

Artificial Intelligence in *Gastrointestinal Endoscopy*

Artif Intell Gastrointest Endosc 2023 January 6; 4(1): 1-11





Artificial Intelligence in Gastrointestinal Endoscopy

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Continuous Publication Volume 4 Number 1 January 6, 2023

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Artificial Intelligence in Gastrointestinal Endoscopy

Continuous Publication Volume 4 Number 1 January 6, 2023

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INDEXING/ABSTRACTING

The AIGE is now abstracted and indexed in Reference Citation Analysis, China Science and Technology Journal Database.

RESPONSIBLE EDITORS FOR THIS ISSUE

Production Editor: Yi-Xuan Cai; Production Department Director: Xu Guo; Editorial Office Director: Jin-Lai Wang.

NAME OF JOURNAL

Artificial Intelligence in Gastrointestinal Endoscopy

ISSN

ISSN 2689-7164 (online)

LAUNCH DATE

July 28, 2020

FREQUENCY

Continuous Publication

EDITORS-IN-CHIEF

Fatih Altintoprak, Sahin Coban, Krish Ragunath

EDITORIAL BOARD MEMBERS

<https://www.wjgnet.com/2689-7164/editorialboard.htm>

PUBLICATION DATE

January 6, 2023

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<https://www.wjgnet.com/bpg/GerInfo/288>

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<https://www.wjgnet.com/bpg/gerinfo/208>

ARTICLE PROCESSING CHARGE

<https://www.wjgnet.com/bpg/gerinfo/242>

STEPS FOR SUBMITTING MANUSCRIPTS

<https://www.wjgnet.com/bpg/GerInfo/239>

ONLINE SUBMISSION

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Kyoto classification of gastritis, virtual chromoendoscopy and artificial intelligence: Where are we going? What do we need?

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Specialty type: Gastroenterology and hepatology

Provenance and peer review: Invited article; Externally peer reviewed.

Peer-review model: Single blind

Peer-review report's scientific quality classification

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

P-Reviewer: Kishikawa H, Japan; Tsuji Y, Japan

Received: September 14, 2022

Peer-review started: September 14, 2022

First decision: September 29, 2022

Revised: October 18, 2022

Accepted: January 3, 2023

Article in press: January 3, 2023

Published online: January 6, 2023



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Abstract

Chronic gastritis (CG) is a widespread and frequent disease, mainly caused by *Helicobacter pylori* infection, which is associated with an increased risk of gastric cancer. Virtual chromoendoscopy improves the endoscopic diagnostic efficacy, which is essential to establish the most appropriate therapy and to enable cancer prevention. Artificial intelligence provides algorithms for the diagnosis of gastritis and, in particular, early gastric cancer, but it is not yet used in practice. Thus, technological innovation, through image resolution and processing, optimizes the diagnosis and management of CG and gastric cancer. The endoscopic Kyoto classification of gastritis improves the diagnosis and management of this disease, but through the analysis of the most recent literature, new algorithms can be proposed.

Key Words: Early gastric cancer; Artificial intelligence; *Helicobacter pylori*; Dysplasia; Image enhanced endoscopy; Kyoto classification of gastritis

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Core Tip: Advances in virtual chromoendoscopy have improved the knowledge and management of chronic gastritis and led to the Kyoto classification. Artificial intelligence promotes progression in the management of gastric cancer and the diffusion of innovation, allowing new diagnostic algorithms that include both active inflammation and dysplasia as evolutionary steps towards cancer.

Citation: Panarese A, Saito Y, Zagari RM. Kyoto classification of gastritis, virtual chromoendoscopy and artificial intelligence: Where are we going? What do we need? *Artif Intell Gastrointest Endosc* 2023; 4(1): 1-11

URL: <https://www.wjgnet.com/2689-7164/full/v4/i1/1.htm>

DOI: <https://dx.doi.org/10.37126/aige.v4.i1.1>

INTRODUCTION

Chronic gastritis (CG) is a widespread and frequent disease, often undiagnosed even after a gastroscopy. Chronic gastritis is relevant to the symptoms that it causes, for the absorption defects that it can entail, but, above all, for the oncological risk with which it is associated[1]. The correct diagnosis improves the management of the disease and, on the endoscopic side, the identification of dysplasia and early gastric cancer is fundamental, possible due to advances in endoscopic technology, which allows the observation of the gastric mucosa in detail[2]. The appropriate classification of CG, defining the etiology, severity, extension, and, in particular, the oncological risk, allows the correct management of the disease and contributes to the results of artificial intelligence, capable of developing algorithms for the diagnosis of CG and gastric cancer[3-6].

Objectively, considering that gastric cancer is still a major cancer, the diagnosis of dysplasia is a relevant outcome[3,7,8], and endoscopic surveillance, important for detecting dysplasia and gastric cancer, is efficient in the high-risk population[9,10]. Early-stage gastric cancer can be cured *via* endoscopic submucosal dissection, which is curative and less invasive than surgery if carried out according to the guidelines[11-13].

Helicobacter pylori (*H. pylori*) infection is the main cause of CG and gastric cancer[14]. *H. pylori* is a type I carcinogen for gastric cancer[15]. However, the risk of gastric cancer in *H. pylori*-positive subjects is related to the development of precancerous conditions, *i.e.*, mucosal atrophy (MA) and intestinal metaplasia (IM)[14,16-18]. Indeed, gastric cancer morbidity and mortality are declining due to *H. pylori* eradication therapy[19]. Therefore, the accurate assessment of *H. pylori* infection status is important[20-22]. The ¹³C-urea breath test, stool antigen test, and serology are non-invasive tests for the diagnosis of *H. pylori* infection[5,22].

The Kyoto classification of gastritis, introduced in 2013 in Kyoto, during the 85th Congress of the Japan Gastroenterological Endoscopy Society, was developed with the aim of endoscopically diagnosing *H. pylori* infection and assessing the risk factors for gastric cancer[23].

This review is an up-to-date study on the Kyoto classification of gastritis[3,23] and highlights advances and future prospects in the endoscopic diagnosis of gastritis and gastric cancer to help improve endoscopic practice.

THE KYOTO CLASSIFICATION OF GASTRITIS

The Kyoto classification of gastritis accurately considers the endoscopic characteristics of gastritis associated with *H. pylori* infection and identifies gastric cancer risk factors[23].

In the Kyoto classification of gastritis, there are 19 characterized endoscopic findings that are related to the presence/absence of *H. pylori* infection, gastritis, and the risk of gastric cancer (Table 1). Among them, MA, IM, enlarged folds, nodularity, and diffuse redness are accounted for in the Kyoto classification score, which is the sum of their scores. The Kyoto score ranges from 0 to 8 (Table 2) and a high score reflects a higher risk of current *H. pylori* infection and gastric cancer[23].

The endoscopic MA (Figure 1A) consists of discolored/pale mucosa with a visible capillary network, and it is classified according to the Kimura and Takemoto classification[24], widely used to diagnose atrophic borders using white light imaging (WLI). In Japan, this classification correlates with histological findings and serum pepsinogen levels observed in the case of MA[24,25], while, in Western countries, WLI cannot correctly diagnose MA and IM according to guidelines, which recommend gastric biopsies for the confirmation of MA, as for IM[26].

The endoscopic IM (Figure 1B) appears as an irregular surface with slightly elevated/flat/depressed grayish-white plaques surrounded by mixed patchy pink and pale areas of the mucosa. Useful indicators for the endoscopic diagnosis of IM are villous patterns, whitish colors, and rough surfaces, distinctly visible with virtual chromoendoscopy (Figure 2). WLI presents low sensitivity for the diagnosis of IM compared to that of the pathological diagnosis[16,25].

Enlarged folds (Figure 1C) are folds of the body with a width ≥ 5 mm, caused by increased mucosal thickness due to foveolar hyperplasia and the massive infiltration of inflammatory cells. Insufflation does not flatten them or does so partially. The thickness of the folds normalizes after the eradication of *H. pylori*[10,23].

Nodularity (Figure 1D), *i.e.*, nodular gastritis, is localized mainly in the antrum and consists of a nodular or micronodular diffuse pattern of the mucosa, similar to "goosebumps". Nodular antral

Table 1 The endoscopic findings of the Kyoto classification of gastritis

Kyoto classification	
Related to gastric cancer risk	Mucosal atrophy
	Intestinal metaplasia
	Enlarged folds
	Nodularity
Related to <i>Helicobacter pylori</i> infection status	Diffuse redness
Others	Regular arrangement of collecting venules
	Map like redness
	Foveolar hyperplastic polyp
	Xanthoma
	Mucosal swelling
	Patchy redness
	Depressed erosion
	Sticky mucus
	Hematin
	Red streak
	Spotty redness
	Multiple white and flat elevated lesions
	Fundic gland polyp
	Raised erosion

gastritis pathologically consists of prominent lymphoid follicles with the infiltration of mononuclear cells. It can be observed more frequently in the stomachs of children than in those of adults, suggesting that it is a characteristic of the early stage of *H. pylori* infection[27-29].

Diffuse redness (Figure 1E) is the uniform redness of the non-atrophic fundic mucosa, an expression of the congestion and dilation of the subepithelial capillary network by inflammation, with the infiltration of neutrophils and mononuclear cells[30].

Regular arrangement of collecting venules (Figure 1F), in the corpus, from a distance, appears as numerous dots and, more closely, as a regular pattern of starfish-like shapes.

THE EFFECTIVENESS OF THE KYOTO CLASSIFICATION OF GASTRITIS

The effectiveness of the Kyoto classification of gastritis is proven by testing scores in patients with CG, gastritis associated with *H. pylori*, and gastric cancer.

