

Artificial Intelligence in *Gastroenterology*

Quarterly Volume 5 Number 2 August 8, 2024



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Artificial Intelligence in Gastroenterology

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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.

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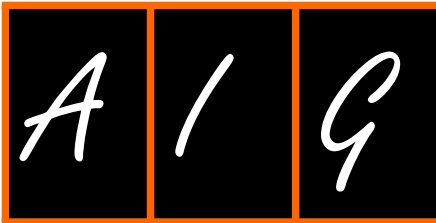
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Will artificial intelligence reach any limit in gastroenterology?

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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.

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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 endocystoscopy[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

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