection as a risk factor for post-surgical bacterial infection. To elaborate, we reported that HCV predisposes to immunosuppression[18] with associated increased post-surgical complications in HCV patients[19], in addition to compromised liver function and wound healing[19]. Pour *et al*[20] confirmed this finding as wound complications requiring antibiotics/wound debridement were noticeably more common in HCV patients post-surgery.

Risk factors for chronic disease – The appearance of rheumatologic diseases

The persistence of the viral genome or proteins in host cells could represent the major risk factor for chronic manifestations after the initial infection. However, no data prove any association between Epstein-Barr and rheumatoid arthritis[40]. In the setting of CHIKV infection, joint manifestations resemble inflammatory arthropathies[41], and their severity depends on the levels of cytokines. We highlight that further studies should be performed to clarify that[42].

Study limitations and implications for future research

We recognize that the lack of a consistent definition of virus-induced rheumatoid arthritis and the wide variety of musculoskeletal manifestations secondary to viral infections complicates the picture for clinicians and health policymakers. In addition, the limited number of studies addressing the above issues and the uncertainty introduced by the moderate-to-low quality of evidence of the included articles further contribute to this vagueness. It has been shown that some tropism exists for cells such as osteocytes, synovial cells, and chondrocytes. However, the pathophysiology of the infection or inflammation, the underlying processes, and the reasons for lingering symptoms are still unknown. Towards this direction, we advocate that future research should aim for the development of novel treatment

options based on the underlying mechanisms.

The role of COVID-19 on the musculoskeletal system

It is highlighted that all articles relating to COVID-19 were excluded as the vast majority were based on expert opinions and observational studies with limited follow-up and sample size. However, some aspects of this pandemic should be commented on. First, it is unknown whether osteoporosis and osteonecrosis are two common findings after COVID-19 infection, but the potential role of corticosteroid administration as a part of the therapeutic regime cannot be overlooked[43]. Another clinical finding worth mentioning is the higher incidence of late (*i.e.*, a few weeks following COVID-19 diagnosis) spinal epidural abscesses. This could be explained by 'patients' immunosuppression or the occurrence of nosocomial superinfection[44]. Finally, the binding of COVID-19 spike protein to functional receptors of ACE2, also expressed in human bone marrow, could be a possible explanation for the decreased bone matrix and early muscle disorders[45]. Although the above considerations represent some early indications of the potential connection of COVID-19 with orthopedic clinical outcomes, we underline that a safe conclusion cannot be drawn, given the limited available literature and considerable risk of bias.

CONCLUSION

Viral infections pose a major concern for microbiologists and orthopedic surgeons, given the high incidence of chronic arthritis and its detrimental effect on patients' quality of life[23]. While the literature on this topic was sparse and heterogenous, the negative influence of viruses on orthopedic surgical outcomes is evident[18-20]. We highlight that arthralgia, myalgia, and transient arthritis could result from viral infection or secondary immune processes, although each mechanism's contribution is still relatively unclear. Therefore, we advocate that the present systematic review raises awareness of the implications of viral infections in orthopedics and acts as a guide for orthopedic surgeons to classify them in a clinical and pathogenetic fashion.

ARTICLE HIGHLIGHTS

Research background

While the influence of microbial infections on orthopedic clinical outcomes is well documented, the impact of viral infections on the musculoskeletal system has been inadequately investigated.

Research motivation

Although microbial infections have been studied extensively in orthopedics, the impact of viral infections on orthopedics has not been sufficiently investigated. In addition, we are unaware of any classifications relating to viral infections in the orthopedic literature.

Research objectives

In this article, we looked at the risk factors for persistent arthritis development after a viral infection and the impact of viral infections on orthopedic clinical outcomes. In addition, we categorized orthopedic manifestations of viral infections relative to their causative mechanism.

Research methods

An extensive literature search was performed to identify completed studies published before January 30, 2021. MEDLINE, Cochrane Central Register of Controlled Trials (CENTRAL), the Reference Citation Analysis, and Scopus were searched for articles evaluating risk factors and bone/joint manifestations of viral infection in animals and humans. In addition, we assessed the quality of the included articles utilizing SYRCLE's risk of bias tool for animal studies, the Moga score for case series, the Wylde score for registry studies, and the Newcastle-Ottawa Scale for Case-control studies.

Research results

Ten articles were included in the systematic review. Of these, two dealt with treatment strategies and another three with arthroplasties in patients with hepatitis C virus (HCV). In addition, six articles addressed human beings investigating Chikungunya, HCV, and RRVs. After major orthopedic surgery, HCV was implicated in several peri- and post-operative complications. Herpes virus may affect the integrity of lumbar discs, whereas Ross River and Chikungunya viruses negatively influence bones and/or joints, resulting in viral arthritis and bone loss.

Research conclusions

Viral infections pose a significant burden in orthopedics due to the significant impact on patient quality of life. We have demonstrated a connection between viral infections and orthopedic surgical outcomes. We highlight that arthralgia, myalgia, and transient arthritis could result from viral infection or secondary immune processes, although each mechanism's contribution is still relatively unclear. We advocate that the present systematic review raises awareness of the implications of viral infections in orthopedics and acts as a guide for orthopedic surgeons to classify them in a clinical and pathogenetic fashion.

Research perspectives

We recommend that a consistent definition of virus-induced rheumatoid arthritis be developed. Furthermore, we suggest that further high-quality articles investigating novel treatment options based on the underlying mechanisms be conducted.

FOOTNOTES

Author contributions: Drago L and Kavarthapu V were involved in the study's conceptualization; Tsikopoulos K and Sidiropoulos K conducted the literature research and extracted relevant information; Tsikopoulos K and Kitridis D assessed the quality of the included studies; Christofilos SI and Meroni G were involved in the generation of tables and writing the paper; Drago L, Kavarthapu V, and Romanò CL supervised the paper and revised the paper accordingly.

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REFERENCES

1 **Metsemakers WJ**, Morgenstern M, Senneville E, Borens O, Govaert GAM, Onsea J, Depypere M, Richards RG, Trampuz A, Verhofstad MHJ, Kates SL, Raschke M, McNally MA, Obremskey WT; Fracture-Related Infection (FRI) group. General treatment principles for fracture-related infection: recommendations from an international expert group. *Arch Orthop Trauma Surg* 2020; **140**: 1013-1027 [PMID: 31659475 DOI: 10.1007/s00402-019-03287-4]
2 **Drago L**, Romanò CL, Morelli I, Benzakour T. Viral Bone Infection: A Neglected Disease? *Microorganisms* 2020; **8** [PMID: 32466516 DOI: 10.3390/microorganisms8060797]
3 **Markowa J**. Osteitis produced experimentally in mice by the virus of tick-borne encephalitis. *J Bone Joint Surg Am* 1962; **44B**: 722-734 [DOI: 10.1302/0301-620X.44B3.722]
4 **Marks M**, Marks JL. Viral arthritis. *Clin Med (Lond)* 2016; **16**: 129-134 [PMID: 27037381 DOI: 10.7861/clinmedicine.16-2-129]
5 **Kildow BJ**, Politzer CS, DiLallo M, Bolognesi MP, Seyler TM. Short and Long-Term Post-operative Complications Following Total Joint Arthroplasty in Patients With Human Immunodeficiency Virus, Hepatitis B, or Hepatitis C. *J Arthroplasty* 2018; **33**: S86-S92.e1 [PMID: 29198873 DOI: 10.1016/j.arth.2017.10.061]
6 **McCarthy MK**, Morrison TE. Persistent RNA virus infections: do PAMPS drive chronic disease? *Curr Opin Virol* 2017; **23**: 8-15 [PMID: 28214732 DOI: 10.1016/j.coviro.2017.01.003]
7 **Wimalasiri-Yapa BMCR**, Yapa HE, Huang X, Hafner LM, Kenna TJ, Frentiu FD. Zika Virus and Arthritis/Arthralgia: A Systematic Review and Meta-Analysis. *Viruses* 2020; **12** [PMID: 33036370 DOI: 10.3390/v12101137]
8 **Mumtaz N**, Koedam M, van den Doel PB, van Leeuwen JPTM, Koopmans MPG, van der Eerden BCJ, Rockx B. Zika

virus infection perturbs osteoblast function. *Sci Rep* 2018; **8**: 16975 [PMID: 30451958 DOI: 10.1038/s41598-018-35422-3]
9 **Mody GM**, Parke FA, Reveille JD. Articular manifestations of human immunodeficiency virus infection. *Best Pract Res Clin Rheumatol* 2003; **17**: 265-287 [PMID: 12787525 DOI: 10.1016/s1521-6942(03)00003-2]
10 **Raynaud-Messina B**, Bracq L, Dupont M, Souriant S, Usmani SM, Proag A, Pingris K, Soldan V, Thibault C, Capilla F, Al Saati T, Gennero I, Jurdic P, Jolicoeur P, Davignon JL, Mempel TR, Benichou S, Maridonneau-Parini I, Vérollet C. Bone degradation machinery of osteoclasts: An HIV-1 target that contributes to bone loss. *Proc Natl Acad Sci USA* 2018; **115**: E2556-E2565 [PMID: 29463701 DOI: 10.1073/pnas.1713370115]
11 **Pattison JR**. B19 virus--a pathogenic human parvovirus. *Blood Rev* 1987; **1**: 58-64 [PMID: 2844330 DOI: 10.1016/0268-960x(87)90020-8]
12 **Hooijmans CR**, Rovers MM, de Vries RB, Leenaars M, Ritskes-Hoitinga M, Langendam MW. SYRCLE's risk of bias tool for animal studies. *BMC Med Res Methodol* 2014; **14**: 43 [PMID: 24667063 DOI: 10.1186/1471-2288-14-43]
13 **Wells GA**, Shea B, O'Connell D, Peterson J, Welch V, Losos M, Tugwell P. The Newcastle-Ottawa Scale (NOS) for assessing the quality of non-randomised studies in meta-analyses. 2011. http://www.ohri.ca/programs/clinical_epidemiology/oxford.htm [DOI: 10.13105/wjma.v5.i4.80]
14 **Wylde V**, Beswick AD, Dennis J, Gooberman-Hill R. Post-operative patient-related risk factors for chronic pain after total knee replacement: a systematic review. *BMJ Open* 2017; **7**: e018105 [PMID: 29101145 DOI: 10.1136/bmjopen-2017-018105]
15 **Moga C**, Guo B, Schopflocher D, Harstall C. Development of a Quality Appraisal Tool for Case Series Studies Using a Modified Delphi Technique. Edmonton AB: Institute of Health Economics. 2012
16 **Chen W**, Foo SS, Rulli NE, Taylor A, Sheng KC, Herrero LJ, Herring BL, Lidbury BA, Li RW, Walsh NC, Sims NA, Smith PN, Mahalingam S. Arthritogenic alphaviral infection perturbs osteoblast function and triggers pathologic bone loss. *Proc Natl Acad Sci USA* 2014; **111**: 6040-6045 [PMID: 24733914 DOI: 10.1073/pnas.1318859111]
17 **Hawman DW**, Stoermer KA, Montgomery SA, Pal P, Oko L, Diamond MS, Morrison TE. Chronic joint disease caused by persistent Chikungunya virus infection is controlled by the adaptive immune response. *J Virol* 2013; **87**: 13878-13888 [PMID: 24131709 DOI: 10.1128/JVI.02666-13]
18 **Best MJ**, Buller LT, Klika AK, Barsoum WK. Increase in perioperative complications following primary total hip and knee arthroplasty in patients with hepatitis C without cirrhosis. *J Arthroplasty* 2015; **30**: 663-668 [PMID: 25492245 DOI: 10.1016/j.arth.2014.11.013]
19 **Chowdhury R**, Chaudhary MA, Sturgeon DJ, Jiang W, Yau AL, Koehlmoos TP, Haider AH, Schoenfeld AJ. The impact of hepatitis C virus infection on 90-day outcomes following major orthopaedic surgery: a propensity-matched analysis. *Arch Orthop Trauma Surg* 2017; **137**: 1181-1186 [PMID: 28674736 DOI: 10.1007/s00402-017-2742-7]
20 **Pour AE**, Matar WY, Jafari SM, Purtill JJ, Austin MS, Parvizi J. Total joint arthroplasty in patients with hepatitis C. *J Bone Joint Surg Am* 2011; **93**: 1448-1454 [PMID: 21915551 DOI: 10.2106/JBJS.J.00219]
21 **Chen W**, Foo SS, Taylor A, Lulla A, Merits A, Hueston L, Forwood MR, Walsh NC, Sims NA, Herrero LJ, Mahalingam S. Bindarit, an inhibitor of monocyte chemotactic protein synthesis, protects against bone loss induced by chikungunya virus infection. *J Virol* 2015; **89**: 581-593 [PMID: 25339772 DOI: 10.1128/JVI.02034-14]
22 **Soden M**, Vasudevan H, Roberts B, Coelen R, Hamlin G, Vasudevan S, La Brooy J. Detection of viral ribonucleic acid and histologic analysis of inflamed synovium in Ross River virus infection. *Arthritis Rheum* 2000; **43**: 365-369 [PMID: 10693876 DOI: 10.1002/1529-0131(200002)43:2<365::AID-ANR16>3.0.CO;2-E]
23 **Chang AY**, Martins KAO, Encinales L, Reid SP, Acuña M, Encinales C, Matranga CB, Pacheco N, Cure C, Shukla B, Ruiz Arteta T, Amdur R, Cazares LH, Gregory M, Ward MD, Porras A, Rico Mendoza A, Dong L, Kenny T, Brueggemann E, Downey LG, Kamalapathy P, Lichtenberger P, Falls O, Simon GL, Bethony JM, Firestein GS. Chikungunya Arthritis Mechanisms in the Americas: A Cross-Sectional Analysis of Chikungunya Arthritis Patients Twenty-Two Months After Infection Demonstrating No Detectable Viral Persistence in Synovial Fluid. *Arthritis Rheumatol* 2018; **70**: 585-593 [PMID: 29266856 DOI: 10.1002/art.40383]
24 **Goupil BA**, McNulty MA, Martin MJ, McCracken MK, Christofferson RC, Mores CN. Novel Lesions of Bones and Joints Associated with Chikungunya Virus Infection in Two Mouse Models of Disease: New Insights into Disease Pathogenesis. *PLoS One* 2016; **11**: e0155243 [PMID: 27182740 DOI: 10.1371/journal.pone.0155243]
25 **Alpantaki K**, Katonis P, Hadjipavlou AG, Spandidos DA, Sourvinos G. Herpes virus infection can cause intervertebral disc degeneration: a causal relationship? *J Bone Joint Surg Br* 2011; **93**: 1253-1258 [PMID: 21911538 DOI: 10.1302/0301-620X.93B9.27002]
26 **Galossi A**, Guarisco R, Bellis L, Puoti C. Extrahepatic manifestations of chronic HCV infection. *J Gastrointestin Liver Dis* 2007; **16**: 65-73 [PMID: 17410291]
27 **Panzer S**, Seel E, Brunner M, Körmöczi GF, Schmid M, Ferenci P, Peck-Radosavljevic M. Platelet autoantibodies are common in hepatitis C infection, irrespective of the presence of thrombocytopenia. *Eur J Haematol* 2006; **77**: 513-517 [PMID: 17042765 DOI: 10.1111/j.0902-4441.2006.t01-1-ejh2888.x]
28 **Buezo GF**, García-Buey M, Rios-Buceta L, Borque MJ, Aragües M, Daudén E. Cryoglobulinemia and cutaneous leukocytoclastic vasculitis with hepatitis C virus infection. *Int J Dermatol* 1996; **35**: 112-115 [PMID: 8850039 DOI: 10.1111/j.1365-4362.1996.tb03273.x]
29 **Mayo MJ**. Extrahepatic manifestations of hepatitis C infection. *Am J Med Sci* 2003; **325**: 135-148 [PMID: 12640289 DOI: 10.1097/00000441-200303000-00006]
30 **Olariu M**, Olariu C, Olteanu D. Thrombocytopenia in chronic hepatitis C. *J Gastrointestin Liver Dis* 2010; **19**: 381-385 [PMID: 21188328]
31 **Cines DB**, Liebman H, Stasi R. Pathobiology of secondary immune thrombocytopenia. *Semin Hematol* 2009; **46**: S2-14 [PMID: 19245930 DOI: 10.1053/j.seminhematol.2008.12.005]
32 **Roberts S**, Caterson B, Menage J, Evans EH, Jaffray DC, Eisenstein SM. Matrix metalloproteinases and aggrecanase: their role in disorders of the human intervertebral disc. *Spine (Phila Pa 1976)* 2000; **25**: 3005-3013 [PMID: 11145811 DOI: 10.1097/00007632-200012010-00007]
33 **Manfredi M**, Corradi D, Vescovi P. Langerhans-cell histiocytosis: a clinical case without bone involvement. *J Periodontol*

2005; **76**: 143-147 [PMID: 15830650 DOI: 10.1902/jop.2005.76.1.143]

34 **Caglioti C**, Lalle E, Castilletti C, Carletti F, Capobianchi MR, Bordi L. Chikungunya virus infection: an overview. *New Microbiol* 2013; **36**: 211-227 [PMID: 23912863]

35 **Edington F**, Varjão D, Melo P. Incidence of articular pain and arthritis after chikungunya fever in the Americas: A systematic review of the literature and meta-analysis. *Joint Bone Spine* 2018; **85**: 669-678 [PMID: 30053609 DOI: 10.1016/j.jbspin.2018.03.019]

36 **Bottini N**, Firestein GS. Duality of fibroblast-like synoviocytes in RA: passive responders and imprinted aggressors. *Nat Rev Rheumatol* 2013; **9**: 24-33 [PMID: 23147896 DOI: 10.1038/nrrheum.2012.190]

37 **Liu XH**, Kirschenbaum A, Yao S, Levine AC. Cross-talk between the interleukin-6 and prostaglandin E(2) signaling systems results in enhancement of osteoclastogenesis through effects on the osteoprotegerin/receptor activator of nuclear factor-{kappa}B (RANK) ligand/RANK system. *Endocrinology* 2005; **146**: 1991-1998 [PMID: 15618359 DOI: 10.1210/en.2004-1167]

38 **Souza PP**, Lerner UH. The role of cytokines in inflammatory bone loss. *Immunol Invest* 2013; **42**: 555-622 [PMID: 24004059 DOI: 10.3109/08820139.2013.822766]

39 **Binder NB**, Niederreiter B, Hoffmann O, Stange R, Pap T, Stulnig TM, Mack M, Erben RG, Smolen JS, Redlich K. Estrogen-dependent and C-C chemokine receptor-2-dependent pathways determine osteoclast behavior in osteoporosis. *Nat Med* 2009; **15**: 417-424 [PMID: 19330010 DOI: 10.1038/nm.1945]

40 **Almohmeed YH**, Avenell A, Aucott L, Vickers MA. Systematic review and meta-analysis of the sero-epidemiological association between Epstein-Barr virus and multiple sclerosis. *PLoS One* 2013; **8**: e61110 [PMID: 23585874 DOI: 10.1371/journal.pone.0061110]

41 **Krutikov M**, Manson J. Chikungunya Virus Infection: An Update on Joint Manifestations and Management. *Rambam Maimonides Med J* 2016; **7** [PMID: 27824550 DOI: 10.5041/RMMJ.1026]

42 **Chirathaworn C**, Chansaenroj J, Poovorawan Y. Cytokines and Chemokines in Chikungunya Virus Infection: Protection or Induction of Pathology. *Pathogens* 2020; **9** [PMID: 32471152 DOI: 10.3390/pathogens9060415]

43 **Disser NP**, De Micheli AJ, Schonk MM, Konnaris MA, Piacentini AN, Edon DL, Toresdahl BG, Rodeo SA, Casey EK, Mendias CL. Musculoskeletal Consequences of COVID-19. *J Bone Joint Surg Am* 2020; **102**: 1197-1204 [PMID: 32675661 DOI: 10.2106/JBJS.20.00847]

44 **Talamonti G**, Colistra D, Crisà F, Cenzato M, Giorgi P, D'Aliberti G. Spinal epidural abscess in COVID-19 patients. *J Neurol* 2021; **268**: 2320-2326 [PMID: 32910251 DOI: 10.1007/s00415-020-10211-z]

45 **Tao H**, Bai J, Zhang W, Zheng K, Guan P, Ge G, Li M, Geng D. Bone biology and COVID-19 infection: Is ACE2 a potential influence factor? *Med Hypotheses* 2020; **144**: 110178 [PMID: 33254500 DOI: 10.1016/j.mehy.2020.110178]

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SYSTEMATIC REVIEWS

Patient-reported dissatisfaction following second side in staged bilateral total knee arthroplasty: A systematic review

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Abstract

BACKGROUND

Around one third of patients who undergo total knee arthroplasty (TKA) will eventually have the contralateral knee replaced. Overall patient satisfaction after staged bilateral total knee arthroplasty procedures performed on different days is reportedly similar to unilateral TKA. Nevertheless, in our anecdotal experience patients often report less satisfying outcomes following the second side. A cursory review of available literature tended to confirm that observation. We sought therefore to consolidate all of the available data on this issue to further investigate this phenomenon.

