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Contents

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Contents

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

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

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OPINION REVIEW

Current situation and prospect of artificial intelligence application in endoscopic diagnosis of *Helicobacter pylori* infection

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Abstract

With the appearance and prevalence of deep learning, artificial intelligence (AI) has been broadly studied and made great progress in various fields of medicine, including gastroenterology. *Helicobacter pylori* (*H. pylori*), closely associated with various digestive and extradigestive diseases, has a high infection rate worldwide. Endoscopic surveillance can evaluate *H. pylori* infection situations and predict the risk of gastric cancer, but there is no objective diagnostic criteria to eliminate the differences between operators. The computer-aided diagnosis system based on AI technology has demonstrated excellent performance for the diagnosis of *H. pylori* infection, which is superior to novice endoscopists and similar to skilled. Compared with the visual diagnosis of *H. pylori* infection by endoscopists, AI possesses voluminous advantages: High accuracy, high efficiency, high quality control, high objectivity, and high-effect teaching. This review summarizes the previous and recent studies on AI-assisted diagnosis of *H. pylori* infection, points out the limitations, and puts forward prospect for future research.

Key Words: Artificial intelligence; *Helicobacter pylori*; Endoscopy; Diagnosis; Deep learning; Machine learning

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Core Tip: In recent years, artificial intelligence (AI) has been rapidly developed and applied in various fields of medicine, including gastroenterology. We witnessed the promising application of AI in endoscopic diagnosis of *Helicobacter pylori* infection. In this review, we summarize the advantages of AI, point out the limitations of current studies, and put forward the direction of future research.

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INTRODUCTION

Helicobacter pylori (*H. pylori*) is a Gram-negative bacterium that infects the human stomach and is closely associated with a variety of diseases, including chronic gastritis, peptic ulcer, gastric adenocarcinoma, mucosa-associated lymphoid tissue lymphoma, and other digestive diseases, as well as extradigestive diseases of the blood system, nervous system, cardiovascular system, skin, and ophthalmology[1,2]. The International Agency for Research on Cancer has categorized *H. pylori* as a group 1 carcinogen. A recent systematic review and meta-analysis pooling 410879 participants showed that the overall prevalence of *H. pylori* infection worldwide was 44.3% [95% confidence interval (CI): 40.9-47.7][3]. Therefore, accurate diagnosis of *H. pylori* infection is extremely important for the prevention and treatment of related diseases. Currently, various diagnostic methods are available for detecting *H. pylori* infections (non-invasive and invasive methods)[4], but endoscopic evaluation to determine the *H. pylori* infection status is an irreplaceable method, which can assist in the screening of early gastric cancer.

Artificial intelligence (AI) is a technology science that studies and develops the theory, method, technology, and application system that is used to simulate, extend, and expand human intelligence. With the emergence and development of deep learning (DL), the application of AI in medicine has also been enthusiastically explored and extensively studied[5-8]. Numerous research studies, using AI technology to identify or distinguish images in different medical fields including gastroenterology, radiology, neurology, orthopedics, pathology, and ophthalmology, have been published[9].

In this review, we focus on the application of AI in the field of endoscopic diagnosis of *H. pylori* infection and discuss future prospect.

SIGNIFICANCE OF ENDOSCOPIC DIAGNOSIS OF *H. PYLORI* INFECTION

Most patients with gastric cancer have or have had *H. pylori* infection[10,11]. A large number of studies have indicated that the eradication of *H. pylori* can effectively reduce the risk of gastric cancer[12-14]. However, the study conducted by Mabe *et al* [15] showed that people after *H. pylori* eradication still have a higher risk of developing gastric cancer than people who have not been infected with *H. pylori*. Therefore, even after *H. pylori* eradication, regular endoscopic and histological surveillance is strongly recommended[16,17]. In consequence, endoscopic assessment of *H. pylori* infection status (non-infection, past infection, and current infection) has become increasingly important.