DIAGNOSIS OF *H. PYLORI*-RELATED CHRONIC GASTRITIS

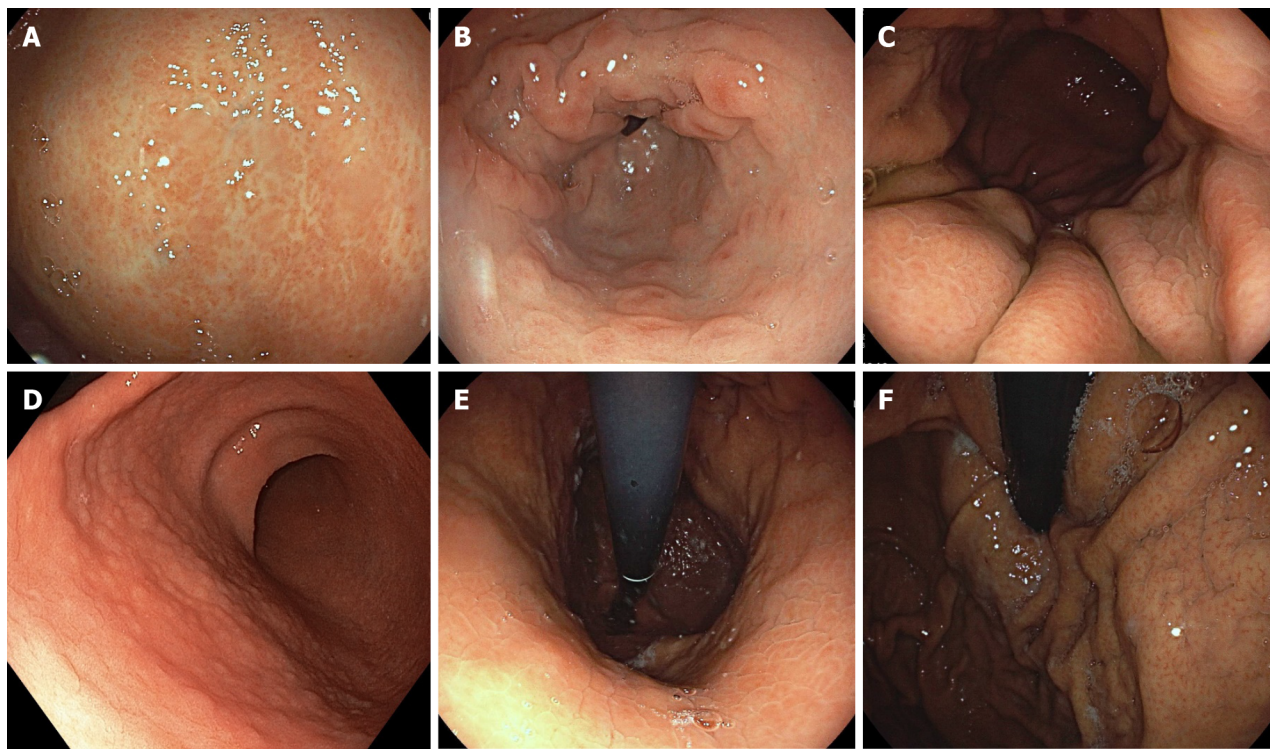
The Kyoto classification proposes the endoscopic diagnosis of *H. pylori* infection status, although the diagnostic confirmation comes from other investigations[5,17]. Endoscopic diagnosis of *H. pylori* infection by WLI has low sensitivity (18%-75%) and poor inter-observer agreement[31,32], while magnified image-enhanced endoscopy (M-IEE) is more accurate[9-10,26].

Regarding active *H. pylori* infection related-gastritis, enlarged folds, nodularity, and diffuse redness have low sensitivity but good specificity, particularly for nodularity (sensitivity: 6.4%-32.1%, specificity: 95.8%-98.8%). On the other hand, regular arrangement of collecting venules has high sensitivity for non-infection (86.7%-100%). Furthermore, for the diagnosis of past *H. pylori* infection, endoscopic MA has lower specificity (75.5%) compared to IM and map-like redness (92.6% and 98.0%, respectively)[33].

Regarding the total Kyoto classification score and serum *H. pylori* antibody titer, Kyoto scores increase in line with the *H. pylori* antibody titer[34,35].

Table 2 The Kyoto classification score			
Endoscopic finding	Score		
Mucosal atrophy	0	None	C0-CI according to Kimura Takemoto classification
	1	Mild	CII-CIII
	2	Severe	OI-OIII
Intestinal metaplasia	0	None	None
	1	Mild	Within the antrum
	2	Severe	Up to the corpus
Enlarged folds	0	Negative	< 5 mm gastric fold width
	1	Positive	≥ 5 mm gastric fold width
Nodularity	0	Negative	None
	1	Positive	Small nodules in the antrum
Diffuse redness	0	None	None
	1	Mild	Mild translucency of collecting venules in the body
	2	Severe	Severe translucency of collecting venules in the body

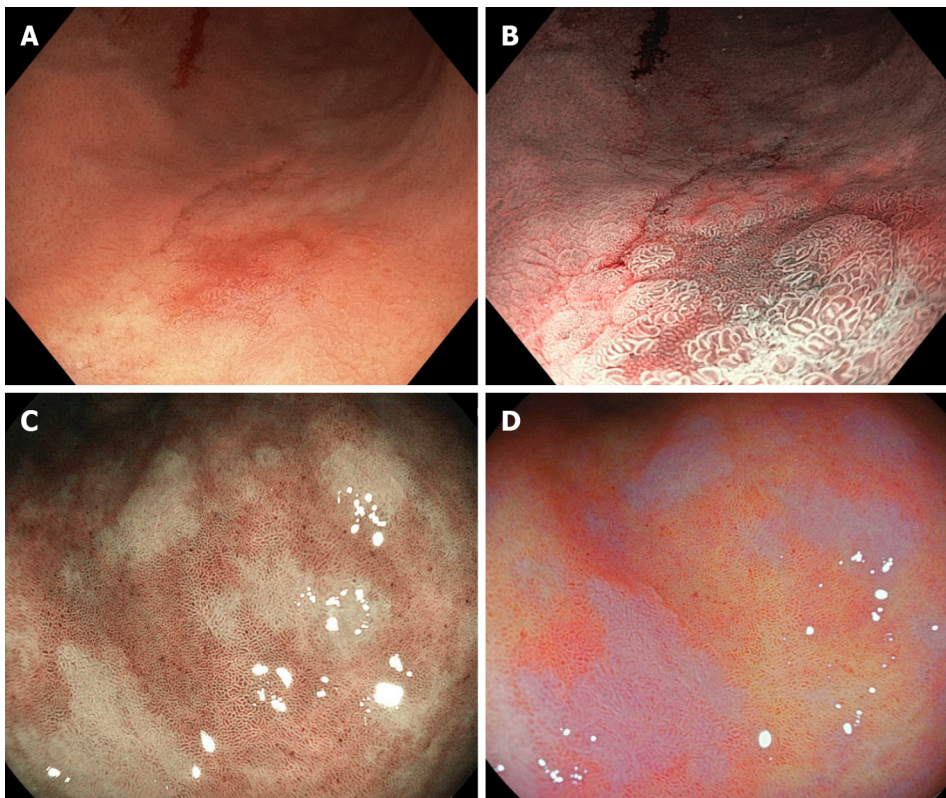
A score of 0 indicates no *Helicobacter pylori* (*H. pylori*) infection, a score of ≥ 2 indicates current *H. pylori* infection, and a score of ≥ 4 indicates higher risk of gastric cancer risk.



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Figure 1 The endoscopic findings of the Kyoto classification of gastritis taken into account in the Kyoto score (magnified white light imaging). A: Mucosal atrophy; B: Intestinal metaplasia; C: Enlarged folds; D: Nodularity; E: Diffuse redness; F: Regular arrangement of collecting venules.

A Kyoto score of 0, 1, and ≥ 2, and no history of *H. pylori* eradication therapy, corresponds to *H. pylori* infection rates of 1.5%, 45%, and 82%. However, an active *H. pylori* infection is not always present in the case of a high Kyoto score, due to a spontaneous negative conversion, IM, or unintentional eradication, after the treatment of other infectious diseases with antibiotics[35,36].



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Figure 2 Endoscopic images of gastric intestinal metaplasia. A: Magnified white light imaging; B: Narrow-band imaging; C: Blue laser imaging; D: Linked color imaging.

ASSESSMENT OF THE RISK OF GASTRIC CANCER

It has been reported that there is good agreement between endoscopic findings for MA and IM and histopathological diagnosis[36]. Endoscopic determination of IM in the corpus is useful because when endoscopic IM is present in the corpus (*i.e.*, the IM 2 score of the Kyoto classification), the pathological IM is significantly associated with a higher risk of gastric cancer[38]. Furthermore, corpus-predominant activity, *i.e.*, the presence of neutrophil activity, has a higher risk of leading to gastric cancer than antral predominant activity[38]. Severe endoscopic MA, enlarged folds, and nodularity correspond to higher neutrophil activity in the corpus than that in the antrum[37].

The topographic distribution of neutrophil activity and IM is strongly associated with gastric cancer risk and corresponds to the separate assessment of pathological gastritis in the corpus and antrum[38].

Regarding gastric cancer as assessed by the Kyoto classification of gastritis, its incidence increases, as %/year, for mild (0.04-0.10), moderate (0.12-0.34), and severe (0.31-1.60) atrophy[38-40]. In detail, over a period of 10 years, the incidence was extremely high (16.0% of patients with severe atrophy)[16] and increased according to the extent of the MA. The prevalence of O-II/O-III-type atrophy according to the Kimura-Takemoto classification is significantly higher in patients with gastric cancer than in subjects with gastritis alone (45.1% *vs* 12.7%, $P < 0.001$)[10,39], and Kyoto gastritis scores of MA and IM are significantly higher in the *H. pylori*-positive cancer group than in subjects with gastritis alone ($P < 0.001$). Furthermore, endoscopic IM is associated with intestinal-type early gastric cancer, with an OR of 5.0; enlarged folds and nodularity are associated with diffuse-type gastric cancer, with an OR of 5.0 and 13.9, respectively[10].

A cross-sectional study suggests that a Kyoto classification score of ≥ 4 might indicate gastric cancer risk, considering that the Kyoto classification score is 4.8 and 3.8, respectively, for patients with and without gastric cancer[10].

VIRTUAL CHROMOENDOSCOPY FOR THE DIAGNOSIS OF CHRONIC GASTRITIS AND GASTRIC CANCER

Virtual chromoendoscopy is necessary for a correct evaluation of CG because it remarkably improves the accuracy in the diagnosis of premalignant lesions and early gastric cancer, increasing the visibility of

endoscopic findings[26]. Image-enhanced endoscopy (narrow-band imaging, NBI, linked color imaging, LCI, blue laser imaging, BLI, texture and color enhancement imaging, TXI, and autofluorescence imaging) achieves significantly better sensitivity and specificity than WLI, due to the examination of the glandular epithelium by observing the microvascular architecture and structure of the microsurface[31, 32,41,42]. However, M-IEE requires skills and experience[43].