AIM

To consolidate available published data revealing satisfaction scores among patients following staged bilateral TKA, and to evaluate the phenomenon of less satisfying results following TKA2.

METHODS

A systematic review of available literature reporting on satisfaction with TKA1 and TKA2 after staged bilateral knee arthroplasty was undertaken using PubMed, Google Scholar, and Embase. From 427 records, five full-length articles met criteria for inclusion in the meta-analysis. The data were then extracted and assessed on the basis of the *Reference Citation Analysis* (https://www.referencecitationanalysis.com/).

RESULTS

A total of 1889 patients with an average age of 68 (range: 38–92) underwent staged bilateral TKA with outcomes reported at 1 year following each TKA with a mean

21.9 mo between surgeries (range: 2 d to 14.5 years). Overall satisfaction with both knees was 83.70% (1581) and dissatisfaction with both knees was 2.75% (52). In the remaining 13.56% (256) who were dissatisfied with one side, 61.0% were dissatisfied with TKA2, and 39.0% were dissatisfied with TKA1. Patient-reported outcome scores for TKA2 were frequently lower than TKA1 even in patients reporting overall satisfaction with both knees.

CONCLUSION

At 1-year follow-up, there was a 50% greater risk of dissatisfaction with TKA2 among the 13.56% of patients reporting dissatisfaction in one knee after staged bilateral TKA. Whether the interval between procedures or long-term follow-up changes these results requires further investigation.

Key Words: Staged; Staggered; Sequential; Bilateral arthroplasty; Total knee arthroplasty; Patient-reported outcomes

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Core Tip: Total knee arthroplasty (TKA) is one of the most popular and successful treatments for end stage arthritis worldwide. Around one third of patients who undergo TKA will eventually have the contralateral knee replaced. Anecdotal experience has shown that patients tend to report decreased satisfaction following the second TKA procedure (TKA2). The primary aim of this review article was to assess patient satisfaction following TKA2 after staged bilateral knee arthroplasty. Ideally, quantifying reported dissatisfaction as well as reporting associated factors.

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INTRODUCTION

Total knee arthroplasty (TKA) is a highly effective procedure for the treatment of end stage arthritis and is the most common arthroplasty procedure performed worldwide[1,2]. As such, it is important to investigate patient satisfaction and quality of life following surgery. Patient-reported outcomes and scoring systems have become essential measurement tools, particularly given the limited correlation that functional outcome scores and other direct measurement data have with patient satisfaction[3,4]. Patient scoring systems were first introduced in the 1990's to investigate function in the context of quality of life and have since been used clinically, and in research, to reaffirm patient wellness in surgical healthcare[4,5]. Although a majority of patients report satisfactory outcomes following TKA, an estimated 10%-20% report being dissatisfied in the absence of clinical complications[1,2,6-8]. Investigation into factors predicting dissatisfaction tend to revolve around failure to meet expectations, recall bias, and physiologic rationale for hypersensitivity to pain[3,5]. Previous studies have also demonstrated associations with variables such as patient gender, patient age, history of rheumatoid arthritis, as well as patient personality traits[3]. There is also evidence that a history of any previous arthroplasty - not necessarily a previous knee replacement - lowered the expectations for the outcome of TKA[9].

In patients who have undergone total knee replacement, 25% or more will go on to have the contralateral side replaced[2,6,10]. Much of the literature on bilateral knee replacement focuses on pain improvement, functional outcomes, safety, efficiency, and cost-effectiveness of simultaneous bilateral TKA (one anesthesia event) compared to staged or staggered TKA (two anesthesia events)[2,7,11]. Unlike unilateral TKA, there is very limited data on patient satisfaction following staged TKA, particularly comparing one side to the other. In our anecdotal experience, many patients who have undergone staged bilateral knee replacement report less satisfying results with the second side (TKA2). Review of available literature on this issue revealed some data that tended to confirm this observation[7,12]. Reported reasons included failure to meet the anticipated improvements of pain and function compared to the first side (TKA1), slower return to activity, and inability to engage in full activity. Still, others provide no specific reasons for preferring TKA1 over TKA2, with some reporting uncertainty about their satisfaction with TKA2[7-9,11,13]. To consolidate these data, and better understand the phenomenon of unilateral dissatisfaction following staged bilateral TKA, we performed a systematic review of available literature reporting on both patient-reported outcomes and satisfaction.

MATERIALS AND METHODS

We queried PubMed, Embase, and Google Scholar for articles using: "staged" or "staggered" or "sequential" and "bilateral arthroplasty" and "patient-reported outcomes." PRISMA guidelines were followed for inclusion and exclusion of articles as shown in Figure 1. This review was submitted for registration with PROSPERO (ID: 299833). Only full-text articles with an English version available were included. Additional inclusion criteria were individually reported Oxford Knee Scores (OKS) as a patient reported outcome measure, and/or a satisfaction score for each knee, with follow-up of at least 1 year. Exclusion criteria included abstracts only, follow-up information missing, individual scores for each knee missing, and simultaneous knee replacement. The initial search returned 427 records; 397 had been excluded after screening, leaving 30 full-text articles. Of these, five articles explicitly reported information comparing outcome data between TKA1 to TKA2 for each patient. To determine the disparity in satisfaction between sides, we recorded the satisfaction scores of TKA1 and TKA2 or the OKS of TKA1 and TKA2 for patients that reported unequal satisfaction.

Patients who reported being uncertain about one knee and dissatisfied with the other were grouped according to the dissatisfied knee. Patients who reported being uncertain with one knee and satisfied with the other were grouped according to the uncertain knee. Patients with an OKS score difference below the minimal clinically important difference (MCID) for only one knee were considered dissatisfied with that knee; patients with an OKS score difference between knees that exceeded the MCID for the study, were considered dissatisfied with knee with the lower OKS. The use of the OKS to predict satisfaction was based on previous literature[14].

STATISTICS

Weighted values were used to calculate the average age and interval between surgeries.

The Q = W/S method was used to test for normality. Frequency data from each study were used to calculate the relative risk (RR) of TKA2 dissatisfaction in patients who reported unequal satisfaction after bilateral TKA. The RR was used under the assumption that unilateral dissatisfaction is relatively rare (< 10% of patients) and that using the odds ratio may result in an inflated rate of dissatisfaction with TKA2. Statistical significance was set at $P < 0.05$, chi-square analysis was used to determine the significance of the resultant RR. The Mann-Whitney *U* test was used to compare the RR of TKA2 dissatisfaction between studies. Calculations were performed using SPSS V.27 (IBM Corp., Armonk, NY, United States).

RESULTS

A total of 1889 patients from five studies underwent staged bilateral TKA with patient reported outcomes and satisfaction recorded at 1 year following each TKA. Two of the five studies (85% of patients) explicitly reported satisfaction. The most common PROMs used were the OKS, the Western Ontario and McMaster Universities Osteoarthritis Index, and short form 12 (SF-12). The average age was 68 years with a range of 38 to 92. The time interval between surgeries was not standardized; the largest study reported the widest interval range of 2 d to 14.5 years between sides, with an average interval of 21.9 mo. Table 1 summarizes the details of the five studies. The results of bias assessment with MINORS criteria are displayed in Table 2. Overall satisfaction with both knees across all studies was 83.70% (1581), and dissatisfaction with both knees was 2.75% (52). Two hundred fifty-six patients (13.56%) reported unequal satisfaction between knees. Assessing each study individually, two cohorts, Suzangar *et al*[4] and Abram *et al*[5], demonstrated a significantly increased relative risk of dissatisfaction with TKA2 *vs* TKA1. Comparing frequencies between studies, chi-square N-1 comparison showed a difference between Clement *et al*[6] and Abram *et al*[5], in the reported frequency of dissatisfaction with TKA1 and TKA2. No other differences were found within or among studies. The pooled data demonstrated a significant increase in the relative risk of dissatisfaction with TKA2 *vs* TKA1 among patients who reported unequal satisfaction (RR = 1.49, $P < 0.01$) shown below in Figure 2. Table 3 summarizes the results.

DISCUSSION

The goal of this review was to consolidate available published data revealing satisfaction scores among patients following staged bilateral TKA, and to evaluate the phenomenon of less satisfying results following TKA2. The overall satisfaction rate for unilateral TKA and bilateral staged TKA is reported at 80%-89% with minimum 2-year follow-up[5,15,16]. Similar to previous reports, we calculated overall satisfaction with both sides of 83.70% after accounting for 52 patients (2.75%) who were dissatisfied with

Table 1 Study information, all studies included for analysis had a minimum follow-up of 1 year after each total knee arthroplasty

Ref.	Participants, *n* (weight %)	Male, *n*	Female, *n*	Mean age, range	Interval between TKAs, mo (range)	PROMs	Conclusions
Suzangar *et al* [4], 2019	1001 (53.0%)	459	542	68.7	25.6 (0.1-174.0)	Satisfaction	More dissatisfaction after TKA2
Clement *et al*[6], 2019	454 (24.0%)	219	235	68.0	16.8 (7.2-44.4)	Satisfaction, OKS	No difference between knees
Abram *et al*[5], 2016	250 (13.2%)	84	166	66.0	23.0 (2.0-74.0)	OKS, WOMAC	Lower TKA2 OKS
Scott *et al*[9], 2014	70 (3.7%)	29	41	71.7	7.8 (2.0-25.0)	Satisfaction, OKS	No difference between knees
Tucker *et al*[10], 2021	114 (6.0%)	31	83	66.5	16.2 (11.4-22.8)	OKS	Females less satisfied than males
Pooled	1889 (100.0%)	822 (43.5%)	1067 (56.5%)	68 (38 to 92)	21.9 (0.1-174.1)		

Age reported in years. OKS: Oxford knee score; TKA1: First side total knee arthroplasty; TKA2: Second side total knee arthroplasty; WOMAC: Western Ontario and McMaster universities.

Table 2 MINORS assessment

Ref.	A clearly stated aim	Inclusion of consecutive patients	Prospective collection of data	Endpoint appropriate to the aim of the study	Unbiased assessment of the study endpoint	Follow-up period appropriate to the aim of the study	Loss of follow-up less than 5%	Prospective calculation of the study size	Total
Suzangar *et al*[4], 2019	2	2	2	1	N/A	2	2	1	12
Clement *et al*[6], 2019	2	2	2	2	N/A	2	2	1	13
Abram *et al*[5], 2016	2	1	2	2	N/A	2	2	2	13
Scott *et al* [9], 2014	2	2	2	1	N/A	2	2	1	12
Tucker *et al*[10], 2021	2	2	2	2	N/A	2	2	1	13

The items are scored 0 (not reported), 1 (reported but inadequate) or 2 (reported and adequate). The global ideal score is 16 for non-comparative studies. N/A: Not applicable.

both sides (not included in tables). The remaining 13.56% of the included patients that were unilaterally dissatisfied varied widely by interval between surgeries, age, indications (osteoarthritis, inflammatory, and post-traumatic arthritis were all represented to unknown degrees) and inclusion/exclusion criteria. Although the studies included in this review reported significant differences in the rates of unilateral dissatisfaction, the proportion of patients reporting a preference for TKA1 over TKA2 was similar. Based on pooled data we found that the risk of an unsatisfying result with one side after staged bilateral TKA is about 50% greater for TKA2 (RR = 1.56) at the 1-year follow-up. We also predicted that the interval between TKA1 and TKA2, and the potential influence of recall bias based on the interval between surgeries and follow-up time, could be associated with unilaterally decreased satisfaction after staged bilateral TKA. Although we only included studies reporting results at 1 year, we could not account for the variation in surgical intervals. Therefore, there was not enough data shared among the included studies to determine additional variables associated with our results.

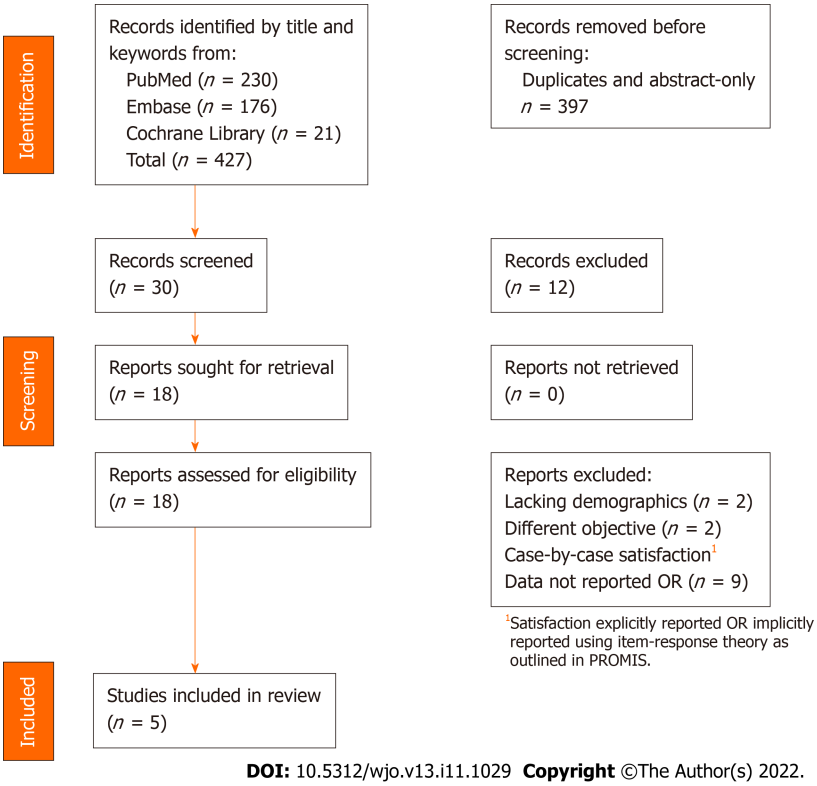
Correlation between Satisfaction and PROMs

Experience with shoulder arthroplasty literature has shown variable strengths of correlation to satisfaction using the Oxford Shoulder Score (moderate correlation, 0.311) and Quick DASH (weak

Table 3 Patients in each study reporting unequal satisfaction between knees after staged bilateral total knee arthroplasty

Ref.	Dissatisfied with TKA1, *n*	Dissatisfied with TKA2, *n*	Study RR	95%CI LL	95%CI UL	Study significance
Suzangar *et al*[4], 2019	61	91	1.49	1.18	1.88	0.025
Clement *et al*[6], 2019[a]	21	19	0.90	0.49	1.66	0.757
Abram *et al*[5], 2016[a]	15	32	2.0	1.11	3.61	0.021[1]
Scott *et al*[9], 2014	4	8	2.0	0.63	6.34	0.239
Tucker *et al*[10], 2021	0	5	12.0	0.67	215.26	0.090[1]
Pooled	101 (39.5%)	155 (60.5%)	1.49	1.17	1.90	0.001

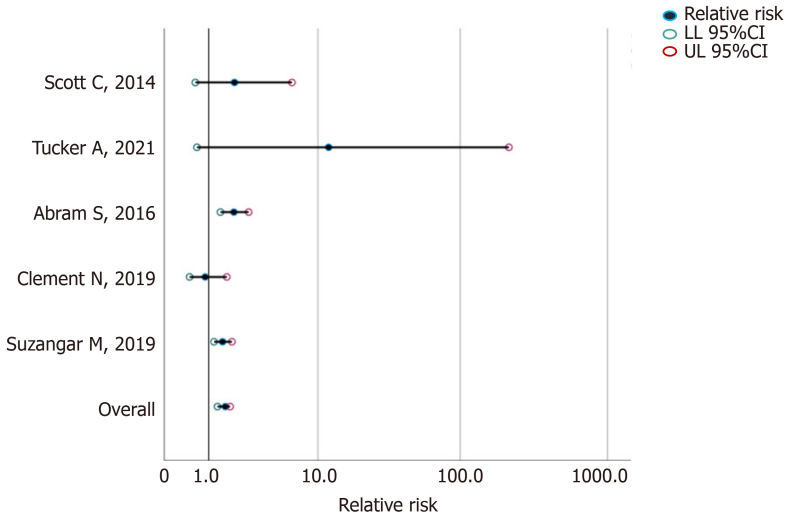
[1]Based on number of patients with OKS score differences between knees exceeding MCID; calculation assumes skewness of distribution < 2.
[a]Pairwise comparison of proportions with Chi square N-1 statistic 17.847, $P < 0.0001$.
Those that more satisfied with TKA2 are classified as "Dissatisfied with TKA1"; those that preferred TKA1 over TKA2 are classified as "Dissatisfied with TKA2" ($n = 256$, 13.6%). LL: Lower limit; TKA1: First side total knee arthroplasty; TKA2: Second side total knee arthroplasty; UL: Upper limit. Significance of the RR of dissatisfaction with TKA2 for each study with significance value set at $P < 0.05$.



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Figure 1 PRISMA flow chart.

correlation, -0.292)[17]. Unlike the Oxford Shoulder Score, the OKS has been shown to be a reliable, reproducible proxy for detecting patient satisfaction. Clement and colleagues further demonstrated the OKS is a highly accurate model for predicting patient satisfaction (AUC = 0.86)[14]. In patients with bilateral knee arthritis undergoing staged bilateral TKA, the most painful knee is typically replaced first. Unsurprisingly, TKA2 tends to have higher initial OKS scores, smaller gains postoperatively (often attributed to the ceiling effect, where the difference in the patient score and maximum score can be less than the minimum clinically important difference), followed by higher scores than TKA1 at 1 year and beyond[18-22]. However, the differences in OKS scores and satisfaction are reported in the context of high overall satisfaction, and do not readily explain the differences among patients that are dissatisfied with one side, nor the preference for one side over the other in this subgroup. The OKS may be an accurate screening tool for satisfaction, but its use in determining individual reasons for dissatisfaction



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Figure 2 Relative risk of unsatisfactory outcome following total knee arthroplasty 2. The studies are ordered along the vertical axis according to power from least (top) to greatest (bottom); the relative risk is given in a log10 scale along the horizontal axis. LL: Lower limit; UL: Upper limit.

has not been validated.