The Kyoto classification of gastritis was proposed, which is used to assess the status of *H. pylori* infection and more accurately evaluate the risk of gastric cancer[18]. According to the characteristics of the gastric mucosa under endoscopy, the gastric mucosa can be divided into the following three situations: *H. pylori*-uninfected gastric mucosa, *H. pylori*-infected gastric mucosa, and *H. pylori*-past infected gastric mucosa [18,19]. It should be noted that the Kyoto classification score is the sum of scores for five endoscopic features (atrophy, intestinal metaplasia, enlarged folds, nodularity, and diffuse redness with or without regular arrangement of collecting venules) and ranges from 0 to 8. The scoring system demonstrated excellent ability to evaluate *H. pylori* infection and predict the risk of gastric cancer[20]. However, above endoscopic features do not have objective indicators, and there is the potential for interobserver or intraobserver variability in the optical diagnosis of *H. pylori*-infected mucosa[21]. In other words, for endoscopic diagnosis of *H. pylori* infection, the diagnostic consistency among endoscopists is not ideal. Moreover, professional endoscopists can determine *H. pylori* infection with punctilious visual inspection of the mucosa during endoscopic examination, but novices need a large amount of time to perform this task effectively.

The significance of endoscopic surveillance is not limited to determining whether *H. pylori* is infected, not, or past, but can make an overall evaluation of the stomach. First of all, the classical Kimura-Takemoto classification is still widely used today to help endoscopists classify the atrophic pattern of the stomach by observing the endoscopic atrophic border[22]. Second, most gastric cancers develop from *H. pylori* associated gastritis. This can occur *via* a multistep pathway of precancerous lesions — in particular, atrophic gastritis, intestinal metaplasia, and dysplasia/intraepithelial neoplasia[16]. We can use histological staging systems such as OLGA and OLGIM to make an assessment of gastric cancer risk by the severity and extent of atrophy and intestinal metaplasia[23-25]. Finally, when one detection method shows *H. pylori* negativity, but there are typical signs of *H. pylori* infection under endoscopy, another different method should be selected for confirmation in this case to avoid missed diagnosis.

WHAT IS AI?

Physicians and endoscopists may be confused about the precise concept of AI, machine learning (ML), and DL. AI is a macro concept with many branches (*e.g.*, Planning and Scheduling, Expert Systems, Multi-Agent Systems, and Evolutionary Computation). In general, there are three approaches to AI: Symbolism (rule based, such as IBM Watson), connectionism (network and connection based, such as DL), and Bayesian (based on the Bayesian theorem)[26]. In AI, computers can imitate humans and display intelligence similar to that of humans.

ML is a subset of AI, which is a method to realize AI. ML is defined as a set of methods that automatically detect patterns in data, and then utilize the uncovered patterns to predict future data or enable decision making under uncertain conditions [27]. ML is approximately divided into supervised and unsupervised methods. Unsupervised learning occurs when the purpose is to identify groups within data according to commonalities, with no *a priori* knowledge of the number of groups or their significance. Supervised learning occurs when training data contain individuals represented as input–output pairs. Input comprises individual descriptors while output comprises outcomes of interest to be predicted — either a class for classification tasks or a numerical value for regression tasks. Then, the supervised ML algorithm learns predictive models that whereafter allow to map new inputs to outputs[28]. The most basic practice of ML [*e.g.*, support vector machine (SVM), random forest, and Gaussian mixture models] is to use algorithms to parse data so as to learn from them, and then make decisions and predictions about events in the real world. Today's ML has made great achievements in computer vision and other fields; however, it has its limitations, requiring a certain amount of manual instruction in the process. The image recognition rate of ML is enough to realize commercialization, but it is still very low in certain fields, which is why image recognition skills are still not as good as human capabilities[29].

DL [*e.g.*, artificial neural network, deep neural network (DNN), convolutional neural network (CNN), and recurrent neural network] is a process in which the computer collects, analyzes, and processes the required data quickly while performing certain tasks, without having to accept the formal data, which is a technique to achieve ML. DL has the characteristics of autonomous learning; once the training data set is provided, the program can extract the key features and quantities by using back-propagation algorithm and changing the internal parameters of each neural network layer, without human instructions[30]. Compared with the conventional hand-crafted algorithm, the recently developed DL algorithm can automatically extract and learn the discriminative features of images, and then classify these images[31]. DL has the potential to automatically detect lesions, classify lesions, prompt differential diagnosis, and write preliminary medical reports, which will be realized in the near future.

CNN is a DNN based on the principle that the visual cortex of the human brain processes and recognizes images, which is now the most popular network architecture for DL for images[29]. CNN uses the multiple network layers (consecutive convolutional layers followed by pooling layers) to extract the key features from an image and provide a final classification through the fully connected layers as the output[30]. Compared to other DL structures, CNN is a prevalent method for image recognition because of its excellent performance in both video and audio applications. For example, CNN performs best in image classification in large image repositories such as ImageNet[32]. Additionally, CNN is easier to train than other DL techniques and has the advantage of using fewer parameters.

