Artificial Intelligence in

Gastroenterology

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ABOUT COVER

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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

There is currently no indexing.

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Artificial intelligence in gastrointestinal diseases

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Abstract

Artificial intelligence (AI) applications are growing in medicine. It is important to understand the current state of the AI applications prior to utilizing in disease research and treatment. In this review, AI application in the diagnosis and treatment of gastrointestinal diseases are studied and summarized. In most cases, AI studies had large amounts of data, including images, to learn to distinguish disease characteristics according to a human's perspectives. The detailed pros and cons of utilizing AI approaches should be investigated in advance to ensure the safe application of AI in medicine. Evidence suggests that the collaborative usage of AI in both diagnosis and treatment of diseases will increase the precision and effectiveness of medicine. Recent progress in genome technology such as genome editing provides a specific example where AI has revealed the diagnostic and therapeutic possibilities of RNA detection and targeting.

Key Words: Artificial intelligence; Gastrointestinal disease; RNA; Therapeutic application; Inflammatory diseases

Core Tip: The application of artificial intelligence (AI) in the diagnosis and treatment of disease is a promising approach in medicine. The application of AI approaches in gastrointestinal diseases is summarized and reviewed. AI holds great promise in

medicine, but to safely and efficiently apply AI in medicine, the advantages and limitations should first be carefully considered.

INTRODUCTION

Recent studies have developed RNA editing using the Clustered Regularly Interspaced Short Palindromic Repeats (CRISPR)/CRISPR-associated protein 9 (Cas9) system, which has made genome editing more accessible and has resulted in the development of many applications[1-3]. These new technologies have many advantages and disadvantages in their utilization, which are already being applied in medicinal situations. RNA editing has been recognized as a potential prognostic biomarker for cancer and prediction models have been developed with machine learning[4]. The utilization of artificial intelligence (AI) is rapidly expanding and is increasingly useful in understanding gastrointestinal (GI) diseases[5-7]. To better understand the use of AI-oriented diagnosis and treatment of diseases, it is important to determine how to raise the potential of AI and manage the human-AI interaction in diagnosis and therapeutics in diseases. AI technology has been combined with a massive amount of data to understand human activities[8]. Increasingly image data such as magnetic resonance imaging, X-ray, computed tomography scanning or endoscope in clinic will be utilized for the diagnosis of the diseases[9-12]. Currently, machine learning algorithms improve performance of gastrointestinal endoscopy by diagnosing the gastrointestinal diseases[13]. The application of AI has increased identification of patients with intestinal malignancies or premalignant lesions, and inflammatory or other nonmalignant diseases or lesions[14]. Computer-aided diagnosis (CAD) for colonoscopy would improve the quality of image-oriented diagnosis of colorectal cancer[15]. Classification of systems in AI-oriented disease management is summarized in Table 1.

APPLICATION OF AI IN DIAGNOSIS OF GASTROINTESTINAL DISEASES

There are several areas in which AI can advance the diagnosis of GI diseases. Diseases of interest for AI-oriented disease management are summarized in Figure 1.

AI application in inflammatory diseases
The diagnosis of GI diseases such as inflammatory bowel disease (IBD) including Crohn's disease, a chronic inflammatory condition in the GI tract, and ulcerative colitis, which occurs in the colon, includes several fundamental laboratory tests including measurement of hemoglobin, hematocrit, blood urea nitrogen, creatinine, liver enzymes and C-reactive protein[16].

AI application in tumor
Recent progress in AI has resulted in predictive tools for the diagnosis of GI cancer classification, where network-based machine learning in colorectal and bladder organoid models predicts drug responders and non-responders using network analysis of pharmacogenomics data and the patient's transcriptome[17]. Bioinformatic analyses of gene expression data have revealed common gene signatures in hypopharyngeal and esophageal squamous cell carcinoma, which may serve as diagnostic and therapeutic targets[18]. Balloon catheter tracking and visualization in GI tracking could be made more precise with AI guidance using image recognition [19]. Deep learning algorithms for image recognition can lead to more precise endoscopic diagnosis with improved sensitivity and specificity in upper GI tract diseases such as gastric cancer and Barrett's esophagus[20]. Convolutional neural networks (CNNs) have generated liver imaging features and shown promise in

Table 1 Classification of systems in artificial intelligence-oriented disease management