Factors affecting satisfaction

Pain was perhaps the most consistently reported factor that strongly correlated with satisfaction after surgery, and there is evidence suggesting the surgical interval and follow-up interval may have a role in actual pain perceived and recall of perceived pain, respectively[3,13,18,22,23]. An interval greater than 1 year has been associated with higher TKA2 satisfaction scores, while intervals less than 6 mo negatively impact TKA2 scores[12,13]. An interval less than 6 mo has also been associated with increased post-operative pain in the first 48 h based on analgesic requirements, suggesting a physiologic rationale for the potential recall bias[3,18]. Conversely, Gabr *et al*[8] found no difference in TKA2 pain or function scores after stratifying patients by intervals greater than or less than 6 mo. However, they reported TKA2 pain scores gathered beyond 1 year continued to improve with time, even exceeding those of TKA1[11]. Similarly, Clement *et al*[6] reported an increased interval from TKA1 correlated with increased TKA1 dissatisfaction, along with higher unilateral dissatisfaction with TKA1 over TKA2. Although their findings are contrary to ours, they were similarly unable to determine consistency in factors related to the preferred side in cases of unilateral dissatisfaction. Expectations and perceptions are also associated with satisfaction to varying degrees[23]. High rates of unmet postoperative expectations for activity and pain levels in TKA patients have been reported despite overall satisfaction (83% expected pain-free recovery, 43% met expectations, 52% expected to be fully active after surgery, and 20% achieved this)[22]. Negative psychosocial factors are shown to exaggerate negative clinical predictors and independently influence surgical outcomes, while general perceptions of the hospital stay have been strongly correlated with TKA satisfaction at 1 year[3,20,21,24]. In a study by Scott *et al*[9], expectations were lowered in younger individuals and those with high expectations before TKA1, and unilateral dissatisfaction occurred most frequently after TKA2[12]. Above average satisfaction was reported for TKA1 (93%) and TKA2 (87%) in the patients, but satisfaction with either side did not correlate within individuals. These findings further display the multifactorial subjectivity of satisfaction, the difficulty in discerning modifiable risk factors for dissatisfaction, and corroborate our experience and the results of this review.

Limitations

This study was primarily limited by the amount of available evidence reporting individual satisfaction and associated patient-specific variables in those who underwent staged bilateral knee arthroplasties. TKA is the most common arthroplasty procedure worldwide[1]. Considering that 25%–30% of patients undergoing TKA will also have a contralateral TKA within 5 years, there is a substantial portion of the population not accounted for in this review of only 1889 total patients[2,6]. The article by Suzangar *et al*[4] accounted for over half of the included patients and stochastically dominated the data. The second largest study, by Clement *et al*[6], was 50% smaller and showed no difference in dissatisfaction between sides while being appropriately powered. Unlike the larger studies, the smaller studies included here did not show a difference in the risk of dissatisfaction between TKA1 and TKA2. They might have found a difference had the study been powered to do so. Additionally, treatment of Likert data as categorical or continuous is arguable, as is the granularity and balance of the scale (how many points, and whether the mid-point of the scale should be neutral and balanced by equal-opposite positive and

negative responses). We treated Likert scales as continuous data, and therefore patients who reported "uncertain" on a 4-point scale were classified as dissatisfied with the uncertain side. Finally, we acknowledge the inherent limitations in use of the OKS as a satisfaction proxy which likely added an element of error, albeit statistically insignificant[9,18]. Nevertheless, the purpose of this review was to consolidate all of the available data to better study the phenomenon of unequal satisfaction following staged bilateral TKA. The OKS has been shown to be accurate for predicting satisfaction, and we believe including the study by Tucker *et al*[10] improved the statistical power and potentially reduced the bias imparted by larger studies[3,9,12,14].

CONCLUSION

In patients undergoing staged bilateral TKA, we calculated a 50% increased risk of dissatisfaction with TKA2 compared to TKA1 (RR = 1.56) but could not establish risk factors causally linked to this phenomenon. Reasons for unilateral dissatisfaction appear to be multifactorial and are inconsistent between and within patients. Patient education preoperatively about the possibility and probability of differences in subjective outcomes may help temper expectations and could potentially improve overall patient satisfaction.

ARTICLE HIGHLIGHTS

Research background

Total knee arthroplasty (TKA) is a highly effective procedure for the treatment of end stage arthritis, and is the most common arthroplasty procedure performed worldwide. Although many patients report satisfaction with their outcomes, an estimated 10%–20% report being dissatisfied in the absence of clinical complications. This is significant given that in patients who have undergone total knee replacement, 25% or more will go on to have the contralateral side replaced in the future. Unlike unilateral TKA, there is very limited data on patient satisfaction following staged TKA, particularly comparing one side to the other.

Research motivation

Our motivation arose from the anecdotal experience that patients who have undergone bilateral knee replacement in a staged fashion indicate that the second side (TKA2) had a less satisfying outcome compared to the first side (TKA1). Our initial cursory reviews of the literature also seemed to confirm this experience. However, little is known about the factors associated with these reports. To better understand the phenomenon of unilateral dissatisfaction, the goal of this study was to perform a systematic review on currently available literature investigating patient reported outcomes and satisfaction following staged bilateral TKA.

Research objectives

The primary aim of this review article was to consolidate available published data revealing satisfaction scores among patients following staged bilateral TKA and to evaluate the phenomenon of less satisfying results following TKA2. Ideally, quantifying reported dissatisfaction as well as trending associated factors.

Research methods

A systematic review of available literature reporting on satisfaction with TKA1 and TKA2 after staged bilateral knee arthroplasty was undertaken using PubMed, Google Scholar, and Embase. Among 427 records, five articles meeting inclusion criteria were included in the meta-analysis. Statistical analysis was performed to calculate relative risk of TKA2 dissatisfaction and compare the relative risk of TKA2 dissatisfaction between studies.

Research results

In the five included studies, a total of 1889 patients with an average age of 68 years underwent staged bilateral TKA with patient reported outcomes and satisfaction recorded at 1 year following each TKA. Average time between surgeries was 21.9 mo. Overall satisfaction with both knees was 83.70 % (1581), and dissatisfaction with both knees was 2.75% (52). In the remaining 13.56% (256) who were dissatisfied with one side, 61.0% were dissatisfied with TKA2, and 39.0% were dissatisfied with TKA1. Patient-reported outcome scores for TKA2 were frequently lower than TKA1 even in patients reporting overall satisfaction with both knees.

Research conclusions

In patients undergoing staged bilateral TKA, we calculated a 50% increased risk of dissatisfaction with TKA2 compared to TKA1. Although we were unable to establish risk factors linked to this phenomenon, there is high suspicion that the factors are multifactorial and often patient specific.

Research perspectives

Future directions include investigating the effects of time between surgeries and scheduled long-term follow-up.

FOOTNOTES

Author contributions: Gruenberger E and Bae AS contributed to data collection, data analysis, and manuscript writing; McGrory J contributed to study design, manuscript writing, and revisions; Ponce BA contributed to study design; Kelly T contributed to data analysis and manuscript revisions.

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REFERENCES

1 Total knee replacement - orthoinfo - aaos. OrthoInfo. Accessed August 2022. https://orthoinfo.aaos.org/en/treatment/total-knee-replacement
2 **Walmsley P**, Murray A, Brenkel IJ. The practice of bilateral, simultaneous total knee replacement in Scotland over the last decade. Data from the Scottish Arthroplasty Project. *Knee* 2006; **13**: 102-105 [PMID: 16481171 DOI: 10.1016/j.knee.2006.01.003]
3 **Memtsoudis SG**, Ma Y, Chiu YL, Poultsides L, Gonzalez Della Valle A, Mazumdar M. Bilateral total knee arthroplasty: risk factors for major morbidity and mortality. *Anesth Analg* 2011; **113**: 784-790 [PMID: 21752942 DOI: 10.1213/ANE.0b013e3182282953]
4 **Suzangar M**, Esler C, Kennedy J, Chatterji U. Bilateral staged primary total knee arthroplasty: Are patients less pleased with their second side? *Orthop Res Traumatol Open J* 2019; **4**: 1-5 [DOI: 10.17140/ORTOJ-4-114]
5 **Abram SG**, Nicol F, Spencer SJ. Patient reported outcomes in three hundred and twenty eight bilateral total knee replacement cases (simultaneous versus staged arthroplasty) using the Oxford Knee Score. *Int Orthop* 2016; **40**: 2055-2059 [PMID: 26861830 DOI: 10.1007/s00264-016-3122-6]
6 **Clement ND**, Merrie KL, Weir DJ, Holland JP, Deehan DJ. Asynchronous Bilateral Total Knee Arthroplasty: Predictors of the Functional Outcome and Patient Satisfaction for the Second Knee Replacement. *J Arthroplasty* 2019; **34**: 2950-2956 [PMID: 31331702 DOI: 10.1016/j.arth.2019.06.056]
7 **Lizaur-Utrilla A**, Serna-Berna R, Vizcaya-Moreno MF, Martinez-Mendez D, Marco-Gomez L, Lopez-Prats FA. Comparison of Functional Outcomes Between the First and Second Knee in Staged Bilateral Total Knee Arthroplasty With Diverse Intervals Between Stages. *J Arthroplasty* 2018; **33**: 2863-2867 [PMID: 29776854 DOI: 10.1016/j.arth.2018.04.033]
8 **Gabr A**, Withers D, Pope J, Santini A. Functional outcome of staged bilateral knee replacements. *Ann R Coll Surg Engl* 2011; **93**: 537-541 [PMID: 22004637 DOI: 10.1308/147870811X13137608454803]
9 **Scott CE**, Murray RC, MacDonald DJ, Biant LC. Staged bilateral total knee replacement: changes in expectations and outcomes between the first and second operations. *Bone Joint J* 2014; **96-B**: 752-758 [PMID: 24891574 DOI: 10.1302/0301-620X.96B6.32793]
10 **Tucker A**, Warnock JM, Cassidy R, Napier RJ, Beverland D. Are patient-reported outcomes the same following second-side surgery in primary hip and knee arthroplasty? *Bone Jt Open* 2021; **2**: 243-254 [PMID: 33881349 DOI: 10.1302/2633-1462.24.BJO-2020-0187.R1]

11 **Sun J**, Li L, Yuan S, Zhou Y. Analysis of Early Postoperative Pain in the First and Second Knee in Staged Bilateral Total Knee Arthroplasty: A Retrospective Controlled Study. *PLoS One* 2015; **10**: e0129973 [PMID: 26068371 DOI: 10.1371/journal.pone.0129973]

12 **Baker PN**, van der Meulen JH, Lewsey J, Gregg PJ; National Joint Registry for England and Wales. The role of pain and function in determining patient satisfaction after total knee replacement. Data from the National Joint Registry for England and Wales. *J Bone Joint Surg Br* 2007; **89**: 893-900 [PMID: 17673581 DOI: 10.1302/0301-620X.89B7.19091]

13 **Scott CE**, Howie CR, MacDonald D, Biant LC. Predicting dissatisfaction following total knee replacement: a prospective study of 1217 patients. *J Bone Joint Surg Br* 2010; **92**: 1253-1258 [PMID: 20798443 DOI: 10.1302/0301-620X.92B9.24394]

14 **Kim MH**, Nahm FS, Kim TK, Chang MJ, Do SH. Comparison of postoperative pain in the first and second knee in staged bilateral total knee arthroplasty: clinical evidence of enhanced pain sensitivity after surgical injury. *Pain* 2014; **155**: 22-27 [PMID: 23994101 DOI: 10.1016/j.pain.2013.08.027]

15 **Elrich M**, Yu D. The benefits of pre-surgery education. Gallup.com. Published May 20, 2015. Accessed August 2022. https://news.gallup.com/businessjournal/183317/benefits-pre-surgery-education.aspx

16 **Daw RLC**, Gibson J, Prescot D, Bonnett L, Smith M. What is the correlation between patient-reported outcome measure (PROM) scores and patient satisfaction following elective reverse total shoulder replacement? *Shoulder Elbow* 2019; **11**: 42-47 [PMID: 31447944 DOI: 10.1177/1758573217744178]

17 **Janse AJ**, Gemke RJ, Uiterwaal CS, van der Tweel I, Kimpen JL, Sinnema G. Quality of life: patients and doctors don't always agree: a meta-analysis. *J Clin Epidemiol* 2004; **57**: 653-661 [PMID: 15358393 DOI: 10.1016/j.jclinepi.2003.11.013]

18 **Kennedy P**, Joshi R, Dhawan A. The Effect of Psychosocial Factors on Outcomes in Patients With Rotator Cuff Tears: A Systematic Review. *Arthroscopy* 2019; **35**: 2698-2706 [PMID: 31500758 DOI: 10.1016/j.arthro.2019.03.043]

19 **Mannion AF**, Kämpfen S, Munzinger U, Kramers-de Quervain I. The role of patient expectations in predicting outcome after total knee arthroplasty. *Arthritis Res Ther* 2009; **11**: R139 [PMID: 19772556 DOI: 10.1186/ar2811]

20 **Neuprez A**, Delcour JP, Fatemi F, Gillet P, Crielaard JM, Bruyère O, Reginster JY. Patients' Expectations Impact Their Satisfaction following Total Hip or Knee Arthroplasty. *PLoS One* 2016; **11**: e0167911 [PMID: 27977711 DOI: 10.1371/journal.pone.0167911]

21 **Bourne RB**, Chesworth BM, Davis AM, Mahomed NN, Charron KD. Patient satisfaction after total knee arthroplasty: who is satisfied and who is not? *Clin Orthop Relat Res* 2010; **468**: 57-63 [PMID: 19844772 DOI: 10.1007/s11999-009-1119-9]

22 **McMahon M**, Block JA. The risk of contralateral total knee arthroplasty after knee replacement for osteoarthritis. *J Rheumatol* 2003; **30**: 1822-1824 [PMID: 12913941]

23 **Clement ND**, Macdonald D, Burnett R. Predicting patient satisfaction using the Oxford knee score: where do we draw the line? *Arch Orthop Trauma Surg* 2013; **133**: 689-694 [PMID: 23525559 DOI: 10.1007/s00402-013-1728-3]

24 **Clement ND**, Macdonald D, Burnett R, Simpson AHRW, Howie CR. A patient's perception of their hospital stay influences the functional outcome and satisfaction of total knee arthroplasty. *Arch Orthop Trauma Surg* 2017; **137**: 693-700 [PMID: 28331990 DOI: 10.1007/s00402-017-2661-7]

25 **Canovas F**, Dagneaux L. Quality of life after total knee arthroplasty. *Orthop Traumatol Surg Res* 2018; **104**: S41-S46 [PMID: 29183821 DOI: 10.1016/j.otsr.2017.04.017]



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Retrospective Study

Accuracy of the rotator cuff reparability score

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Abstract

BACKGROUND

The reparability of large or massive rotator cuff tears is difficult to determine pre-operatively. We previously identified age ≥ 65 years, acromiohumeral interval ≤ 6 mm, and anteroposterior tear size ≥ 22 mm as risk factors for rotator cuff repair failure. We therefore developed a rotator cuff reparability score where each of the above risk factors is assigned a score of one point.

AIM

To determine the accuracy of a rotator cuff reparability score.

METHODS

This was a retrospective cohort study of recruited patients with large or massive rotator cuff tears treated at our institution between January 2013 and December 2019. Exclusion criteria were revision surgery and patients with contraindications for surgery. All patients underwent arthroscopic rotator cuff repair and were categorized into either complete or partial rotator cuff repair. Rotator cuff reparability scores were calculated for each patient. The sensitivity, specificity, positive and negative predictive value, and positive and negative likelihood ratio were assessed. A receiver operating characteristic curve was plotted to determine the optimal cut-off rotator cuff reparability score.

RESULTS

Eighty patients (mean age, 61 years; range, 25–84 years; 41 females and 39 males) were recruited. Intra- and inter-observer reliabilities were good to excellent. The

number of patients with 0, 1, 2, and 3 risk factors for rotator cuff repair failure were 24, 33, 17, and 6, respectively. Complete repair was performed in all patients without risk factors. Two of the 33 patients with one risk factor and seven of the 17 patients with two risk factors underwent partial repair. One of the six patients with three risk factors underwent complete repair. The area under the curve was 0.894. The optimal cut-off score was two points with a sensitivity of 85.71% and a specificity of 83.33%.

CONCLUSION
A rotator cuff reparability score of two was determined to be the optimal cut-off score for predicting the reparability of large or massive rotator cuff tears.

Key Words: Rotator cuff tear; Reparability; Prognostic factors; Rotator cuff reparability score

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Core Tip: This is retrospective study to evaluate the accuracy of a novel rotator cuff reparability score. In large or massive rotator cuff tears, arthroscopic rotator cuff repair is not always feasible. The reparability of large or massive rotator cuff tears can be more accurately determined after intra-operative arthroscopy. The identification of pre-operative risk factors for rotator cuff tear repair failure may facilitate improvements in management and provide patients with more accurate treatment information. Accordingly, we developed a novel scoring system to predict the likelihood of rotator cuff repair failure.

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INTRODUCTION

The recommended treatment option for rotator cuff tears is arthroscopic surgery. Complete rotator cuff repair yields superior functional outcomes with a lower rate of recurrent tears compared to partial rotator cuff repair or arthroscopic debridement[1,2]. Partial rotator cuff repair may initially improve functional outcomes; however, half of patients are reportedly dissatisfied with the results of partial rotator cuff repair at long-term follow-up[3]. Prior to arthroscopic rotator cuff surgery, a variety of salvage operations, such as superior capsular reconstruction, tendon transfer, subacromial balloon spacer, and reverse total shoulder arthroplasty, should be planned. Furthermore, arthroscopic repair of large or massive rotator cuff tears may not always be feasible. The reparability of large or massive rotator cuff tears can be more accurately determined during intra-operative arthroscopy. Pre-operative risk factors for rotator cuff repair failure may improve management planning and provide patients with more reliable treatment information.

Age, tendon retraction, rotator cuff tendon tear size, fatty infiltration, muscle atrophy, and superior humeral head migration are reported predictors of the reparability of large rotator cuff tears[4-7]. Our previous study identified age, acromiohumeral interval (AHI), anteroposterior (AP) tear size, and AHI as pre-operative clinical and radiographic parameters associated with the reparability of rotator cuff tears[5]. Pre-operative evaluations have been shown to facilitate better treatment outcomes and lower re-tear rates after complete rotator cuff repair[1,2]. In cases where complete repair is not feasible, alternative salvage techniques with superior results to partial rotator cuff repair should be considered [8].

Accordingly, we developed a novel scoring system for predicting the reparability of large or massive rotator cuff tears. The objective of the present study was to determine the accuracy of our novel pre-operative scoring system in predicting the probability of the reparability of large or massive rotator cuff tears. We hypothesized that higher rotator cuff reparability scores predict rotator cuff repair failure.

MATERIALS AND METHODS

The present retrospective cohort study collected data from January 1, 2013 to December 31, 2019 after the Queen Savang Vadhana Memorial Hospital's Research Ethics Committee gave its approval to the study protocol. All patients with large or massive rotator cuff injuries identified by magnetic resonance

imaging (MRI) prior to surgery and verified during surgery by arthroscopy were included in the current study. Rotator cuff tears were classified using the Snyder classification and modified Millstein[9,10].

The term "complete supraspinatus tendon tears" was used to describe large rotator cuff tears. At least two tendons must be involved for a rotator cuff injury to be considered massive. The current study excluded patients with recurrent rotator cuff injuries or surgical contraindications.

Our rotator cuff reparability scoring system consisted of three factors: age ≥ 65 years, AHI ≤ 6 mm, and AP tear size ≥ 22 mm[2]. AHI was used to assess superior humeral head migration and was measured as the distance between the inferior border of the acromion and the superior aspect of the humeral head on AP plain radiography[11] (Figure 1). AP tear size was determined using T2-weighted MRI in the sagittal oblique view as the largest straight distance from anterior to posterior tendon edge [12]. No measurements were performed for frayed tissues at the tendon edge (Figure 2). Two independent observers measured both imaging parameters twice.