In recent years, AI has flourished in the field of gastroenterology, with applications throughout the digestive tract, especially in image recognition and classification. van der Sommen *et al*[33] reported an automated computer algorithm for the detection of early neoplasia in Barrett's esophagus based on 100 images from 44 patients with Barrett's esophagus. At per-image level, the sensitivity and specificity of the algorithm were both 0.83, and at the patient level, 0.86 and 0.87, respectively. Everson *et al*[34] trained a CNN to classify intrapapillary capillary loops for the real time prediction of early squamous cell cancer of the esophagus, demonstrating strong diagnostic performance with a sensitivity of 93.7% and accuracy of 91.7%, which is comparable to an expert panel of endoscopists. Xu *et al*[35] established a deep CNN system to detect gastric precancerous conditions (including gastric atrophy and intestinal metaplasia) by image-enhanced endoscopy (IEE). In the internal test set, the multicenter external test set, and the prospective video test set, the diagnostic accuracy for gastric atrophy was 0.901, 0.864, and 0.878, and that of intestinal metaplasia was 0.908, 0.859, and 0.898, respectively. To assist endoscopists in distinguishing early gastric cancer, Kanesaka *et al*[36] studied a computer-aided diagnosis (CAD) system utilizing SVM technology to facilitate the use of magnifying narrow band imaging (NBI), which revealed an accuracy of 96.3%, sensitivity of 96.7%, and specificity of 95%. Since capsule endoscopic image viewing and diagnosis is an extremely time-consuming process, Park *et al*[37] developed an AI-assisted reading model based on the Inception-Resnet-V2 model to identify different types of lesions and evaluate the clinical significance of this model. The results showed that the model not only helped the operator to improve the lesion detection rates, but also reduced the reading time. Urban *et al*[38] constructed a deep CNN model, including 8641 images from 2000 patients, to locate and identify colorectal polyps, which revealed an area under the receiver operating characteristic curve of 0.991 and accuracy of 96.4%. Also, several studies have proved the feasibility and prospect of AI-assisted endoscopy in the diagnosis of *H. pylori* infection.

AI-ASSISTED ENDOSCOPIC DIAGNOSIS OF *H. PYLORI* INFECTION

As early as 2004, Huang *et al*[39] independently developed a CAD model based on a refined feature selection with neural network (RFSNN) technique which is planned for predicting *H. pylori*-related gastric histological features. A total of 104 dyspeptic patients were enrolled in this study and all subjects were prospectively evaluated by endoscopy and gastric biopsy. The authors used endoscopic images and histological features of 30 patients (15 with and 15 without *H. pylori* infection) to train the RFSNN model, and then used image parameters of the remaining 74 patients to construct a predictive model of *H. pylori* infection. At the same time, six endoscopic physicians (three novices and three skilled seniors) were invited to predict the histological features of the gastric antrum from endoscopic images. The results showed that the sensitivity and specificity for detecting *H. pylori* infection were 85.4% and 90.9%, respectively, when the RFSNN model included images of the same patient's antrum, body, and cardia for analysis. Together, the accuracy of the six endoscopists in predicting *H. pylori* infection was 67.5%, 64.8%, 72.9%, 74.3%, 79.7%, and 81.1%, respectively (the first three were novices and the second three were skilled elderly). Obviously, the accuracy of RFSNN model in predicting *H. pylori* infection by the antrum images was 85.1% higher than that of endoscopists. Notably, the prediction system has a high sensitivity and specificity in the diagnosis of atrophy and intestinal metaplasia, which was also superior to that of endoscopists. This RFSNN system provides real-time and comprehensive information about the stomach during endoscopy and has the potential to overcome the shortcomings of the localized biopsy. For various reasons, white-light endoscopy was used throughout the study, instead of IEE, which is more conducive to the diagnosis of *H. pylori* infection. As an early study of AI in diagnosing *H. pylori* infection, this paper provides reference data and innovative ideas for subsequent studies.