Narrow-band imaging, through the use of narrower-band light *via* blue and green filters, enhances the visualization of the vascular, rather than the surface, structure of the mucosa[44]. Magnified narrow-band imaging can accurately diagnose inflammation and premalignant conditions with sensitivity higher than that of WLI[31,41,42]. Yellowish-white nodules are a predictive marker of nodular gastritis because they have high specificity for the histological finding of lymphoid follicles in the *H. pylori*-positive stomach[42]. The presence of a fine blue-white line on the crests of the epithelial surface, a light blue crest, and a white opaque substance an accumulation of lipid micro-droplets in the superficial area of certain IM are highly accurate signs of IM[31,41]. The correspondence between histology and magnified narrow-band imaging has been verified regarding the diagnosis of IM and MA[31,41].

Autofluorescence imaging detects the natural fluorescence of some components of the gastric mucosa in real time during endoscopy to differentiate between non-atrophic mucosa, in purple, and atrophic mucosa infected with *H. pylori*, in green[45]. However, current endoscopic systems do not have the autofluorescence imaging function. Otherwise, texture and color enhancement imaging clearly define subtle tissue differences due to the enhancement of three image factors in WLI (texture, brightness, and color). This is available on the new-generation Olympus instruments[46].

Blue laser imaging-bright and linked color imaging use narrow-band, short-wavelength light because they separately correct blue, green, and red color information. Blue laser imaging, as in narrow-band imaging, produces red-colored, high-intensity, contrast-enhanced images, through blue and green color information, allowing the superior visualization of microvascular and microsurface patterns. In blue laser imaging-bright, a spotty pattern is correlated with an active *H. pylori* infection, while a cracked pattern corresponds to a post-inflammatory change after the eradication of *H. pylori* and the mottled pattern to IM[46-47]. Linked color imaging uses the information of all three colors and returns images with color enhancement in its own color range (*e.g.*, red is changed to vivid red and white to clear white) *via* unique image processing. Regardless of *H. pylori* infection status, linked color imaging, compared to WLI, increases the color difference around the atrophic border. Linked color imaging identifies diffuse redness of the fundus as a crimson red color, and, compared to WLI, it offers significantly higher overall diagnostic accuracy in patients with an *H. pylori*-positive stomach and those with an *H. pylori*-negative stomach after eradication. On the contrary, regarding the presence of the regular arrangement of collecting venules or diffuse redness, WLI, linked color imaging, and magnifying endoscopy with WLI have similar diagnostic accuracy for *H. pylori* infection. Linked color imaging identifies IM as a lavender color and the diagnostic accuracy is significantly higher than in WLI. Moreover, it increases the visibility of diffuse redness, spotty redness, map-like redness, patchy redness, red streaks, and atrophic borders. Bright-blue laser imaging improves the IM visibility[48].

Magnified-IEE allows the correct endoscopic diagnosis of gastritis with the application of the Kyoto classification of gastritis, and it guarantees the accuracy and reproducibility of endoscopic diagnosis for premalignant lesions related to *H. pylori* infection throughout the stomach, during active infection and after the eradication of *H. pylori*[49].

ARTIFICIAL INTELLIGENCE FOR THE DIAGNOSIS OF CHRONIC GASTRITIS AND GASTRIC CANCER

Artificial intelligence, based on deep learning which has allowed considerable progress in various fields through the convolutional neural network (CNN), a method for image recognition can be trained with endoscopic images and could detect gastric cancer accurately[4,50]. Artificial intelligence autonomously extracts and learns the discriminative features of the images and analyzes their complex features, including shapes, colors, and textures. Thus far, several artificial intelligence-assisted CNN computer-aided diagnosis systems have been built, whose diagnostic accuracy in detecting CG and gastric cancer is based on WLI and/or IEE[4,51-53], thus allowing better performance among endoscopists. However, since their introduction in this field occurred recently, the results of most studies need to be further validated, considering all the aspects of endoscopy and formulating increasingly advanced algorithms.

Prospective studies suggest that the deep-learning-based real-time video monitoring diagnostic model works better than endoscopists in the diagnosis of CG and gastric cancer[6,52] and that computer-aided diagnosis systems based on deep learning algorithms have significantly higher accuracy for IEE than for WLI[54]. Computer-aided diagnosis has been studied with the Kyoto classification of gastritis for the endoscopic diagnosis of *H. pylori* infection, demonstrating accuracy similar to that of experienced endoscopists, being superior with IEE rather than using WLI. Real-time analyses are validating, in prospective studies, the accuracy of computer-aided diagnosis with IEE, using the Kyoto classification of gastritis, for the diagnosis of *H. pylori* infection and the evaluation of the gastric cancer risk[55].

FUTURE PERSPECTIVES IN THE ASSESSMENT OF CHRONIC GASTRITIS

Technological developments in IEE allow high diagnostic performance to identify CG and determine the risk of gastric cancer according to the Kyoto classification of gastritis[33]. Magnified narrow-band imaging identifies MA and IM due to its detailed examination of the gastric mucosal pattern, *e.g.*, a light blue crest and white opaque substance[26,31]. At a distant view, non-magnified narrow-band imaging, blue laser imaging-bright, and autofluorescence imaging are useful in evaluating MA and IM, and linked color imaging can be used to identify MA, IM, diffuse redness, and a regular arrangement of collecting venules, compared with WLI. Linked color imaging allows the highest visibility among the findings of the Kyoto classification of gastritis and early gastric cancer after *H. pylori* eradication. Blue laser imaging has the highest visibility for the microvascular pattern, microsurface pattern, and demarcation line in magnifying observations[41,42,47,48]. Matsumura *et al*[49] suggest that the best methods for the detection and early diagnosis of gastric cancer after *H. pylori* eradication are linked color imaging observation of the stomach and magnifying blue laser imaging, respectively[33].

Furthermore, in the evaluation of gastric cancer risk, the total score of the grading system is useful in patients with active *H. pylori* gastritis[10,39], but after *H. pylori* eradication, it may not be accurate due to the disappearance of diffuse redness, enlarged folds, and nodularity. Moreover, the absence of a regular arrangement of collecting venules is identified as an independent risk factor for gastric cancer after *H. pylori* eradication[56,57]. Therefore, studies with IEE, applying the Kyoto classification of gastritis, require prospective confirmation and a new grading system, which includes the findings of MA, IM, and regular arrangement of collecting venules to assess the risk of gastric cancer in patients with past *H. pylori* infection.

Secondly, GC is a disease with two important etiologies, *H. pylori* infection and autoimmunity, worthy of different treatments and surveillance to reduce the risk of gastric cancer, which could remain a frequent cancer, precisely because the prevalence of *H. pylori* infection will decrease but the incidence of autoimmune gastritis will increase[21,58]. Definitive endoscopic diagnostic criteria should be established for autoimmune gastritis, in addition to the dosage of antibodies, and they should be considered as endoscopic findings[3,59]. A new endoscopic classification that considers *H. pylori* gastritis as well as autoimmune gastritis is desirable. Regarding *H. pylori*-related gastritis, the endoscopic diagnosis of *H. pylori* infection must be confirmed by an additional test for *H. pylori*, including histology or a 13C-urea breath test. Endoscopic diagnosis is not sufficient to prescribe antibiotic therapy, even if, due to recent advances in IEE, the diagnostic accuracy is improved and the Kyoto classification of gastritis unifies the endoscopic diagnostic criteria for gastritis, allowing an association between gastritis and *H. pylori* infection. Eradication therapy for *H. pylori* is prescribed if positivity is confirmed by the 13C-urea breath test, histological examination, or a fecal test[21]. In conclusion, currently, it is not possible to obtain a conclusive diagnosis of active *H. pylori* infection only endoscopically.

Thirdly, MA, enlarged folds, nodularity, diffuse redness, and regular arrangement of collecting venules have been considered to assess the correlation between endoscopic findings and histopathology [33], with the limitation that only the combination of different endoscopic findings can improve the diagnostic accuracy, because no single endoscopic feature is highly specific for histological MA and inflammation[23]. However, endoscopic MA and IM are associated with pathological atrophy and IM, respectively, according to several studies[37-59], and the Kyoto classification of gastritis score correlates with the activity and distribution of neutrophils, which are related to the risk of cancer[60]. It is necessary to point out, however, that studies on the consistency between the Kyoto classification of gastritis and histology based on the updated Sydney system are few.

Fourthly, the endoscopy-based Kyoto classification of gastritis score, which predicts the risk of gastric cancer, changes after *H. pylori* eradication. Toyoshima *et al*[61], in a retrospective study, concluded that the Kyoto classification score decreases after *H. pylori* eradication for enlarged folds, nodularity, and diffuse redness. It is probably necessary to calculate the score after the eradication of *H. pylori* infection to better define the cancer risk and the need for surveillance. As for other preneoplastic conditions of the digestive tract, *e.g.*, Barrett's esophagus, it is necessary to estimate the score when the inflammation is not active. High-resolution WLI, in association with narrow-band imaging, increases low-grade dysplasia detection on visible lesions after the regression of active *H. pylori*-induced chronic gastritis. Extensive gastric mapping is required in patients with an overlap between autoimmune atrophic gastritis and *H. pylori*-induced gastritis[40,49,61,62].

In a future consensus setting, a new algorithm should be published[3]. Considering that *H. pylori* is oncogenic, we should screen for *H. pylori* infection, treat positives, and then perform gastroscopy when the infection is no longer active and the possibility of detecting dysplasia is greater. Indeed, dysplasia is the real condition that increases the risk for gastric cancer[63,64]. Current technologies make it possible to detect dysplasia[64], which must be included in the final score as a new finding. Of course, we must perform high-quality gastroscopy, and, currently, biopsies must be carried out with M-IEE, for an accurate histological assessment of gastritis[26]. The accuracy of M-IEE in trained hands further increases the yield of targeted biopsies, necessary for correct risk stratification with OLGA – OLGIM histological staging systems (Operative Link for Gastritis Assessment, Operative Link for Gastric Intestinal Metaplasia Assessment)[65]. Patients in OLGA and OLGIM stage III or IV have a higher

gastric cancer risk, and a surveillance endoscopy should be offered to these patients. In this regard, considering the technological advances that make dysplasia visible, it may be the case that the updated Sydney system undergoes further evolutions and, ultimately, also the OLGA-OLGIM system.

