

Artificial Intelligence in *Gastroenterology*

Quarterly Volume 5 Number 1 April 30, 2024





Artificial Intelligence in Gastroenterology

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Zhang W, Song LN, You YF, Qi FN, Cui XH, Yi MX, Zhu G, Chang RA, Zhang HJ. Application of artificial intelligence in the prediction of immunotherapy efficacy in hepatocellular carcinoma: Current status and prospects. *Artif Intell Gastroenterol* 2024; 5(1): 90096 [DOI: [10.35712/aig.v5.i1.90096](https://doi.org/10.35712/aig.v5.i1.90096)]

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The primary aim of *Artificial Intelligence in Gastroenterology* (AIG, *Artif Intell Gastroenterol*) is to provide scholars and readers from various fields of artificial intelligence in gastroenterology with a platform to publish high-quality basic and clinical research articles and communicate their research findings online.

AIG mainly publishes articles reporting research results obtained in the field of artificial intelligence in gastroenterology and covering a wide range of topics, including artificial intelligence in gastrointestinal cancer, liver cancer, pancreatic cancer, hepatitis B, hepatitis C, nonalcoholic fatty liver disease, inflammatory bowel disease, irritable bowel syndrome, and *Helicobacter pylori* infection.

INDEXING/ABSTRACTING

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

RESPONSIBLE EDITORS FOR THIS ISSUE

Production Editor: *Yu-Qing Zhao*; Production Department Director: *Xu Guo*; Cover Editor: *Jin-Lei Wang*.

NAME OF JOURNAL

Artificial Intelligence in Gastroenterology

ISSN

ISSN 2644-3236 (online)

LAUNCH DATE

July 28, 2020

FREQUENCY

Quarterly

EDITORS-IN-CHIEF

Rajvinder Singh, Ferruccio Bonino

EDITORIAL BOARD MEMBERS

<https://www.wjgnet.com/2644-3236/editorialboard.htm>

PUBLICATION DATE

April 30, 2024

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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

<https://www.f6publishing.com>

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E-mail: office@baishideng.com <https://www.wjgnet.com>

Application of artificial intelligence in the prediction of immunotherapy efficacy in hepatocellular carcinoma: Current status and prospects

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Specialty type: Computer science, artificial intelligence

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

P-Reviewer: Liakina V, Lithuania

Received: November 23, 2023

Peer-review started: November 23, 2023

First decision: January 12, 2024

Revised: January 28, 2024

Accepted: March 12, 2024

Article in press: March 12, 2024

Published online: April 30, 2024



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Abstract

Artificial Intelligence (AI) has increased as a potent tool in medicine, with promising oncology applications. The emergence of immunotherapy has transformed the treatment terrain for hepatocellular carcinoma (HCC), offering new hope to patients with this challenging malignancy. This article examines the role and future of AI in forecasting the effectiveness of immunotherapy in HCC. We highlight the potential of AI to revolutionize the prediction of therapy response, thus improving patient selection and clinical outcomes. The article further outlines the challenges and future research directions in this emerging field.

Key Words: Artificial intelligence; Hepatocellular carcinoma; Immunotherapy; Predictive modeling

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Core Tip: Recently, there has been a lot of progress in predicting the effect of immunotherapy for hepatocellular carcinoma using artificial intelligence, but it also faces serious challenges. Therefore, in this article we summarize and discuss these issues.

Citation: Zhang W, Song LN, You YF, Qi FN, Cui XH, Yi MX, Zhu G, Chang RA, Zhang HJ. Application of artificial intelligence in the prediction of immunotherapy efficacy in hepatocellular carcinoma: Current status and prospects. *Artif Intell Gastroenterol* 2024; 5(1): 90096

URL: <https://www.wjgnet.com/2644-3236/full/v5/i1/90096.htm>

DOI: <https://dx.doi.org/10.35712/aig.v5.i1.90096>

INTRODUCTION

Hepatocellular carcinoma (HCC), the most prevalent primary liver cancer and a top contributor to global cancer mortality, is frequently detected at an advanced stage, offering few treatment choices and a bleak prognosis[1,2]. Traditional treatment modalities, such as surgery, radiotherapy, and chemotherapy, have been the mainstay of HCC management, but their efficacy is frequently limited by tumor recurrence and adverse side effects[3-5]. With the advent of immunotherapy, the treatment landscape for HCC has been changed, offering new hope to patients with this aggressive form of liver cancer[6,7]. Immunotherapy has shown promising results in improving survival rates. It is being evaluated in various stages of HCC treatment, from its role in the adjuvant setting to its use in advanced stages of the disease[4,6,8].

Despite progress, the heterogeneity of HCC and the complexity of the tumor microenvironment (TME) hinder consistent, durable responses across all patient groups[9]. Predicting which patients will benefit from these treatments remains a significant challenge. Currently, ongoing clinical trials and research efforts are focused on understanding the mechanisms of resistance and identifying biomarkers to predict immunotherapy response[10,11]. This is where artificial intelligence (AI) comes into play, offering a new dimension to these efforts. AI has the potential to analyze complex biomedical data, identifying patterns that could predict treatment outcomes. Integrating AI into clinical practice may lead to more personalized, effective treatment strategies, optimizing patient care and resource use[12].

AI models have achieved remarkable success in various medical applications, such as diagnostic imaging, genomics, and drug discovery. In the context of HCC, AI applications extend to predicting patient prognosis, and treatment response, and even suggesting potential therapeutic targets[13,14]. However, the application of AI in predicting the efficacy of immunotherapy for HCC remains nascent, with numerous challenges yet to be overcome.

The evolution of immunotherapy for HCC

Historically, the initial attempts to harness the immune system to combat HCC centered around cytokine-based therapies, such as interferon-alpha and interleukin-2. Later, it was realized that immune checkpoints, such as CTLA-4 and PD-(L)1, could be manipulated to improve anti-tumor immunity[15].

The first breakthrough in the immunotherapy of HCC came with the approval of nivolumab, a PD-1 inhibitor, for use in patients with advanced HCC who had previously received sorafenib[7]. More recently, researchers have explored combination therapies, such as PD-L1 inhibitors with CTLA-4 inhibitors or with other therapeutic modalities like targeted therapies and locoregional treatments, which are predicated on the potential to synergize different mechanisms of action to enhance anti-tumor responses[16]. For example, the combination of atezolizumab and bevacizumab demonstrated improved survival outcomes relative to sorafenib in the IMbrave150 trial[5].

Despite these advances, the response to immunotherapy in HCC remains variable, with a significant proportion of patients not experiencing benefit. Consequently, this variability has spurred ongoing research into biomarkers that can predict response to immunotherapy.

The potential of AI in oncology

AI, encompassing a wide area of computer science, works toward building systems able to accomplish functions commonly needing human cognition. Among these subfields are machine learning (ML), deep learning (DL), natural language processing, and robotics[17,18]. In the field of oncology, the potential role of AI is to enhance diagnosis, and treatment, and predict treatment outcomes or disease progression.

For diagnosis, DL algorithms that analyze low-dose computed tomography (CT) scans can detect early-stage lung cancer with precision comparable to expert radiologists, potentially leading to earlier and more effective interventions [19]. Similarly, applying DL algorithms to whole-slide pathology images can aid pathologists in identifying cancerous tissues, thus significantly expediting the diagnostic process and enhancing diagnostic accuracy and efficiency[20]. Using AI integrated with machines and DL in radiomics can help to more accurately define tissue characteristics[21].

Regarding treatment, AI's integration and analysis of genomic data alongside clinical histories enable the creation of personalized treatment plans that predict patient benefits from specific therapies. Zhang *et al*[22] utilized Garson's algorithm, Lek's profile, local interpretable model-agnostic explanations, and partial dependence plots to aid clinicians and medical policymakers in understanding artificial neural networks, powerful tools for effectively predicting outcome variable relationships.

Additionally, AI also aids in anticipating treatment outcomes, helping to optimize treatment regimens by forecasting patient responses and potential side effects based on historical data. For instance, DL algorithms, in particular convolutional networks, utilize imaging data to track tumor advancement or decline, offering impartial markers for modifying the treatment process[23]. AI models integrate various patient data, such as genetic information, clinical histories, and imaging findings, to predict disease progression. This comprehensive approach leads to more accurate prognostic assessments than traditional methods, which often consider fewer data points[24]. Survival convolutional neural networks integrate histology images and genomic biomarkers using DL to predict patient outcomes, surpassing current clinical methods for predicting overall survival (OS) in glioma patients[25]. Huang *et al*[26] identified 10 signature genes from a pool of 166 stem cell-related genes using the least absolute shrinkage operator (LASSO) and multivariate Cox regression analysis. They found that this signature effectively predicted the response to chemotherapy in lung adenocarcinoma patients. Furthermore, in Ding *et al*'s experiment, the mirlncRNA signature, comprising five notable lncRNAs, not only differentiates molecular typing and identifies the related tumor immune subtypes and their chromatin accessibility, but also underscores the immune efficacy and drug sensitivity of tumor immune subtypes[27].

The role of AI in predicting immunotherapy efficacy in HCC

ML, a subset of AI, may become a powerful tool for predicting the response of HCC patients to immunotherapy. ML models, like support vector machines (SVMs), have been utilized for predicting HCC recurrence, screening drugs, identifying potential targets, and determining which patients are more likely to experience recurrence with specific treatments[24,28-30]. Shi *et al*[31] examined peripheral blood mononuclear cells from various cohorts, creating an AdaBoost-SVM logistic model that can identify early-stage HCC *via* immune markers, surpassing alpha-fetoprotein in accuracy.

DL, another subset of AI, uses algorithms to model and understand complex patterns in data. Zeng *et al*[32] explored three DL approaches (patch-based, classic MIL, and CLAM) to create and verify AI-based pathology models for predicting immune and inflammatory gene signatures. Their findings suggest that these signatures could be associated with heightened sensitivity to immunotherapy in patients with advanced HCC.

Additionally, genomic data also play a crucial role in predicting treatment responses. AI models have been trained to identify genetic mutations and expression profiles that correlate with better immunotherapy outcomes. Gong *et al*[33] utilized ML to develop a risk scoring system known as 'neutrophil-derived signature' (NDS), comprising 10 crucial genes. The RiskScore of NDS showed higher accuracy compared to clinical variables and was associated with increased malignancy levels. Consequently, the predictive prowess of DL models can guide clinicians in identifying patients who stand to gain the most from immunotherapy, fostering personalized and efficacious treatment approaches. Xie *et al*[34] found that the m6A- and ferroptosis-lncRNA signature, which has significant prognostic value, provides new perspectives in distinguishing 'cold' and 'hot' tumors and could have important implications for personalized therapy to improve the survival rate of HCC patients. Feng *et al*[35] utilized the LASSO and CoxBoost algorithms to combine and create a signature from 11 natural killer cell-related genes. This provided a new method for evaluating the prognosis and immunotherapeutic response of HCC patients. Dai *et al*[36] employed the LASSO regression model to create an immune-related gene-based prognostic index. This index can predict immune cell infiltration in the HCC TME, as well as the response to immunotherapy. Shen *et al*[37] used genes related to aging to create a predictive model. Through Spearman correlation analysis, they found that the model's risk score was closely related to Mismatch Repair and expression of immune checkpoints.

AI models, particularly those based on ML and DL, have several advantages over traditional statistical methods in predicting outcomes and treatment responses in HCC. Traditional methods often rely on predefined clinical and pathological criteria, which may not capture the complex biological interactions underlying HCC progression and response to treatment. In contrast, AI models can integrate a wide range of data types and identify non-linear relationships within the data[30,38]. Comparative studies have shown that AI models can outperform traditional scoring systems and clinical judgment in prognostication and treatment prediction. For instance, the random survival forests model showed greater accuracy in predicting early recurrence of HCC after surgery compared to COX proportional hazard models[39]. Moreover, AI-driven tools can continuously learn and improve as they are exposed to new data, a feature that static traditional models lack.

Moreover, AI has been instrumental in discovering novel biomarkers for HCC. Through the analysis of large datasets, DL can uncover subtle correlations between biomarkers and treatment responses that may not be apparent to human investigators. Liang *et al*[40] introduced an interpretable human-centric DL-guided framework, Pathological-biomarker-finder, to aid pathologists in identifying new tissue biomarkers using effective DL models.