In 2008, Huang *et al*[40] conducted a further study in the field of AI-assisted endoscopy in the diagnosis of *H. pylori* infection. They designed a CAD system combining SVM and sequential forward floating selection (SFFS) to diagnose gastric histology of *H. pylori* using the features of white-light endoscopic images. This study aimed to use SFFS to select the most suitable feature to describe the relationship between histology and a large number of candidate image features, and then use SVM for classification. A total of 236 dyspepsia patients were enrolled in this study, 130 of whom were defined as *H. pylori*-infected patients using histological examination as the gold standard. The results showed that the accuracy of diagnosing *H. pylori* infection was 87.8%, 87.6%, and 86.7%, respectively, when the SVM with SFFS system was used to analyze the images of the antrum, body, and cardia. Compared with SVM without SFFS, the SVM with SFFS system had a higher diagnostic accuracy in most cases. This indicates that it is of great significance to use SFFS for screening before the classification of image features, which not only improves the diagnostic accuracy by excluding features with low correlation, but also reduces the time of training and testing system. Furthermore, 1000 repeated tests were carried out on the classification results, which proved the experiment reliability. In addition, the authors compared the new diagnostic system with the previous system[39] that used a neural network with feature selection to detect *H. pylori* infection, and it was shown that the new system had a higher classification rate. It is a pity that both studies classified *H. pylori* infection status only as infected and uninfected, and the authors did not consider cases where the infection disappeared or was eradicated with drugs.

In 2017, Shichijo *et al*[41] developed two deep CNN systems, one based on 32208 unclassified images either positive or negative for *H. pylori* (as a development data set) and the other based on images classified according to eight anatomical locations (cardia, upper body, middle body, lesser curvature, angle, lower body, antrum, and pylorus). Then, the test data set included a total of 11481 images from 397 patients (72 *H. pylori* positive and 325 negative). Patients who tested positive on any of these assays (including blood or urine anti-*H. pylori* immunoglobulin (Ig) G levels, fecal antigen test, or urease breath test) were classified as *H. pylori* positive. To compare the diagnostic performance of the two CNNs, 23 endoscopists were invited to evaluate the test data sets, together. According to their experience, the endoscopists were divided into three groups: "Certified group," "relatively experienced group," and "beginner group". The test results showed that for the first CNN constructed with unclassified images, the area under the receiver operating curve (ROC) curve (AUC) was 0.89 at a cut off value of 0.43. The sensitivity, specificity, accuracy, and diagnostic time of the first CNN were 81.9%, 83.4%, 83.1% and 3.3 min, respectively. These values for the secondary CNN were 88.9%, 87.4%, 87.7%, and 3.2 min, respectively, and the AUC was 0.93 at a cutoff value of 0.34. Furthermore, these values for the overall endoscopists were 79.0%, 83.2%, 82.4%, and 230.1 min, respectively. After statistical analysis, there was no difference in sensitivity, specificity, or accuracy between the first CNN and the 23 endoscopists in the diagnosis of *H. pylori* infection. However, the secondary CNN which was constructed with categorized images according to the location of the stomach was found to have a significantly higher accuracy than the endoscopists (by 5.3%; 95%CI: 0.3-10.2). Besides, the board-certified group was found to have a significantly higher specificity (89.3% *vs* 76.3%, $P < 0.001$) and accuracy (88.6% *vs* 75.6%, $P < 0.001$) than the beginner group. Similarly, a significant difference was observed between the relatively experienced group and the beginner group. In brief, the diagnostic ability of the second CNN is almost as good as that of a skilled endoscopist. In terms of diagnosis time, CNN even completely surpassed the endoscopists. However, still images were adopted to construct CNN algorithm in this study, and whether real-time diagnosis could be realized based on dynamic images remains to be researched.