Considering all the above, computer-aided diagnosis CNN systems using IEE and the Kyoto score should be refined to confirm the diagnosis of *H. pylori* infection and to accurately estimate the risk of gastric cancer. Artificial intelligence, through IEE and future advances, will allow us to overcome the problem of subjectivity related to the training and experience of operators[66].

CONCLUSION

Given that the assessment of gastritis can be considered complete only when a gastroscopy with M-IEE is performed by an experienced operator, who determines the Kyoto score and performs gastric biopsies, which are evaluated by a pathologist, who establishes the OLGA-OLGIM stage, it may be the case that the artificial intelligence allows some steps to be reduced. M-IEE, especially magnified narrow-band imaging and blue laser imaging-bright, has surpassed WLI in terms of sensitivity and specificity for the diagnosis of MA and IM in gastric mucosa, while linked color imaging accurately evaluates all segments of the stomach by searching for endoscopic findings according to the Kyoto classification of gastritis. Artificial intelligence may be able to further support an update of the Kyoto classification of gastritis that would allow us to improve the diagnosis of chronic gastritis, precancerous gastric conditions, lesions of the stomach, and early-stage gastric cancer.

FOOTNOTES

Author contributions: Panarese A conceived and wrote the manuscript, reviewed and analyzed the literature; Panarese A and Zagari RM edited the manuscript; all the authors revised and approved the final article.

Conflict-of-interest statement: All the authors declare no conflict of interests for this article.

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S-Editor: Liu JH

L-Editor: A

P-Editor: Liu JH

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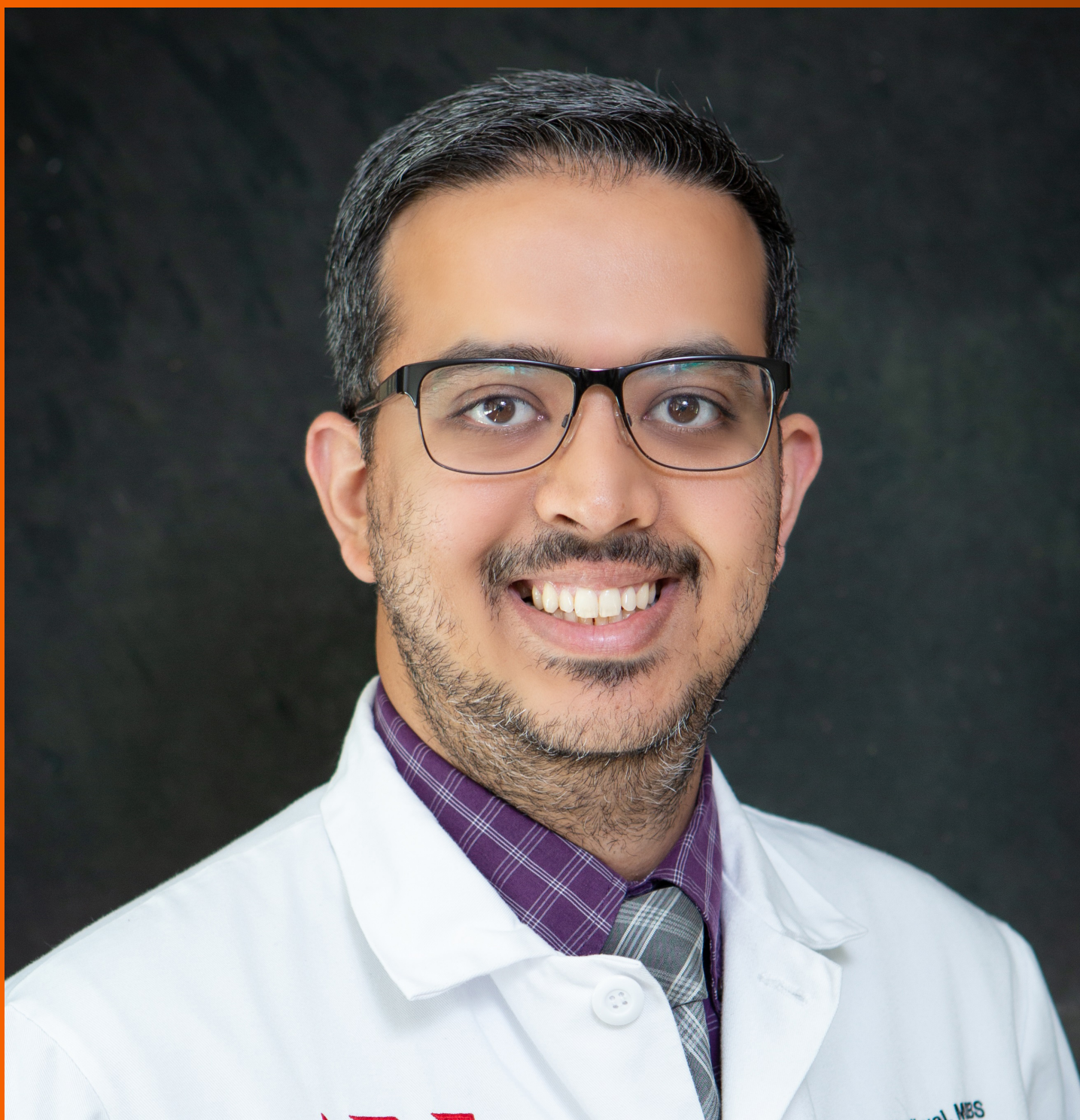
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Artificial Intelligence in *Gastrointestinal Endoscopy*

Artif Intell Gastrointest Endosc 2023 December 8; 4(2): 12-26





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ABOUT COVER

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The primary aim of *Artificial Intelligence in Gastrointestinal Endoscopy* (AIGE, *Artif Intell Gastrointest Endosc*) is to provide scholars and readers from various fields of artificial intelligence in gastrointestinal endoscopy with a platform to publish high-quality basic and clinical research articles and communicate their research findings online.

AIGE mainly publishes articles reporting research results obtained in the field of artificial intelligence in gastrointestinal endoscopy and covering a wide range of topics, including artificial intelligence in capsule endoscopy, colonoscopy, double-balloon enteroscopy, duodenoscopy, endoscopic retrograde cholangio-pancreatography, endosonography, esophagoscopy, gastrointestinal endoscopy, gastroscopy, laparoscopy, natural orifice endoscopic surgery, proctoscopy, and sigmoidoscopy.

INDEXING/ABSTRACTING

The AIGE is now abstracted and indexed in Reference Citation Analysis, China Science and Technology Journal Database.

RESPONSIBLE EDITORS FOR THIS ISSUE

Production Editor: *Yi-Xuan Cai*, Production Department Director: *Xiang Li*, Editorial Office Director: *Jin-Lei Wang*.

NAME OF JOURNAL

Artificial Intelligence in Gastrointestinal Endoscopy

ISSN

ISSN 2689-7164 (online)

LAUNCH DATE

July 28, 2020

FREQUENCY

Quarterly

EDITORS-IN-CHIEF

Fatih Altintoprak, Sahin Coban, Krish Ragunath

EDITORIAL BOARD MEMBERS

<https://www.wjgnet.com/2689-7164/editorialboard.htm>

PUBLICATION DATE

December 8, 2023

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INSTRUCTIONS TO AUTHORS

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PUBLICATION ETHICS

<https://www.wjgnet.com/bpg/gerinfo/288>

PUBLICATION MISCONDUCT

<https://www.wjgnet.com/bpg/gerinfo/208>

ARTICLE PROCESSING CHARGE

<https://www.wjgnet.com/bpg/gerinfo/242>

STEPS FOR SUBMITTING MANUSCRIPTS

<https://www.wjgnet.com/bpg/gerinfo/239>

ONLINE SUBMISSION

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Role of endoscopic ultrasound in non-variceal upper gastrointestinal bleeding management

Cosmas Rinaldi Adithya Lesmana

Specialty type: Gastroenterology & hepatology

Provenance and peer review:
Invited article; Externally peer reviewed.

Peer-review model: Single blind

Peer-review report's scientific quality classification

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

P-Reviewer: Rodrigo L, Spain

Received: July 28, 2023

Peer-review started: July 28, 2023

First decision: September 29, 2023

Revised: October 14, 2023

Accepted: December 4, 2023

Article in press: December 4, 2023

Published online: December 8, 2023



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Abstract

Non-variceal upper gastrointestinal bleeding (NVUGIB) is one of the challenging situations in clinical practice. Despite that gastric ulcer and duodenal ulcer are still the main causes of acute NVUGIB, there are other causes of bleeding which might not always be detected through the standard endoscopic evaluation. Standard endoscopic management of UGIB consists of injection, thermal coagulation, hemoclips, and combination therapy. However, these methods are not always successful for rebleeding prevention. Endoscopic ultrasound (EUS) has been used recently for portal hypertension management, especially in managing acute variceal bleeding. EUS has been considered a better tool to visualize the bleeding vessel in gastroesophageal variceal bleeding. There have been studies looking at the role of EUS for managing NVUGIB; however, most of them are case reports. Therefore, it is important to review back to see the evolution and innovation of endoscopic treatment for NVUGIB and the role of EUS for possibility to replace the standard endoscopic haemostasis management in daily practice.

Key Words: Non-variceal upper gastrointestinal bleeding; Endoscopic haemostasis; Endoscopic ultrasound; Bleeding vessel; Doppler image

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Core Tip: Non-variceal upper gastrointestinal bleeding is still one of the challenging situations in clinical practice. Standard endoscopic hemostasis has shown to have a high successful bleeding control rate; however, in some types of bleeding, there is still a possibility for endoscopic treatment failure. Endoscopic ultrasound can give a better bleeding vessel visualization, and it has shown to be a promising tool for non-variceal upper gastrointestinal bleeding management.