Disease of interest	Purpose of AI	User	Limitation of use	Ref.
Acute appendicitis	Diagnosis	Specialist	The study is designed in retrospective nature	Reismann *et al* [5]
Colon cancer	Diagnosis	Specialist	The design of the analysis is post hoc and the number of patients is limited	Reichling *et al* [6]
Ulcerative colitis	Diagnosis	Specialist	Long-term clinical prognosis is not clear	Maeda *et al*[7]
Spinal stenosis in degenerative lumbar kyphoscoliosis	Surgery navigation	Specialist	The number of patients is limited. Long-term follow-up data is needed	Ho *et al*[9]
Coronavirus infectious disease (COVID-19)	Screening, diagnosis	Specialist	Privacy of the patient data should be considered	Bhattacharya *et al*[10]
Diseases in general	Diagnosis	Specialist	The burden on specialists may increase	Karako *et al*[11]
Diseases in general	Screening	Specialist	Careful and thorough investigation is necessary	Shiyam Sundar *et al*[12]
Gastrointestinal disease	Diagnosis	Specialist	There is a difference in the definition of anomaly detection between the area of computer science and medical domain	de Lange *et al* [13]
Gastrointestinal disease, hepatic diseases	Diagnosis	Specialist	High-quality datasets are needed	Le Berre *et al* [14]
Colorectal cancer	Diagnosis	Specialist	The quality of previous study designs is limited, and practical usefulness of computer-associated diagnosis systems is unknown	Kudo *et al*[15]
Colorectal cancer, bladder cancer	Prediction of anti-cancer drug efficacy	Specialist	Further molecular layer profiling in organoids may be needed	Kong *et al*[17]
Hypopharyngeal squamous cell carcinoma, esophageal squamous cell carcinoma	Identification of diagnostic and therapeutic targets	Specialist	Further studies are needed to validate the findings of the study	Zhou *et al*[18]
Arterial stenosis, coronary arterial diseases, stricture of the gastrointestinal tract	Guiding of balloon catheter	Specialist	The systemic performance needs to be improved	Kim *et al*[19]
Gastrointestinal disease	Diagnosis	Specialist	Further studies are needed to improve the performance	Marlicz *et al*[20]
Colorectal cancer	Prediction of liver metastasis	Specialist	The investigation of another dataset is needed	Lee *et al*[21]
Colon cancer	Diagnosis	Specialist	The change of protein expression level needs to be investigated	Xue *et al*[22]
Gastrointestinal disease	Diagnosis	Specialist	Investigation and development of newly improved methods are encouraged	Borgli *et al*[23]
Gastrointestinal disease	Diagnosis	Specialist	Further development is needed	Adler and Bjarnason[24]
Upper gastrointestinal cancer	Diagnosis	Specialist	Only high-quality endoscopic images for the training and validation analyses were used	Luo *et al*[25]
Gastric cancer	Diagnosis	Specialist	The associations of the quality or the number of training images and the CNN accuracy needs to be examined	Hirasawa *et al* [26]
Gastrointestinal disease	Diagnosis	Specialist	The possibilities to improve the medical performance, to reduce the medical cost, and to improve the satisfaction of the patient and medical staff are unknown	Min *et al*[27]
Functional gastrointestinal disorder	Diagnosis	Specialist	Evaluation of the feasibility of AI on studies on the gut-brain-microbiome axis is needed	Mukhtar *et al* [28]
Colorectal cancer	Diagnosis	Specialist	The uncertainty about the true efficacy of CAD in "real-world" practice remains	Ahmad *et al*[29]
Colorectal cancer	Diagnosis	Specialist	Further accumulation of lesion images for training is needed	Yamada *et al* [30]
Small-bowel disease	Diagnosis	Specialist	Further multicenter, prospective studies and external validation are needed	Yang[31]