One weakness of this study was that it did not include the situation after the eradication of *H. pylori*. To address this issue, the authors soon conducted a new study to further elaborate on the role of AI in assessing *H. pylori* infection status. A deep CNN which was constructed by Shichijo *et al*[42] in 2019 was pre-trained and fine-tuned on a dataset of 98564 endoscopic images from 5236 patients (742 *H. pylori*-positive, 3649 *H. pylori*-negative, and 845 *H. pylori*-eradicated). As in the previous study, this AI-based diagnostic system was developed using classified images following eight regions of the stomach (cardia, upper body, middle body, lesser curvature, angle, lower body, antrum, and pylorus). An independent test data set including a total of 23699 images from 847 patients (70 *H. pylori* positive, 493 *H. pylori*-negative, and 284 *H. pylori*-eradicated) was prepared to evaluate the diagnostic accuracy of the constructed CNN. According to the statistical analysis, the proportions of accurate diagnoses were 80% (465/582) for negative, 84% (147/174) for eradicated, and 48% (44/91) for positive. The performance of this diagnostic system is comparable to that of skilled endoscopists who, in one study, diagnosed these statuses in 88.9%, 55.8%, and 62.1% of cases, respectively[43]. Subsequently, the authors assessed the diagnostic ability of CNN for distinguishing *H. pylori* positive from eradicated (excluding *H. pylori* negative patients). Among 70 positive patients, the CNN diagnosed correctly as positive in 46 (66%), while out of 284 eradicated patients, the CNN diagnosed correctly as eradicated in 243 (86%). Nevertheless, this study did not take into account the time after *H. pylori* eradication, but the histological features of atrophic gastritis may disappear a few years after eradication[44]. Then, endoscopic features also change possibly in the diagnosis.

In 2019, Zheng *et al*[45] designed a novel computer-aided decision support system combined with a CNN model (ResNet-50, a state-of-the-art CNN consisting of 50 Layers). This system was expected to be used to retrospectively evaluate *H. pylori* infection based on white-light images (WLI) of the stomach. Totally 1507 patients (11729 gastric images) including 847 with *H. pylori* infection as the derivation cohort were used to train the algorithm. The authors created three DL models: (1) Single gastric image for all gastric images; (2) Single gastric image by different gastric locations (fundus, corpus, angularis, and antrum); and (3) Mmultiple gastric images for the same patient. Afterwards, 452 patients (3755 images) including 310 with *H. pylori* infection as the validation cohort were used to evaluate the diagnostic accuracy CNN for the evaluation of *H. pylori* infection. The evaluation results showed that for a single gastric image, the AUC, sensitivity, specificity, and accuracy were 0.93, 81.4%, 90.1%, and 84.5%, respectively. When evaluating a single gastric image by different anatomical locations, the AUCs from high to low were 0.94 (corpus), 0.91 (angularis), 0.90 (antrum), and 0.82 (fundus). According to statistical analysis, the CNN model using a single corpus image had the highest AUC ($P < 0.01$) compared with the antrum or fundus. More importantly, when multiple stomach images per patient were applied to the CNN model, the AUC, sensitivity, specificity, and accuracy were as high as 0.97, 91.6%, 98.6% and 93.8%, respectively. Consequently, the CNN model using multiple gastric images had a higher AUC compared with a single gastric image ($P < 0.001$) or body gastric image ($P < 0.001$). When selecting endoscopic images to be included in this study, images of poor quality (*i.e.*, blurred images, excessive mucus, food residue, bleeding, and/or insufficient air insufflation) were excluded, which however could not be avoided in the actual operation of endoscopy. Therefore, the CNN's ability to recognize low-quality images needs to be further exploited.

In 2020, Yoshii *et al*[19] established a prediction model based on an ML procedure to prospectively evaluate *H. pylori* infection status (non-infection, past infection, and current infection) and compared it with general assessment by seven well-experienced endoscopists using the Kyoto classification of gastritis. The study recruited a total of 498 subjects (315 non-infection, 104 past infection, and 79 current infection) and the gold standard for determining the *H. pylori* infection status was the history of eradication therapy and the presence of *H. pylori* IgG antibody. The results showed that the overall diagnostic accuracy rate of the seven endoscopists was 82.9%. The diagnostic accuracy of the prediction model without *H. pylori* eradication history was 88.6% and with eradication history was 93.4%. Obviously, the results improved in the model with eradication history. There was no significant difference in diagnostic accuracy between the predictive model and skilled endoscopists. One of the limitations of this study was that only one test method was used to evaluate current status of *H. pylori* infection. In addition, urea breath test or fecal antigen test would evaluate current situation of *H. pylori* infection more surpassingly than that of *H. pylori* IgG antibody levels, especially in patients with an *H. pylori* antibody titer of 3-10 U/mL.