Citation: Lesmana CRA. Role of endoscopic ultrasound in non-variceal upper gastrointestinal bleeding management. *Artif Intell Gastrointest Endosc* 2023; 4(2): 12-17

URL: <https://www.wjgnet.com/2689-7164/full/v4/i2/12.htm>

DOI: <https://dx.doi.org/10.37126/aige.v4.i2.12>

INTRODUCTION

Upper gastrointestinal bleeding (UGIB) is one of the challenging situations in clinical practice due to its etiology, location, types of bleeding, and severity. It comprises of non-variceal and variceal bleeding[1,2]. In the past, there has been no significant change from time to time regarding the etiology of non-variceal upper gastrointestinal bleeding (NVUGIB). Gastric ulcer (GU) and duodenal ulcer (DU) are still the main causes of acute NVUGIB, where hemorrhage and perforation are the major causes for mortality[3,4]. A recent large multicenter study showed that the bleeding etiology for NVUGIB was dominated by DU, followed by GU, whereas neoplasia was ranked as the fourth common cause of NVUGIB when compared to other non-malignant causes, such as Mallory-Weiss, esophagitis, and Dieulafoy's lesion. Recurrent bleeding was found in 3.2% of patients, with a 4.5% mortality rate in 30 d. Standard endoscopic treatment, which consists of injection, thermal coagulation, hemoclips, and combination therapy, has shown a good bleeding control rate. However, endoscopic treatment failure was still found to be higher in patients with several predictors, such as in-hospital bleeding, hematemesis, renal failure, neoplasia, and liver cirrhosis[5]. Recently, there has been innovation management using endoscopic ultrasound (EUS) for managing variceal bleeding as it can target the bleeding vessel much better than conventional endoscopic management[6]. Therefore, in this review, the role of EUS will be discussed further.

METHODS

We collected all articles which have been published on standard endoscopic management as well as endoscopic ultrasound guided management in UGIB through the Medline/PubMed databases. The keywords used were EUS-guided vascular therapy, upper gastrointestinal bleeding, and non-variceal upper gastrointestinal bleeding. The purpose of this review was to elaborate the standard endoscopic management, limitations, new development or technique innovation, bleeding causes, and patient's outcome.

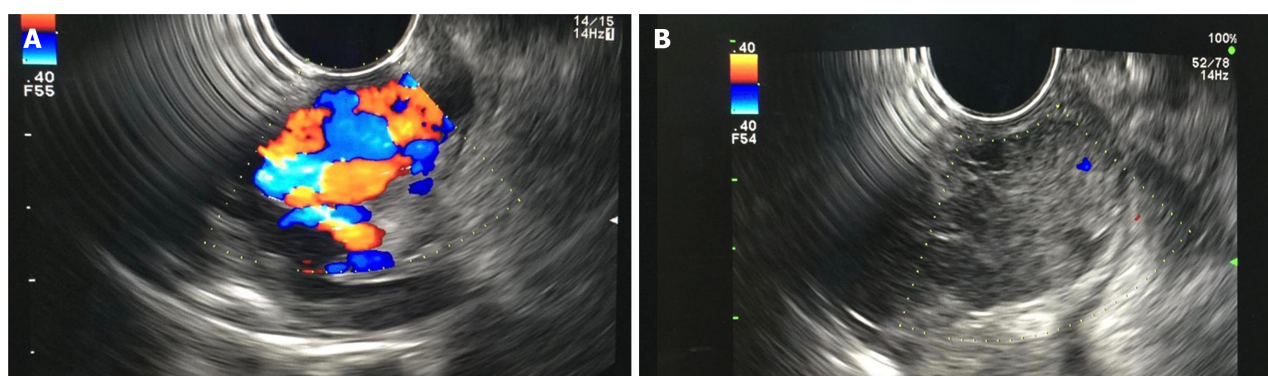
ENDOSCOPIC MANAGEMENT FOR NON-VARICEAL UPPER GASTROINTESTINAL BLEEDING

Standard endoscopic hemostasis treatment for NVUGIB consists of drug injection (epinephrine, cyanoacrylate, and other sclerosing agents), thermal coagulation, mechanical method, as well as topical treatment[7]. Endoscopic findings and bleeding ulcer stratification based on Forrest class have been routinely used as a standard parameter for the decision of endoscopic treatment options. Based on the Forrest classification, active bleeding (classes IA and B) has a 55% rebleeding rate with a 11% mortality rate, followed by visible vessel (class IIA) with a 43% rebleeding rate and 11% mortality rate, adherent clot (class IIB) with a 22% rebleeding rate and 7% mortality rate, flat spot (class IIC) with a 10% rebleeding rate and 3% mortality rate, and clean base ulcer (class III) with a 5% rebleeding rate and 2% mortality rate[8]. A randomized controlled trial by Chau *et al*[9] looking at the role of epinephrine injection combined with heat probe coagulation therapy *vs* epinephrine injection combined with argon plasma coagulation treatment in patients with bleeding peptic ulcers showed no significant difference between the two combined methods in achieving successful hemostasis (95.9% *vs* 97.7%). This study mostly included patients with Forrest classes IB and IIA. However, the rebleeding rate from both of groups was still high (21.6% and 17.0%), and the hospital mortality was 6.2% and 5.7%, respectively. Another randomized controlled trial by Lo *et al*[10] showed that combined therapy using epinephrine injection with hemoclip therapy *vs* epinephrine injection alone was more effective in reducing the rebleeding rate (100% *vs* 33%, $P = 0.02$). In fact, no surgery was even required in the combination treatment group when compared to the single treatment group ($P = 0.023$). The use of clips in NVUGIB might be associated with less mucosal injury when compared to thermal therapy[11]. In 2010, a novel endoscopic method using electrocautery forceps alone or with combined method based on retrospective multicenter data from patients with nonmalignant gastroduodenal ulcer bleeding in Japan showed that the rate of successful bleeding control was achieved in 96.8% of peptic ulcer patients, and 100% of artificial ulcer patients. However, there were 12 patients with rebleeding, which consisted of seven (11.5%) peptic ulcer patients and five (7.6%) artificial ulcer patients. In the rebleeding management, only one patient needed repeat endoscopic hemostasis treatment, and one patient required surgery after undergoing combination treatment. However, this study has been limited by the patient's selection bias as

well as the endoscopist's procedure skill[12]. Another innovation on endoscopic management on UGIB using a novel hemostatic powder (the "GRAPHE" registry), TC-325, showed that the immediate bleeding control effect was achieved by 96.5% of the patients; however, recurrent bleeding was found in 26.7% of patients at day 8 and 33.5% at day 30. Melena and pulsatile bleeding were the two most important factors for recurrent bleeding[13]. A large multicenter prospective study by Kawaguchi *et al*[14] showed that the most frequent cause of NVUGIB was gastric ulcer (GU; 69%), followed by DU (27%) and gastroduodenal ulcer (4%). The in-hospital 4-wk mortality rate was 5%, where two patients who died were associated with the bleeding itself. Patients with DU had a significantly higher mortality rate when compared to patients with GU (16% *vs* 4%, $P = 0.014$). In this study, 20 patients (8%) had unsuccessful endoscopic treatment. Other factors were comorbidities, the use of antithrombotic agent, and in-hospital onset. Based on the guideline recommendations from the international consensus group for NVUGIB management, it has been suggested that TC-325 can become a temporary treatment option with low evidence. This is due to its high rebleeding rates after 72 h and 1 wk. Endoscopic treatment, such as epinephrine injection, thermal coagulation, and clipping, is still considered as the main treatment. However, there was no significant difference in term of mortality rate even with combination therapy [15].

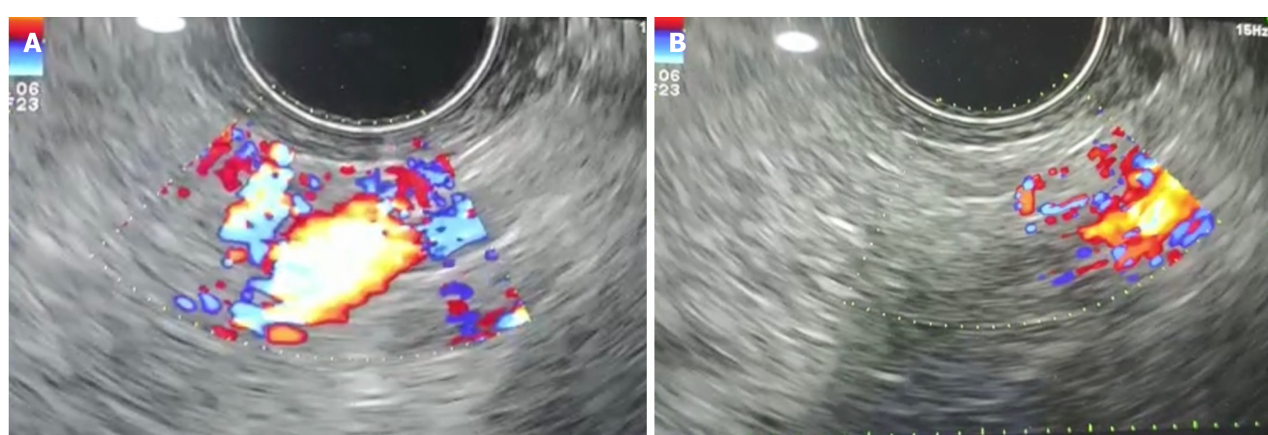
ENDOSCOPIC ULTRASOUND EVOLUTION AND INNOVATION IN MANAGING NON-VARICEAL UPPER GASTROINTESTINAL BLEEDING