Arthroscopic repair was performed by three fellowship-trained sports medicine surgeons. General anesthesia was used to sedate the patients, who were then placed in a beach chair position. If an acromial spur was identified, acromioplasty was performed. Arthroscopic capsular release and manipulation under anesthesia were performed in cases of adhesive capsulitis. After confirming the size of the tear using an arthroscopic probe, tendon adhesions were released and mobilized to cover as much of the native footprint as feasible. The interval sliding technique was used where necessary. Where feasible, double-row rotator cuff repair or trans-osseous equivalent repair could improve tendon healing, lower the risk of re-rupture, and improve functional outcomes compared to single-row repair[13-15]. Single-row or partial repair was performed in cases where double-row repair was not possible.

Partial repair was defined as having less than 50% of the anatomical footprint covered by tendon. Complete repair was defined as 50% tendon coverage or greater[7,11] (Figure 3A and B). On the first post-operative day, passive range-of-motion exercises were permitted for all patients. Patients were provided an arm sling for 6 wk post-operatively. In the third or fourth post-operative week, progressive active-assisted passive motion exercises were initiated for muscle strengthening.

Statistical analyses were performed using SPSS version 26. Each risk factor score's sensitivity, specificity, positive and negative predictive value, and positive and negative probability ratio were assessed. The optimal cut-off score and values of area under the curve (AUC) were determined using receiver operating characteristics (ROC) curves. Intra-observer and inter-observer reliabilities were calculated using Kappa analysis and the intra-class correlation coefficient for categorical and continuous data, respectively.

RESULTS

Eighty patients (mean age, 61 years; range, 25–84 years; 41 females and 39 males) met the study inclusion criteria. A total of 64 massive rotator cuff tears (82.5%) and 14 Large rotator cuff tears (17.5%) were identified by MRI and confirmed by arthroscopic examination.

AP distance and AHI had intra-observer reliability values of 83.8 and 84.6 %, respectively. The inter-observer reliability values for AP distance and AHI were 81.2 and 81.6 %, respectively. Both outcomes were rated as good to excellent. Sixty-six patients underwent complete arthroscopic rotator cuff repair. Partial arthroscopic rotator cuff repairs were performed in 14 patients. All 24 patients who had no risk factors for rotator cuff surgery failure had complete arthroscopic repair of their rotator cuffs. Only two of the 33 patients with one risk factor underwent partial repair. Seven patients with two risk factors underwent partial repair, while ten patients with two risk factors underwent complete repair. One of the six patients with all three risk factors underwent complete repair. The numbers of patients undergoing complete or partial repair according to number of risk factors for rotator cuff repair failure are shown in Table 1.

For each rotator cuff reparability score, sensitivity, specificity, positive and negative predictive value, as well as positive and negative likelihood ratios, were investigated (Table 2). The AUC of ROC curve was 0.894 (Figure 4). Two was the optimal cut-off score for rotator cuff reparability, with a sensitivity of 85.71% and a specificity of 83.33%.

DISCUSSION

Arthroscopic rotator cuff repair is currently the standard treatment for rotator cuff tears. However, arthroscopic surgery is technically challenging in cases of large or massive rotator cuff tears. Previous studies have demonstrated that complete rotator cuff repair leads to superior functional results compared to partial rotator cuff repair[1,2,16,17]. Shon *et al*[3] suggested that arthroscopic partial repair may result in initial clinical improvements at two-year follow-up; however, over half of the study participants were dissatisfied with surgical outcomes which had worsened over time[3]. Heuberer *et al*[1] conducted a 45-mo follow-up study and demonstrated that partial rotator cuff repair was associated with higher re-rupture rates compared to complete rotator cuff repair.

Table 1 Number of patients undergoing complete or partial repair according to number of risk factors

No. of risk factors	Partial repair	Complete repair	Total
3	5	1	6
2	7	10	17
1	2	31	33
0	0	24	24
Total	14	66	80

Table 2 Diagnostic values of rotator cuff repair score in patients undergoing complete or partial rotator cuff repair

Rotator cuff reparability score	Sensitivity	Specificity	PPV	NPV	Positive likelihood ratio	Negative likelihood ratio
1	100%	36.36%	25%	NA	1.57	0
2	85.71%	83.33%	52.17%	96.49%	5.14	0.17
3	35.71%	98.47%	83.33%	87.84%	23.57	0.65

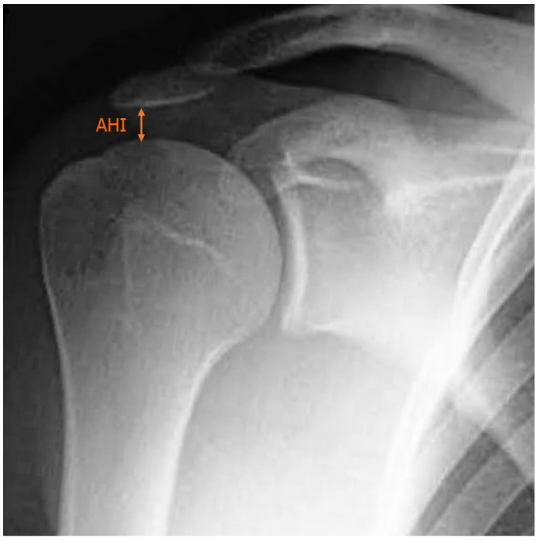
PPV: Positive predictive value; NPV: Negative predictive value; NA: Not available.



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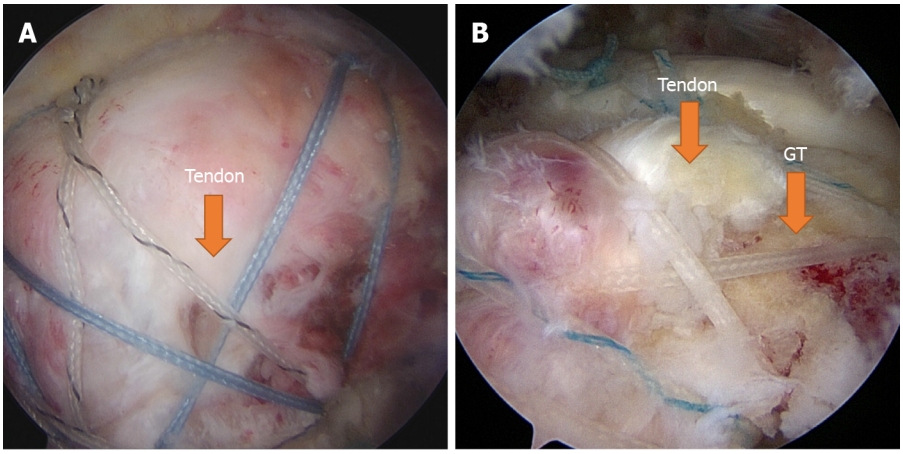
Figure 1 Anteroposterior tear size was measured as the greatest distance between the anterior tendon edge and the posterior tendon edge in sagittal oblique magnetic resonance imaging slices.

Many salvage procedures have recently been developed for irreparable rotator cuff tears. However, there is a lack of studies comparing partial rotator cuff repair with other salvage procedures. A recent prospective cohort study comparing a latissimus dorsi muscle transfer with a partial rotator cuff repair in irreparable posterosuperior rotator cuff tears showed higher the University of California-Los Angeles (UCLA) shoulder scale, forward flexion, and shoulder strength in the muscle transfer group[8]. A cost-effective study by Makhni *et al*[18] revealed that arthroscopic rotator cuff repair may be a more cost-effective initial treatment for massive rotator cuff tears compared with primary reverse total shoulder arthroplasty. However, reverse total shoulder arthroplasty had superior outcomes in cases of rotator cuff repair failure or re-tear. The results of the study by Makhni *et al*[18] demonstrate the importance of comprehensive evaluation of the reparability of rotator cuff tears. Salvage procedures including superior capsular reconstruction, subacromial spacer, tendon transfer, and reverse total shoulder arthroplasty, are recommended in cases of irreparable rotator cuff tears after their utility in significantly improving functional outcomes was confirmed[19,20]. To our knowledge, no comparative studies of



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Figure 2 The acromiohumeral interval was measured as the distance between the inferior border of acromion and the superior aspect of the humeral head on true anteroposterior plain radiography. AHI: Acromiohumeral interval.



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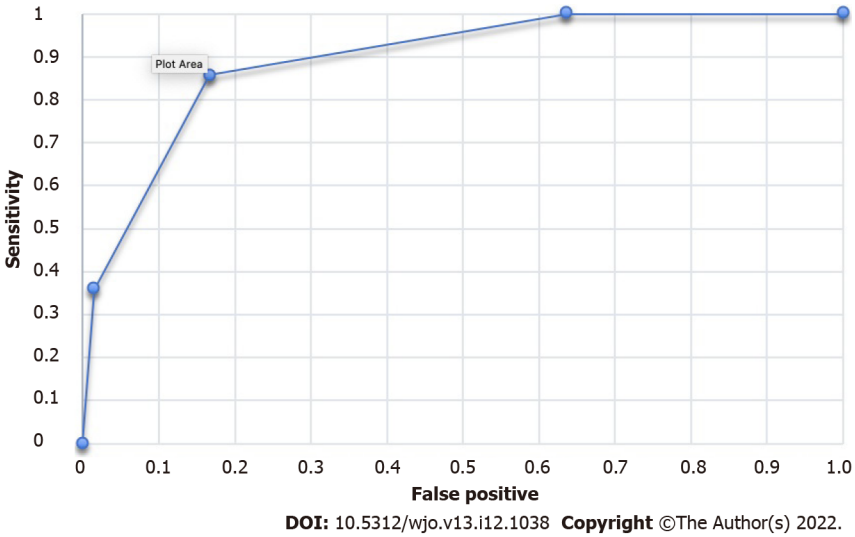
Figure 3 Arthroscopic view of rotator cuff repair. A: After arthroscopic rotator cuff repair, the tendon is seen to over more than 50% of the anatomical footprint following complete repair. B: In partial repair, the tendon covers less than 50% of the anatomical footprint. GT: Greater tuberosity.

partial rotator cuff repair and salvage procedures have been reported to date. Accordingly, the assessment of rotator cuff reparability is clinically challenging, particularly in cases of large or massive rotator cuff tears. However, many factors have been reported to be associated with rotator cuff tear reparability and have utility in predicting treatment outcomes pre-operatively[1-3,17].

Rotator cuff injuries are a phenomenon of natural aging[21]. The majority of rotator cuff injuries are asymptomatic. However, 30% – 40% of patients with asymptomatic tears developed symptoms in the subsequent 2 to 5 years[22-23]. Larger rotator cuff tears are typically associated with degeneration and fatty infiltration[21,24]. Moreover, increasing age, particularly ≥ 65 years, has been shown to significantly correlate with rotator cuff tear irreparability[5-6].

Rotator cuff tears cause an imbalance between the forces acting on the glenohumeral joint, which can result in the humeral head superior migration, [25] which is one of the earliest signs of rotator cuff tear arthropathy[26]. The humeral head superior migration, as measured by the AHI or inferior glenohumeral distance, is an important factor in predicting the reparability and clinical outcomes of rotator cuff tears[4-7,27]. Previous studies have reported that an AHI ≤ 6 mm is associated with rotator cuff tear irreparability[4-5].

Tear size is another significant factor, which many studies reported as a main predicting factor of reparability[4-7,11,21]. Previous studies have determined rotator cuff tear size using different imaging modalities and in coronal and sagittal oblique views. Our previous study reported that both mediolateral tear size ≥ 36 mm and AP tear size ≥ 22 were associated with rotator cuff tear irreparability. This result corroborates a previous study by Di Benedetto *et al*[4]; however, their multiple logistic



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Figure 4 Receiver operating characteristics curve of the rotator cuff reparability score.

regression model demonstrated that only AP tear size was significantly correlated with rotator cuff tear irreparability.

A previous retrospective study reported the development of a quantitative scoring system for large-to-massive rotator cuff tears[6]. Their scoring system, which included AP tear size, mediolateral tear size, muscle atrophy, and fatty infiltration, had a sensitivity of 73.5% and a specificity of 96.2%. However, this study included only pre-operative MRI factors and not clinical and radiographic factors.

Our previous study analyzed all pre-operative clinical and radiographic factors to estimate the reparability of large and massive rotator cuff tears[5], demonstrating that age, AHI, and AP tear size were correlated with rotator cuff reparability. As all three factors had similar odd ratios, we weighted them equally to develop the present three-point scoring system.

In this study, the AUC for our rotator cuff reparability score was 0.894, indicating good accuracy. A score of two, which had a sensitivity of 85.71% and a specificity of 83.33%, was found to be the optimal cut-off rotator cuff reparability score. Accordingly, rotator cuff tears are most likely to be irreparable in patients with a score rotator cuff reparability of two or three. We recommend pre-operative consideration of backup procedures in such cases.

This study had several limitations. First, the retrospective nature of the present study may have introduced selection or information into the study analysis. Second, there was a wide range of participant ages which may have affected tissue quality and the likelihood of traumatic rotator cuff tears. Third, the small sample size and small number of patients in the partial repair group may have influenced the study results. Finally, clinical outcomes and follow-up were not assessed in the present study. Further studies are required to validate the clinical utility of our rotator cuff reparability score in improving clinical outcomes and provided satisfactory results after long-term follow-up.

CONCLUSION

A score of two is the optimal rotator cuff reparability score for predicting the reparability of large or massive rotator cuff tears. Patients with a pre-operative rotator cuff reparability score of two or greater are likely to have irreparable rotator cuff tears.

ARTICLE HIGHLIGHTS

Research background

It is challenging to predict the reparability of a large and massive rotator cuff injury before surgery. Age, tendon retraction, tendon tear size, fatty infiltration, muscle atrophy, and superior humeral head migration are factors that influence whether or not large or massive rotator cuff tears can be repaired.

Research motivation

The better result and lower recurrent rate of complete rotator cuff repair, make the pre-operative evaluation much more important. If a complete repair is not possible, alternative salvage techniques

with better results than partial rotator cuff repair should be considered.

Research objectives
The aim of the current study was to determine the accuracy of the rotator cuff reparability score.

Research methods
This was a retrospective cohort diagnostic study including all patients with large and massive rotator cuff tears between January 2013 and December 2019. All patients underwent an arthroscopic rotator cuff repair and were classified as having either complete or partial rotator cuff repair. The sensitivity, specificity, positive and negative predictive value, and positive and negative likelihood ratio were assessed. The receiver operating characteristic curve was analyzed to define the optimal cut-off level for the reparability of the rotator cuff tear.

Research results
Eighty patients were recruited for this study. The intra- and inter-observer reliabilities were good to excellent. The number of patients with 0, 1, 2, and 3 positive factors were 24, 33, 17, and 6 respectively. The complete repair was done in all patients without any positive factors. Two of 32 patients with one positive factor and seven of 17 patients with two positive factors were partially repaired. Only one of six patients with three positive factors was completely repaired. The area under the curve was 0.894. The optimal cut-off point was two with the sensitivity of 85.71% and the specificity of 83.33%.

Research conclusions
The optimal cut-off point for predicting the reparability of a large or massive rotator cuff tear is a rotator cuff reparability score of two. If the pre-operative score is two or more, the rotator cuff tear is likely to be irreparable.

Research perspectives
Further studies are required to validate the clinical utility of our rotator cuff reparability score in improving clinical outcomes and provide satisfactory results after long-term follow-up.

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FOOTNOTES
Author contributions: Prasathaporn N designed and performed the research and supervised the report; Kuptniratsaikul V designed the study and contributed to the analysis; Thamrongskulsiri N wrote the manuscript; Itthipanichpong T contributed to the analysis and wrote the manuscript and supervised the study; All authors have read and approved the final manuscript.

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REFERENCES

1 **Heuberer PR**, Kölblinger R, Buchleitner S, Pauzenberger L, Laky B, Auffarth A, Moroder P, Salem S, Kriegleder B, Anderl W. Arthroscopic management of massive rotator cuff tears: an evaluation of debridement, complete, and partial repair with and without force couple restoration. *Knee Surg Sports Traumatol Arthrosc* 2016; **24**: 3828-3837 [PMID: 26254089 DOI: 10.1007/s00167-015-3739-9]
2 **Lee YS**, Jeong JY, Park CD, Kang SG, Yoo JC. Evaluation of the Risk Factors for a Rotator Cuff Retear After Repair Surgery. *Am J Sports Med* 2017; **45**: 1755-1761 [PMID: 28319431 DOI: 10.1177/0363546517695234]
3 **Shon MS**, Koh KH, Lim TK, Kim WJ, Kim KC, Yoo JC. Arthroscopic Partial Repair of Irreparable Rotator Cuff Tears: Preoperative Factors Associated With Outcome Deterioration Over 2 Years. *Am J Sports Med* 2015; **43**: 1965-1975 [PMID: 26015444 DOI: 10.1177/0363546515585122]
4 **Di Benedetto P**, Beltrame A, Cicuto C, Battistella C, Gisonni R, Cainero V, Causero A. Rotator cuff tears reparability index based on pre-operative MRI: our experience. *Acta Biomed* 2019; **90**: 36-46 [PMID: 30714997 DOI: 10.23750/abm.v90i1-S.8074]
5 **Kuptniratsaikul V**, Laohathaimongkol T, Umprai V, Yeekian C, Prasathaporn N. Pre-operative factors correlated with arthroscopic reparability of large-to-massive rotator cuff tears. *BMC Musculoskelet Disord* 2019; **20**: 111 [PMID: 30885179 DOI: 10.1186/s12891-019-2485-4]
6 **Kim SJ**, Park JS, Lee KH, Lee BG. The development of a quantitative scoring system to predict whether a large-to-massive rotator cuff tear can be arthroscopically repaired. *Bone Joint J* 2016; **98-B**: 1656-1661 [PMID: 27909128 DOI: 10.1302/0301-620X.98B12.BJJ-2016-0316]
7 **Dwyer T**, Razmjou H, Henry P, Gosselin-Fournier S, Holtby R. Association between pre-operative magnetic resonance imaging and reparability of large and massive rotator cuff tears. *Knee Surg Sports Traumatol Arthrosc* 2015; **23**: 415-422 [PMID: 24170190 DOI: 10.1007/s00167-013-2745-z]
8 **Paribelli G**, Boschi S, Randelli P, Compagnoni R, Leonardi F, Cassarino AM. Clinical outcome of latissimus dorsi tendon transfer and partial cuff repair in irreparable postero-superior rotator cuff tear. *Musculoskelet Surg* 2015; **99**: 127-132 [PMID: 25904348 DOI: 10.1007/s12306-015-0353-4]
9 **Millstein ES**, Snyder SJ. Arthroscopic evaluation and management of rotator cuff tears. *Orthop Clin North Am* 2003; **34**: 507-520 [PMID: 14984190 DOI: 10.1016/s0030-5898(03)00095-6]
10 **Aliprandi A**, Messina C, Arrigoni P, Bandirali M, Di Leo G, Longo S, Magnani S, Mattiuz C, Randelli F, Sdao S, Sardanelli F, Sconfienza LM, Randelli P. Reporting rotator cuff tears on magnetic resonance arthrography using the Snyder's arthroscopic classification. *World J Radiol* 2017; **9**: 126-133 [PMID: 28396726 DOI: 10.4329/wjr.v9.i3.126]
11 **Koh KH**, Lim TK, Park YE, Lee SW, Park WH, Yoo JC. Preoperative factors affecting footprint coverage in rotator cuff repair. *Am J Sports Med* 2014; **42**: 869-876 [PMID: 24496508 DOI: 10.1177/0363546513518581]
12 **Davidson JF**, Burkhart SS, Richards DP, Campbell SE. Use of preoperative magnetic resonance imaging to predict rotator cuff tear pattern and method of repair. *Arthroscopy* 2005; **21**: 1428 [PMID: 16376230 DOI: 10.1016/j.arthro.2005.09.015]
13 **Prasathaporn N**, Kuptniratsaikul S, Kongrukgreatiyos K. Single-row repair versus double-row repair of full-thickness rotator cuff tears. *Arthroscopy* 2011; **27**: 978-985 [PMID: 21693349 DOI: 10.1016/j.arthro.2011.01.014]
14 **Zhang Q**, Ge H, Zhou J, Yuan C, Chen K, Cheng B. Single-row or double-row fixation technique for full-thickness rotator cuff tears: a meta-analysis. *PLoS One* 2013; **8**: e68515 [PMID: 23874649 DOI: 10.1371/journal.pone.0068515]
15 **Xu C**, Zhao J, Li D. Meta-analysis comparing single-row and double-row repair techniques in the arthroscopic treatment of rotator cuff tears. *J Shoulder Elbow Surg* 2014; **23**: 182-188 [PMID: 24183478 DOI: 10.1016/j.jse.2013.08.005]
16 **Holtby R**, Razmjou H. Relationship between clinical and surgical findings and reparability of large and massive rotator cuff tears: a longitudinal study. *BMC Musculoskelet Disord* 2014; **15**: 180 [PMID: 24884835 DOI: 10.1186/1471-2474-15-180]
17 **Jenssen KK**, Lundgreen K, Madsen JE, Kvakestad R, Dimmen S. Prognostic Factors for Functional Outcome After Rotator Cuff Repair: A Prospective Cohort Study With 2-Year Follow-up. *Am J Sports Med* 2018; **46**: 3463-3470 [PMID: 30383411 DOI: 10.1177/0363546518803331]
18 **Makhni EC**, Swart E, Steinhaus ME, Mather RC 3rd, Levine WN, Bach BR Jr, Romeo AA, Verma NN. Cost-Effectiveness of Reverse Total Shoulder Arthroplasty Versus Arthroscopic Rotator Cuff Repair for Symptomatic Large and Massive Rotator Cuff Tears. *Arthroscopy* 2016; **32**: 1771-1780 [PMID: 27132772 DOI: 10.1016/j.arthro.2016.01.063]
19 **Catapano M**, de Sa D, Ekhtiari S, Lin A, Bedi A, Lesniak BP. Arthroscopic Superior Capsular Reconstruction for Massive, Irreparable Rotator Cuff Tears: A Systematic Review of Modern Literature. *Arthroscopy* 2019; **35**: 1243-1253 [PMID: 30878327 DOI: 10.1016/j.arthro.2018.09.033]
20 **Dickerson P**, Pill SG, Longstaffe R, Shanley E, Thigpen CA, Kissenberth MJ. Systematic review of reversing pseudoparalysis of the shoulder due to massive, irreparable rotator cuff tears. *J Shoulder Elbow Surg* 2020; **29**: S87-S91 [PMID: 32643613 DOI: 10.1016/j.jse.2020.04.039]
21 **Keener JD**, Patterson BM, Orvets N, Chamberlain AM. Degenerative Rotator Cuff Tears: Refining Surgical Indications Based on Natural History Data. *J Am Acad Orthop Surg* 2019; **27**: 156-165 [PMID: 30335631 DOI: 10.5435/JAAOS-D-17-00480]
22 **Keener JD**, Galatz LM, Teefey SA, Middleton WD, Steger-May K, Stobbs-Cucchi G, Patton R, Yamaguchi K. A prospective evaluation of survivorship of asymptomatic degenerative rotator cuff tears. *J Bone Joint Surg Am* 2015; **97**: 89-98 [PMID: 25609434 DOI: 10.2106/JBJS.N.00099]