Given the promising prospects of AI in predicting the immunotherapy efficacy of HCC, an increasing array of predictive variables is being incorporated into clinical practice. These variables include risk-scoring systems, gene phenotypes, and other types of biomarkers. For instance, Hatanaka *et al*[41] conducted a multicenter retrospective analysis that employed the modified Gustave Roussy Immune (GRIm) score as a new prognostic tool for HCC patients treated with atezolizumab and bevacizumab. Their findings indicated that a high GRIm score is a significant adverse factor for both progression-free survival (PFS) and OS. The retrospective analysis by Sangro *et al*[42] revealed an inflammatory gene signature consisting of four genes: CD274, CD8A, LAG3, and STAT1, which correlated with improved response rates and OS in advanced HCC patients treated with nivolumab. Similarly, the atezolizumab-bevacizumab response signature (ABRS), associated with PFS after starting treatment with atezolizumab-bevacizumab, includes genes like CXCR2P1, ICOS, and TIMD4[43]. Building on this, Zeng *et al*[44] developed a prediction model (ABRS-P) and found that patients with ABRS-P-high tumors had a significantly longer median PFS than those with ABRS-P-low tumors. In addition, Sun *et al*[45] used specific patient cohorts with advanced solid tumors to develop and validate a radiomic signature capable of predicting immunotherapy responses by assessing CD8 T cell infiltration in tumors. In another

clinical trial, researchers identified pre-existing CD8 T cells as a promising biomarker for forecasting responses to combined lenvatinib and PD-1 inhibitors in unresectable HCC[46].

Challenges in AI application to HCC immunotherapy

Despite these advancements, several challenges still impede the broader application of AI in predicting HCC immunotherapy efficacy. A significant challenge is the availability of high-quality, annotated datasets. AI models require large amounts of data to learn effectively; however, the scarcity of such datasets can limit the performance of these models[47]. Furthermore, AI models predicting immunotherapy outcomes need to be updated regularly to incorporate the latest clinical knowledge and patient data. Additionally, the heterogeneity of HCC presents another challenge, as it can vary greatly in its genetic makeup and clinical presentation. This variability can hinder AI models from generalizing their predictions effectively across different patient populations[11]. Furthermore, the interpretability of AI models, particularly DL models, remains a significant concern. The unclear and puzzling nature of these models can make it tough for healthcare professionals to comprehend the logic behind the predictions, which is essential for making well-informed clinical decisions[48].

The use of AI in healthcare also raises important ethical and regulatory considerations. Issues including patient privacy, data security, and informed consent must be addressed to ensure the ethical application of AI in predicting immunotherapy response[49].

Prospects and future directions

The integration of AI into clinical practice for predicting HCC immunotherapy response is an ongoing endeavor. A crucial part of this integration process is the thorough validation of AI models across various patient groups to ensure that the predictions are strong and dependable[50]. Additionally, the development of user-friendly AI platforms that healthcare professionals can easily access and utilize is another important aspect. To facilitate their adoption in routine practice, these platforms must be explicitly designed with a focus on clinical workflow integration[51].

As biomedical data continuously accumulates and AI technology advances, we can expect the predictive capabilities of AI models to improve correspondingly. One promising area of future development involves integrating AI with other emerging technologies, such as liquid biopsy and single-cell sequencing. Analyses of circulating nucleic acids, often called 'liquid biopsies', can monitor treatment response, evaluate drug resistance emergence, and measure minimal residual disease[52]. Compared to traditional bulk sequencing, single-cell sequencing can analyze HCC at single-cell resolution, accurately identify different cell types, and uncover the heterogeneity of HCC cells[53]. Lu *et al*[54] previously developed a new diagnostic model for HCC using single-cell RNA sequencing data and discovered that patients with high-risk scores were less likely to benefit from immunotherapy. Another area of exploration is AI's role in dynamic prediction models, which can monitor patient responses in real time and adjust predictions accordingly. This approach has the potential to result in more predictable outcomes and treatment strategies that are personalized and adaptable[55].

In the future, AI applications are expected to benefit from the development of more advanced algorithms capable of processing complex biological data, which includes genomics, proteomics, and metabolomics. The goal of these algorithms will be to identify novel biomarkers and molecular signatures that can predict immunotherapy response in HCC patients[56]. The effectiveness of immunotherapy often relies on the interaction of immunomodulation in the TME[57]. By integrating multi-omics data, we will gain a more comprehensive understanding of the TME and its interactions with the immune system[58,59]. In addition, AI is poised to play a critical role in the design and implementation of clinical trials for HCC immunotherapy by identifying patient subgroups that are more likely to benefit from specific treatments. This will help categorize participants and improve the results of trials (Figure 1).

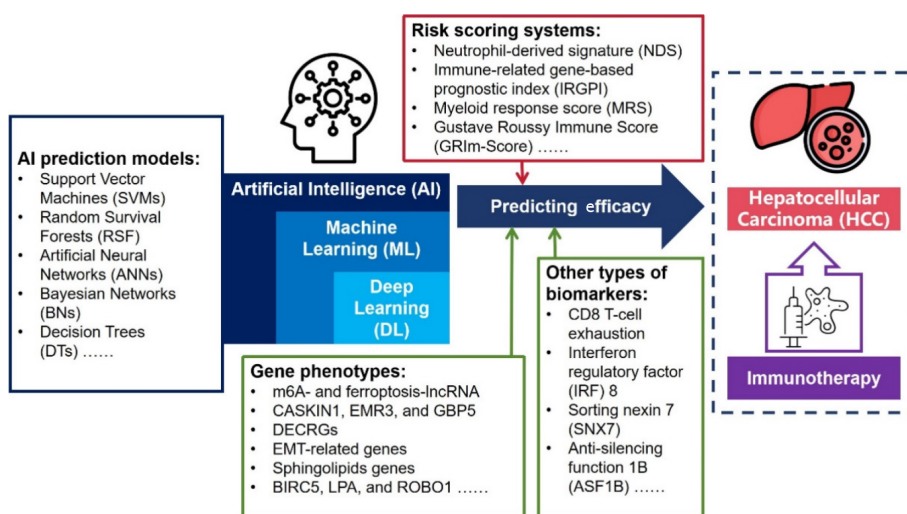


Figure 1 Schematic diagram of artificial intelligence in the prediction of immunotherapy efficacy in hepatocellular carcinoma. This

schematic diagram displays the application of artificial intelligence in the prediction of immunotherapy efficacy in hepatocellular carcinoma. It mentions several artificial intelligence prediction models closely connected to this article, along with risk scoring systems, gene phenotypes, and other types of biomarkers that have surfaced in recent research. AI: Artificial intelligence.

CONCLUSION

The current status of AI in predicting the efficacy of immunotherapy for HCC is marked by significant advancements and potential, tempered by challenges and considerations that must be addressed. The schematic diagram in **Figure 1** displays the application of AI in predicting the effectiveness of immunotherapy for HCC. As AI technology evolves and becomes more integrated into healthcare, it possesses the potential to transform HCC prognosis and treatment through personalized and precise predictions for immunotherapy.

FOOTNOTES

Author contributions: Zhang W and Zhang HJ have access to all the data in this study and take responsibility for the integrity and accuracy of the data analyses. Zhang HJ, Zhu G, and Chang RA study concept and design; Zhang W drafted the manuscript; Song LN revised the manuscript; You YF, Qi FN, Cui XH, and Yi MX supervised the study and provided modification suggestions; All authors have read and approved the final manuscript; Zhang W and Song LN contributed equally to this work.

Supported by the National Natural Science Foundation of China, No. 81401988; China Postdoctoral Science Foundation, No. 2019M661907; Jiangsu Postdoctoral Science Foundation, No. 2019K159, and No. 2019Z153; General Project of Jiangsu Provincial Health Committee, No. H2023136; General Project of Nantong Municipal Health Committee, No. MS2023013; Jiangsu Provincial Research Hospital, No. YJXY202204-YSB28; and College Student Innovation Program, No. 202210304128Y, and No. 2023103041055.

Conflict-of-interest statement: All authors certify that they have no conflicts of interest related to this work.

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S-Editor: Liu JH

L-Editor: Webster JR

P-Editor: Zhao YQ

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Scope and caveats: Artificial intelligence in gastroenterology

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

P-Reviewer: Soreq L, United Kingdom

Received: January 23, 2024

Peer-review started: January 23, 2024

First decision: February 6, 2024

Revised: February 18, 2024

Accepted: March 29, 2024

Article in press: March 29, 2024

Published online: April 30, 2024



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Abstract

The use of Artificial intelligence (AI) has evolved from its mid-20th century origins to playing a pivotal tool in modern medicine. It leverages digital data and computational hardware for diverse applications, including diagnosis, prognosis, and treatment responses in gastrointestinal and hepatic conditions. AI has had an impact in diagnostic techniques, particularly endoscopy, ultrasound, and histopathology. AI encompasses machine learning, natural language processing, and robotics, with machine learning being central. This involves sophisticated algorithms capable of managing complex datasets, far surpassing traditional statistical methods. These algorithms, both supervised and unsupervised, are integral for interpreting large datasets. In liver diseases, AI's non-invasive diagnostic applications, particularly in non-alcoholic fatty liver disease, and its role in characterizing hepatic lesions is promising. AI aids in distinguishing between normal and cirrhotic livers and improves the accuracy of lesion characterization and prognostication of hepatocellular carcinoma. AI enhances lesion identification during endoscopy, showing potential in the diagnosis and management of early-stage esophageal carcinoma. In peptic ulcer disease, AI technologies influence patient management strategies. AI is useful in colonoscopy, particularly in detecting smaller colonic polyps. However, its applicability in non-academic settings requires further validation. Addressing these issues is vital for harnessing the potential of AI. In conclusion, while AI offers transformative possibilities in gastroenterology, careful integration and balancing of technical possibilities with ethical and practical application, is essential for optimal use.

Key Words: Machine learning; Neural networks; Diagnosis; Work-flow; Ethics; Image; Polyps; Hepatoma

Core Tip: Artificial intelligence helps in the early identification, management and prognostication of gastrointestinal diseases through applications in endoscopy and histopathological interpretation. Proof of concept studies exist for all of these, but need validation by randomized clinical trials before they can be incorporated into clinical work flow.

Citation: Sridhar GR, Siva Prasad AV, Lakshmi G. Scope and caveats: Artificial intelligence in gastroenterology. *Artif Intell Gastroenterol* 2024; 5(1): 91607

URL: <https://www.wjgnet.com/2644-3236/full/v5/i1/91607.htm>

DOI: <https://dx.doi.org/10.35712/aig.v5.i1.91607>

INTRODUCTION

Artificial intelligence (AI) has origins dating back to the mid-20th century[1]. Its application, particularly in gastroenterology, has been more recent, being dependent on the availability of digital data and powerful computational hardware. AI is now used in diagnosing and predicting treatment responses for a spectrum of gastrointestinal and hepatic disorders [2-5].

AI encompasses multiple fields and is often defined as a computer's ability to perform tasks requiring human-like cognition[5], or as a machine that simulates complex human thinking[2].

In contrast to traditional statistical methods, AI processes data using a large number of variables and sophisticated formulas, making it possible to perform otherwise impractical analyses[2].

NOMENCLATURE AND CLASSIFICATION OF AI

AI broadly includes three areas: (1) Machine learning, which involves artificial neural networks, deep learning, and convolutional neural networks; (2) Natural language processing; and (3) Robotics. Machine learning techniques are principally used in gastroenterology[6].

Machine learning can be considered an advanced statistical approach to uncover relationships among various parameters; it utilizes algorithms such as linear regression for predicting relationships between variables, and classification algorithms like support vector machines and random forests for categorizing data.

Neural networks are more complex, utilizing nodes to determine calculated parameters, thereby allowing the use of intricate formulas. Deep learning networks, which are multi-layered, enable more advanced learning, are used in image processing[2].

Machine learning models are categorized into supervised and unsupervised. Supervised models label each sample, while unsupervised models aim to discover data structures without labels.

APPLICATIONS OF AI IN GASTROENTEROLOGY

AI's applications in gastroenterology promise to enhance patient care by reducing diagnostic errors[6]. They are employed in various conditions including gastritis, gastrointestinal bleeding, gastric malignancy, non-alcoholic fatty liver disease (NAFLD), cirrhosis, inflammatory bowel disease, colorectal polyps and cancer, and computer-aided endoscopy. Other potential applications include *Helicobacter pylori* infection, celiac disease, and pancreatic lesions[5]. A MEDLINE database search indicates that China and the USA are leading in AI research in this field[3].

LIVER DISEASES

In liver diseases, AI applications span from hepatocellular carcinoma to NAFLD, benign tumours, and viral hepatitis.

Non-invasive methods like ultrasound or transient elastography are used to identify NAFLD, now classified as metabolic dysfunction-associated steatohepatitis[7]. Probabilistic neural networks differentiate normal livers from those with cirrhosis in NAFLD patients, with the gold standard being liver biopsy. The area under the curve for this method ranges between 0.857 and 0.901[8]. AI also aids in automating histopathological examination, achieving high accuracy in characterizing alterations found in NAFLD[9]. Predictive models using multiple data sources, including electronic medical records, imaging, and biomarkers, have improved accuracy in identifying at-risk patients[10,11].