In the evolution of therapeutic EUS development, a pioneer study by Boustière *et al*[16] performed EUS in liver cirrhotic patients, where gastric varices could be identified and stratified much better than esophageal varices. All cases suspected with the presence of GV was confirmed by EUS examination. In 2000, Lee *et al*[17] published a study on EUS-guided cyanoacrylate injection for bleeding GV showed that repeated injection under EUS guidance might improve patient survival as the recurrent bleeding incidence was decreased significantly when compared to on-demand treatment. Another small case series study by Romero-Castro *et al*[18] showed successful EUS-guided cyanoacrylate injection for the perforating veins related to GV. These innovation studies also have been supported by a recent acute variceal bleeding case series study[19], which concluded that EUS can give accurate approach in varices treatment (Figure 1). In 2011, a study by Binmoeller *et al*[20] showed that EUS-guided transesophageal combined treatment using coil and cyanoacrylate for GV management achieved a success in all cases. The rebleeding was noted to be not associated with the variceal bleeding. This was followed and supported by a recent study published by Bick *et al*[21], where they showed that by using EUS, the GV can be covered in a larger number when compared to the standard endoscopic injection. In fact, the use of EUS for NVUGIB management also has been studied in the past; however, most of them were only case report studies[22]. The first well-known case series study was published in 1996, which described the use of EUS examination for Dieulafoy's lesion evaluation and management. Three patients underwent sclerotherapy injection using 1% polidocanol under EUS guidance successfully without any adverse events[23]. This study was supported by other two case reports in patients who experienced bleeding due to Dieulafoy's lesion. One case report described the treatment using thermal contact with 7F Bicap probe (Boston Scientific). This probe was passed through the EUS channel combined with 2.5 mL absolute alcohol, which resulted in deep mucosal thermal burn, thus reducing the amplitude of arterial wave form. Another case underwent endoscopic band ligation after EUS evaluation. There was no rebleeding after the first procedure in both cases[24,25]. In 2008, Levy *et al*[26] published a study on EUS-guided angiotherapy for refractory NVUGIB, which consisted of bleeding due to hemosuccus pancreaticus, Dieulafoy's lesion, DU, and gastrointestinal stromal tumor (GIST), and occult GI bleeding. In this case series study, absolute alcohol injection was performed for hemosuccus pancreaticus bleeding and Dieulafoy's lesion, and cyanoacrylate injection for DU and GIST patients. All patients in this study did not have any rebleeding episodes, even after more than 12 mo. A larger case series study by Law *et al*[27] on the use of EUS-guided hemostasis treatment in patients with resistant non-variceal bleeding (GIST, colorectal vascular malformations, duodenal masses or polyps, Dieulafoy's lesions, DUs, and rectally invasive prostate cancer), showed that the complete vascular cessation was achieved in 63% of patients and the flow decrease in 37% of patients. There were no adverse events observed after the procedure. No patients had rebleeding within 12 mo follow-up after the procedure. Two studies reported only bleeding due to pancreatic pseudoaneurysm. One study reported a patient with chronic pancreatitis and splenic vein thrombosis with portal hypertension, who underwent EUS-guided pancreatic pseudocyst drainage and endoscopic retrograde cholangiopancreatography, followed by laparoscopic cholecystectomy for biliary tract stones. The late bleeding was due to the presence of pseudoaneurysm close to the pancreatic pseudocyst drainage area. The bleeding was controlled with *n*-butyl cyanoacrylate injection under EUS guidance. No recurrent bleeding was observed after the hemostatic procedure. The other case was a patient experiencing pseudoaneurysm induced by hemosuccus pancreaticus which has been confirmed by computed tomography angiography. This patient underwent EUS-guided coil embolization. No bleeding was recorded after more than a year[28,29]. The role of EUS-guided vascular therapy also has been reported in visceral pseudoaneurysm. The first case was reported by Lameris *et al* [30], where a thrombin-collagen compound was injected into pseudoaneurysm and the Doppler study revealed complete obliteration. No rebleeding occurred during 10 mo follow-up. Sharma *et al*[31] reported bleeding from visceral pseudoaneurysm due to acute pancreatitis, and it was successfully controlled by human thrombin injection. A recent single-blind study by Jensen *et al*[32] in 148 patients with severe NVUGIB who underwent endoscopic hemostasis under Doppler guidance showed that the rebleeding rate was significantly lower when compared to the control group (11.1% *vs* 26.3%, $P = 0.0214$). However, the use of EUS with Doppler guidance would give more accuracy and advantage to detect the bleeding source and manage severe NVUGIB due to possible poor visualization during standard endoscopic hemostasis procedure (Figure 2).



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Figure 1 Gastric varices images before and after endoscopic ultrasound guided cyanoacrylate injection. A: Endoscopic ultrasound (EUS) image of large gastric varices; B: EUS image of gastric varices post cyanoacrylate injection. Endoscopy database Medistra Hospital, Jakarta.



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Figure 2 Deep vascular bleeding source detection through endoscopic ultrasound (EUS) and after EUS-guided cyanoacrylate injection. A: Deep vascular bleeding source detection based on endoscopic ultrasound (EUS); B: EUS image after cyanoacrylate injection to control the bleeding source. Endoscopy database Medistra Hospital, Jakarta.

CONCLUSION

NVUGIB is still a challenging situation where there are a variety of causes which sometimes cannot be detected through standard endoscopic examination. EUS has shown that it has an important role in managing UGIB, especially in NVUGIB. However, it still needs larger study before it can be recommended as the first-line approach in managing NVUGIB.

FOOTNOTES

Author contributions: Lesmana CRA conceptualized the review, and wrote and edited the manuscript.

Conflict-of-interest statement: Cosmas Rinaldi Adithya Lesmana has no conflict of interest to disclose.

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S-Editor: Liu JH

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Retrospective Cohort Study

Artificial intelligence fails to improve colonoscopy quality: A single centre retrospective cohort study

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Specialty type: Gastroenterology and hepatology

Provenance and peer review: Unsolicited article; Externally peer reviewed.

Peer-review model: Single blind

Peer-review report's scientific quality classification

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

P-Reviewer: Rodrigo L, Spain

Received: September 4, 2023

Peer-review started: September 4, 2023

First decision: November 1, 2023

Revised: November 7, 2023

Accepted: November 30, 2023

Article in press: November 30, 2023

Published online: December 8, 2023



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Abstract

BACKGROUND

Limited data currently exists on the clinical utility of Artificial Intelligence Assisted Colonoscopy (AIAC) outside of clinical trials.

AIM

To evaluate the impact of AIAC on key markers of colonoscopy quality compared to conventional colonoscopy (CC).

METHODS

This single-centre retrospective observational cohort study included all patients undergoing colonoscopy at a secondary centre in Brisbane, Australia. CC outcomes between October 2021 and October 2022 were compared with AIAC outcomes after the introduction of the Olympus Endo-AID module from October 2022 to January 2023. Endoscopists who conducted over 50 procedures before and after AIAC introduction were included. Procedures for surveillance of inflammatory bowel disease were excluded. Patient demographics, proceduralist specialisation, indication for colonoscopy, and colonoscopy quality metrics were collected. Adenoma detection rate (ADR) and sessile serrated lesion detection rate (SSLDR) were calculated for both AIAC and CC.

RESULTS

The study included 746 AIAC procedures and 2162 CC procedures performed by seven endoscopists. Baseline patient demographics were similar, with median age of 60 years with a slight female predominance (52.1%). Procedure indications, bowel preparation quality, and caecal intubation rates were comparable between groups. AIAC had a slightly longer withdrawal time compared to CC, but the difference was not statistically significant. The introduction of AIAC did not significantly change ADR (52.1% for AIAC vs 52.6% for CC, $P = 0.91$) or SSLDR (17.4% for AIAC vs 18.1% for CC, $P = 0.44$).

CONCLUSION

The implementation of AIAC failed to improve key markers of colonoscopy quality, including ADR, SSLDR and withdrawal time. Further research is required to assess the utility and cost-efficiency of AIAC for high performing endoscopists.

Key Words: Artificial intelligence; Colonoscopy quality; Adenoma detection rate; Sessile serrated lesion detection rate; Withdrawal time

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Core Tip: This paper investigates the utility of Artificial Intelligence Assisted Colonoscopy (AIAC) in enhancing colonoscopy quality, particularly adenoma detection rate. Using a retrospective design, we compare AIAC with conventional colonoscopy in a real-world setting, finding no significant improvement in surrogate markers of colonoscopy quality. We explore challenges in artificial intelligence-human interaction and emphasise the need for further validation.

Citation: Goetz N, Hanigan K, Cheng RKY. Artificial intelligence fails to improve colonoscopy quality: A single centre retrospective cohort study. *Artif Intell Gastrointest Endosc* 2023; 4(2): 18-26

URL: <https://www.wjgnet.com/2689-7164/full/v4/i2/18.htm>

DOI: <https://dx.doi.org/10.37126/aige.v4.i2.18>

INTRODUCTION

Screening colonoscopy has been instrumental in reducing the incidence and mortality from colorectal cancer (CRC). However, up to 9% of CRCs develop in patients up-to-date on surveillance colonoscopies, termed interval cancers, thought to overwhelmingly result from suboptimal examination[1]. In defining colonoscopy quality, the most widely used quality metric is adenoma detection rate (ADR), which is the proportion of screening colonoscopies where at least one adenoma is found[2]. As ADR is inversely correlated to the interval cancer rate[3], technology that can aid adenoma detection has been the focus of intense research.

Artificial Intelligence Assisted Colonoscopy (AIAC) has emerged as a potential tool for improving colonoscopy quality and mitigating factors such as proceduralist fatigue or inattention in a procedure that is substantially operator dependent. Early robust randomised controlled trial (RCT) data on computer-aided polyp detection (CADE), which involves neural networks processing colonoscopy images in real time and superimposing a visual alert over suspected polyps on the endoscopy display, has garnered strong enthusiasm for this field[4]. Indeed, meta-analysis of published RCTs suggest that CADE can improve ADR by as much as 10%[5,6]. However, the majority of included trials were single-center studies conducted largely in Chinese institutions with relatively low baseline ADRs and using proprietary technology not available commercially[7]. As such, published data on the utility and cost-effectiveness in real-world clinical settings is limited. The objective of our study was to assess the effect of AIAC on key benchmarks of colonoscopy quality including ADR, sessile serrated lesion detection rate (SSLDR), and withdrawal time in comparison to conventional colonoscopy (CC).

MATERIALS AND METHODS

This was a single-centre retrospective observational cohort study conducted at Redcliffe Hospital, a public secondary hospital in Brisbane, Australia, which provides an open-access endoscopy service. All consecutive colonoscopies from October 2021 until January 2023 were included in the study. Patients were identified through a prospectively maintained departmental database of all patients undergoing colonoscopy. The introduction of the Olympus End-AID module in October 2022 allowed us to compare outcomes for CC in the preceding year with those of AIAC in the subsequent three months. For inclusion, proceduralists must have performed at least 50 colonoscopies both before and after the introduction of the Endo-AID module. We also only included patients with an intact colon. Colonoscopies performed for the surveillance of inflammatory bowel disease were excluded. All endoscopists included in the study had at least five years of independent endoscopy experience.

The primary endpoint for the study was change in three surrogate markers of colonoscopy quality with artificial intelligence (AI): ADR, SSLDR and withdrawal time. Additional variables collected included patient demographics, proceduralists specialisation, indication for colonoscopy, polyp size and colonoscopy quality metrics including bowel preparation and caecal intubation rate.