23 **Moosmayer S**, Tariq R, Stiris M, Smith HJ. The natural history of asymptomatic rotator cuff tears: a three-year follow-up of fifty cases. *J Bone Joint Surg Am* 2013; **95**: 1249-1255 [PMID: 23864172 DOI: 10.2106/JBJS.L.00185]

24 **Gumina S**, Carbone S, Campagna V, Candela V, Sacchetti FM, Giannicola G. The impact of aging on rotator cuff tear size. *Musculoskelet Surg* 2013; **97** Suppl 1: 69-72 [PMID: 23588834 DOI: 10.1007/s12306-013-0263-2]

25 **Nam D**, Maak TG, Raphael BS, Kepler CK, Cross MB, Warren RF. Rotator cuff tear arthropathy: evaluation, diagnosis, and treatment: AAOS exhibit selection. *J Bone Joint Surg Am* 2012; **94**: e34 [PMID: 22438007 DOI: 10.2106/JBJS.K.00746]

26 **Hamada K**, Yamanaka K, Uchiyama Y, Mikasa T, Mikasa M. A radiographic classification of massive rotator cuff tear arthritis. *Clin Orthop Relat Res* 2011; **469**: 2452-2460 [PMID: 21503787 DOI: 10.1007/s11999-011-1896-9]

27 **Vad VB**, Warren RF, Altchek DW, O'Brien SJ, Rose HA, Wickiewicz TL. Negative prognostic factors in managing massive rotator cuff tears. *Clin J Sport Med* 2002; **12**: 151-157 [PMID: 12011722 DOI: 10.1097/00042752-200205000-00002]

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ORIGINAL ARTICLE

Retrospective Study

Taper-wedge stem suitable for anterior approach total hip arthroplasty: Adequate biomechanical reconstruction parameters and excellent clinical outcome at mid-term follow-up

Carlo Trevisan, Antonino Salvatore Lombardo, Gianluca Gallinari, Marco Zeppieri, Raymond Klumpp

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Abstract

BACKGROUND

The direct anterior approach (DAA) for total hip arthroplasty (THA) is a less invasive and muscle-sparing approach that seems to improve early function and patient satisfaction. Several studies, however, have reported high complication and revision rates due to the technical difficulties related to the femoral preparation.

AIM

To evaluate the usefulness and safety of a new stem equipped with a morphometric design and a size-specific medial curvature in DAA for THA.

METHODS

This retrospective study was based on 130 patients that underwent mini-invasive DAA procedures for THA using the Accolade II stem. A total of 144 procedures were included in the assessment, which was based on postoperative complications, survival rates, functional parameters, and patient related outcomes.

RESULTS

Overall complications were recorded in 6 procedures (4.2%). There were no complications related to the stem implantation and no intraoperative fractures. Only one patient was revised for deep infection. On radiographs, biomechanical hip reconstruction was satisfactory and no stem showed any subsidence greater

than 2 mm. Full osseointegration based on Engh scores was seen in all of the implanted stems. Median Harris hip score at final follow-up was 99 points (range 44-100 points), which resulted excellent in 91.3% of patients. The median values of the osteaorthritis outcome score ranged from 87.5 to 95.

CONCLUSION
The mid-term positive outcomes and low complication rate in our consecutive series of patients support the safety and suitability of this new stem design in DAA for THA.

Key Words: Total hip arthroplasty; Orthopedics; Direct anterior approach; Orthopedic surgery; Stem implantation; Accolade II stem

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Core Tip: The direct anterior approach can provide a less invasive and muscle-sparing technique for total hip arthroplasty. New stems used in the direct anterior approach have been designed to reduce complication rates, and enhance postoperative morphologic and functional outcomes. The Accolade II stem is equipped with a morphometric design and a size-specific medial curvature, which can be advantageous for this type of surgery.

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INTRODUCTION

Total hip arthroplasty (THA) is one of the surgical procedures with the highest levels of safety, efficacy, and clinical satisfaction[1]. In the last decade, there have been numerous improvements in techniques and technologies, which have given rise to better clinical outcomes and less need for early surgical THA revisions[2,3]. New technology, methods and implants, however, need to be carefully tested and assessed in long term studies on large cohorts to determine the clinical usefulness and safety before widespread use.

The direct anterior approach (DAA) for THA has been a debatable issue in current literature. Several studies supporting this surgical technique have reported that this less invasive and muscle-sparing approach can improve early functional and patient-reported outcomes. Others studies, however, have reported the limitations of using this approach, which include high complication and revision rates, usually dependent on long and difficult surgeon learning curves[4,5]. The technical difficulties in the DAA have been reported to be linked with the implantation of undersized stems[6] and early femoral failure[7].

The design of the femoral stem used in surgery can be an additional contributing factor in postoperative early aseptic loosening. Lindgren *et al*[8] found that stems with an "anatomic" design were more likely to loosen when implanted through an anterolateral approach. Janssen *et al*[9] reported that cementless femoral stems with a proximal shoulder tend to be associated with early aseptic loosening when inserted through an anterior or anterolateral approach, while an anatomically shaped stem may be preferred with these approaches.

The choice of a suitable stem to be used in an anterior approach should preferably consider a reduction in possible complications rates related to the difficulties of femoral exposure. A new second-generation cementless stem (Accolade II) with its short length and smooth tapered tip could be considered a good candidate when using the DAA for THA. This new stem was created to better adapt to the anatomy of the femoral canal thanks to a more anthropomorphic dimension ratio between its proximal and distal portions and to the variation, size to size, of the radius of curvature of its medial side[10].

The aim of our study was to evaluate the feasibility, utility and safety of this second-generation cementless stem (Accolade II) for the DAA. The assessment in our study was based on data regarding complications, survival of the implanted prostheses, biomechanical hip reconstructions, radiographic evolutions, functional results, and patient-related outcomes.

MATERIALS AND METHODS

Study design

This retrospective observational study analyzed consecutive patients that underwent THA with DAA using the Accolade II stem (Stryker Orthopedics) in the Department of Traumatology and Orthopedics at a public Italian hospital located in Seriate, Bergamo between November 2013 and March 2019. The analysis was based on data obtained from outpatient reports, medical records, and radiographs. The investigation was performed in accordance with the tenets of the Declaration of Helsinki and informed consent was obtained from all participants before surgery. The study was in compliance with Institutional Review Boards and the Health Insurance Portability and Accountability Act requirements of the hospital. The study was approved by the Ethics Committee of Bergamo (n. 144/19, August 5, 2019).

Hip-fractured patients and patients with a final follow-up of less than 12 mo were excluded. All the surgical procedures were performed *via* a mini-invasive DAA without a traction table. A preoperative radiological 2D plan, using TraumaCad® software, and intraoperative fluoroscopy evaluation of trials for stem positioning were performed for each patient. The stems were used in combination with an uncemented Trident HA-coated cup (Stryker orthopedics). In all cases, a highly cross-linked polyethylene on Biolox Delta femoral head bearing was used.

One hundred forty-eight subjects (161 hips) were treated in the time interval considered. Seventeen patients were lost to follow-up. At the last outpatient follow-up visit, these patients were stable from a clinical and radiographic point of view. Four patients died for reasons unrelated to their hip surgery. Thirteen patients, contacted by phone, refused to come to the follow-up visit for logistical or work reasons. They all reported that no other surgical revisions were performed on the operated hip.

Data collection

Body mass index (BMI), American Society of Anesthesiologists (ASA) Score, Charlson Comorbidity Index (CCI)[11], and Charnley classification were calculated for each patient[12]. The postoperative outcome assessments included data based on complications, implant survival, and clinical and radiological outcomes. Complications and adverse events were coded according to the Hip Society THA Complications workgroup[13]. Clinical outcomes were obtained at the last follow-up visit. Functional results were evaluated by the Harris Hip Score (HHS)[14]. Patient-related outcomes were assessed by the Hip disability and Osteoarthritis Outcome Score Italian version LK 2.0 (HOOS)[15].

Standardized pre- and post-operative anteroposterior radiographs of the pelvis and the lateral view of the operated hip were used for the radiological assessment. Occurrence of radiolucent lines, osteolytic changes, or cortical hypertrophy were recorded using Gruen's zones for the stem and the DeLee Charnley zones for the cup[16,17]. Stem subsidence was calculated using the method reported by Grant *et al*[18]. Femoral component fixation and stability were assessed by the Engh score[19]. Adequate radiographs to measure the biomechanical parameters for hip reconstruction as described by Asayama *et al*[20] and Schmidutz *et al*[21] were available in 104 hips. Acetabular cup positioning was evaluated by referring to the safe zones defined by Lewinnek *et al*[22].

Statistical analysis

Data regarding quantitative variables included mean, standard deviation, range and/or median, and qualitative variables as a percentage. The student *t*-test for independent samples was used to compare continuous variables in normally distributed data among groups. The Wilcoxon rank-sum test was used for data not normally distributed. The implant survival probabilities were computed using Kaplan–Meier analysis (revision of any component for any reason as the terminating event or at the end of the follow-up period). The statistical analysis was performed using the STATA11 software package (Statistic Data Analysis, StataCorp, College Station, TX). *P* values lower than 0.05 were considered significant.

RESULTS

One hundred and thirty patients were included in the study. Surgery was carried out bilaterally in 14 cases for a total of 144 hips that underwent DAA for THA. One hundred and twenty cases were performed by a senior experienced surgeon; twenty-four cases by two other surgeons in their learning curve.

The demographic and clinical data of the patients are shown in Table 1.

Complications

Complications were recorded in 6 procedures (4.2%). Analytical data are reported in Table 2.

No significant differences in terms of complications were observed between the senior surgeon and the training surgeons (5 complications out of 120 procedures *vs* 1 complication in 24 procedures – not significant, Fisher exact test).

Table 1 Demographic and clinical data of the 144 hips included in the study

Demographic and clinical data	*n* = 144
Male/female, *n* (%)	70 (49)/74 (51)
Right hip/left hip, *n* (%)	83 (58)/61 (42)
Age avg. (range)	68.6 (43-88)
BMI avg. (range)	26.3 (17.5-39.8)
Diagnosis primary OA, *n* (%)	135 (94)
AVN, *n* (%)	7 (5)
Post-traumatic OA, *n* (%)	2 (1)
ASA, *n* (%)	
1	9 (6)
2	89 (62)
3	44 (30)
4	2 (1)
CCI, *n* (%)	
0	6 (4)
1-2	39 (27)
≥ 3	99 (69)
Charnley classification, *n* (%)	
A	79 (54.9)
B	33 (22.9)
BB	28 (19.4)
C	4 (2.8)

BMI: Body mass index; AVN: Avascular necrosis; ASA: American Society of Anesthesiologists; OA: Osteoarthritis; CCI: Charlson comorbidity index.

Table 2 Data of the six patients with complications

Patient, *n* (age)	Gender	Charnely	Complications	Grade[13]	HHS	HOOS	Remarks
12 (50)	F	A	2-wound complication	2	93	89	
53 (77)	M	B2	9-PJI	3	85	52	Two stage procedure with resolution
55 (63)	M	A	1-bleeding	3	100	96	Hematoma that required surgical drainage
115 (55)	M	B1	10-heterotopic calcification	3	93	84	
139 (69)	F	B1	2-wound complication	3	79	78	Surgical debridement, no patogens, healed in 3 wk
141 (44)	F	B1	2-wound complication	2	100	96	

HHS: Harris Hip Score; HOOS: Hip disability and Osteoarthritis Outcome Score; F: Female; M: Male.

No intra-operative complications and no dislocations were reported.

Survivorship

At 69 mo, the cumulative survival of the stem and cup (that did not require surgical revisions) was 98.6% (95%CI: 90.7-99.8). Only one implant was revised due to deep infection (0.7%). No failures were observed for aseptic loosening.

Component positioning

Stem alignment averaged -0.3° ± 1.9°; 97 out of 104 stems (93.3%) were within 3° of varus/valgus. The mean cup inclination was 38° ± 5.7° and the mean anteversion was 15° ± 5.2°. Eighty-eight out of 104

cups (84.6%) were within the Lewinnek safe zone.

No significant differences were seen between the senior surgeon and the training surgeons regarding stem alignment and cup position.

Hip center of rotation, femoral offset and abduction lever arm reconstruction and leg length

When compared to the contralateral side, hip center of rotation (CoR) was postoperatively elevated by 3.7 mm ± 4.3 mm and medialized by 3.4 mm ± 4.5 mm on average. Femoral offset (FO), abduction lever arm (ALA), and leg length (LL) after surgery are shown in Figure 1. FO increased in 83 out of 104 cases (79.8%); when compared to the contralateral side, only 8 out of 104 cases (7.7%) showed a decrease of FO greater than 15%. Compared to the contralateral side, the leg length of the operated hip was longer by 2 mm ± 6.1 mm on average. In 56.7% of cases, leg length discrepancy was within ± 5 mm.

Radiographic outcomes

No lines of radiolucency or lysis were observed around any of the implanted acetabular components. One stem showed an area of lysis in Gruen zone 1 and radiolucencies in zones 3, 4, and 5 at 24 mo. This patient was asymptomatic with an Engh score of 15.

No stem showed any subsidence greater than 2 mm. The Engh score provided results between 15 and 26 suggesting osseointegration of all implanted stems. Distal femoral cortical hypertrophy (DFCH) was observed around 32 femoral stems (22.2%) (Figure 2). Gruen zone 3 was the most affected (28 cases), followed by zones 2 and 5 (respectively 13 and 11 cases). None of the patients involved were symptomatic nor showed any functional impairment. HHS and HOOS total scores were not significantly different between those with DFCH and those without it (respectively 95.8 ± 9.6 *vs* 97.4 ± 2.9 and 86.9 ± 16.6 *vs* 89.5 ± 9.9, Wilcoxon rank-sum test).

Functional outcomes and patient-related outcome

The HHS median at final follow-up was 96.2 points (range 44-100 points). The score was excellent in 119 patients (91.5%), good in 5 (3.8%), fair in 3 (2.3%) and poor in 3 (2.3%).

The patients with poor HHS included 3 Charnley class C females with disabling chronic low back pain. HOOS results at final follow-up for all patients are presented in Figure 3. Median values range from 87.5 to 95.

Two multivariate analysis was performed to identify potential risk factors for a poor outcome using HHS and total HOOS at final follow-up as independent variable and age, gender, BMI, ASA, CCI and Engh Score as dependent variables. Regarding HHS, male gender was a significant positive factor whilst age, ASA and CCI were significantly inversely correlated with the score. Age and ASA were also significantly inversely correlated with final HOOS total score.

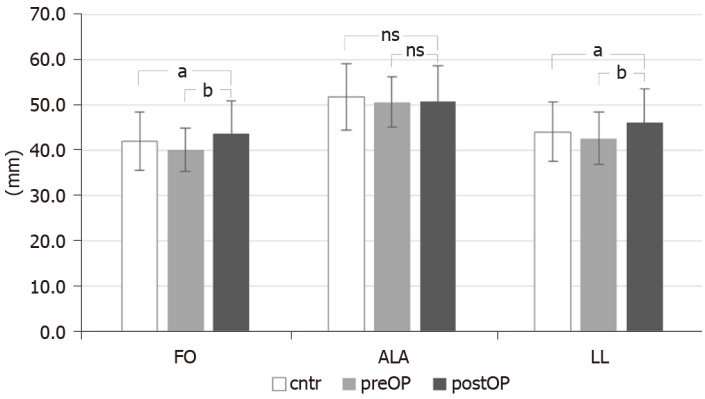
DISCUSSION

The results of our study showed that the Accolade stem is suitable, safe, and efficient when used in the DAA for THA. The overall complication rate was low even for surgeons during the learning curve. None of the complications were related to the difficulties of exposure of the femur during the surgical procedure, intraoperative fractures or stem subsidence. Failures due to infection was very rare, with only one of the 144 cases that showed failure for periprosthetic infection at a mean follow-up of 35 mo.

Femoral exposure and preparation through the DAA is a complex part of the operation. Meneghini *et al*[7] found that the revisions due to early femoral failure were more common in patients who had undergone the DAA. In this regard, the design of the stem can play an important role during surgery, and data from the literature suggests that the shape of the stem can induce specific problems. Janssen *et al*[9] found that there was a stem-approach interaction, in which shoulder stems showed a greater likelihood of early aseptic loosening when the anterolateral or the anterior approach was used.