Hepatic mass lesions can be interpreted with high accuracy by the use of AI. Deep learning methods achieved receiver operating curves of 0.93 in lesion differentiation and 0.916 in characterization[12]. AI also aids in prognosticating established hepatocellular carcinoma[11] and predicting graft failure following liver transplantation[4].

However, when compared with standard scores, AI did not significantly improve the accuracy of short-term predictions for readmission and mortality risks in patients with cirrhosis[13].

ESOPHAGEAL LESIONS

AI methodologies improved the identification of suspicious lesions during upper GI endoscopy; this was reported in the differentiation of dysplasia and early neoplastic changes in Barrett's esophagus[14]. Other technologies such as white-light endoscopy/narrow band imaging, wide-area transepithelial sampling, and volumetric laser endomicroscopy lend themselves to machine learning[14]. As of 2020, AI algorithms were shown to be effective in diagnosing and thereby improving the outcomes of early-stage esophageal carcinoma.

ACID PEPTIC DISORDERS

In peptic ulcer disease, AI is useful in diagnosis, management, and complications[15]. *Helicobacter pylori*, a significant pathogenic factor, can be identified using AI. The first application was reported in 2004[16]; recent studies employ convoluted neural network models on large datasets, achieving high sensitivity, specificity, and accuracy[17].

AI also assists in diagnosing and differentiating peptic ulcers with wireless capsule endoscopic images by the use of deep learning[18,19]. It achieved an overall sensitivity of 89.7%. AI can also help identify infections, ulcers, polyps, and submucosal xanthomas[20,21].

For rare cases requiring surgical intervention, AI finds application in robot-assisted minimally invasive surgery, and in predicting complications like bleeding and perforation by the use of data from electronic medical records[15,22].

COLONOSCOPY

AI aids in classifying structures and has notably improved polyp detection rates, particularly in identifying polyps less than 5cm in size[2]; these are often missed by conventional procedures.

AI is also effective in grading remission of ulcerative colitis[23,24] and in assessing video capsule endoscopy for ulcers and bleeding detection, which is a time-consuming task[25].

However, mixed results were reported for polyp detection using computer-aided endoscopy in non-academic community-based practice[26], indicating the need for further studies[27].

PROS AND CONS OF AI IN GASTROENTEROLOGY

The potential of AI to enhance quality of care is significant, but integration into clinical workflows remains a challenge [28]. In specific tasks, AI-based devices match or even surpass expert gastroenterologists in identifying and differentiating neoplasms in the gastrointestinal tract. However, for adoption into routine clinical practice, randomized trial validation is necessary[28].

Other factors such as disease prevalence, physician competence, and human-machine interaction also affect AI's clinical benefit[29]. Despite the availability of commercial AI tools in the USA and Europe, their integration into clinical workflows is still a work in progress before the full potential is realized[30].

ETHICAL AND LEGAL ASPECTS

The growing use of AI in clinical practice brings ethical and legal challenges such as data privacy and security, method reliability and safety, and ensuring fairness, inclusivity, transparency, and accountability[31]. The extent of reliance on AI for decision-making is a key consideration[28], given that the ultimate responsibility rests on the end user, viz the physician.

AI has the potential for bias in clinical problem selection, variable choices, algorithm development, and system use [32]. In gastroenterology, as in other fields, training sets must be inclusive and diverse to avoid bias in diagnosing diseases with varying prevalence rates.

To mitigate potential biases, health equity goals should be incorporated early in algorithm development by involving technically diverse research teams. Regulatory standards should include pre-deployment audits to ensure algorithmic performance equality[32].

CONCLUSION

AI in gastroenterology has primarily been applied in endoscopic image analysis, radiology, and histopathology to aid in early detection of lesions and appropriate treatment. While its role in diagnostic endoscopy is expanding, evidence for improved clinical outcomes in real-life scenarios remains to be established.

Issues surrounding human-machine interaction, AI integration into clinical culture and practice, and the balance between AI-assisted management and practitioner skill maintenance need to be addressed[33]. Generative AI, such as ChatGPT, launched in late November 2022[34], has become pervasive in medicine, including gastroenterology. While beneficial in diagnosis in complex scenarios[35], privacy and legal concerns arise, especially when scientific publications could eventually heavily rely on AI-generated results[36].

ACKNOWLEDGEMENTS

We thank Mr Venkat Yarabati for assistance in the preparation of this manuscript.

FOOTNOTES

Author contributions: All three authors contributed to this manuscript; Sridhar GR designed the concept and outline; Siva Prasad AV provided inputs to the discussion and design; Lakshmi G contributing to the writing and editing of the manuscript.

Conflict-of-interest statement: The authors declare no conflict of interest.

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S-Editor: Gong ZM

L-Editor: A

P-Editor: Zhao YQ

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Observational Study

Evaluating the accuracy and reproducibility of ChatGPT-4 in answering patient questions related to small intestinal bacterial overgrowth

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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 classification****Scientific Quality:** Grade C, Grade C, Grade C, Grade D, Grade D**Novelty:** Grade A, Grade B, Grade B, Grade B, Grade B**Creativity or Innovation:** Grade A, Grade B, Grade B, Grade B, Grade B**Scientific Significance:** Grade B, Grade B, Grade B, Grade B, Grade C**P-Reviewer:** Caboclo JLF, Brazil;

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Received: December 7, 2023**Revised:** March 27, 2024**Accepted:** April 16, 2024**Published online:** April 30, 2024**Lauren Schlusell, Jamil S Samaan, Yin Chan, Bianca Chang, Yee Hui Yeo, Ali Rezaie**, Division of Gastroenterology and Hepatology, Cedars-Sinai Medical Center, Los Angeles, CA 90048, United States**Wee Han Ng**, Bristol Medical School, University of Bristol, BS8 1TH, Bristol, United Kingdom**Ali Rezaie**, Medically Associated Science and Technology Program, Cedars-Sinai Medical Center, Los Angeles, CA 90048, United States**Corresponding author:** Ali Rezaie, MD, MSc, FRCPC, Medical Director, Medically Associated Science and Technology Program, Cedars-Sinai Medical Center, Cedars-Sinai, 8730 Alden Drive, Thalians Bldg, #E240, Los Angeles, CA 90048, United States. Ali.rezaie@cshs.org

Abstract

BACKGROUND

Small intestinal bacterial overgrowth (SIBO) poses diagnostic and treatment challenges due to its complex management and evolving guidelines. Patients often seek online information related to their health, prompting interest in large language models, like GPT-4, as potential sources of patient education.

AIM

To investigate ChatGPT-4's accuracy and reproducibility in responding to patient questions related to SIBO.

METHODS

A total of 27 patient questions related to SIBO were curated from professional societies, Facebook groups, and Reddit threads. Each question was entered into GPT-4 twice on separate days to examine reproducibility of accuracy on separate occasions. GPT-4 generated responses were independently evaluated for accuracy and reproducibility by two motility fellowship-trained gastroenterologists. A third senior fellowship-trained gastroenterologist resolved disagreements. Accuracy of responses were graded using the scale: (1) Comprehensive; (2) Correct but inadequate; (3) Some correct and some incorrect; or (4) Completely incorrect. Two responses were generated for every question to evaluate reproducibility in accuracy.

RESULTS

In evaluating GPT-4's effectiveness at answering SIBO-related questions, it provided responses with correct information to 18/27 (66.7%) of questions, with 16/27 (59.3%) of responses graded as comprehensive and 2/27 (7.4%) responses graded as correct but inadequate. The model provided responses with incorrect information to 9/27 (33.3%) of questions, with 4/27 (14.8%) of responses graded as completely incorrect and 5/27 (18.5%) of responses graded as mixed correct and incorrect data. Accuracy varied by question category, with questions related to "basic knowledge" achieving the highest proportion of comprehensive responses (90%) and no incorrect responses. On the other hand, the "treatment" related questions yielded the lowest proportion of comprehensive responses (33.3%) and highest percent of completely incorrect responses (33.3%). A total of 77.8% of questions yielded reproducible responses.

CONCLUSION

Though GPT-4 shows promise as a supplementary tool for SIBO-related patient education, the model requires further refinement and validation in subsequent iterations prior to its integration into patient care.

Key Words: Small intestinal bacterial overgrowth; Motility; Artificial intelligence; Chat-GPT; Large language models; Patient education

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Core Tip: ChatGPT-4 demonstrates promise in enhancing patient understanding of basic concepts related to small intestinal bacterial overgrowth (SIBO). However, it exhibits limitations in accurately addressing questions about the diagnosis and treatment of SIBO, which are areas where up-to-date medical guidance is crucial. As such, artificial intelligence can be beneficial for general patient education but should not replace professional medical advice, especially for conditions with complex care protocols. Continuous refinement and updating of Chat-GPT's knowledge are essential for its safe and effective application in healthcare. Rigorous scrutiny of artificial intelligence-generated content is imperative to prevent the dissemination of potentially harmful misinformation.

Citation: Schlussel L, Samaan JS, Chan Y, Chang B, Yeo YH, Ng WH, Rezaie A. Evaluating the accuracy and reproducibility of ChatGPT-4 in answering patient questions related to small intestinal bacterial overgrowth. *Artif Intell Gastroenterol* 2024; 5(1): 90503

URL: <https://www.wjgnet.com/2644-3236/full/v5/i1/90503.htm>

DOI: <https://dx.doi.org/10.35712/aig.v5.i1.90503>

INTRODUCTION

Small intestinal bacterial overgrowth (SIBO) is a medical condition characterized by an excessive amount of bacteria in the small intestine, which can lead to a variety of symptoms, including bloating, abdominal pain, diarrhea, and constipation[1]. The diagnosis and treatment of SIBO varies across institutions and by healthcare provider[2]. Though various tests exist, including glucose and lactulose breath tests and small intestine aspiration and culture, there is a lack of universal approach regarding how and when to utilize these tests, as well as how to interpret the results[3].

Due to the need for specialized tests, lack of dedicated International Classification of Diseases codes, and differences in the diagnostic methods across studies, it is challenging to estimate the prevalence of SIBO with studies showing rates ranging from 4% to 79%[2] and 38% to 84% in patients with IBS[4]. Importantly, SIBO has adverse effects on quality of life and may be associated with significant healthcare costs. Though the impact on quality of life for patients with SIBO has not been independently examined, one study showed that the presence of SIBO among patients with IBS was associated with more severe symptoms and led to a decreased quality of life[5]. Patients with IBS constitute a major proportion of patients who seek consultation in gastroenterology specialist clinic[6] and is associated with considerable healthcare resource use[7]. Given the high prevalence of SIBO among patients with IBS and its association with more severe symptoms, it's very likely that SIBO has a significant impact on patients and our healthcare system. Moreover, patients have limited access to motility specialists or physicians that are capable of managing SIBO, and may even encounter health care providers that question the legitimacy of SIBO as a medical condition[8].

The advent of artificial intelligence (AI) and natural language processing technologies has led to the development of large language models (LLMs), such as ChatGPT, which have the potential to revolutionize healthcare communication and patient education[9]. GPT-4, created by OpenAI, is able to produce easy to understand and conversational responses to inquiries by users based on their inquiries. It functions on the principle of predicting subsequent words in a sentence, much akin to an expert player in a game of 'guess the next word'[9]. There is a growing body of evidence demonstrating ChatGPT's ability to answer patient questions related to medical diseases such as cardiovascular disease, bariatric surgery and cirrhosis[10-12]. In a study comparing chatbot and physician responses, evaluators preferred chatbot answers 78.6% of the time[10]. The chatbot's responses were not only more comprehensive but also of higher quality and more empa-

thetic, with a 3.6 times higher prevalence of good or very good quality answers and a 9.8 times higher prevalence of empathetic or very empathetic responses than physicians[10]. Given the increasing trends of patients seeking healthcare related information from online sources, examining the strengths and limitations of LLMs as sources of information for patients is critical to ensuring safe, effective and responsible use of these models[13].

SIBO is a complex medical condition, with differing diagnostic and treatment approaches across institutions and healthcare providers as well as geographic variations in access to specialists. The gap in patient needs versus accessibility may lead individuals to seek information from alternative sources, such as the internet or ChatGPT. If proven safe and effective, emerging AI technologies like ChatGPT offer potential benefits in this space, providing accessible, easy to understand, and informed responses to patient inquiries, which may supplement or complement patient education provided by licensed healthcare professionals. In light of this, our study aimed to evaluate the accuracy of GPT-4 in providing accurate and reproducible responses to patient questions related to SIBO. This involved assessing the quality of information provided by the AI tool against evidence-based guidelines and expert opinions. Furthermore, our research will identify the limitations and potential risks associated with using GPT-4 as a supplementary tool for patient education and support, in order to inform the development of best practices for its implementation in the healthcare context.