Proceduralists were able to switch the AI assistance mode on and off and use adjunctive techniques to enhance polyp detection, such as distal cap, narrow band imaging or chemical chromoendoscopy at their discretion. All patients underwent split bowel preparation, and the quality of preparation was evaluated and graded using the Boston Bowel

Preparation Scale by the performing proceduralist. All procedures were performed under conscious sedation using a combination of fentanyl and midazolam. The final decision regarding polyp resection was at the discretion of the proceduralist. Procedures were conducted in one of two dedicated endoscopy rooms equipped with identical high-definition colonoscopes (Olympus EVIS EXTRA) and histopathology was performed at a single laboratory, Queensland Pathology.

Statistical analysis

Statistical analysis was performed using Stata Corp STATA software (Boston, United States). Using ADR as the primary outcome and anticipating an effect size of 0.10, we calculated a minimum sample size of 236 patients to achieve a 95% confidence interval. Univariate comparisons of baseline parameters were conducted using the unpaired *t*-test after confirming normal distribution. Non-parametric data was assessed using the Mann-Whitney U test, while categorical data was analysed using the Chi-squared or Fisher's exact test. We set statistical significance at a *P* value of < 0.05.

RESULTS

We compared 746 AIACs with 2126 CCs, which were conducted by seven endoscopists, comprising four gastroenterologists and three surgeons. Patient demographics were similar between patients undergoing AIAC and CC at baseline, with a median age of 60 years (interquartile range 49-70) and a slight female predominance of 52.1% (Table 1). Procedure indications in order of frequency were symptoms (35.1%), surveillance following previous polyps (31.2%) and investigation of a positive faecal occult blood test (14.8%). The indication for the procedure, quality of bowel prep and caecal intubation rates were well matched between the study populations (*P* > 0.05).

AIAC introduction ultimately had no significant impact on either ADR (52.1% for AIAC *vs* 52.6% for CC, *P* = 0.91) or SSLDR (17.4% for AIAC *vs* 18.1% for CC, *P* = 0.44) on an institutional level. However, a per-proceduralist analysis (Figure 1) demonstrated a significant change for two endoscopists, with ADR increasing by 16.8% for one (CC 61.4%, AIAC 78.2%, *P* = 0.004) and decreasing by 21% for another (CC 58.6%, AIAC 37.6%, *P* = 0.006). By-proceduralist analysis of SSLDR did not yield significant results. The AIAC group exhibited a longer mean withdrawal time (13 min 18 sec) compared with the CC group (12 min 29 sec), though this difference was not statistically significant (*P* = 0.48) (Figure 2). Analysis by adenoma or sessile serrated lesion (SSL) size was not significant between groups, with the majority of adenomas detected being < 5 mm in size in both groups (Figure 3).

DISCUSSION

We demonstrate that AI in colonoscopy yielded no benefit in our unit and failed to improve either ADR or SSLDR. One possible explanation for our experience being discordant to trial data is that the baseline ADR of 52% in our unit is substantially higher than many of the published RCTs to date, and there may be a ceiling effect to polyp detection among high performing endoscopists. Furthermore, results from RCTs may be overly optimistic as proceduralists were not blinded to the intervention, which may have impacted their performance and prompted a more thorough mucosal exposure or conscientious lesion assessment[8]. A more concerning explanation would be that CADe instilled a false sense of security and unwittingly resulted in a degradation of mucosal exposure quality, though a consistent withdrawal time would argue against this. It is also possible that proceduralists did not utilize CADe to the full extent and ignored lesions highlighted by CADe because they either deemed these to be clinically unimportant or incorrectly believed them to be false-positive signals. As such, exploration of endoscopist attitudes and behavior in the face of a nascent technology and formal training in CADe may be critical for successfully integrating AIAC across a range of practice settings.

Interestingly, per-proceduralist analysis of ADR yielded significant results for two individuals, including one interventional gastroenterologist whose ADR deteriorated with AIAC. Given the comparatively short period of observation of AIAC compared with CC, this may reflect a type II error due to the smaller number of AIAC procedures or alternatively stem from an altered referral pattern during this limited time period. Again, there was no change in withdrawal time to suggest a degradation in examination quality due to overreliance on AI. In terms of SSL detection, these are known to be more challenging to detect given they are often located in the proximal colon and have a non-polypoid configuration with inconspicuous borders[9]. There has been no substantial improvement in SSLDR in the majority of published AIAC studies except for two tandem colonoscopy RCTs which demonstrated reduced SSL miss rates with AIAC, although detection rates compared unfavorably with our 18% baseline SSLDR[10,11].

Our study is not an outlier, but rather follows a series of recent disappointing results from AIAC implementation in high-performing Western endoscopy units that challenge the generalizability of the benefits of CADe demonstrated in early RCTs across broader clinical settings. Most notably, Wei *et al*[12] performed a multi-center RCT across four community-based endoscopy centers in the United States and found no change in the number of adenomas per colonoscopy (0.73 for AIAC *vs* 0.67 for CC, *P* = 0.496) or the ADR (35.9% for AIAC *vs* 37.2% for CC, *P* = 0.774). This study is particularly salient as it offered a more pragmatic trial design, allowing proceduralists to choose how they employed the AI assistance mode (*i.e.* 'on' during insertion or only once the cecum was reached). Similarly, a United Kingdom RCT found that AIAC resulted in a higher polyp detection rate (85.7% for AIAC *vs* 79.7% for CC; *P* = 0.05) but no change in ADR (71.4% for AIAC *vs* 65.0% for CC, *P* = 0.09)[13]. Furthermore, a large volume endoscopy center in Israel retrospectively demonstrated a deterioration in ADR with AIAC implementation (30.3% for AIAC *vs* 35.2% for CC, *P* < 0.001)[14]. While there are challenges to comparing results of different CADe systems across various clinical settings,

Table 1 Baseline patient demographics, procedure characteristics and detection rate for both conventional colonoscopy and Artificial Intelligence Assisted Colonoscopy

	AIAC (n = 746)	CC (n = 2162)
Age, median (IQR)	58.2 (47-69)	60 (49-71)
Sex		
Male	359 (48.1)	1034 (47.8)
Female	387 (51.9)	1128 (52.2)
Indication for colonoscopy		
Symptoms	292 (39.1)	729 (33.7)
Surveillance	201 (26.9)	706 (32.7)
Positive FOBT	128 (18.5)	293 (13.6)
Other	125 (16.8)	434 (20.1)
Bowel Prep Quality		
Not stated	0 (0)	1 (0.05)
Poor	39 (5.2)	107 (4.9)
Fair	101 (13.5)	225 (10.4)
Good	514 (68.9)	1582 (73.2)
Excellent	92 (12.3)	247 (11.4)
Caecum intubated	733 (98.3)	2104 (97.3)
Withdrawal time (min), median (IQR)	13.31 (9.13-19.06)	12.49 (8.38-19.0)
PDR	620 (85.3)	1596 (73.9)
Polyps removed		
0	176 (23.6)	566 (26.2)
1	126 (16.9)	446 (20.6)
2	99 (13.3)	325 (15.0)
3	81 (10.9)	216 (10.0)
4	57 (7.6)	128 (5.9)
5	52 (7.0)	118 (5.5)
6	35 (4.7)	84 (3.9)
7	29 (3.9)	62 (2.9)
8	18 (2.4)	38 (1.8)
9	12 (1.6)	33 (1.5)
10-19	52 (7.0)	129 (6.0)
20-99	9 (1.2)	17 (0.8)
Adenoma detection rate	392 (52.6)	1125 (52.1)
Villous histology	26/392 (6.6)	80/1125 (7.1)
HGD	2.3/392 (9.0)	43 (3.8)
Adenomas removed		
0	354 (47.5)	1037 (48.0)
1	167 (42.6)	478 (42.5)
2	74 (18.9)	232 (20.6)
3	39 (10.0)	138 (12.3)
4	31 (7.9)	88 (7.8)

5	22 (5.6)	69 (6.1)
6	15 (3.8)	33 (2.9)
7	10 (2.5)	32 (2.8)
8	12 (3.06)	22 (2.0)
9	5 (1.3)	11 (1.0)
10-19	17 (4.3)	20 (1.8)
20-99	0 (0)	2 (0.2)
Adenoma size		
≤ 5 mm	234 (59.7)	683 (60.7)
5-10 mm	101 (25.8)	269 (23.9)
10-20 mm	49 (12.5)	126 (11.2)
≥ 20 mm	8 (2.0)	47 (4.2)
SSLDR	130 (17.4)	392 (18.1)
SSLs with Dysplasia	1 (0.7)	3 (0.7)
SSLs removed		
1	65 (50)	211 (53.8)
2	34 (26.2)	86 (21.9)
3	12 (10)	27 (6.9)
4	4 (3.1)	16 (4.1)
≥ 5	12 (10.8)	52 (13.2)
SSL size		
≤ 5 mm	58 (44.6)	173 (44.1)
5-10 mm	43 (33.1)	118 (30.1)
10-20 mm	23 (17.7)	92 (23.5)
≥ 20 mm	6 (4.6)	9 (2.3)

Data are presented as median (IQR) or number of patients (% of patients). AIAC: Artificial Intelligence Assisted Colonoscopy; CC: Conventional colonoscopy; FOBT: Fecal Occult Blood Test; IQR: Interquartile range; PDR: Polyp detection rate; HGD: High grade dysplasia; SSLDR: Sessile serrated lesion detection rate; SSL: Sessile serrated lesion.

these studies highlight that real-world CAde implementation without attention to the AI-human interaction may fail to achieve intended outcomes.

Withdrawal time is a key marker of colonoscopy quality that is strongly correlated with ADR[15]. In our study, withdrawal time did not change, though our median of 12.82 min for CC significantly exceeds the grouped averages for controls in early RCTs which ranged from 4.76 min to 6.99 min[6]. In these RCTs, improvements in ADR with CAde have paralleled increases in withdrawal time. Similarly, a New Zealand center demonstrated increased ADR with AIAC deployment (47.9% for AIAC *vs* 38.5% for CC; $P = 0.03$), though the AIAC group also had a significantly longer withdrawal time (15 min for AIAC *vs* 13 min for CC; $P < 0.001$)[16]. Arguably, ADR improvements could therefore merely be the result of a more thorough examination, reflected in the longer withdrawal time, rather than AI. Notably, in the study by Wei *et al*[12], ADR did not improve despite a prolonged withdrawal time in the AIAC group, possibly reflecting increased time spent assessing activations from the AI module, including possible false positives.