Studies have reported that longer stems or those with particular designs were associated with more perioperative complications, especially periprosthetic fractures. Dietrich *et al*[23] found an odds ratio of 1.98 for intraoperative fractures when a Quadra-H stem was used compared to the Fitmore and AMIStem. Tamaki *et al*[24] and Greco *et al*[25] reported an increase in femur complication rate using the Taperloc Microplasty short stem with full profile taper concerning the standard length Taperloc. Rivera *et al*[6] reported that the Fitmore stem was associated with a higher probability of undersizing when implanted by DAA.

New stem designs may reveal new problems with other surgical approaches as well, as suggested by the data from Tootsi *et al*[26], which reported a 5% incidence of intraoperative femoral fracture in 222 THA performed using the novel SP-CL® implant. With regards to the Accolade II, the morphometric design with a size-specific medial curvature and optimized length potentially renders this stem suitable for DAA. Our radiographic results on the reconstruction of the biomechanics of the operated hip also seem to promote the design of this stem. Stem positioning and the reconstruction of FA, ALA, and LL resulted comparable to those reported by Schmidutz *et al*[21] This study compared a short-stem hip with a conventional stem implanted with a minimally invasive anterolateral Hardinge approach in the



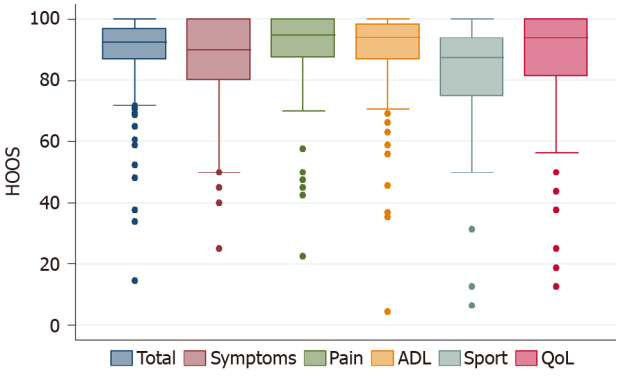
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Figure 1 Comparison of postoperative femoral offset, abductors lever arm and leg length with preoperative and contralateral parameters. [a]*P* < 0.05, [b]*P* < 0.01; ns: Not significant. postOP: Postoperative; FO: Femoral offset; ALA: Abductors lever arm; LL: Leg length; preOP: Preoperative; cntr: Contralateral.



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Figure 2 Patient with bilateral prosthesis. Right hip at 36 mo since surgery with distal femoral cortical hypertrophy in Gruen zones 2 and 3; left hip at 18 mo postoperative without cortical hypertrophy.



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Figure 3 Box plot for Hip disability and Osteoarthritis Outcome scores at final follow-up (median, 25th and 75th percentile, max and min values, outliers). HOOS: Hip disability and Osteoarthritis Outcome Score; ADL: Activities of daily living; QoL: Quality of life.

supine position. The achieved degree of precision of the joint reconstruction was such as not affecting patient-related outcomes[27].

The performance of the Accolade II stem has also been described in other studies. Pierce *et al*[28] reported the results of 68 hips implanted at a high-volume institution using an anterolateral approach. No stem complications were shown, with an all-cause survivorship of 99.2% at a mean follow-up of 3.5 years. Kolisek *et al*[29] examined 202 Accolade II femoral stems implanted in 4 different hospitals with a 2-year follow-up. They reported two surgical complications related to stem implantation, which included a posterior trochanteric avulsion and a periprosthetic fracture. Aseptic and all-cause survival

rates of 100% and 99.5% were reported. Berndt *et al*[30] reviewed 151 THA procedures with the Accolade II/Trident implant system using DAA. With regards to complications, this study reported one intraoperative stem perforation and one aseptic stem loosening at 45 mo with a total implant survival of 96.9% at 5 years.

Our study showed that all patients had favorable radiographic outcomes. The Engh scores suggested that all stems were well integrated and showed a low incidence of radiolucency lines (reported in 1 of the 115 hips). These results are indicative of a satisfactory fit and fill of the femoral canal and adequate adhesion of the circumferential porous coating to the surrounding bone[31].

A better "fit and fill" of the Accolade II stems when compared to the previous models has been reported in a preclinical study by Faizan *et al*[32], which showed a more uniform proximal-distal grip in a large sample of femoral sizes. Studies by Issa *et al*[10] reported a significant improvement in both proximal and distal fixation in the current version. Numerous evidences affirms that excellent "fit and fill" correlate with better clinical-functional results[33-35]. Our data confirm the excellent results in HHS and HOOS in addition to the absence of radiological subsidence in the stems.

We detected DFCH in 22% of our stems, but this did not appear to influence the implant survival and functional and subjective outcomes. Previous studies have shown that DFCH prevalence ranges from 6% to 56% in different cementless stem designs without determining any functional impairment[36,37].

Our study has several limitations. The data is based on a retrospective study in which the lack of complication related to the stem may be due to the relatively limited number in the cohort. Similar types of study in literature, however, have reported incidence rates of perioperative fractures ranging from 1 to 7 cases[23,25], which was not seen in our cohort. Moreover, our study was based on a rather short follow-up (3.5 years), thus does not provide information regarding the long-term success rates of this stem.

CONCLUSION

The design of the stem can have an effect on the risk of adverse events in DAA for THA. Studies are needed to confirm the safety and success rates when new models are proposed for implantable stems for THA are desirable. Our preliminary data shows that the Accolade II stem tends to provide a low complication rate and satisfactory biomechanical reconstruction. The mid-term positive outcomes concerning survivorship, functional scores, and activity levels in our consecutive series of patients support the safety and suitability for DAA of this new stem design, which can be a long-term predictor of success. Further multicenter studies with longer follow-up are needed to confirm these preliminary positive results.

ARTICLE HIGHLIGHTS

Research background

The direct anterior approach for total hip arthroplasty is a less invasive and muscle-sparing approach that seems to improve early function and patient satisfaction.

Research motivation

To study the results of this surgery in a cohort of patients.

Research objectives

To report outcomes, advantages and indications for this surgery.

Research methods

Analysis of outcomes after surgery.

Research results

Result outcomes were good. Complication rates were relatively low.

Research conclusions

The mid-term positive outcomes and low complication rate in our consecutive series of patients support the safety and suitability of this new surgery.

Research perspectives

New models to enhance surgery can improve outcomes.

FOOTNOTES

Author contributions: Trevisan C designed the research study, performed data acquisition, and wrote the manuscript; Lombardo AS, Gallinari G, and Klumpp R designed the research study and performed data acquisition; Trevisan C, Lombardo AS, Gallinari G, Zeppieri M and Klumpp R contributed towards conception of the study and final editing; All authors revised the article critically for important intellectual content, and provided final approval for the paper to be published.

Institutional review board statement: The study was reviewed and approved by the Ethics Committee of Bergamo, Italy (No. 144/19, August 5, 2019).

Informed consent statement: Patients were not required to give informed consent to the study because the data was collected retrospectively and anonymized. Clinical data were obtained after each patient agreed to treatment by written consent.

Conflict-of-interest statement: All authors report no relevant conflict of interest for this article.

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REFERENCES

1 **Metha JS**, Kiryluk S, Fordyce MJ. Pain and satisfaction after hip replacement: The patients perspective at 5 - 12 years. *Hip Int* 2005; **15**: 112-118 [PMID: 28224567 DOI: 10.5301/HIP.2008.2998]
2 **Dobzyniak M**, Fehring TK, Odum S. Early failure in total hip arthroplasty. *Clin Orthop Relat Res* 2006; **447**: 76-78 [PMID: 16505710 DOI: 10.1097/01.blo.0000203484.90711.52]
3 **Melvin JS**, Karthikeyan T, Cope R, Fehring TK. Early failures in total hip arthroplasty -- a changing paradigm. *J Arthroplasty* 2014; **29**: 1285-1288 [PMID: 24444568 DOI: 10.1016/j.arth.2013.12.024]
4 **de Steiger RN**, Lorimer M, Solomon M. What is the learning curve for the anterior approach for total hip arthroplasty? *Clin Orthop Relat Res* 2015; **473**: 3860-3866 [PMID: 26394641 DOI: 10.1007/s11999-015-4565-6]
5 **Graw BP**, Woolson ST, Huddleston HG, Goodman SB, Huddleston JI. Minimal incision surgery as a risk factor for early failure of total hip arthroplasty. *Clin Orthop Relat Res* 2010; **468**: 2372-2376 [PMID: 20352391 DOI: 10.1007/s11999-010-1300-1]
6 **Rivera F**, Leonardi F, Evangelista A, Pierannunzii L. Risk of stem undersizing with direct anterior approach for total hip arthroplasty. *Hip Int* 2016; **26**: 249-253 [PMID: 27013489 DOI: 10.5301/hipint.5000337]
7 **Meneghini RM**, Elston AS, Chen AF, Kheir MM, Fehring TK, Springer BD. Direct Anterior Approach: Risk Factor for Early Femoral Failure of Cementless Total Hip Arthroplasty: A Multicenter Study. *J Bone Joint Surg Am* 2017; **99**: 99-105 [PMID: 28099299 DOI: 10.2106/JBJS.16.00060]
8 **Lindgren V**, Garellick G, Kärrholm J, Wretenberg P. The type of surgical approach influences the risk of revision in total hip arthroplasty: a study from the Swedish Hip Arthroplasty Register of 90,662 total hipreplacements with 3 different cemented prostheses. *Acta Orthop* 2012; **83**: 559-565 [PMID: 23116440 DOI: 10.3109/17453674.2012.742394]
9 **Janssen L**, Wijnands KAP, Janssen D, Janssen MWHE, Morrenhof JW. Do Stem Design and Surgical Approach Influence Early Aseptic Loosening in Cementless THA? *Clin Orthop Relat Res* 2018; **476**: 1212-1220 [PMID: 29481346 DOI: 10.1007/s11999.0000000000000208]
10 **Issa K**, Pivec R, Wuestemann T, Tatevossian T, Nevelos J, Mont MA. Radiographic fit and fill analysis of a new second-generation proximally coated cementless stem compared to its predicate design. *J Arthroplasty* 2014; **29**: 192-198 [PMID: 23706811 DOI: 10.1016/j.arth.2013.04.029]
11 **Charlson M**, Szatrowski TP, Peterson J, Gold J. Validation of a combined comorbidity index. *J Clin Epidemiol* 1994; **47**: 1245-1251 [PMID: 7722560 DOI: 10.1016/0895-4356(94)90129-5]
12 **Halley DK**, Charnley J. Results of low friction arthroplasty in patients thirty years of age or younger. *Clin Orthop Relat Res* 1975; 180-191 [PMID: 1192631]
13 **Healy WL**, Iorio R, Clair AJ, Pellegrini VD, Della Valle CJ, Berend KR. Complications of Total Hip Arthroplasty:

Standardized List, Definitions, and Stratification Developed by The Hip Society. *Clin Orthop Relat Res* 2016; **474**: 357-364 [PMID: 26040966 DOI: 10.1007/s11999-015-4341-7]

14 **Harris WH**. Traumatic arthritis of the hip after dislocation and acetabular fractures: treatment by mold arthroplasty. An end-result study using a new method of result evaluation. *J Bone Joint Surg Am* 1969; **51**: 737-755 [PMID: 5783851]

15 **Nilsdotter AK**, Lohmander LS, Klässbo M, Roos EM. Hip disability and osteoarthritis outcome score (HOOS)--validity and responsiveness in total hip replacement. *BMC Musculoskelet Disord* 2003; **4**: 10 [PMID: 12777182 DOI: 10.1186/1471-2474-4-10]

16 **Gruen TA**, McNeice GM, Amstutz HC. "Modes of failure" of cemented stem-type femoral components: a radiographic analysis of loosening. *Clin Orthop Relat Res* 1979; 17-27 [PMID: 477100]

17 **DeLee JG**, Charnley J. Radiological demarcation of cemented sockets in total hip replacement. *Clin Orthop Relat Res* 1976; 20-32 [PMID: 991504]

18 **Grant TW**, Lovro LR, Licini DJ, Warth LC, Ziemba-Davis M, Meneghini RM. Cementless Tapered Wedge Femoral Stems Decrease Subsidence in Obese Patients Compared to Traditional Fit-and-Fill Stems. *J Arthroplasty* 2017; **32**: 891-897 [PMID: 27793497 DOI: 10.1016/j.arth.2016.09.023]

19 **Engh CA**, Massin P, Suthers KE. Roentgenographic assessment of the biologic fixation of porous-surfaced femoral components. *Clin Orthop Relat Res* 1990; 107-128 [PMID: 2199114]

20 **Asayama I**, Chamnongkich S, Simpson KJ, Kinsey TL, Mahoney OM. Reconstructed hip joint position and abductor muscle strength after total hip arthroplasty. *J Arthroplasty* 2005; **20**: 414-420 [PMID: 16124955 DOI: 10.1016/j.arth.2004.01.016]

21 **Schmidutz F**, Beirer M, Weber P, Mazoochian F, Fottner A, Jansson V. Biomechanical reconstruction of the hip: comparison between modular short-stem hip arthroplasty and conventional total hip arthroplasty. *Int Orthop* 2012; **36**: 1341-1347 [PMID: 22262250 DOI: 10.1007/s00264-011-1477-2]

22 **Lewinnek GE**, Lewis JL, Tarr R, Compere CL, Zimmerman JR. Dislocations after total hip-replacement arthroplasties. *J Bone Joint Surg Am* 1978; **60**: 217-220 [PMID: 641088]

23 **Dietrich M**, Kabelitz M, Dora C, Zingg PO. Perioperative Fractures in Cementless Total Hip Arthroplasty Using the Direct Anterior Minimally Invasive Approach: Reduced Risk With Short Stems. *J Arthroplasty* 2018; **33**: 548-554 [PMID: 28993084 DOI: 10.1016/j.arth.2017.09.015]

24 **Tamaki T**, Jonishi K, Miura Y, Oinuma K, Shiratsuchi H. Cementless Tapered-Wedge Stem Length Affects the Risk of Periprosthetic Femoral Fractures in Direct Anterior Total Hip Arthroplasty. *J Arthroplasty* 2018; **33**: 805-809 [PMID: 29107490 DOI: 10.1016/j.arth.2017.09.065]

25 **Greco NJ**, Lombardi AV Jr, Morris MJ, Hobbs GR, Berend KR. Direct Anterior Approach and Perioperative Fracture With a Single-Taper Wedge Femoral Component. *J Arthroplasty* 2019; **34**: 145-150 [PMID: 30301574 DOI: 10.1016/j.arth.2018.09.003]

26 **Tootsi K**, Lees L, Geiko B, Märtson A. Intraoperative complications in total hip arthroplasty using a new cementless femoral implant (SP-CL®). *J Orthop Traumatol* 2020; **21**: 8 [PMID: 32451636 DOI: 10.1186/s10195-020-00548-6]

27 **Trevisan C**, Klumpp R, Piscitello S, Compagnoni R, Grattieri R, Cazzaniga C. Biomechanical reconstruction parameters obtained after direct anterior approach total hip arthroplasty do not compromise clinical outcome. *Eur J Orthop Surg Traumatol* 2020; **30**: 1463-1470 [PMID: 32613469 DOI: 10.1007/s00590-020-02727-x]

28 **Pierce TP**, Jauregui JJ, Kapadia BH, Elmallah RK, Cherian JJ, Harwin SF, Mont MA. Second-Generation Versus First-Generation Cementless Tapered Wedge Femoral Stems. *Orthopedics* 2015; **38**: 550-554 [PMID: 26375526 DOI: 10.3928/01477447-20150902-04]

29 **Kolisek FR**, Chughtai M, Mistry JB, Elmallah RK, Jaggard C, Malkani AL, Masini MA, Harwin SF, Mont MA. Outcomes of Second-Generation Tapered Wedge Femoral Stem. *Surg Technol Int* 2016; **28**: 275-279 [PMID: 27042781]

30 **Berndt K**, Rahm S, Dora C, Zingg PO. Total hip arthroplasty with accolade/trident through the direct minimally invasive anterior approach without traction table: Learning curve and results after a minimum of 5 years. *Orthop Traumatol Surg Res* 2019; **105**: 931-936 [PMID: 31255503 DOI: 10.1016/j.otsr.2019.05.008]

31 **Kim YH**, Oh SH, Kim JS. Primary total hip arthroplasty with a second-generation cementless total hip prosthesis in patients younger than fifty years of age. *J Bone Joint Surg Am* 2003; **85**: 109-114 [PMID: 12533580 DOI: 10.2106/00004623-200301000-00017]

32 **Faizan A**, Wuestemann T, Nevelos J, Bastian AC, Collopy D. Development and verification of a cementless novel tapered wedge stem for total hip arthroplasty. *J Arthroplasty* 2015; **30**: 235-240 [PMID: 25449589 DOI: 10.1016/j.arth.2014.09.023]

33 **Engh CA**, Bobyn JD, Glassman AH. Porous-coated hip replacement. The factors governing bone ingrowth, stress shielding, and clinical results. *J Bone Joint Surg Br* 1987; **69**: 45-55 [PMID: 3818732 DOI: 10.1302/0301-620X.69B1.3818732]

34 **Itami Y**, Akamatsu N, Tomita Y, Nagai M, Nakajima I. A clinical study of the results of cementless total hip replacement. *Arch Orthop Trauma Surg (1978)* 1983; **102**: 1-10 [PMID: 6639306 DOI: 10.1007/BF00443031]

35 **Bourne RB**, Rorabeck CH, Ghazal ME, Lee MH. Pain in the thigh following total hip replacement with a porous-coated anatomic prosthesis for osteoarthrosis. A five-year follow-up study. *J Bone Joint Surg Am* 1994; **76**: 1464-1470 [PMID: 7929493 DOI: 10.2106/00004623-199410000-00005]

36 **Maier MW**, Streit MR, Innmann MM, Krüger M, Nadorf J, Kretzer JP, Ewerbeck V, Gotterbarm T. Cortical hypertrophy with a short, curved uncemented hip stem does not have any clinical impact during early follow-up. *BMC Musculoskelet Disord* 2015; **16**: 371 [PMID: 26627999 DOI: 10.1186/s12891-015-0830-9]

37 **Cho YJ**, Chun YS, Rhyu KH, Baek JH, Liang H. Distal femoral cortical hypertrophy after hip arthroplasty using a cementless doubletapered femoral stem. *J Orthop Surg (Hong Kong)* 2016; **24**: 317-322 [PMID: 28031498 DOI: 10.1177/1602400309]

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ORIGINAL ARTICLE

Observational Study

Occupational injuries and burn out among orthopedic oncology surgeons

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Abstract

BACKGROUND

Orthopedic oncology surgeons commonly engage in prolonged and complex surgical procedures. These types of surgeries increase the risk of physical and psychological stressors, which may in turn make these physicians prone to work-related occupational injuries.

AIM

The aim of this study was to explore in orthopedic oncologists, the prevalence of work-related physical injuries and psychological disturbances.

METHODS

A modified version of the physical discomfort survey was developed to assess occupational injuries among orthopedic oncology surgeon members of the Musculoskeletal Tumor Society, the Canadian Orthopedic Oncology Society and European Musculoskeletal Oncology Societies. The survey was sent by email, and it explored musculoskeletal complaints, psychological disturbances, treatment required for these complaints and the requirement of time off work.

RESULTS

A total of 67 surgeon responses were collected. A high number of orthopedic

oncologists (84%) reported an occupational injury. Low back pain (39%) was the most prevalent musculoskeletal condition, followed by lumbar disk herniation (16%), shoulder tendinitis (15%) and lateral epicondylitis (13%). Of the cohort, 46% required surgery and 31% required time off work due to their injury. Thirty-three respondents reported a psychological disorder. Burnout (27%), anxiety (20%) and insomnia (20%) were the most commonly reported. Time required off work due to injury was associated with old age and years in practice.