MATERIALS AND METHODS

Question curation

A total of 38 patient questions related to SIBO were collected from professional societies and institutions as well as Facebook support groups ("SIBO lifestyle", "SIBO SOS Community") and the Reddit thread r/SIBO. Each question was screened to ensure it was directly related to SIBO. Questions that were not specific to SIBO or were outside the scope of typical patient concerns were excluded. Duplicate and similar questions were excluded to prevent redundancy and to ensure a broad coverage of topics. One question was removed after it was deemed incorrectly worded and containing incorrect information. The final set of 27 questions included in our study represents a diverse range of patient inquiries, covering aspects of basic knowledge, diagnosis, treatment, and other concerns related to SIBO.

ChatGPT

ChatGPT is an AI LLM developed by OpenAI, based on the GPT (Generative Pre-trained Transformer) architecture. The model was designed to generate human-like text based on input, allowing the model to answer questions, engage in conversation, and perform various tasks. ChatGPT was trained on a large corpus of text from the internet, learning grammar, facts, and some reasoning abilities. It does not have a traditional "database" to retrieve information from; instead, the model generates text based on patterns and knowledge learned from the training data. However, it is essential to note the model's knowledge is limited to data up until September 2021, lacking awareness of more recent information. The latest iteration of the model, GPT-4, was released in March of 2023 and has shown promise across multiple domains of tasks[14].

Response generation

GPT-4 was used on 4/23/23 and 4/24/23 to generate responses. Each question was entered as an individual prompt using the "New Chat" function. Each question was entered into GPT-4 twice on separate days to examine reproducibility of accuracy on separate occasions.

Response grading

Responses to questions were first independently graded for accuracy and reproducibility by two board certified, motility fellowship-trained, academic gastroenterologist reviewers actively practicing in a tertiary medical center. The following grading scale was used to grade the accuracy of each response similar to previous publications[11,12]: (1) Comprehensive (Grade 1): The response provides a complete and thorough answer as one would expect from a board-certified gastroenterologist. This grade implies that there is no additional relevant information that a specialist would deem necessary to include; (2) Correct but inadequate (Grade 2): The response is accurate but lacks certain critical details or depth that a board-certified gastroenterologist would consider important for a patient's understanding or management of SIBO; (3) Some correct and some incorrect (Grade 3): The response contains both correct and incorrect elements, indicating partial knowledge but with significant gaps or errors that require correction; and (4) Completely incorrect (Grade 4): The response does not provide accurate information related to the question asked and is considered misleading or wrong.

Reproducibility was graded based on the similarity in accuracy of the two responses per question generated by GPT-4. Any disagreement in reproducibility or accuracy grading was resolved by a third senior board-certified, motility fellowship trained gastroenterologist reviewer with greater than 10 years of experience in the field of gastrointestinal motility.

Statistical analysis

Descriptive analysis is presented as counts and percentages. For statistical analysis purposes, questions were categorized into multiple subgroups: Basic knowledge, diagnosis, treatment, and others. All statistical analysis was performed in Excel version 2308.

RESULTS

In total, 27 questions related to SIBO were inputted into GPT-4. The model provided 16/27 (59.3%) comprehensive, 2/27 (7.4%) correct but inadequate, 5/27 (18.5%) mixed with correct and incorrect data, and 4/27 (14.8%) completely incorrect responses. When examined by category, the model provided "comprehensive" responses to 90% of "basic knowledge questions", 60% of "diagnosis" questions, and 33.3% of "treatment" questions (Table 1). The model provided reproducible responses to 21/27 (77.8%) of questions (Table 2).

Most of the "completely incorrect" responses were noted to be in the "treatment" subcategory with 33.3% (3/9) of these responses rated as "completely incorrect". For example, when asked "What probiotic strain is recommended for constipation predominant SIBO?" GPT-4 stated that there is evidence that shows certain strains of probiotics helps constipation, which is not in line with current evidence and guidelines. Importantly, the model did recommend consulting with a health professional before starting new supplements. Questions, responses, and reviewer gradings are shown in [Supplementary Table 1](#).

DISCUSSION

SIBO is a common medical condition with variable approaches to management and diagnosis across institutions. The literature shows patients frequently pursue health-related information in lieu of their healthcare providers, with the internet emerging as a common source. Due to its user-friendly interface as well as its easy to understand and conversational responses, patients may utilize ChatGPT as a source of information regarding SIBO. In light of this, we examined ChatGPT's ability to accurately and reliably answer SIBO related questions. While the model provided comprehensive answers to 59.3% of questions, 14.8% of questions were graded as completely incorrect. Our findings show GPT-4's promising future in serving as an adjunct source of information for patient with SIBO but highlight its current limitations and need for further fine tuning, training and validation prior to incorporation into clinical care.

The model provided completely inaccurate responses to 4 (14.8%) questions and mixed correct and incorrect information to 5 (18.5%) questions, which is not in line with previous data which shows its proficiency in areas such as cirrhosis, congestive heart failure, and bariatric surgery[11,12,15]. For example, GPT-3.5 provided comprehensive responses to 86.8% of questions related to bariatric surgery and 83.2% of questions related to heart failure[11,15]. The reason for the difference in performance seen in our study may be related to the dataset used to train ChatGPT. There are well-established, thoroughly researched, and widely accepted guidelines governing the diagnosis and treatment of these conditions. Such robust guidelines offer a standardized framework, enabling ChatGPT to provide accurate and reliable responses. SIBO, however, presents a unique challenge due to its less definitive guidelines that often diverge across institutions and among physicians. Further compounding this issue is ChatGPT's knowledge constraints to information prior to 2021, restricting its ability to integrate the latest studies or consensus in the rapidly evolving field of SIBO and gut microbiome. This data limitation, paired with the inherent variability in SIBO management, showcases the system's vulnerabilities in areas where medical guidelines are either in flux or less established. Considering our analysis shows a considerable number of responses contained incorrect and potentially harmful information, this underscores the importance of exercising caution when utilizing AI-generated information in the context of patient education, particularly related to complex medical conditions like SIBO. Ongoing refinement and development of LLMs are imperative to mitigate the potential risks and enhance their potential role in patient education.

GPT-4 also showed a relatively low reproducibility, only delivering consistent accuracy of responses for 77.8% of questions. This again is in contrast with previous studies which found LLMs deliver high reproducibility of quality of responses[10-12]. Such reproducibility is critical for a tool intended to educate and inform, as consistent messaging is key in enhancing understanding, mitigating confusion and establishing trust among users.

Examining GPT-4's accuracy across different domains of patient questions allowed for a more granular analysis of its performance. In line with previous studies examining ChatGPT's knowledge in cirrhosis and hepatocellular carcinoma, bariatric surgery, and heart failure[11,12,15], we found GPT-4 provided comprehensive and accurate responses to the vast majority of basic knowledge questions. This suggests that AI has the potential to serve as a reliable resource of information for patients to enhance their basic understanding of their condition. Such an application aligns with a growing body of evidence pointing to the potential of AI in augmenting patient education[16]. However, our findings also underscore key limitations of this technology. Most notably, GPT-4's responses related to the diagnosis and treatment of SIBO contain a significant amount of inaccuracies. This finding is particularly concerning given that these areas often present the greatest challenges for patients in terms of understanding and self-management. Misinformation can lead to suboptimal patient decision-making and potential harm. It underlines the importance of caution when using AI for health-related advice and re-emphasizes the need for these tools to be used in tandem with professional medical guidance[9]. This suggests that while LLMs like GPT-4 in their current form may provide beneficial support for patients looking to enhance their general understanding of a condition, they are not yet equipped to offer reliable advice on more complex aspects of medical care. It is consistent with prior research noting the limitations of AI in understanding complex diseases and suggesting tailored, expert human intervention for such scenarios[17,18].

Beyond accuracy, comprehensiveness, and reproducibility, it's important to ensure LLMs produce materials that are easy to understand by patients of all health literacy levels. There is a growing body of literature showing LLMs are able to adjust the readability of outputs when prompted[19,20]. This ensures that access to information is democratized, and patients of all health literacy levels have personalized education materials. One study showed that GPT-4 was able to improve the readability of bariatric surgery patient education materials from 12th grade-college level to 6th-9th grade[19].

Table 1 Grading of responses generated by ChatGPT-4 to questions related to small intestinal bacterial overgrowth categorized by subgroup and overall

	%
Basic knowledge (<i>n</i> = 10)	
Comprehensive	90
Correct but inadequate	10
Mixed with correct and incorrect data	0
Completely incorrect	0
Diagnosis (<i>n</i> = 5)	
Comprehensive	60
Correct but inadequate	0
Mixed with correct and incorrect data	40
Completely incorrect	0
Treatment (<i>n</i> = 9)	
Comprehensive	33.3
Correct but inadequate	0
Mixed with correct and incorrect data	33.3
Completely incorrect	33.3
Other (<i>n</i> = 3)	
Comprehensive	33.3
Correct but inadequate	33.3
Mixed with correct and incorrect data	0
Completely incorrect	33.3
Overall (<i>n</i> = 27)	
Comprehensive	59.3
Correct but inadequate	7.4
Mixed with correct and incorrect data	18.5
Completely incorrect	14.8

Table 2 Reproducibility of ChatGPT-4 responses overall and categorized by subgroup

	%
Overall (<i>n</i> = 27)	77.8
Basic knowledge (<i>n</i> = 10)	90
Diagnosis (<i>n</i> = 5)	80
Treatment (<i>n</i> = 9)	77.8
Other (<i>n</i> = 3)	33.3

Access to high quality patient education materials can also be impacted by patient language preference. Patients who prefer non-English languages have unique barriers to access to patient education materials. Some studies have shown the ability of LLMs in generating patient education materials in languages other than English with promising results[21-23]. Lastly, it's important to ensure outputs do not perpetuate known stereotypes and biases in medicine. There is a growing body of literature examining the presence of implicit bias in LLM outputs, with some studies showing LLMs may propagate racial and gender biases[24,25]. Future research should thoroughly investigate how LLMs can produce patient education materials that are not only accurate and of high quality but also accessible to patients from diverse backgrounds, with an emphasis on minimizing implicit bias and discrimination.

Limitations specific to the design of this study include the use of only two responses generated by GPT-4 to evaluate its reproducibility. While our findings provide initial insights, expanding the number of responses and questions in future research will be crucial to thoroughly assess consistency and reliability. Such expansions will help to substantiate the AI model's utility in patient education. Another limitation of this study is the use of the paid GPT-4 model over the free GPT-3.5, which was selected for its advanced linguistic capabilities and enhanced accuracy in medical contexts. While this choice aligns with our objective to evaluate the most current and sophisticated AI technology for patient education, it may affect the generalizability and accessibility of our findings. Future research could explore the trade-offs between cost and performance by comparing different AI models, including the cost-free GPT-3.5, to optimize the balance between accessibility and quality of information in AI-assisted patient care. Future studies would also benefit from exploring the differences in accuracy and reproducibility amongst different AI tools such as GPT-3.5, GPT-4, and Google Bard. For example, in a study comparing GPT-4 and Google Bard in their ability to diagnose and triage patients' ophthalmologic complaints, GPT-4 performed significantly better than Bard by generating more accurate triage suggestions, responses that experts were satisfied with for patient use, and lower potential harm rates[26]. Another study comparing GPT-3.5 and Bard in their ability to provide appropriate informational responses to patient questions regarding vascular surgery demonstrated that GPT-3.5 responses were more complete and more appropriate compared with Bard responses[27]. Similarly, GPT-3 exhibited greater accuracy and consistency over Google Bard, as well Google and Bing search engines, when addressing patient questions related to lung cancer[28]. These comparative evaluations underscore the evolving landscape of AI tools in healthcare and the importance of ongoing, meticulous analysis to harness their full potential for patient care.

Finally, we must consider other limitations of ChatGPT that pose a challenge for its future utilization in healthcare. OpenAI has not released specific details about the exact datasets used to train GPT-4. This raises concerns regarding the quality of data the model uses to respond to questions, especially when discussing healthcare related topics. The literature in healthcare is rapidly evolving and requires staying up to date with the literature to ensure good practice of medicine. ChatGPT's lack of continuous updates limits its generalized applicability in patient care. Another constraint of GPT-4 and LLMs in general is the "hallucination effect," where the model produces outputs that seem plausible and believable but are incorrect, misleading, or entirely fabricated[29,30]. This is a significant limitation that should be considered when implementing such AI tools in the healthcare setting. Our study design also has its limitations. Responses from ChatGPT were graded based on expert opinion which is subjective and prone to bias. Notably, this is a limitation across the majority of literature examining the clinical knowledge of ChatGPT, given expert opinion guided by the literature and guidelines is currently the gold standard in the practice of medicine. Our study utilized a sample of 27 patient questions, which is not inclusive of all possible patient questions pertaining to SIBO. We performed a systematic approach when curating questions to reduce the risk of selection bias. Furthermore, questions were not removed after the generation of responses from ChatGPT.