Colorectal cancer	Diagnosis	Specialist	Complaints of system malfunctions and reports of patient injuries could lead to lawsuits against stakeholders	Ciuti *et al*[32]
Cholangiocarcinoma, pancreatic adenocarcinoma	Diagnosis	Specialist	Case-control and single-center design, and the lack of an independent validation cohort should be considered	Urman *et al*[33]
Colorectal cancer	Screening	Specialist	The applicability to other types of cancer needs optimization	Misawa *et al*[34]
Gastrointestinal disease	Diagnosis	Specialist	Most studies were designed in retrospective manner. Ethical issues on misdiagnosis or misclassification need to be handled	Yang and Bang [35]
Gastrointestinal cancer	Prediction of microsatellite instability for immunotherapy	Specialist	Larger training cohorts are needed	Kather *et al*[36]
Colorectal cancer	Diagnosis	Specialist	The CNN architecture needs to be improved for colonoscopy	Azer[37]
Barrett esophagus cancer	Diagnosis	Specialist	The number of patients is limited. Further optimization is needed	Ebigbo *et al*[38]
Celiac disease	Diagnosis	Specialist	The preliminary results need to be followed-up with a real clinical setting	Tenório *et al*[39]
Esophageal squamous cell carcinoma	Prediction of prognosis	Specialist	Further experimental studies to verify the results are needed	Zhang *et al*[40]
Advanced rectal adenocarcinoma	Prediction of response to neoadjuvant chemoradiotherapy	Specialist	The size of the cohort is limited. The confirmation of the findings with another data set is needed	Ferrando *et al* [41]
Inflammatory bowel disease	Prediction of prognosis	Specialist	Interventional study to confirm the efficacy of the stratifying therapy is needed	Biasci *et al*[42]
Inflammatory bowel disease	Mapping	Specialist	The application of advanced natural language processing algorithms to the text-mining step may improve the current process	Sarntivijai *et al* [43]

AI: Artificial intelligence; CAD: Computer-aided diagnosis; CNN: Convolutional neural network.

Disease of interest
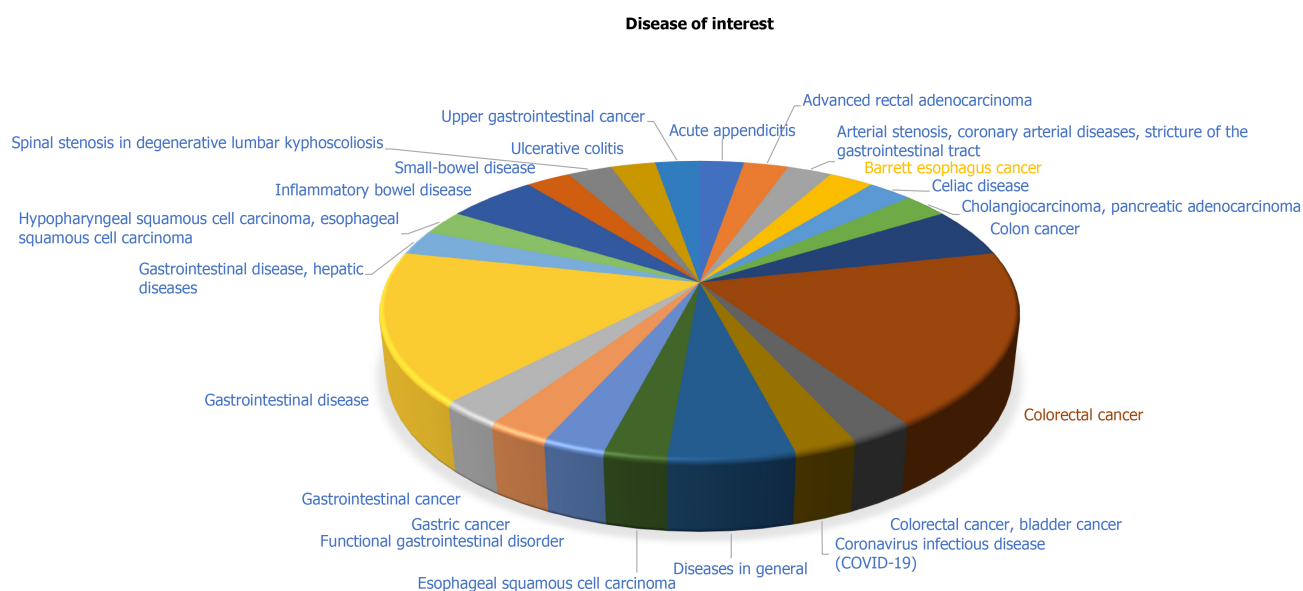
Figure 1 Disease of interest in references surveyed in artificial intelligence-oriented disease management. AI: Artificial intelligence; COVID-19: Coronavirus disease 2019.

predicting the metachronous liver metastasis in stage I-III colorectal cancer patients [21]. Deep learning of immunohistochemistry images of human colon tissues are used to improve the performance in detection of protein subcellular localization[22]. AI is poised to have a greater impact on GI endoscopy with publication of large datasets

including multi-class images and video datasets that are useful for AI deep learning [23]. It seems that the performance of capsule endoscopy for diagnosing small bowel disease is improved using AI approaches[24]. An AI deep learning algorithm that can diagnose upper GI cancers with clinical endoscopic imaging data has been developed and validated[25]. CNNs in AI deep learning using numerous endoscopic image data have been developed that can detect and diagnose gastric cancer[26].