All of the above studies used WLI to build the CAD systems based on AI technology. Besides, some reports have shown the potential of image-enhanced endoscopies (IEEs) in diagnoses of *H. pylori* infection, such as blue laser imaging (BLI), linked color imaging (LCI), and NBI[46-48]. In 2018, Nakashima *et al*[49] built an AI diagnostic system based on a deep CNN algorithm for prospective diagnosis of *H. pylori* infection. A total of 222 subjects (105 *H. pylori*-positive) were recruited and received esophagogastroduodenoscopy and a serum test for *H. pylori* IgG antibodies. A serum *H. pylori* IgG antibody titer ≥ 10 U/mL was considered positive for *H. pylori* infection, while a titer < 3.0 U/mL was considered negative. In addition, subjects with serum *H. pylori* IgG antibody titers between 3.0 and 9.9 U/mL were excluded. In this study, 162 subjects (1944 images) including 75 with *H. pylori* infection were enrolled as a training group for AI training. For the remaining 60 subjects (30 *H. pylori*-positive and 30 *H. pylori*-negative), one WLI, one BLI-bright, and one LCI image of the lesser curvature of the gastric body were collected as a test group to evaluate the diagnostic performance of AI. According to statistical analysis, the AUC, sensitivity, and specificity for WLI were 0.66, 66.7%, and 60.0%, respectively. These indicators were 0.96, 96.7%, and 86.7% for BLI-bright, and 0.95, 96.7%, and 83.3% for LCI, respectively. The AUCs obtained for BLI-bright and LCI were markedly larger than that for WLI ($P < 0.01$). Obviously, this new AI diagnostic system was efficiently adapted to those laser IEEs rather than WLI; hence, it demonstrated an excellent ability to diagnose *H. pylori* infection using the IEEs. It is a pity that patients with a history of *H. pylori* eradication therapy were not included in this study, because this AI system is only an elementary tool and cannot fully evaluate the complex features of the stomach.

In 2020, Yasuda *et al*[21] constructed an automatic diagnosis system based on the SVM algorithm for *H. pylori* infection using LCI images. The authors expected to use this system to retrospectively diagnose *H. pylori* infection and compared its accuracy with that of endoscopists. In this study, endoscopic images of 32 patients (128 images in total) were included as training data, and four images were collected from each patient from the lesser (angle-lower body and middle-upper body) and greater (angle-lower body and middle-upper body) curvature. The diagnosis of *H. pylori* infection was based on more than two different tests: A histological examination, a serum antibody test, a stool antigen test, and/or a 13C-urea breath test. Regarding *H. pylori* infection of the subjects, 14 cases were *H. pylori* positive and 18 were negative. The authors used 525 LCI images from 105 patients (42 *H. pylori* infected, 46 post-eradication, and 17 uninfected) collected from the lesser (angle-lower body and middle-upper body) and greater (angle-lower body and middle-upper body) curvature and the fornix to evaluate the diagnostic capabilities of the system. It was worth noting that for the *H. pylori* post-eradicated subjects, more than 1 year (average of 5.6 years) had passed since *H. pylori* was successfully eradicated after undergoing endoscopy. At the same time, three doctors with different experiences (A, an expert involved in the development of LCI; B, a gastroenterology specialist; and C, a senior resident) also evaluated the same LCI images. The results showed that the accuracy of the AI system, A, B, and C in the diagnosis of *H. pylori* infection was 87.6%, 90.5%, 89.5%, and 86.7%, respectively. Accuracy of the AI system was higher than that of the inexperienced doctor (doctor C), but there was no significant difference between the diagnosis of the doctors and the AI system (P > 0.05). According to the sub-analysis of the patients divided with respect to state of *H. pylori* infection, the accuracy of the AI system, doctors A, B ,and C in the diagnosis of *H. pylori* post-eradication were 82.6%, 87.0%, 89.1%, and 76.1%, respectively. According to the sub-analysis of AI diagnosis for each image of stomach area, accuracy of the lesser curvature of the middle-upper body (88.6%) was significantly higher than that of the fornix (69.5%) and the greater curvature of the middle-upper body (73.3%). However, due to the small number of samples included in this study, there may be a risk of large sampling error.