CONCLUSION

Our study underscores the potential future value of large language models, like GPT-4, in patient education related to SIBO, especially in providing basic knowledge. However, we highlight the limitations of GPT-4 in its current form due to a significant number of its responses containing inaccurate or out of date information and low reproducibility in accuracy of its responses. While AI may supplement traditional patient education methods in the future, it is not a substitute for professional medical advice. Continued evaluation and development of these technologies are crucial to harness their potential while minimizing potential harm. This iterative process will be key to the future integration of AI into healthcare systems, with the ultimate aim of improving patient understanding, engagement, and outcomes. Our research underscores the need for rigorous scrutiny and cautious application when relying on AI technologies for diseases with complex and less standardized diagnosis and treatments. Given the prevalence and impact of SIBO on patients and the healthcare system, the need for accurate, accessible patient education remains critical. Our research serves as a valuable step in identifying the challenges and opportunities for integrating AI tools in this capacity.

FOOTNOTES

Author contributions: Rezaie A was the guarantor, participated in the acquisition, analysis, and interpretation of the data, and revised the article for critically important intellectual content; Schlussel L drafted the initial manuscript and participated in the acquisition, analysis, and interpretation of the data; Samaan J designed the study and revised the article for critically important intellectual content; Chan Y and Chang B participated in the acquisition, analysis, and interpretation of the data, and revised the article for critically important intellectual content; Yeo YH revised the article for critically important intellectual content; Ng WH participated in the acquisition, analysis, and interpretation of the data.

Institutional review board statement: Our study did not require IRB approval, given our research does not involve human subjects.

Informed consent statement: Our research does not involve human subjects. Therefore, no signed informed consent or documents were obtained.

Conflict-of-interest statement: All the authors declare that they have 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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S-Editor: Liu JH

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Artificial Intelligence in *Gastroenterology*

Quarterly Volume 5 Number 2 August 8, 2024





Artificial Intelligence in Gastroenterology

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Quarterly Volume 5 Number 2 August 8, 2024

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MINIREVIEWS

Mubarak M, Rashid R, Sapna F, Shakeel S. Expanding role and scope of artificial intelligence in the field of gastrointestinal pathology. *Artif Intell Gastroenterol* 2024; 5(2): 91550 [DOI: [10.35712/aig.v5.i2.91550](https://doi.org/10.35712/aig.v5.i2.91550)]

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Artificial Intelligence in Gastroenterology
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AIMS AND SCOPE

The primary aim of *Artificial Intelligence in Gastroenterology* (AIG, *Artif Intell Gastroenterol*) is to provide scholars and readers from various fields of artificial intelligence in gastroenterology with a platform to publish high-quality basic and clinical research articles and communicate their research findings online.

AIG mainly publishes articles reporting research results obtained in the field of artificial intelligence in gastroenterology and covering a wide range of topics, including artificial intelligence in gastrointestinal cancer, liver cancer, pancreatic cancer, hepatitis B, hepatitis C, nonalcoholic fatty liver disease, inflammatory bowel disease, irritable bowel syndrome, and *Helicobacter pylori* infection.

INDEXING/ABSTRACTING

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

RESPONSIBLE EDITORS FOR THIS ISSUE

Production Editor: *Yun-Qing Zhao*; Production Department Director: *Xu Guo*; Cover Editor: *Jin-Lei Wang*.

NAME OF JOURNAL

Artificial Intelligence in Gastroenterology

ISSN

ISSN 2644-3236 (online)

LAUNCH DATE

July 28, 2020

FREQUENCY

Quarterly

EDITORS-IN-CHIEF

Rajvinder Singh, Ferruccio Bonino

EDITORIAL BOARD MEMBERS

<https://www.wjgnet.com/2644-3236/editorialboard.htm>

PUBLICATION DATE

August 8, 2024

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STEPS FOR SUBMITTING MANUSCRIPTS

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ONLINE SUBMISSION

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Will artificial intelligence reach any limit in gastroenterology?

Joseph Bou Jaoude, Rose Al Bacha, Bassam Abboud

Specialty type: Gastroenterology and hepatology

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

Peer-review model: Single blind

Peer-review report's classification

Scientific Quality: Grade C

Novelty: Grade C

Creativity or Innovation: Grade C

Scientific Significance: Grade C

P-Reviewer: Yu HG, China

Received: December 27, 2023

Revised: April 25, 2024

Accepted: June 7, 2024

Published online: August 8, 2024

Processing time: 225 Days and 1.3 Hours



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Abstract

Endoscopy is the cornerstone in the management of digestive diseases. Over the last few decades, technology has played an important role in the development of this field, helping endoscopists in better detecting and characterizing luminal lesions. However, despite ongoing advancements in endoscopic technology, the incidence of missed pre-neoplastic and neoplastic lesions remains high due to the operator-dependent nature of endoscopy and the challenging learning curve associated with new technologies. Artificial intelligence (AI), an operator-independent field, could be an invaluable solution. AI can serve as a “second observer”, enhancing the performance of endoscopists in detecting and characterizing luminal lesions. By utilizing deep learning (DL), an innovation within machine learning, AI automatically extracts input features from targeted endoscopic images. DL encompasses both computer-aided detection and computer-aided diagnosis, assisting endoscopists in reducing missed detection rates and predicting the histology of luminal digestive lesions. AI applications in clinical gastrointestinal diseases are continuously expanding and evolving the entire digestive tract. In all published studies, real-time AI assists endoscopists in improving the performance of non-expert gastroenterologists, bringing it to a level comparable to that of experts. The development of DL may be affected by selection biases. Studies have utilized different AI-assisted models, which are heterogeneous. In the future, algorithms need validation through large, randomized trials. Theoretically, AI has no limit to assist endoscopists in increasing the accuracy and the quality of endoscopic exams. However, practically, we still have a long way to go before standardizing our AI models to be accepted and applied by all gastroenterologists.

Key Words: Artificial intelligence; Digestive tract; Gastroenterology; Gastroscopy; Colonoscopy

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Core Tip: The field of gastrointestinal endoscopy is an essential tool in the management of digestive diseases. Despite ongoing advancements in endoscopic technology, the incidence of missed pre-neoplastic and neoplastic lesions remains high. This is attributed to the operator-dependent nature of endoscopy, resulting in variability in detection rates and the characterization of lesions among endoscopists. To enhance endoscopic performance, it is imperative to minimize the "cognitive errors" made by the endoscopist. Artificial Intelligence, being operator-independent, could potentially serve as an unlimited solution.

Citation: Bou Jaoude J, Al Bacha R, Abboud B. Will artificial intelligence reach any limit in gastroenterology? *Artif Intell Gastroenterol* 2024; 5(2): 91336

URL: <https://www.wjgnet.com/2644-3236/full/v5/i2/91336.htm>

DOI: <https://dx.doi.org/10.35712/aig.v5.i2.91336>

INTRODUCTION

The field of gastrointestinal (GI) endoscopy (GE) is an essential tool in the management of digestive diseases. Technology is essential for the advancement of endoscopy. Presently, white-light endoscopy (WLE) with high resolution stands as the standard technology that enables endoscopists to detect and characterize lesions more accurately. However, despite this, even expert endoscopists can overlook several lesions, including small and flat ones.

To morphologically predict the malignant potential of digestive lesions in real-time, several classification systems have been endorsed by scientific societies. These systems categorize lesions based on morphology (sessile, slightly raised, or excavated) or through a detailed examination of vascular and mucosal patterns using optical image-enhancing technology known as virtual chromo-endoscopy. Consequently, the assessment of invasion depth or lymph node involvement plays a crucial role in clinical decision-making, determining whether the lesion is surgically or endoscopically resectable.

Despite the ongoing development of endoscopic technology, the incidence of missed pre-neoplastic and neoplastic lesions remains high. This is attributed to the operator-dependent nature of endoscopy, resulting in variability in detection rates and the characterization of lesions among endoscopists. The existence of this skills gap can be explained by the extended learning curve associated with adopting new technologies.

To enhance the performance of the endoscopic procedure, it is imperative to minimize the "cognitive errors" made by the endoscopist. Artificial intelligence (AI), being operator-independent, could potentially serve as an unlimited solution.

As endoscopy fundamentally depends on high-quality images, it presents an appealing domain for AI, which comprises computer processes performing complex tasks to simulate the human brain. Alan Turing, one of AI's founders, defined it as "the ability of a computer to achieve human performance in cognitive tasks". Thus, this concept combined the fields of medical knowledge and machine tools. Deep learning (DL) was innovated as a major transformation of machine learning (ML), allowing machines to learn and make decisions independently. DL automatically extracts input features from targeted images, demonstrating the ability to explore all pixels without experiencing transitory lapses in attention or fatigue. As a result, DL emerges as a promising technology, serving as a reliable "second observer" independent of the endoscopist's performance. DL encompasses two primary tasks: real-time detection or computer-aided detection (CADE) and real-time characterization or computer-aided diagnosis (CADx). Given that navigation software enhances mucosal exposure, CADE assists endoscopists in reducing the miss rate of lesion detection. Simultaneously, CADx aims to predict the histologic and optical diagnosis of pre-neoplastic lesions without the need for biopsy, as well as estimating the depth of invasion in malignant lesions to facilitate optimal therapeutic decision-making.

Moreover, DL can reduce the cost and the procedure time by abandoning random biopsies in favor of targeted ones and avoiding unnecessary resection of non-neoplastic lesions. DL can also evaluate the quality of endoscopic procedures by identifying parameters such as land marks, blind spots, measurement of withdrawal speed and mucosal cleansing assessment, making surveillance protocols more effective.

Thus, AI allows human-machine interaction, transferring expert knowledge to the entire gastroenterological community.

AI APPLICATIONS IN DIAGNOSTIC GE

AI applications in clinical GI diseases are continuously expanding and evolving into new areas. AI is embraced for its robust self-learning capability and unbiased nature. Real-time AI assists endoscopists throughout the entire digestive tract, including the upper, middle, and lower parts, as well as the hepato-biliary tree and pancreatic gland.

LOWER GI TRACT

Colorectal polyps

In the GI field, the primary application of AI involves DL convolution neural network (CNN) models for detecting and diagnosing polyps during colonoscopy.

Detection of colorectal polyps using CADe: It has been established that the removal of pre-neoplastic polyps reduces the risk of colorectal cancer (CRC). However, endoscopy is operator-dependent, and the adenoma detection rate (ADR) varies widely from 7% to 53% among colonoscopists[1] while post-colonoscopy interval CRC constitutes nearly 8% of all diagnosed CRC[2]. The initial application of AI technology in GE was the detection of colorectal polyps, with most research focusing on the management of colorectal polyps. In 2018, Urban *et al*[3] and Misawa *et al*[4] reported the two earliest applications of CADe on video clips. Their algorithms demonstrated an accuracy of $\geq 90\%$. In 2019, Wang *et al*[5] conducted the first randomized controlled trial. Since then, numerous prospective randomized controlled trials[6-10], as well as meta-analyses[11], have been published, involving different AI systems and training. Consequently, CADe for polyp detection has been shown to increase the ADR, at least comparable to that assessed by experienced endoscopists, as recommended by the European Society of Gastrointestinal Endoscopy (ESGE) guidelines[12].

Characterization of colorectal polyps using CADx (polyp ≤ 5 mm): According to the current ESGE guidelines, polyps ≤ 5 mm with adenomatous structures need to be removed and sent for histopathological analysis. Diminutive polyps located in the recto-sigmoid, characterized as hyperplastic by virtual chromo-endoscopy, can either be "left in situ" or undergo the "resect and discard" approach. CADx tools, when combined with CADe, can assist endoscopists in real-time colonoscopy by distinguishing between neoplastic (adenoma or serrated) and non-neoplastic (hyperplastic) polyps. Consequently, in the case of non-neoplastic polyps, the "diagnose and leave" strategy reduces the need for polypectomy. Similarly, for neoplastic diminutive polyps, the "resect and discard" strategy minimizes the necessity for histopathological processing. In clinical practice, these two strategies, supported by CADe systems, contribute to reduced costs and procedure time. Indeed, many centers have developed CADx tools with WLE, narrow-band imaging (NBI), and endocytoscopy[13-15]. Their published results align with the parameters outlined by the American Society of Gastrointestinal Endoscopy Preservation and Incorporation of Valuable Endoscopic Innovation (PIVI).