CONCLUSION

Orthopedic oncology surgeons report a high prevalence of work-related disorders. Lower back related injury and burnout were the most reported disorders. Improving operative room ergonomics and prevention of stress related to the work environment should be areas to explore in upcoming research.

Key Words: Orthopedic oncology; Surgeons; Occupational; Musculoskeletal; Injuries.

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Core Tip: Orthopedic oncologists reported a high prevalence of occupational injury and work-related stress. Futures studies should be directed towards exploring areas to improve the operative environment and methods to decrease conditions associated with stress at work.

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INTRODUCTION

Alarming rates of occupational injuries have been previously reported in different surgical fields including orthopedic surgery[1-5]. It has been an area of interest and investigation due to the implications of these injuries on surgeons, health care system and the quality of provided care[6-9]. Occupational injuries are either work-related injuries or illnesses caused by incidents at a workplace or previous illnesses aggravated by work-related injuries, that could negatively impact the well-being of the affected workers or the quality of provided care[10-12]. Orthopedic surgeons are more vulnerable to a variety of work-related injuries and hazards associated with the nature of their profession such as blood born infections, sharp injuries, noise-induced hearing impairment, exposure to radiation and chemicals, heavy physical workload, emotional and psychological disturbances[13-16].

Several studies have suggested that orthopedic surgeons are at increased rates of occupational injuries[17-20]. When compared to general surgeons, orthopedic surgeons were found to have higher rates of subjective physical injuries. The most reported injuries were back pain, neck pain and upper extremity related complaints[15,21,22]. Furthermore, the psychological disturbances including burnout rates, were found to be higher among orthopedic surgeons as compared to other medical professions and the general population, which in turn may negatively impact the quality of patient care due to increased medical errors and depersonalization[10,23].

Orthopedic oncology is a subspecialty of orthopedics that is physically and psychologically challenging as it involves prolonged and complex surgical procedures, as well as higher rates of serious surgical complications and limited survivorship and functional outcome relating to the oncology patient population. Consequently, such physical and psychological stressors may subject orthopedic oncology surgeons to higher rates of work-related "occupational" injuries that can impact their quality of life, wellness and the quality of delivered patient care. These occupational stressors can lead to preventable musculoskeletal injuries, time off work, increased burnout rates, emotional and psychological disturbances. Investigating this aspect among orthopedic oncology surgeons can help institutions and occupational health agencies to develop preventive strategies to minimize the negative implications of these injuries on the quality of provided care and promote surgeons' personal well-being.

To our knowledge, there are no studies to date investigating the occupational injuries among orthopedic oncology surgeons. The aim of this survey is to explore occupational injuries in orthopedic oncologists, including their prevalence and characteristics.

MATERIALS AND METHODS

An anonymous online, web-based, modified version of the Physical Discomfort Survey (originally developed by the Workplace Safety and Health Division of Manitoba, Canada)[24] and modified version of Maslach Burnout Inventory-Human services survey for medical personnel[25] was emailed to all surgeon members of Musculoskeletal Tumor Society (MSTS), Canadian Orthopedic Oncology Society (CANOOS), and European Musculoskeletal Oncology Society (EMSOS). Only practicing orthopedic oncology surgeon members of the above-mentioned societies were eligible to participate in our study. The first invitation email was sent out in November 2016 and a reminder email was sent out in January 2017. The survey was closed by mid-February 2017. To minimize the magnitude of potential selection and response biases, we sent our survey to all surgeon members of three large orthopedic oncology societies in North America and Europe. Furthermore, we attempted to reduce the potential response bias by sending a subsequent reminder email.

The survey was divided into 3 parts, the first part included questions about participant's demographic data (age, gender, hand dominance), practice setting (academic, community or private), practice duration in years and the average operative caseload *per* year. The second part of the survey was about the musculoskeletal complaints by region (neck, lower back, upper extremity and lower extremity). For each question, participants were asked about the diagnosis, medical or surgical treatments (if any) and if they ever required work stoppage consequently. The third part of the survey involved questions concerning psychological disturbances (anxiety, depression, insomnia, suicidal thoughts and burnout symptoms) and symptoms of "burnout" (emotional exhaustion, depersonalization, low job satisfaction), treatments required (if any) and any time off work needed as a result.

Descriptive statistics were used to report participants' demographics. The prevalence of occupational injury was estimated as the number of injuries *per* total number of respondents. To determine significant associations between patient demographics and occupational hazards, we performed classical tests of hypothesis as well as logistic regression analysis. Statistical significance was set at an alpha of 0.05 and analysis was carried out using Stata v12.1 (Statacrop).

RESULTS

Sixty-seven orthopedic oncology surgeons (58 male and 9 female surgeons) completed the survey (22% response rate). Of the respondent, 40.3%, 43.3% and 6% of respondents were from MSTS, EMSOS and CANOOS, respectively. Most of the participant surgeons are practicing in academic setting (83.3%). The oncologic yearly caseload was seventy-five cases or more in 38.8% of the surgeons.

Eighty four percent of surveyed orthopedic oncology surgeons reported an occupational injury. Musculoskeletal injuries were reported by 76% of participating surgeons, psychological injuries by 50% and both by 43%. The most common musculoskeletal injuries were low back pain (39%), shoulder symptoms (27%), neck pain (24%), lumbar disc herniation (16%), shoulder tendinitis (15%), lateral epicondylitis (13%), hip or knee osteoarthritis and varicose veins (10 % each) (Figure 1). Consequently, time off work was reported by 33.3% surgeons and 27% required treatment including either medical or surgical treatment. Exacerbation of musculoskeletal injuries was experienced by 18% of respondents (Table 1).

Thirty-three surgeons reported a psychological disturbance (50%). The most prevalent were burnout (27%), anxiety and insomnia (20% each) and depression (11%). More seriously, suicidal thought was reported by one participant (Figure 2). Medical and/or psychiatric treatment was required by 18% of respondents and the time off work was required by 3% (Table 2). Young age (35-45 years) was the only significant factor associated with developing symptoms of burnout ($P < 0.015$).

Eighteen surgeons (26.9%) required time off work due to occupational injuries (17 musculoskeletal injuries and 1 psychological disturbance). Factors significantly associated with time off work were age and years of practice of the surgeon ($P < 0.011$) in the logistic regression analysis models performed.

DISCUSSION

Our study revealed a concerning prevalence of occupational injuries among orthopedic oncology surgeons (84%), which is much higher than the previously reported rates in other orthopedic subspecialties[11,17-20]. This could lead to consequences not only on the surgeon's career, but also on the quality and cost of provided health care. One third (33.3%) of participating surgeons reported periods of work stoppage due to work-related injuries and 27% required either medical or surgical treatments. Fifty percent of respondents reported symptoms of occupational psychological disturbances, with burnout being the most reported (27%) followed by insomnia and anxiety (20% each). Orthopedic surgeons in general have higher work-related subjective musculoskeletal symptoms when compared to general surgeons[15]. However, orthopedic oncology is a unique field in orthopedics which deals with complex osseous and soft tissue tumors and therefore, orthopedic oncologists are involved in prolonged

Table 1 Proportion of orthopaedic oncologists' surgeons with diagnosed musculoskeletal disorders per region requiring treatment and time off work

Region	Proportion of injured respondents (%)	Proportion of injured respondents requiring treatment (%)	Proportion of injured respondents requiring surgery (%)	Proportion of treated respondents requiring time off work (%)
Neck	24	56	6	13
Shoulder	27	72	22	22
Elbow	13	67	0	0
Forearm, wrist and hand	39	62	23	23
Hip and thigh	7	80	20	17
Knee and lower leg	13	56	56	40
Ankle/foot	7	100	20	40
Lower back	55	51	8	24

Table 2 Proportion of orthopaedic oncologists' surgeons with diagnosed psychological disorders requiring treatment and time off work

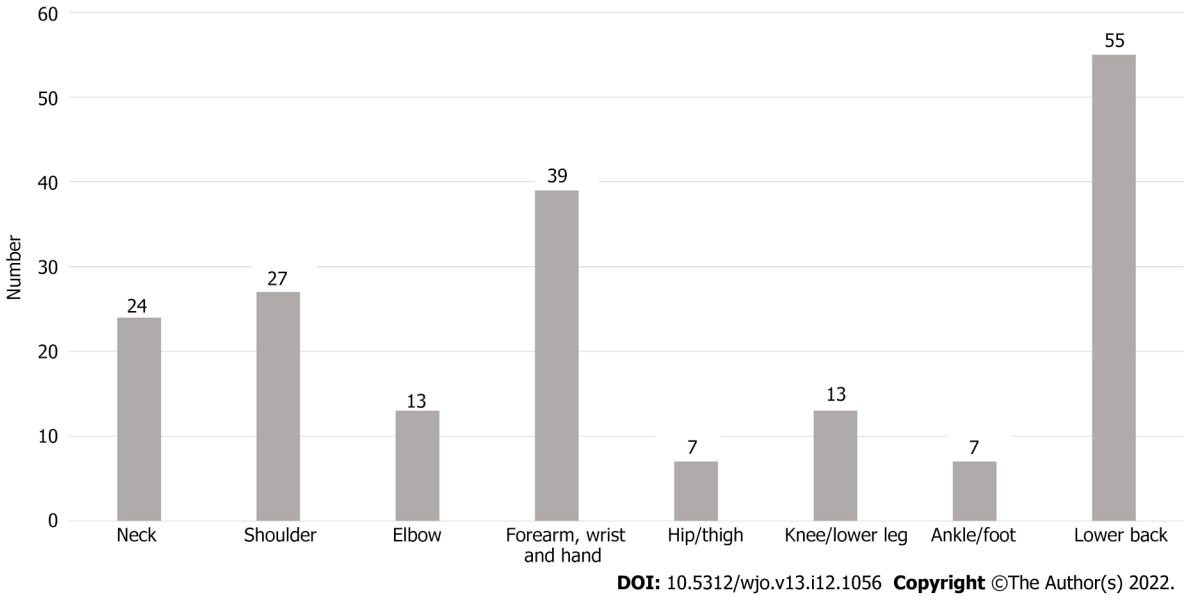
Disorder	Number of respondents with disorders	Number of treated respondents requiring treatment	Proportion of treated respondents requiring medical treatment	Proportion of treated respondents requiring time-off
Anxiety	20	5	2	1
Depression	11	5	3	1
Insomnia	20	2	1	0
Suicidal thoughts	2	1	1	0
Burnout	27	5	2	1
Other	6	1	1	0
Total	33	19	10	3

meticulous surgical procedures with relatively higher complication rates than any other orthopedic specialties. Furthermore, Orthopedic oncologists face psychological stressors as they are involved in psychological and emotional aspects associated with the management of oncology patients. Hence, it is not surprising that this surgeon population have higher rates of occupational injuries including musculoskeletal and psychological disturbances as shown in the results of this study.

Several factors have been shown in the literature as contributing factors to the high rates of occupational injuries among surgeons[4-8]. The nature of their work involves poor ergonomics such as lengthy non-neutral postures while operating, repetitive intra-operative physically demanding tasks, the height of operating table and the non-ergonomically designed surgical instruments[5-8]. New ergonomic innovations have been suggested to improve the operating room environment and minimize the risks of occupational injuries; however, the utilization of these devices is not yet popularized. These factors are applicable even more to orthopedic oncologists due to the complexity and nature of their profession. However, if such work-related injuries are not addressed early, it may progress to more sever morbidity and adversely influence the surgeon's wellbeing and career lifespan.

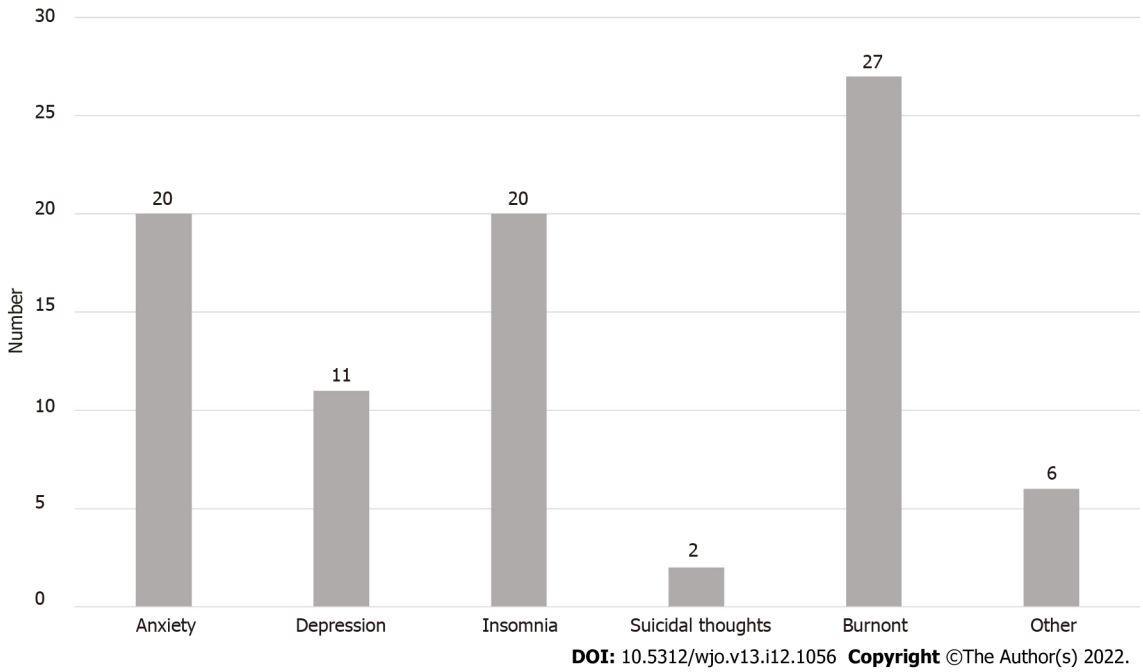
In addition, psychological disturbances were also found to be high in surgeons, especially in surgical oncologists in the current literature[26]. This is consistent with our results showing high psychological morbidity rates among orthopedic oncologists. Nevertheless, many surgeons may neglect their occupational health issues and thus not pursue the appropriate help when needed, likely due to lack of mindfulness about the potential occupational health injuries and the heavy workload nature of their professions[8].

The limitations of our survey study are similar to most survey studies in the literature. One of the limitations is the subjective nature of self-reported occupational musculoskeletal and psychological complaints. However, our participants are practicing surgeons and most likely they are accurately reporting their health issues. Additionally, the primary focus of our study is to assess the magnitude of occupational injuries among orthopedic oncologist and the characteristics of these injuries. Most work-



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Figure 1 Percentages of reported musculoskeletal disorders and complaints among survey participants.



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Figure 2 Percentages of reported psychological disorders among survey participants.

related symptoms are subjective complaints and may not be associated with objective clinical findings. Therefore, it is widely accepted to evaluate the prevalence of occupational injuries by self-administered surveys. Another possible argument is the significantly higher prevalence rate of occupational injuries reported in our study. This possibly inflated prevalence could be related to that some participants in such surveys are currently or have previously been affected by occupational injuries, thus probably leading to possible response or selection bias. Although we believe this is certainly a valid concern, we still anticipate a high rate of occupational injuries among orthopedic oncologists if we assume the non-respondents are not affected with occupational injuries. The surveys used in our current study included modified self-reported outcomes, which could be an area of limitation. Future research should be directed at studying the reliability, validity, and area of weaknesses of these surveys. One of the strengths of our study is that the study sample, although relatively small, is representative of the orthopedic oncology surgeons' population in North America and Europe, which is considered not a large population.

CONCLUSION

The purpose of this survey was to increases the mindfulness of work-related health issues and its possible consequences on surgeons' wellness, patient care delivery and institutional health quality measures. Our data should help health institutions and occupational health services develop early educational programs directed to surgeons and provide preventive and supportive ergonomic measures in order to improve the surgeons' wellness and minimize the undesirable consequences of occupational injuries on the health care system.

ARTICLE HIGHLIGHTS

Research background

Orthopedic oncology surgeons commonly perform complex and prolonged surgical. This places the surgeon at increased risk of not only physical but also psychological stressors.

Research motivation

The effect of these physical and mental burdens on both the surgeon and healthcare system has not been adequately studied.

Research objectives

We aimed to explore occupational injuries among orthopedic oncology surgeons, especially prevalence, characteristics and their effect on practice.

Research methods

A modified version of the physical discomfort web-based survey was used to determine prevalence and patterns of occupational injuries among orthopedic oncology and this survey was sent to multiple orthopedic oncology societies.

Research results

The overall prevalence of occupational injury among our surgeon cohort was 84% (musculoskeletal 76%; psychological 50%; and both 43%). Low back pain was the most prevalent musculoskeletal conditions and burnout was the most prevalent psychological disorder. Old age and years in practice were associated with requirement of time off work.

Research conclusions

We found a high prevalence of occupational injuries in orthopedic oncologists, with a large proportion of them requiring time off due to these injuries.

Research perspectives

Future research should be directed towards exploring strategies directed at decreasing the prevalence of these injuries through improved ergonomics and optimized working environments to minimize stress associated with the workplace.

FOOTNOTES

Author contributions: Alaseem AM, Turcotte RE, Alzahrani MM, Al-Qahtani SM, Goulding KA contribute to study design; Alaseem AM, Turcotte RE, Ste-Marie N, Alzahrani MM, Al-Qahtani SM, Goulding KA contribute to manuscript preparation; Turcotte RE, Alzahrani MM, Al-Qahtani SM, Goulding KA contribute to methodology; Ste-Marie N contribute tostatistical analysis.

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Informed consent statement: This study is a survey and informed consent was not required.