Even though polyp size was comparable between groups in our study, it is worth noting that improvements in ADR with AI in previous RCTs have primarily been driven by an increased in the detection of diminutive adenomas of 5 mm in size or lower[6]. In our study, adenomas < 5 mm constituted 60.7% of resected adenomas in the control group, compared with a mean of 19% in RCT controls[6]. Coupled with high baseline ADRs and SSLDRs in our unit, this likely reflects astute mucosal exposure and examination in our institution. Furthermore, the merit of increased detection and removal of diminutive polyps is a point of controversy, particularly with respect to the degree this mitigates cancer risk [17].

A significant strength of our study is its real-world setting, which confers less risk of operator bias than a trial framework. Important limitations include the retrospective design, relatively short period of observation for AIAC and lack of patient randomization, though enrollment of consecutive patients resulted in well-matched baseline characteristics. Furthermore, the CAde mode could be switched on and off by proceduralists at their discretion, generating a

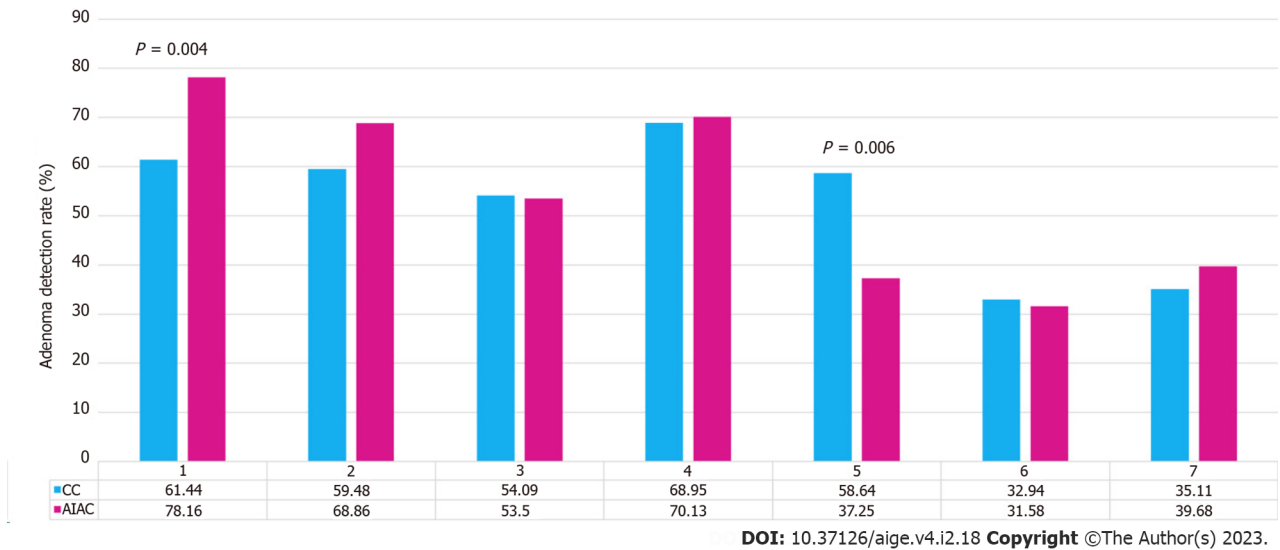


Figure 1 By-proceduralist analysis of adenoma detection rate for both conventional colonoscopy and Artificial Intelligence Assisted Colonoscopy. CC: Conventional colonoscopy; AIAC: Artificial Intelligence Assisted Colonoscopy.

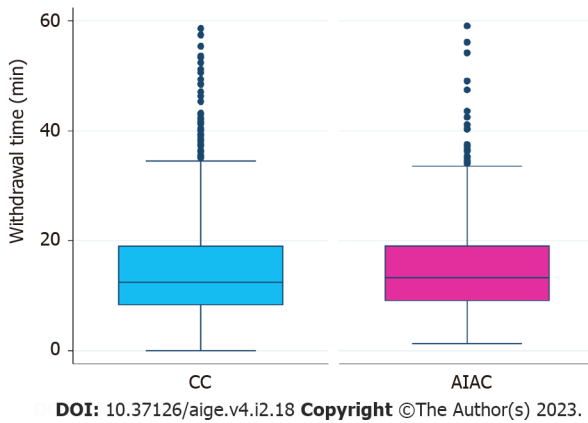


Figure 2 Median withdrawal time for both conventional colonoscopy and Artificial Intelligence Assisted Colonoscopy. CC: Conventional colonoscopy; AIAC: Artificial Intelligence Assisted Colonoscopy.

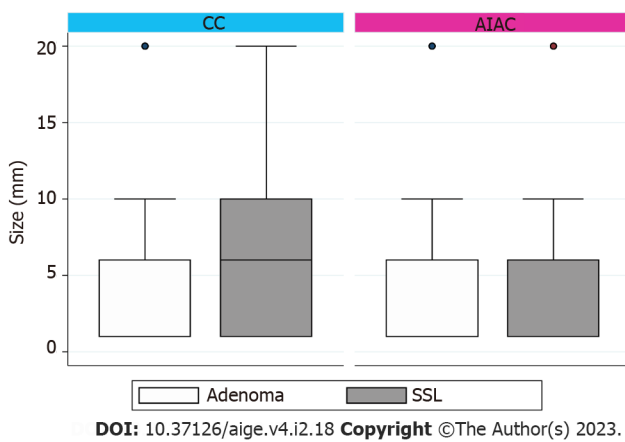


Figure 3 Median adenoma and sessile serrated lesion size (mm) for both conventional colonoscopy and Artificial Intelligence Assisted Colonoscopy. CC: Conventional colonoscopy; AIAC: Artificial Intelligence Assisted Colonoscopy; SSL: Sessile serrated lesion.

further variable of "on time" for CADe, which was not documented. In addition, though intuitive, no formal training was provided for CADe prior to implementation.

CONCLUSION

Ultimately, while AIAC has shown promise in early RCTs, further validation is required to assess its effectiveness and cost-efficiency in institutions with high performance metrics at baseline, where gains from AI are likely to be far more incremental. Specifically, longitudinal studies that assess the impact of AIAC on interval cancer rates are required. Beyond CADe, additional applications of AI in colonoscopy may increase its utility. For example, the development of computer-assisted diagnosis, which promises to confidently distinguish diminutive hyperplastic polyps from neoplastic lesions through optical pathology, could lead to significant cost-savings by allowing proceduralists to adopt a 'resect and discard' policy rather than sending these specimens for histopathology[18]. Similarly, novel AI systems can recognize key endoscopic landmarks, specific tools, and quality of bowel preparation and integrate this information into an automatically generated colonoscopy report, reducing peri-procedural documentation burden[19]. As such, it may be that a comprehensive suite of AI tools is necessary to fully realize the benefits in this field.

ARTICLE HIGHLIGHTS

Research perspectives

While Artificial Intelligence Assisted Colonoscopy (AIAC) has shown promise in early randomised controlled trials (RCTs), further validation is required to assess its utility and cost-effectiveness in centres with high baseline performance metrics, where gains from artificial intelligence (AI) are likely to be far more incremental. Specifically, longitudinal studies that assess the impact of AIAC on interval cancer rates are required.

Research conclusions

In our institution, introduction of AIAC failed to improve key benchmarks of colonoscopy quality, including adenoma detection rate (ADR), sessile serrated lesion detection rate (SSLDR) and withdrawal time. An important limitation of our investigation is the relatively brief observation period following AIAC implementation, that the 'on time' of the AI assistance mode was not recorded as well as the retrospective design.

Research results

The study included 746 AIAC procedures and 2162 conventional colonoscopy (CC) procedures performed by seven endoscopists. Baseline patient demographics were similar, with a median age of 60 years and a slight female predominance (52.1%). Procedure indications, bowel preparation quality, and caecal intubation rates were comparable between groups. AIAC had a slightly longer withdrawal time compared to CC, but the difference was not statistically significant. The introduction of AIAC did not significantly change ADR (52.1% for AIAC *vs* 52.6% for CC, $P = 0.91$) or SSLDR (17.4% for AIAC *vs* 18.1% for CC, $P = 0.44$).

Research methods

This retrospective observational cohort study was conducted at a single center in Brisbane, Australia, encompassing all patients who underwent colonoscopy during the study period. Colonoscopy quality markers for CCs conducted from October 2021 to October 2022 were compared with AIAC markers following the implementation of the Olympus Endo-AID module from October 2022 to January 2023. Proceduralists who conducted over 50 procedures before and after AIAC introduction were included. Procedures for surveillance of inflammatory bowel disease were excluded. Patient demographics, proceduralist specialisation, indication for colonoscopy, and colonoscopy quality metrics were collected. We determined the ADR and SSLDR for both CC and AIAC.

Research objectives

The objective of our investigation was to assess the effect of AIAC on key benchmarks of colonoscopy quality including the detection rate of adenomas (ADR) and SSLDR as well as withdrawal time in comparison to CC.

Research motivation

In recent years, rapid technological advancements and a focus on quality improvement have garnered significant enthusiasm for AIAC as a means of improving key markers of colonoscopy quality. While early data appears promising, this technology requires validation in day-to-day clinical practice.

Research background

AIAC has emerged as a potential tool for improving colonoscopy quality and mitigating factors such as proceduralist fatigue or inattention in a procedure that is substantially operator dependent. However, published data on the utility and cost-effectiveness in real-world clinical settings is limited.

FOOTNOTES

Author contributions: All authors conceived the idea. KH collated the data from the departmental database; Goetz N performed the statistical analysis and was primarily responsible for writing the manuscript; Cheng RKY provided substantial revisions to the manuscript.

Institutional review board statement: The study was approved by the local Human Research Ethics Committee (HREC/2023/MNHA/100582).

Informed consent statement: A waiver of consent was obtained from the HREC.

Conflict-of-interest statement: The authors declare there is no potential sources of conflict of interest. This study was not funded, with research work conducted *in-kind*.

Data sharing statement: The datasets generated during and/or analysed 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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S-Editor: Liu JH

L-Editor: A

P-Editor: Liu JH

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