Advanced subtle neoplastic (flat and serrated)

The increased detection of non-advanced adenomas alone cannot reduce the interval CRC. Consequently, developing AI systems to enhance the detection of advanced polyps is now considered a priority, as they pose the highest risk of developing CRC. Most CADx studies lack data about sessile serrated lesions (SSL) and flat polyps. When SSL are described, the majority is located in the recto-sigmoid and is diminutive. Only one recent prospective study, utilizing video datasets enriched with flat, SSL, and advanced colorectal polyps, evaluated AI performance against endoscopists. The AI-based algorithm achieves high per-polyp sensitivities for the diagnosis of advanced polyps[16].

Malignancy in colorectal polyps

Endoscopists must assess the level of submucosal invasion in T1 CRC without resorting to biopsy to decide whether to perform endoscopic or surgical resection. AI emerges as an ideal tool to offer valuable guidance to endoscopists. Two Japanese AI studies were conducted using CNN algorithms to differentiate between T1a and T1b. The initial study was a randomized one and achieved 94% of accuracy; however, the second one ranged only 81.4% of accuracy[17,18].

Computer-aided quality assessment of colonoscopy technique: AI, functioning as a virtual endoscopist, can complement the expertise of endoscopists in reducing the rate of missed polyps visible on the screen. However, the quality of a colonoscopy procedure relies on additional parameters such as incomplete mucosal exposure, blind spots, withdrawal speed, and the degree of bowel cleansing. Currently, AI is developing new systems to measure these parameters during the procedure, alongside CADe and CADx, to address exposure errors. Consequently, computer-aided quality assessment objectively evaluates the time spent exploring different segments of the colon, the quality of fold examination, and mucosal cleansing[19]. Therefore, in the future, we can objectively determine the quality of colonoscopy for the optimal surveillance protocol of CRC.

UPPER GI TRACT

Esophagus

In a recent multicenter study of upper GI endoscopies, a 6.4% esophageal cancer miss rate was reported[20]. Due to the capability of DL to explore images beyond the reach of the human eye, it has been employed in the analysis of endoscopic images related to esophageal and stomach diseases. Wu *et al*[21] utilized a DL model and demonstrated promising outcomes in the classification and segmentation of individual esophageal lesions. Consequently, several CADe systems have been recently tested in clinical settings.

Precursor lesion of esophageal squamous cell neoplasia: Intrapapillary capillary loops (IPCL) observed through virtual chromoendoscopy (NBI) have been classified as a precancerous lesion of esophageal squamous cell neoplasia (ESCC), correlating with depth invasion. Everson *et al*[22] demonstrated that a DL model was an efficient, accurate, and reliable tool for classifying IPCL patterns as normal or abnormal. In two separate studies, Zhao *et al*[23] and Yuan *et al*[24] compared the accuracy of AI systems to that of endoscopists. AI models significantly enhance the ability of junior endos-

copists to diagnose IPCL abnormalities and depth invasion of ESCC.

ESCC: A recent literature review demonstrated high diagnostic accuracy for AI in ESCC[25]. Extensive datasets have supported the overall diagnostic performance of AI for both superficial and advanced esophageal squamous cancer. Numerous studies have indicated that, AI accuracy in detection was comparable to or even higher than that experienced endoscopists[26-28]. In therapeutic decisions for ESCC, which depend on the depth of invasion, Zhang *et al*[29] conducted a multicenter study using an AI-based CADx model that simulated radiologists' diagnoses of lymph node metastasis. The results from AI systems significantly outperformed those of human diagnostics. Additionally, Tokai *et al*[30] published a comparative study between a DL CNN model and endoscopists to determine ESCC depth invasion. The results demonstrated that AI algorithms surpassed the performance of all endoscopists. Given these promising results, AI-assisted diagnostic techniques should be considered for adoption in future clinical practice.

Barrett's esophagus-related neoplasia: It is established that Barrett's esophagus (BE) is a precursor of esophageal adenocarcinoma (EAC). BE represents an exemplary application of AI systems, showcasing their capability in lesion identification and determining the degree of malignancy. Pan *et al*[31] demonstrated the ability of an AI model in identifying and classifying BE according to the Prague classification. To enable endoscopists to successfully detect dysplasia or EAC in BE, several AI studies have achieved high sensitivity, specificity, and accuracy, meeting the parameters outlined by the PIVI[32-35]. Two meta-analyses have reached similar conclusions[36,37].

To choose the optimal treatment, the identification of sub-mucosal invasion of BE-related neoplasia is mandatory. A retrospective multicenter study evaluated the performance of DL algorithms in discriminating between T1a and T1b cancer[38]. The AI model demonstrated comparable performance to experienced endoscopists.

Stomach

Gastric precancerous lesions: *Helicobacter pylori* (HP) infection can produce chronic atrophic gastritis (CAG) and gastric intestinal metaplasia (GIM). CAG and GIM are precancerous lesions associated with an increased risk of gastric cancer (GC) development[39]. Thus, endoscopic surveillance of the precancerous lesions is mandatory to detect GC in an early stage, termed early GC (EGC). The diagnosis of EGC is difficult because the sensitivity of endoscopic diagnosis of CAG is only 42% in a large study and the overall rate of missed neoplasia at endoscopy varies between 8.3% and 10%[40].

AI models may improve the diagnostic accuracy and aid the endoscopist in the detection and staging of precancerous lesions.

AI in the detection of gastric precancerous lesions and HP infection: Regarding CAG, in two studies, AI models were compared to endoscopists. Zhang *et al*[41] used the CNN model to detect CAG in 1699 patients. It outperformed three expert endoscopists with a sensitivity, specificity, and accuracy of 95%, 94%, and 94% respectively. Guimaraes *et al*[42] reported a 93% accuracy with WLE images.

Concerning GIM, Yan *et al*[43] developed a CNN-CAD model with ME-NBI. It reached an accuracy of 89% compared to 84% accuracy for expert endoscopists.

Concerning HP infection, Zheng *et al*[44] developed a CAdE system to detect HP infection status based on endoscopic images without the need for biopsies. The CNN systems reached an accuracy of 92%. Nakashima *et al*[45] used a DL model with WLE and blue light imaging (BLI). The DL model had an area under the curve (AUC) of 0.96 with BLI, and 0.66 with WLE.

AI in the detection of EGC: Li *et al*[46] developed a CNN model on images of benign lesions and EGC. The AI model has a diagnostic accuracy of 91% compared to an accuracy of 87% when used by experts and 70%-74% for non-expert endoscopists. Horiuchi *et al*[47] used a CAdE system to detect EGC using NBI videos and compared to 11 expert endoscopists in NBI. Only two endoscopists were outperformed by the CAdE systems.

AI in the prediction of invasion depth of EGC: Nagao *et al*[48] developed a CNN-CAD system by using images of GC that underwent endoscopic resection or radical surgery to evaluate the accuracy of AI to determine invasion depth. They found that the CAdE system can predict the invasion depth with a sensitivity of 75%-84%, specificity of 80%-99%, and accuracy of 94% during WLE and NBI images, respectively. Yoon *et al*[49] analyzed images of GC (T1a and T1b) to predict invasion depth with AUC of 0.85. This accuracy was significantly lower in undifferentiated lesions.

SMALL BOWEL

Inflammatory bowel disease

Recently, the therapeutic goals for patients with inflammatory bowel disease (IBD) have shifted toward mucosal healing, defined by endoscopic evaluation. However, histologic evaluation is essential to predict the risk of relapse and colon cancer.

This GI field has emerged as a new area for AI, utilizing data from endoscopic images, video capsule endoscopy images, histology, magnetic resonance imaging images, laboratory studies, and genetics. Numerous studies with meta-analyses using ML and DL systems have aimed to detect Crohn's disease and ulcerative colitis with high sensitivity and accuracy[49]. Additionally, AI studies utilizing ML and DL CNN systems have achieved a high level of accuracy in predicting disease severity for IBD[50,51].

Villous atrophy

Celiac disease is the primary cause of villous atrophy and remains undiagnosed in 50% of cases. A study conducted by Gadermayr *et al*[52] achieved a high accuracy of 94%, but that requires water immersion. Also, studies with video capsule endoscopy showed an accuracy > 90% [52-54]. These studies were conducted under special conditions with high probability of suspicion. It is mandatory to make the diagnosis in routine endoscopy. A recent retrospective study done by Scheppach *et al*[55] compared AI algorithms to performance of fellows and experts on routine endoscopy. The results showed that AI significantly improved the performance of all endoscopists with stable performance.

PANCREAS

Endoscopic ultrasound (EUS) is a reliable tool for the detection and staging of pancreatic lesions, particularly pancreatic cancer (PC). EUS-FNB is a well-established diagnostic tool for PC, demonstrating a specificity and sensitivity greater than 90%. However, the EUS technique is operator-dependent, exhibiting inter-observer variability, making it an ideal platform for AI applications.

AI in EUS for detection of PC

Three retrospective studies were conducted using DL algorithms, demonstrating high sensitivity, specificity, and accuracy in diagnosing PC [56-58]. Additionally, Goyal *et al*[59] conducted a systematic review of 11 studies on the role of AI-assisted EUS models in diagnosing PC, revealing that AI algorithms had high potential for detecting PC.

AI in EUS differentiation PC from benign lesions

Chronic pancreatitis: Chronic pancreatitis still mimics PC in radiologic features and is also considered a risk factor for the development of PC. Five studies were conducted with DL algorithms, reporting high accuracy, sensitivity, and specificity [60-64]. However, these studies were heterogeneous with a small patient population. Hence, two recent prospective multicenter studies using DL models were published, validating the aforementioned findings [65,66]. Therefore, AI-assisted EUS can be a validated tool in clinical practice to differentiate PC from chronic pancreatitis with accepted results.

Autoimmune pancreatitis: Marya *et al*[67] conducted a unique study using a DL model to differentiate between PC and autoimmune pancreatitis. The high sensitivity and specificity encourage the use of AI to assist EUS endoscopists in this field.

LIMITATIONS

Input data

DL tasks rely on databases used to train AI algorithms, which must be manually annotated and propagated through frames using dedicated software. The development of DL may be affected by selection biases, which include the chosen disease, its prevalence, the endoscopic center's characteristics, the patient population, and the number of patients enrolled. Spectrum biases in DL performance can arise from variations in patient population, the number and skills of endoscopists, and the technical characteristics used, such as WLE, advanced imaging, and optical magnification. Consequently, a database from a single institution, lacking diversity and failing to capture all possible variations, can impact the quality of input data, as well as the reproducibility and generalizability of the results. To mitigate these biases, it is essential to establish a quality-monitored central data collection server that aggregates data from all institutions.

Algorithm

Studies utilize different AI-assisted models that require images prepared in specific ways. These algorithms may not consistently achieve a high degree of accuracy. Therefore, it is essential to establish a universal protocol for input data to enhance the efficacy and accuracy of AI-assisted models.

Validation

AI findings must undergo clinical validation before being introduced into clinical practice. AI has a valuable advantage when the reference standard is based on histologic verification. However, if not, the reference standard relies on expert endoscopist raters, introducing potential bias. Therefore, AI systems should be validated through randomized trials comparing the standard and new endoscopic modalities. Additionally, these algorithms must be tested on large and cross-institutional datasets. Long-term data on the accuracy of AI-assisted models is lacking. Consequently, there are no results regarding the impact of AI on reducing the incidence and mortality of GI cancer. Clinical efficacy evaluation must adhere to established guidelines. The two recommended guidelines are the PIVI statement as a guide for new imaging technology and the ESGE guidelines. For example, in cases requiring targeted biopsies, PIVI recommends a per-patient sensitivity of 90% or greater and a specificity of 80% or greater to allow a reduction in biopsies. Therefore, studies must meet these parameters to be approved for clinical practice. Additionally, according to ESGE, the results of AI studies must be comparable to those of experts.

Output

There are "black boxes" in the logic of DL algorithm decision-making processes that are not understood or controlled by humans[68]. Consequently, AI can make mistakes, and humans cannot explain or justify the computer's decisions. For instance, physicians have concerns regarding the number of false-positive signals generated by AI. This may cause distraction, prolong procedure time, and frustrate the endoscopist, making some users hesitant to use it. Therefore, humans must make the final decision and should not become entirely dependent on AI technology for both diagnostic and therapeutic endoscopies; otherwise, they risk losing their cognitive abilities.

CONCLUSION

In conclusion, because the GI field relies on imaging, AI-assisted algorithms continue to explore new GI organs and diseases. The growth and applications of AI increase exponentially with the development of computer science and may reach no limit. However, we must be careful about how we use it and preserve our independence in the final decision. Additionally, to achieve better results in AI studies in the future, collaboration between academic and private gastroenterologists and the industry must be closer, aiming to improve the quality, utility, ease of use, and accuracy of AI models. We hope that AI-assisted diagnostic techniques will be widely used in GI diseases because AI is an unavoidable tool in GI endoscopy.