AI application in other diseases and endoscopy

Min *et al*[27] pointed out that one drawback of AI approaches is the need for large datasets to train the system; therefore, the quality of CNN-based AI endoscopy is limited by the need for a large number of high-quality endoscopic images. Machine learning and AI are important to diagnose functional GI disorders and aid healthcare professionals and researchers[28]. Ahmad *et al*[29] suggested that the level of AI and CAD in colonoscopy has reached that of human expert performance. A real-time AI system with deep learning technology has been developed to diagnose colorectal cancer[30]. An AI-oriented automated CAD system can identify histologic inflammation associated with ulcerative colitis[7]. Reismann *et al*[5] used AI to identify biomarker signatures to diagnose and classify the pediatric acute appendicitis.

APPLICATION OF AI IN THERAPEUTICS OF GI DISEASES

The application of AI in therapeutics of GI diseases has been expanding. The roles of AI in capsule endoscopy and other recent advanced diagnostic technologies have increased in therapeutics of GI diseases[31,32]. AI analysis was implemented to build neural network models enabling the classification of patients with biliary strictures and identify potential biomarkers in human bile[33]. Machine learning on medical examination records has stimulated the development of preventative measures for colorectal cancer[34]. Retrospective and prospective clinical studies have been conducted to diagnose and predict the prognosis of GI diseases including gastroesophageal reflux disease, atrophic corpus gastritis, acute pancreatitis, acute lower GI bleeding, esophageal cancer, nonvariceal upper GI bleeding, ulcerative colitis after cytoapheresis therapy, IBD, lymph node metastasis in T1 colorectal cancer and postoperative distant metastasis in esophageal squamous cell carcinoma[35]. Kather *et al*[36] found that deep learning can be used to predict microsatellite instability from histology in GI cancer. Azer[37] developed CNN models that can detect and classify colorectal polyps, which may increase colonoscopy application in appropriate colorectal cancer therapeutics. AI-guided tissue analysis has been developed that predicts stage III colon cancer outcomes, which may improve patient care with pathologists' assistance[6]. Ebigbo *et al*[38] found that AI utilization can be used to classify the Barret esophagus cancer. An AI-based clinical decision-support system has been developed to diagnose celiac disease[39]. Bioinformatics analyses have identified important genes associated with the pathogenesis and prognosis of esophageal squamous cell carcinoma, which may contribute to the molecular-targeted therapy [40]. Long non-coding RNA signature has been identified in locally advanced rectal adenocarcinoma, which may predict the response to neoadjuvant chemoradiotherapy in the patients[41]. Machine learning has been utilized for identifying prognostic biomarkers in the whole blood of IBD patients to support the personalized therapy [42]. Ontology tools such as Experimental Factor Ontology or the Ontology of Biomedical Association may be useful for mining the disease-phenotype associations for IBD[43]. Since the responsiveness toward drug alters in cancer cell phenotypes such as epithelial-mesenchymal transition in diffuse-type gastric cancer, the AI application in the identification of cancer subtype would lead to establish therapeutic strategy[44,45]. The machine learning algorithms may be applied to the therapy of the GI diseases in terms of gut-brain axis[28,46].

FUTURE PERSPECTIVES OF AI APPLICATION IN GI DISEASES

Despite the rapid advances of the application of AI in GI diseases, there still remains some concern in terms of the precision of AI-based diagnosis and the criteria for the therapeutics. Further evidence is needed to solely rely on CAD in colonoscopy to determine an appropriate endpoint[15]. Some regulatory coordination may be needed to use the combination of an AI-assisted device and CAD software[15]. The differences

in levels of AI performance would be considered and adjusted for application in clinical situations[14]. More high-quality datasets are needed to establish deep learning algorithms[14].

CONCLUSION

The area for AI application is rapidly expanding in the diagnosis and therapeutics of GI diseases. AI utilization in image recognition is currently being used to diagnose diseases and assist with personalized therapy. Future studies on disease-phenotype association are needed to maximize the capacity and performance of AI to aide in practical situations.

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