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REFERENCES

1 **Giberti C**, Gallo F, Francini L, Signori A, Testa M. Musculoskeletal disorders among robotic surgeons: a questionnaire analysis. *Arch Ital Urol Androl* 2014; **86**: 95-98 [PMID: 25017587 DOI: 10.4081/aiua.2014.2.95]
2 **Davis WT**, Fletcher SA, Guillamondegui OD. Musculoskeletal occupational injury among surgeons: effects for patients, providers, and institutions. *J Surg Res* 2014; **189**: 207-212.e6 [PMID: 24721601 DOI: 10.1016/j.jss.2014.03.013]
3 **Capone AC**, Parikh PM, Gatti ME, Davidson BJ, Davison SP. Occupational injury in plastic surgeons. *Plast Reconstr Surg* 2010; **125**: 1555-1561 [PMID: 20440174 DOI: 10.1097/PRS.0b013e3181d62a94]
4 **Dianat I**, Bazazan A, Souraki Azad MA, Salimi SS. Work-related physical, psychosocial and individual factors associated with musculoskeletal symptoms among surgeons: Implications for ergonomic interventions. *Appl Ergon* 2018; **67**: 115-124 [PMID: 29122182 DOI: 10.1016/j.apergo.2017.09.011]
5 **Park A**, Lee G, Seagull FJ, Meenaghan N, Dexter D. Patients benefit while surgeons suffer: an impending epidemic. *J Am Coll Surg* 2010; **210**: 306-313 [PMID: 20193893 DOI: 10.1016/j.jamcollsurg.2009.10.017]
6 **Soueid A**, Oudit D, Thiagarajah S, Laitung G. The pain of surgery: pain experienced by surgeons while operating. *Int J Surg* 2010; **8**: 118-120 [PMID: 19944192 DOI: 10.1016/j.ijsu.2009.11.008]
7 **Szeto GP**, Ho P, Ting AC, Poon JT, Cheng SW, Tsang RC. Work-related musculoskeletal symptoms in surgeons. *J Occup Rehabil* 2009; **19**: 175-184 [PMID: 19381790 DOI: 10.1007/s10926-009-9176-1]
8 **Vijendren A**, Yung M, Sanchez J. The ill surgeon: a review of common work-related health problems amongst UK surgeons. *Langenbecks Arch Surg* 2014; **399**: 967-979 [PMID: 25113227 DOI: 10.1007/s00423-014-1233-3]
9 **Vijendren A**, Yung M, Sanchez J, Duffield K. Occupational musculoskeletal pain amongst ENT surgeons - are we looking at the tip of an iceberg? *J Laryngol Otol* 2016; **130**: 490-496 [PMID: 27095554 DOI: 10.1017/S0022215116001006]
10 **Daniels AH**, DePasse JM, Kamal RN. Orthopaedic Surgeon Burnout: Diagnosis, Treatment, and Prevention. *J Am Acad Orthop Surg* 2016; **24**: 213-219 [PMID: 26885712 DOI: 10.5435/JAAOS-D-15-00148]
11 **Davis WT**, Sathiyakumar V, Jahangir AA, Obremskey WT, Sethi MK. Occupational injury among orthopaedic surgeons. *J Bone Joint Surg Am* 2013; **95**: e107 [PMID: 23925752 DOI: 10.2106/JBJS.L.01427]
12 **Lester JD**, Hsu S, Ahmad CS. Occupational hazards facing orthopedic surgeons. *Am J Orthop (Belle Mead NJ)* 2012; **41**: 132-139 [PMID: 22530210]
13 **Maniar HH**, Tawari AA, Suk M, Bowen TR, Horwitz DS. Percutaneous and Mucocutaneous Exposure Among Orthopaedic Surgeons: Immediate Management and Compliance With CDC Protocol. *J Orthop Trauma* 2015; **29**: e391-e394 [PMID: 25967855 DOI: 10.1097/BOT.0000000000000360]
14 **Matityahu A**, Duffy RK, Goldhahn S, Joeris A, Richter PH, Gebhard F. The Great Unknown-A systematic literature review about risk associated with intraoperative imaging during orthopaedic surgeries. *Injury* 2017; **48**: 1727-1734 [PMID: 28648410 DOI: 10.1016/j.injury.2017.04.041]
15 **Mirbod SM**, Yoshida H, Miyamoto K, Miyashita K, Inaba R, Iwata H. Subjective complaints in orthopedists and general surgeons. *Int Arch Occup Environ Health* 1995; **67**: 179-186 [PMID: 7591176 DOI: 10.1007/BF00626350]
16 **Romanova K**, Vassileva J, Alyakov M. Radiation exposure to the eye lens of orthopaedic surgeons during various orthopaedic procedures. *Radiat Prot Dosimetry* 2015; **165**: 310-313 [PMID: 25944961 DOI: 10.1093/rpd/ncv122]
17 **AlQahtani SM**, Alzahrani MM, Harvey EJ. Prevalence of musculoskeletal disorders among orthopedic trauma surgeons: an OTA survey. *Can J Surg* 2016; **59**: 42-47 [PMID: 26812408 DOI: 10.1503/cjs.014415]
18 **Alqahtani SM**, Alzahrani MM, Tanzer M. Adult Reconstructive Surgery: A High-Risk Profession for Work-Related Injuries. *J Arthroplasty* 2016; **31**: 1194-1198 [PMID: 26791046 DOI: 10.1016/j.arth.2015.12.025]
19 **Alzahrani MM**, Alqahtani SM, Tanzer M, Hamdy RC. Musculoskeletal disorders among orthopedic pediatric surgeons: an overlooked entity. *J Child Orthop* 2016; **10**: 461-466 [PMID: 27538942 DOI: 10.1007/s11832-016-0767-z]
20 **Auerbach JD**, Weidner ZD, Milby AH, Diab M, Lonner BS. Musculoskeletal disorders among spine surgeons: results of a survey of the Scoliosis Research Society membership. *Spine (Phila Pa 1976)* 2011; **36**: E1715-E1721 [PMID: 21508887 DOI: 10.1097/BRS.0b013e31821cd140]
21 **Alzahrani MM**, Alqahtani SM, Pichora D, Bicknell R. Work-related musculoskeletal injuries among upper extremity surgeons: A web-based survey. *World J Orthop* 2021; **12**: 891-898 [PMID: 34888149 DOI: 10.5312/wjo.v12.i11.891]
22 **Alqahtani SM**, Alzahrani MM, Bicknell R, Pichora D. Prevalence and factors of work-related musculoskeletal disorders among hand surgeons. *World J Orthop* 2022; **13**: 465-471 [PMID: 35633751 DOI: 10.5312/wjo.v13.i5.465]
23 **Sargent MC**, Sotile W, Sotile MO, Rubash H, Barrack RL. Quality of life during orthopaedic training and academic

practice. Part 1: orthopaedic surgery residents and faculty. *J Bone Joint Surg Am* 2009; **91**: 2395-2405 [PMID: 19797575 DOI: 10.2106/JBJS.H.00665]

24 **Physical Discomfort Survey-Workplace Safety and Health Division of Manitoba, Canada**. [Internet] [accessed 20 October 2022]. Available from: http://www.gov.mb.ca/inr/publications/safe_workplace/section-i/section-i-c/pubs/appendix-i-c-2-symptoms-survey.pdf

25 **Maslach C**, Jackson SE, Leiter MP. Maslach Burnout Inventory Manual (4th Edition). Menlo Park, CA: Mind Garden, Inc, 2018

26 **Taylor C**, Graham J, Potts HW, Richards MA, Ramirez AJ. Changes in mental health of UK hospital consultants since the mid-1990s. *Lancet* 2005; **366**: 742-744 [PMID: 16125591 DOI: 10.1016/S0140-6736(05)67178-4]

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CASE REPORT

Wooden foreign body impalement through the right shoulder region – an unusual penetrating injury: A case report

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Abstract

BACKGROUND

Impalement of the body is a rare injury and comes with varied presentation. There is no set classification or defined protocols for managing this injury. This case report aims to create awareness among trauma surgeons about unusual presentation and management of such case.

CASE SUMMARY

A 45-year-old man presented to the emergency department with a sharp penetrating wooden plank at right clavicular region between the neck and shoulder following a road traffic accident. The vehicle had crashed into a roadside wooden hut, thus causing an impalement injury. He was meticulously worked up and taken to emergency theatre. The wooden plank was removed and the wound healed uneventfully. Postoperatively, he had fairly good shoulder function and was able to return back to work successfully.

CONCLUSION

Each impalement injury brings in challenges in management as no two cases are the same. The varied presentation and risks involved should be known to medical professionals handling the emergency. Coordinated multidisciplinary team approach is needed for successful outcome.

Key Words: Impaling; Wooden; Foreign body; Sharp object; Trunk; Case report

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Core Tip: Penetration of the body, cavity, or region by an elongated object which remains *in situ* is called impalement injury. It can result from both penetrating and blunt trauma, with the severity of injury being factored by mechanism and velocity of trauma. Associated crushing, penetration, tissue loss, wound contamination, major fractures, and massive blood loss bring great challenges to surgeons besides posing difficulty in administering anesthesia.

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INTRODUCTION

Impalement injuries have been defined as penetration of a body cavity or region by an elongated object which remains *in situ* following the injury[1]. It can result from both penetrating and blunt trauma, with the severity of injury being factored by mechanism and velocity of trauma[2]. Associated crushing, penetration, tissue loss, wound contamination, major fractures, and massive blood loss bring great challenges to surgeons besides posing difficulty in administering anesthesia[3].

CASE PRESENTATION

Chief complaints

A 45-year-old male driver who lost control of a four-wheeler and hit against a roadside wooden hut, presented to the emergency department with a sharp penetrating wooden plank at right clavicular region between the neck and shoulder following the accident.

History of present illness

The vehicle had crashed into a roadside wooden hut, thus causing an impalement injury (Figure 1A).

History of past illness

Not significant.

Personal and family history

Not significant.

Physical examination

An initial assessment in the emergency room (ER) revealed a conscious patient with stable vitals and no respiratory distress. There was a large piece of wood passing through-and-through the right trapezius muscle just above the clavicle and midway between the neck and shoulder (Figure 1A). He had no evidence of any neurological deficit and the peripheral pulses were comparable in both upper limbs. He was administered Inj Tetanus Diphtheria, started on intravenous antibiotic, and immediately mobilized for radiological assessment.

Laboratory examinations

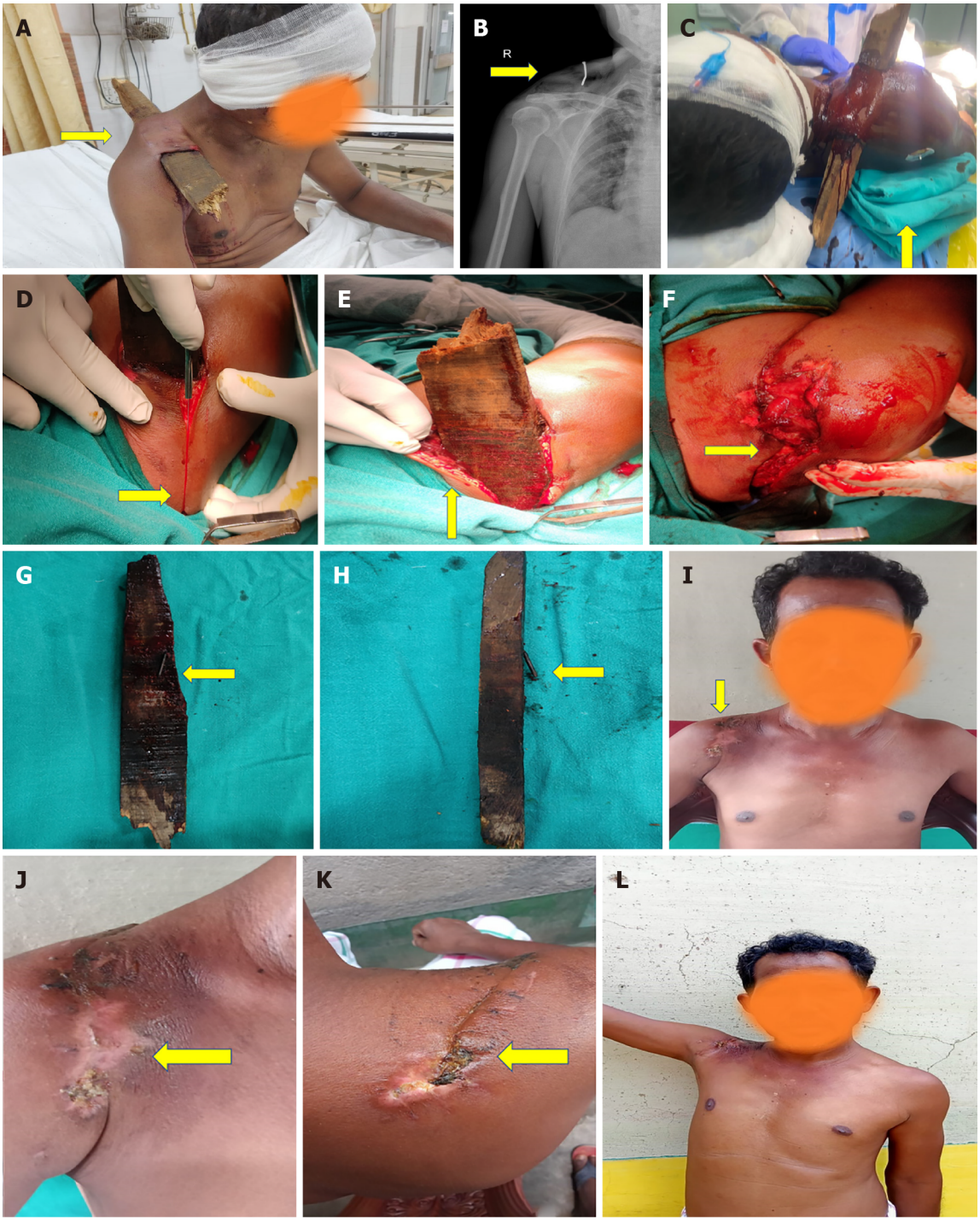
All laboratory parameters were within normal limits. However, the case was further confronted by a positive coronavirus disease 2019 (COVID-19) test report.

Imaging examinations

A rectangular cast with a slightly crooked radio-opaque shadow was seen jutting cranio-caudally, on the radiograph (Figure 1B). No other bony injury was observed.

FINAL DIAGNOSIS

Wooden foreign body (FB) impalement of right shoulder region without any neurovascular deficits following a road traffic accident.



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Figure 1 Chronological figures showing impaled foreign body with its outcome. A: Emergency presentation of the injured right side with the wooden foreign body *in situ*; B: X-ray showing a rectangular cast with a metallic shadow (iron nail) embedded within the FB and tissues; C: Post intubation, folded sheets were kept underneath the scapula for better access and vision; D: After proper positioning and draping, lateral entry and exit points were connected; E: A medial based flap was raised to expose the FB. The iron nail was directed inferiorly, which was carefully dissected out; F: Condition of wound post FB removal showing crushing of edges with minimal skin loss; G and H: 30 cm × 5 cm × 1.5 cm dimension wooden FB with jagged edges at both ends and an embedded bent nail within itself; I-K: Healed flap without any evidence of secondary infection or necrosis; L: Near normal shoulder function seen 2 mo after surgery.

TREATMENT

The patient was scheduled for immediate surgery for the removal of the said FB, debridement, and repair in consultation with the general surgeon and anesthesiologist.

Upon arrival, at the operation theatre and after attaching all requisite monitoring, the patient was gently placed in the supine position with the help of multiple pillows supporting the back and head of the patient, leaving a gap in between for the posterior half of the FB protruding out through his back. General anesthesia was administered, airway secured, and the patient was repositioned with pillows

under the right shoulder for better surgical access (Figure 1C).

A vertical incision was made connecting the lateral points of entry and exit wounds (Figure 1D). A medial based flap was raised to expose the FB (Figure 1E). It was found that it had grazed over the superior surface of the clavicle at the entry point and pierced the trapezius muscle at the exit point. The FB also had a bent nail stuck within the muscle-fibres close to the exit point. It was carefully dissected out, with care being taken not to cause any injury to the adjoining tissues. The wooden FB retrieved measured 30 cm × 5 cm × 1.5 cm in dimension with the bent nail embedded within its body (Figure 1G and H). The wound was given a thorough lavage and damaged structures were looked for. Fortunately, none was noticed, and hence the wound was closed in layers (Figure 1F). The patient was reversed from anesthesia with stable hemodynamic and respiratory parameters. Subsequently, he was shifted to high dependency unit for further monitoring. The postoperative course was uneventful, and the patient was discharged after 2 d.

OUTCOME AND FOLLOW-UP

The patient on discharge was put on an arm pouch sling and intermittent shoulder mobilization was started as the glenohumeral joint escaped injury. The flaps healed well without any secondary infection and necrosis (Figure 1I-K). Passive and active range of motion exercises were initiated post suture removal. At the end of 2 mo, he had good recovery with near normal function of his right upper limb. Partial overhead abduction was present due to scarring and contracture which ensued after healing (Figure 1L).

DISCUSSION

Penetration of the body, cavity or region by an elongated object which remains *in situ* is called impalement injury[1]. Eachempati *et al*[4] classified it under two broad categories. Type 1 injuries occur when the human body strikes an immobile object. Usually, it is seen in industrial and car accidents when persons involved are ejected from their automobiles. Type 2 injuries occur due to penetration of a moving object into an immobile human body.

In prehospital management of penetrating injuries, it is of paramount importance that impaled object should not be removed, so that possible vascular lesions can remain buffered by the object, avoiding major bleeding and cataclysmic hemorrhage. High grade thoracic impalement injuries are rare and complex. It holds a high mortality rate due to associated thoracic wall and lung injuries[5]. Impalement injuries traversing the abdomen and injuring multiple organs too have high rates of morbidity and mortality[6,7].

In our case, the site of the injury was peculiar as the wooden FB grazed superiorly over the right clavicle, between the neck and shoulder presenting a horrific picture, a type 1 injury. Understanding the complexity of the injury, the general surgeon was kept on standby. The presence of the bent nail directed caudally into the tissues ameliorated any chances of removing the FB without proper dissection and assessment. The entry and exit points of the FB were not far apart unlike many reported cases. The lateral corners of both the points were connected, and a flap was raised to expose the FB. Being unusually on the right side, above the clavicle and cranial trajectory, the neurovascular bundle escaped unhurt. The above reason also minimized the chances of lung parenchymal injury. Post FB removal, the flap was approximated without any tension, which healed uneventfully.

The patient also presented with difficult anesthesia as the nature of FB orientation precluded a normal supine position[8]. Additional innovative measures had to be taken to place the patient supine by using multiple pillows behind the back and head. This made it difficult to attain the usual position for laryngoscopy and intubation, especially compounded by the presence of a COVID-19 infection.

Despite the difficulties in the management of the surgical removal of this unusual FB, a multi-disciplinary team with proper coordination and comprehension along with innovative ideas to circumvent the problems unique to this case, made it possible for us to achieve a favorable surgical outcome.

CONCLUSION

Impalement injuries are indeed challenging cases which require early mobilization to hospital and multidisciplinary team approach. As our case demonstrated, right sided supraclavicular anteroposterior impalement usually has a good functional outcome without any sequelae.

FOOTNOTES

Author contributions: Kerketta AH and Kumar R contributed equally to this work; Kerketta AH and Sahu S designed the case study; Kumar R, Laik JK, and Rajak MK performed the research; Kerketta AH and Sahu S wrote the manuscript and analyzed the data; all authors have read and approved the final manuscript.

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REFERENCES

1 **Hyde MR**, Schmidt CA, Jacobson JG, Vyhmeister EE, Laughlin LL. Impalement injuries to the thorax as a result of motor vehicle accidents. *Ann Thorac Surg* 1987; **43**: 189-190 [PMID: 3813709 DOI: 10.1016/s0003-4975(10)60394-3]
2 **Paul S**, Lee CL. Trauma case review: survival following impalement. *Crit Care Nurse* 1994; **14**: 55-59 [PMID: 7882691]
3 **Oya S**, Miyata K, Yuasa N, Takeuchi E, Goto Y, Miyake H, Nagasawa K, Kobayashi Y. Impalement injury to the left buttock with massive bleeding: a case report. *Nagoya J Med Sci* 2013; **75**: 147-152 [PMID: 23544279]
4 **Eachempati SR**, Barie PS, Reed RL 2nd. Survival after transabdominal impalement from a construction injury: a review of the management of impalement injuries. *J Trauma* 1999; **47**: 864-866 [PMID: 10568713 DOI: 10.1097/00005373-199911000-00008]
5 **Ruano RM**, Pereira BM, Biazzoto G, Bortoto JB, Fraga GP. Management of severe thoracic impalement trauma against two-wheeled horse carriage: a case report and literature review. *Indian J Surg* 2014; **76**: 297-302 [PMID: 25278654 DOI: 10.1007/s12262-013-0825-4]
6 **Angelopoulos S**, Mantzoros I, Kyziridis D, Fontalis A, Parpoudi S, Konstandaras D, Tsalis C. A rare case of a transabdominal impalement after a fall from a ladder. *Int J Surg Case Rep* 2016; **22**: 40-43 [PMID: 27046102 DOI: 10.1016/j.ijscr.2016.03.011]
7 **Muhammad Afzal R**, Armughan M, Javed MW, Rizvi UA, Naseem S. Thoracic impalement injury: A survivor with large metallic object in-situ. *Chin J Traumatol* 2018; **21**: 369-372 [PMID: 30348473 DOI: 10.1016/j.cjtee.2018.08.002]
8 **Kaur K**, Singhal SK, Bhardwaj M, Kumar P. Penetrating abdomino-thoracic injury with an iron rod: An anaesthetic challenge. *Indian J Anaesth* 2014; **58**: 742-745 [PMID: 25624541 DOI: 10.4103/0019-5049.147172]



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