FOOTNOTES

Author contributions: Abboud B designed the research; Bou Jaoude J and Al Bacha R performed the research; Bou Jaoude J, Al Bacha R and Abboud B analyzed the data; Bou Japude J, Al Bacha R and Abboud B wrote the paper.

Conflict-of-interest statement: The authors declare no conflicts of interest.

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S-Editor: Lin C

L-Editor: Filipodia

P-Editor: Zhao YQ

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Expanding role and scope of artificial intelligence in the field of gastrointestinal pathology

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Specialty type: Pathology

Provenance and peer review:

Invited article; Externally peer reviewed.

Peer-review model: Single blind

Peer-review report's classification

Scientific Quality: Grade B, Grade E

Novelty: Grade A, Grade D

Creativity or Innovation: Grade C, Grade D

Scientific Significance: Grade A, Grade D

P-Reviewer: Andreev DN; Zulkifli MH

Received: December 30, 2023

Revised: July 6, 2024

Accepted: July 29, 2024

Published online: August 8, 2024

Processing time: 190 Days and 21.5 Hours



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Abstract

Digital pathology (DP) and its subsidiaries including artificial intelligence (AI) are rapidly making inroads into the area of diagnostic anatomic pathology (AP) including gastrointestinal (GI) pathology. It is poised to revolutionize the field of diagnostic AP. Historically, AP has been slow to adopt digital technology, but this is changing rapidly, with many centers worldwide transitioning to DP. Coupled with advanced techniques of AI such as deep learning and machine learning, DP is likely to transform histopathology from a subjective field to an objective, efficient, and transparent discipline. AI is increasingly integrated into GI pathology, offering numerous advancements and improvements in overall diagnostic accuracy, efficiency, and patient care. Specifically, AI in GI pathology enhances diagnostic accuracy, streamlines workflows, provides predictive insights, integrates multimodal data, supports research, and aids in education and training, ultimately improving patient care and outcomes. This review summarized the latest developments in the role and scope of AI in AP with a focus on GI pathology. The main aim was to provide updates and create awareness among the pathology community.

Key Words: Gastrointestinal pathology; Digital pathology; Artificial intelligence; Machine learning; Deep learning; Precision diagnostics

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Core Tip: Anatomic pathology remains largely subjective compared to other diagnostic laboratory fields. However, the digitization of tissue sections and the development of artificial intelligence-based technologies are rapidly advancing image-based diagnostics in anatomic pathology including gastrointestinal pathology. These technologies allow pathologists to make diagnoses more quickly and accurately, particularly for time-consuming and repetitive tasks, leading to higher volumes and faster turnaround times. Increasing awareness of the potential uses and benefits of these emerging technologies is essential for the pathology community.

Citation: Mubarak M, Rashid R, Sapna F, Shakeel S. Expanding role and scope of artificial intelligence in the field of gastrointestinal pathology. *Artif Intell Gastroenterol* 2024; 5(2): 91550

URL: <https://www.wjgnet.com/2644-3236/full/v5/i2/91550.htm>

DOI: <https://dx.doi.org/10.35712/aig.v5.i2.91550>

INTRODUCTION

Anatomic pathology (AP), particularly histopathology, represents the ground truth of medicine, providing the final and definitive test on which crucial treatment decisions are based, especially for cancer (Figure 1). Despite its critical role, AP has remained an analog enterprise, using processes developed in the early 20th century. Tissue preparation and diagnosis are still largely manual and subjective[1,2]. Diagnoses are based on the visualization and assessment of tissue sections on glass slides under a light microscope, making the process highly dependent on the pathologist's interpretation.

The diagnostic process is a complex mental exercise requiring multitasking and the coordination of observation, interpretation, and integration of information. This process yields continuous variables that pathologists use to drive classification systems, which clinicians use to make major therapeutic decisions (Figure 1). While cost-effective, this process is prone to significant inter- and intra-pathologist variation and diagnostic errors and is often time-consuming and tedious. The integration of multiple ancillary diagnostic tests, such as immunohistochemistry and molecular assays, adds to the complexity and demands on pathologists. Moreover, the shortage of pathologists globally exacerbates these challenges, highlighting the need for precision diagnostics, particularly in cancer treatment[3-5].

Traditionally, AP has been slow to embrace digital technology, but this is steadily changing. Many pathology laboratories worldwide have partially or completely transitioned to digital pathology (DP) workflows[6-10]. Advanced artificial intelligence (AI) techniques, such as machine learning (ML) and deep learning (DL), are set to transform AP into a more objective, efficient, and transparent discipline[11,12]. However, many pathologists, particularly in developing countries, have limited knowledge of AI and its vast potential[13,14].

This review aimed to provide a simplified overview of the latest developments in the role and scope of AI in pathology, with a specific focus on gastrointestinal (GI) pathology. It explored how AI can be used to diagnose and predict diseases, highlighting its benefits for routine histopathology practice. The goal was to update pathologists and other healthcare providers about these emerging diagnostic technologies and raise awareness.

LITERATURE REVIEW

A comprehensive search was conducted across multiple databases, including PubMed, Google Scholar, Scopus, and Web of Science, covering publications from 2010 to 2024. Keywords included "Artificial Intelligence," "Machine Learning," "Deep Learning," "Gastrointestinal Pathology," "Diagnosis," and "Histopathology." All types of studies in the English language were selected based on relevance, focusing on AI applications in GI pathology. The full texts of these articles were carefully read to extract the relevant points for writing this review article.

DEFINITION OF AI AND ITS APPLICATIONS

AI is a field of computer science that enables computers to perform tasks that typically require human intelligence, such as learning, pattern recognition, planning, problem-solving, and reasoning[15-17]. AI relies heavily on data for its operations, and the digitization of glass slides in DP workflows provides vast amounts of pixel data for AI applications. AI can be considered a part of data science[18-21].

Initially, AI comprised simple "if-then" algorithms but has since advanced to include complex algorithms that perform tasks akin to the human brain. The advent of DL has expanded the capabilities of AI, allowing systems to analyze data and images using multiple layers and learn from big data. ML and DL are subsets of AI (Figure 2), with DL being a more advanced form capable of solving complex problems using neural networks (Figure 3)[22-24].

AI represents a significant turning point for human society, comparable to the industrial revolution. It is a general purpose technology applicable in various fields, much like electricity. The role of AI in healthcare is growing rapidly, particularly in biomedical research and clinical practice. Modern techniques now generate vast amounts of data, which AI can analyze for patterns, enhancing diagnostics and treatment decisions[25-29]. AI can detect subtle pathological

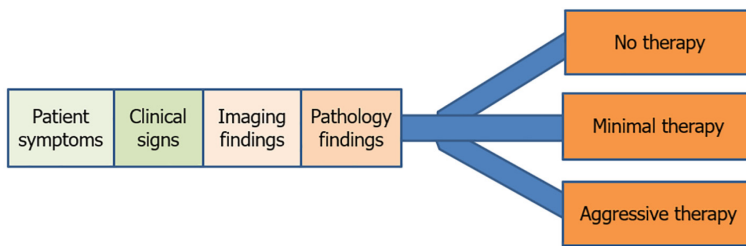


Figure 1 Pathological diagnosis is the final and definitive test that informs all subsequent therapy decisions by clinicians, particularly in oncology.

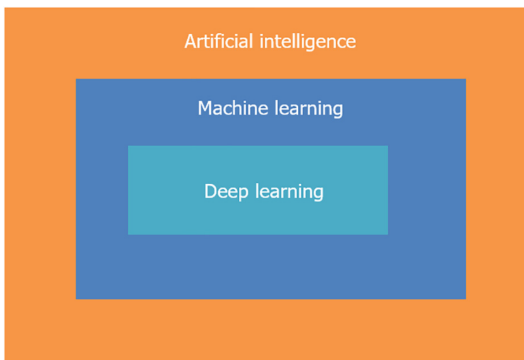


Figure 2 Relationship of artificial intelligence and its more advanced forms, machine learning and deep learning.

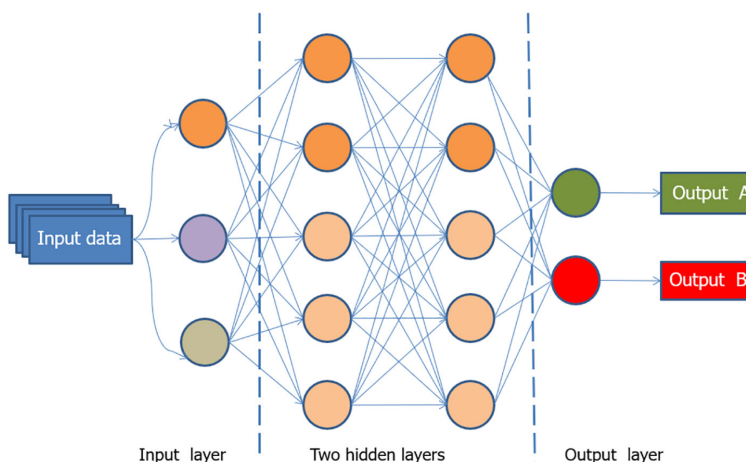


Figure 3 A simplified version of artificial neural network utilized in artificial intelligence algorithms.

alterations, predict therapy responses, and improve workflow efficiency in pathology[30].

In the diagnostics arena, radiologists have been early adopters of AI for image processing and interpretation[31,32]. Pathologists, facing greater visual data complexity in microscopic images, have been slower to adopt AI. However, the shift towards DP and whole slide imaging (WSI) is laying the groundwork for computational pathology technologies. With the recent advancements in AI for computer vision, it is expected that AI will soon support pathologists in various DP tasks. Concurrently, significant progress in DL has created a synergy with AI, enabling image-based diagnostics within the DP context. Efforts are underway to develop AI tools that save pathologists time and reduce errors[33]. Integrating AI systems into AP practices will require fully digital imaging platforms, updating outdated information technology infrastructures, modifying laboratory and pathologist workflows, establishing appropriate reimbursement models, and ensuring pathologists' active participation for buy-in and oversight. New regulations, designed to address the unique aspects and limitations of AI, are being developed to ensure its safe and effective use[34]. The recent Food and Drug Administration approval of WSI systems opens significant opportunities for AI-assisted pathological diagnosis, promising faster, more accurate, and cost-effective diagnostics[35-40].

ROLE OF AI IN ROUTINE AP DIAGNOSTIC WORKFLOW

AI is increasingly being integrated into AP to enhance diagnostic efficiency and accuracy, reduce turnaround times, and improve patient care[41,42]. AI algorithms can analyze DP images with high speed and accuracy, assisting pathologists in identifying and quantifying specific features such as cell structures, mitoses, tissue patterns, and abnormalities. This reduces subjectivity, minimizes diagnostic errors, and ensures consistent results[43-47].

AI-driven workflow management tools can streamline daily tasks, prioritize cases based on urgency, and help pathologists allocate their time effectively. AI can also integrate patient data, provide decision support tools, and assist in quality control and compliance with regulatory standards. AI tools can develop predictive models for disease outcomes and support research by analyzing vast datasets[48,49]. Although technical implementation has become less challenging, much work is needed to integrate AI into routine AP workflows. AI can also enhance the understanding of disease biology by analyzing DP images to identify patterns and features not visible to the human eye. This can aid in discovering new biomarkers and treatments, benefiting both diagnostics and research[50,51].

ROLE OF AI IN GI PATHOLOGY

AI technology is poised to revolutionize GI pathology, offering numerous current and potential applications (Figure 4). By processing digitized images of tissue samples, AI tools enhance the precise and effective identification of various GI disease processes, including inflammatory and neoplastic conditions such as colitis, Crohn's disease, and colorectal cancer (CRC). The integration of AI in GI pathology significantly improves the precision, speed, and quality of diagnostic and therapeutic decision-making processes, ultimately benefiting patient care. Additionally, AI can standardize quality control in GI pathology, ensuring accurate and consistent results across samples[52-55].

AI has been extensively studied for endoscopic diagnosis of GI tract disorders, demonstrating significant promise. It is expected that AI will primarily assist endoscopists with tasks such as detection, characterization, and segmentation. AI has the potential to enhance colonoscopy-based colorectal screening and monitoring by reducing unnecessary expenses and improving quality. Real-time computer-assisted polyp identification can enhance screening and monitoring quality, as measured by adenoma detection rates. Optical biopsies using computer-assisted diagnosis can identify low-risk polyps, supporting resect-and-discard or diagnose-and-leave strategies, thereby reducing unnecessary costs. Recent meta-analyses indicated that AI tools significantly increased colorectal neoplasia detection, regardless of initial adenoma features[56-58]. Furthermore, AI is useful in identifying upper GI pathological processes, including both neoplastic and non-neoplastic lesions[59,60].

In the GI tract, precancerous lesions and invasive tumors are routinely biopsied or excised for histopathological workup. Early and accurate diagnosis is a primary responsibility of pathologists, and AI can assist in achieving this objective. Numerous reports have documented AI-assisted diagnosis of both neoplastic and non-neoplastic GI diseases. For instance, Korbar *et al*[61] trained a model to distinguish between five prevalent types of colorectal polyps with an overall accuracy of 93% using a dataset of over 400 WSIs. Wei *et al*[62] demonstrated that neural networks trained to identify colorectal polyps on WSIs from one institution performed similarly to local pathologists when applied to WSIs from other institutions. Efforts have also been made to automate the diagnosis of preneoplastic and neoplastic lesions, such as Barrett's esophagus or gastric adenomas/adenocarcinomas[60].

AI models also show promise in predicting therapy response or prognosis from WSI analysis. Among all cancer types, GI and liver tumors have notably driven computational oncology forward. AI can extract complex information from digital images of GI and hepatic malignancies, providing clinical, biological, and molecular insights that are not accessible to the naked eye. By identifying the most predictive tissue areas, AI reduces the cognitive burden on pathologists, enhancing their efficacy in histopathological characterization and risk assessments of GI preneoplastic and neoplastic lesions. In biliary tract cancer, DL can identify tissue features predictive of clinical outcomes. DP images and tissue microarrays from CRC have shown the efficacy of DL in prognostic prediction across all tumor stages. The histomorphology of gastric cancer (GC) is more complex and variable than CRC, leading to fewer investigations using DL for GC. Most of this research has focused on tumor detection rather than prognostication[63-66].

Routine processing of surgical and biopsy specimens from various GI tract tumors involves investigating molecular biomarkers that predict responses to targeted therapy. Specific genetic events in GI and hepatobiliary cancers are linked to morphological features identified in hematoxylin and eosin sections. AI-based algorithms on WSIs have been successfully used as surrogate markers for these alterations[66-69]. For example, CRC serves as a model disease due to the abundance of pathology samples. Identifying microsatellite instability (MSI) is crucial because immune-modulating treatments significantly affect MSI tumors. MSI identification has major implications for patients and their families, necessitating further investigation to identify Lynch syndrome. Although immunohistochemistry techniques are typically used to identify MSI, not all patients are routinely screened. A study by Echle *et al*[70] examined 8836 CRC cases across all stages, developing an AI model that could identify MSI tumors from hematoxylin and eosin sections, maintaining performance even in biopsy samples with limited tissue and varying preprocessing methods. Other efforts have created models that accurately predict gene alterations from WSIs of hepatocellular carcinoma (HCC), GC, and other conditions.

AI-based pathology can predict gene expression and RNA sequencing data, holding great promise for clinical application. Developing DL models for prognostication that integrate clinical, biological, and genetic data is a promising approach. For example, Chaudhary *et al*[71] used RNA sequencing, microRNA sequencing, and methylation data to create a DL model predicting survival in HCC patients, demonstrating its efficacy across different HCC patient cohorts.

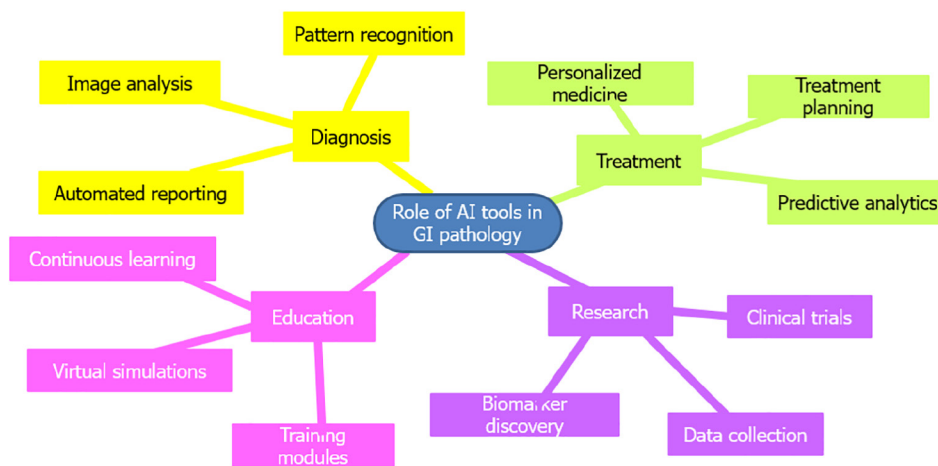


Figure 4 Four main roles of artificial intelligence-based tools in gastrointestinal pathology. AI: Artificial intelligence; GI: Gastrointestinal.

AI ALGORITHMS IN GI PATHOLOGY

AI algorithms, particularly those based on ML and DL, have shown substantial potential in analyzing complex pathological data and are central to the advancements in GI pathology (Table 1). ML algorithms such as support vector machines, random forests, and k-nearest neighbors have been employed to classify and predict various GI conditions. These include supervised, unsupervised, and reinforcement learning algorithms (Figure 5). Supervised learning algorithms, such as support vector machines and random forests, are widely used for classification tasks. These algorithms require extensive feature engineering and domain expertise to identify relevant features from pathology images and clinical data. They are relatively simpler to implement and interpret compared to DL algorithms. They are also effective for structured data analysis and smaller datasets and feature faster training times and lower computational requirements. The need for manual feature extraction limits their use, and ML algorithms may not perform as well as DL in recognizing complex patterns in unstructured data like histopathological images[72-75].

DL models, particularly convolutional neural networks, have revolutionized image analysis in GI pathology[76,77]. Convolutional neural networks can automatically learn hierarchical features from raw images, making them highly effective for tasks such as tumor detection and classification. They possess superior performance in image recognition tasks and are able to handle large and complex datasets. Automated feature extraction reduces the need for domain-specific knowledge. However, it requires substantial computational resources and large annotated datasets. It is difficult to interpret and explain the decision-making process (black-box nature). Recurrent neural networks, including their variants like long short-term memory networks, are used for sequential data analysis. They are particularly useful in analyzing time-series data from endoscopic videos to detect abnormalities[78-84]. While ML algorithms are generally more interpretable, DL algorithms often provide higher accuracy due to their ability to learn complex patterns from large datasets. However, DL models require substantial computational resources and large labeled datasets, which can be a limitation[73,75,79,85].

DATA SOURCES IN GI PATHOLOGY

The performance of AI algorithms heavily depends on the quality and diversity of data sources. Common data sources in GI pathology include: (1) Histopathological images in the form of WSIs and tissue microarrays as the primary data sources; (2) Clinical data, such as electronic health records, patient demographics, clinical history, and endoscopy images; and (3) Publicly available datasets such as The Cancer Genome Atlas and Gastrointestinal Image Data Collection. Each of these sources has merits and demerits. Integration of clinical data, including patient demographics, medical history, and laboratory results, enhances the contextual understanding of GI pathology and improves the predictive power of AI models. The availability of large, well-annotated datasets is a significant challenge. Variability in image quality and staining techniques and differences in pathological practices across institutions can affect the generalizability of AI models. Additionally, integrating clinical data requires sophisticated data management systems to handle patient privacy and data security concerns.

PERFORMANCE METRICS OF AI ALGORITHMS

Sensitivity measures the ability of an AI algorithm to correctly identify positive cases (*e.g.*, detecting cancerous lesions). Specificity measures the ability of an AI algorithm to correctly identify negative cases (*e.g.*, ruling out benign conditions). Achieving high sensitivity and specificity is challenging due to the inherent variability in pathological samples. DL

Table 1 Main artificial intelligence-based algorithms for use in the gastrointestinal pathology field

AI algorithms	Role in gastrointestinal pathology	Key uses	Examples
Machine learning	Assisting in diagnosis and classification of gastrointestinal diseases	Improved diagnostic accuracy, personalized treatment plans	Predictive models for colorectal cancer risk, classification of polyps in colonoscopy images
Deep learning	Analyzing endoscopic and histopathologic images	Enhanced image recognition, reduced human error	Convolutional neural networks for detecting and classifying lesions in endoscopic images
Natural language processing	Extracting relevant information from medical records and literature	Efficient data mining, real-time clinical decision support	Automated extraction of patient data from electronic health records for research and clinical use
Computer vision	Real-time analysis of endoscopic videos	Immediate feedback during procedures, increased detection rates of abnormalities	Detection of bleeding, polyps, and other abnormalities during live endoscopy procedures
Reinforcement learning	Optimizing treatment plans and clinical pathways	Adaptive learning from real-world outcomes, improved clinical decision-making	Personalized treatment strategies for inflammatory bowel disease based on patient response
Predictive analytics	Forecasting disease progression and patient outcomes	Proactive patient management, early intervention	Predicting flare-ups in Crohn's disease, forecasting outcomes after gastrointestinal surgeries
Robotics integration	Enhancing precision in minimally invasive surgeries	Increased surgical precision, reduced recovery time	AI-assisted robotic surgery for gastrointestinal procedures, such as robotic-assisted colectomy
Genomic data analysis	Identifying genetic markers associated with gastrointestinal diseases	Personalized medicine, targeted therapies	Analyzing genetic data to find markers for conditions like Lynch syndrome and hereditary pancreatitis

AI: Artificial intelligence.

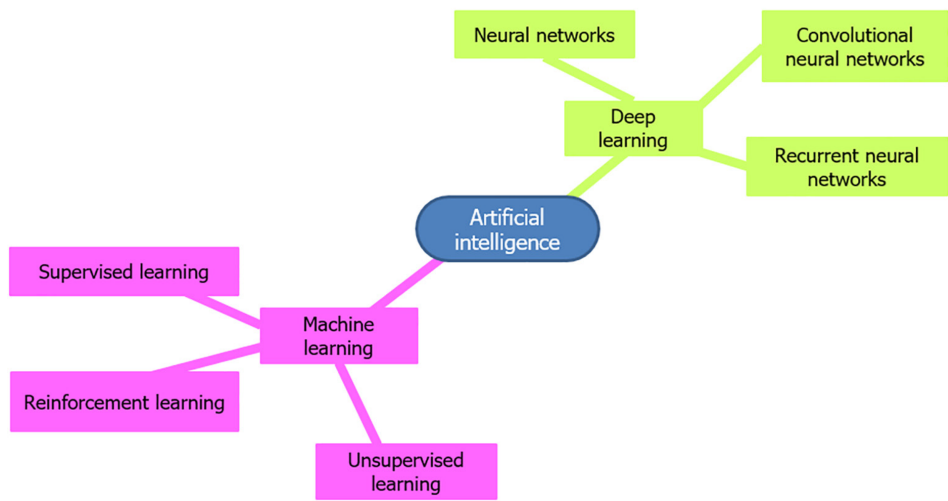


Figure 5 Main artificial intelligence-based algorithms for use in gastrointestinal pathology.

models often outperform traditional ML models in sensitivity and specificity due to their ability to learn intricate features from large datasets. However, there is a trade-off; models with high sensitivity might produce more false positives, reducing specificity. Balancing these metrics is essential to avoid misdiagnoses and unnecessary treatments[74,76,81,82].

CHALLENGES AND FUTURE PROSPECTS

AI is still in its early stages, and many pathology laboratories worldwide have yet to transition to a digital workflow to fully benefit from AI technologies. There are numerous obstacles to the widespread implementation of AI solutions in routine clinical practice, even in developed countries. Bringing an AI solution for pathology to market poses significant technological, business, and regulatory challenges. Although some clinical applications exist, the overall introduction of AI into medical practice has been slow and not without ethical concerns[86-90].

Despite significant research developments in AI-based techniques in recent years, only a few AI solutions have become commercial products for routine use. Consequently, much of the potential of AI remains untapped. Research models need further development, improvement, and integration into the information technology infrastructure of clinical laboratories before they can be used in routine pathology workflows. Additionally, commercial success requires a profitable business model in most countries, and pathologists need to be reimbursed for using the product. AI solutions are also classified as medical devices and thus require regulatory approval before they can be sold as products[91-94].

CONCLUSION

The role and scope of AI are expanding in GI pathology, with the potential to improve diagnostic accuracy, efficiency, and patient care. Increasing awareness among the pathology community about these emerging technologies is essential to realize their full potential and revolutionize diagnostics, prognostics, and theranostics in GI pathology.

FOOTNOTES

Author contributions: Mubarak M and Rashid R designed the research study and wrote the manuscript; Mubarak M, Rashid R, Sapna F, and Shakeel S performed the research; All authors contributed equally to this work, and read and approved the final manuscript.

Conflict-of-interest statement: All the authors report no relevant conflicts of interest for this article.

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S-Editor: Wang JJ

L-Editor: Filipodia

P-Editor: Yu HG

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