LIMITATIONS AND FUTURE DIRECTION

The above studies show to a great extent that the application of AI in endoscopic diagnosis of *H. pylori* infection is practical, feasible, and promising. The detailed information of these studies is shown in Table 1. Compared with the manual identification and diagnosis by endoscopists, the CAD system based on AI technology has many irreplaceable advantages: (1) High accuracy: According to the current studies, AI is better than novice endoscopists in the diagnosis of *H. pylori* infection in terms of sensitivity, specificity, and accuracy, and is almost comparable to skilled endoscopists; (2) High efficiency: Thanks to today's highly developed computers, AI can classify thousands of endoscopic images in minutes, which can take a great deal of time and energy on the part of endoscopists. At the same time, the efficient image recognition lays a foundation for the real-time diagnosis of *H. pylori* infection under endoscopy; (3) High quality control: Some studies have found that adenoma detection rate decreases gradually with the extension of the working hours of endoscopists. This also suggests that endoscopist fatigue may lead to a decrease in the effectiveness of screening colonoscopy[50,51]. However, the CAD system based on AI technology is not disturbed by external factors and provides excellent quality control; (4) High objectivity: As we all know, it is completely subjective for endoscopists to judge *H. pylori* infection by observing the features of the gastric mucosa under endoscopy. Although the decision-making power is still in the hands of endoscopists, AI assisted endoscopy can help to provide an objective second opinion as a reference[52]; and (5) High-effect teaching: AI is capable of undertaking the teaching work of skilled endoscopists, and provides novices with more accessible, convenient, and objective guidance.

However, the application of AI in endoscopic diagnosis of *H. pylori* infection is still in the preliminary research stage at present, which has many limitations to be overcome. It is promising to put this technology into real clinical practice, but much research and further refinement are needed before that can happen. First of all, all of the above studies are single-center studies and most of them only used images from a single endoscopic device. Different images at different endoscopy centers may not guarantee compatibility and extensibility of the CAD system developed by the researchers and limit the generalization of the results. Next, so far, most of the studies

Table 1 Characteristics of current studies about AI-assisted endoscopic diagnosis of *Helicobacter pylori* infection

Ref.	Type of AI	Type of endoscopy	Training set	Validation set	AUC	Sensitivity (%)	Specificity (%)	Accuracy (%)
Huang *et al*[39], 2004	RFSNN	WLI	30 patients	74 patients	NA	85.4	90.9	NA
Huang *et al*[40], 2008	SVM with SFFS	WLI	236 patients	236 patients	NA	82.6 (antrum); 89.1 (body); 100 (cardia)	94.0 (antrum); 85.8 (body); 72.0 (cardia)	87.8 (antrum); 87.6 (body); 86.7 (cardia)
	SVM without SFFS	WLI	236 patients	236 patients	NA	98.5 (antrum); 98.7 (body); 99.1 (cardia)	70.8 (antrum); 71.5 (body); 70.3 (cardia)	86.3 (antrum); 86.4 (body); 86.0 (cardia)
Shichijo *et al* [41], 2017	CNN (first)	WLI	1750 patients, 32208 images	397 patients, 11481 images	0.89	81.9	83.4	83.1
	CNN (second, constructed according to anatomical locations)	WLI	1750 patients, 32208 images	397 patients, 11481 images	0.93	88.9	87.4	87.7
Shichijo *et al* [42], 2019	CNN	WLI	5236 patients, 98564 images	847 patients, 23699 images	NA	NA	NA	48 (*H. pylori*-positive); 84 (*H. pylori*-eradicated); 80 (*H. pylori*-negative)
Zheng *et al*[45], 2019	CNN (first, single image for all image)	WLI	1507 patients, 76146 images	452 patients, 3755 images	0.93	81.4	90.1	84.5
	CNN (second, single image by different locations)	WLI	1507 patients, 76146 images	452 patients, 3755 images	0.90 (antrum); 0.91 (angularis); 0.94 (corpus); 0.82 (fundus)	76.1 (antrum); 78.8 (angularis); 81.6 (corpus); 72.4 (fundus)	88.5 (antrum); 90.5 (angularis); 92.1 (corpus); 80.5 (fundus)	80.3 (antrum); 82.8 (angularis); 85.6 (corpus); 75.3 (fundus)
	CNN (third, multiple images per patient)	WLI	1507 patients, 76146 images	452 patients, 3755 images	0.97	91.6	98.6	93.8
Yoshii *et al*[19], 2020	ML (model without *H. pylori* eradication history)	WLI	NA	498 patients	NA	91.6 (non-infection); 75.0 (past infection); 59.5 (current infection)	88.6 (non-infection); 89.9 (past infection); 94.7 (current infection)	88.6
	ML (model with *H. pylori* eradication history)	WLI	NA	498 patients	NA	94.0 (non-infection); 94.0 (past infection); 88.1 (current infection)	93.4 (non-infection); 100.0 (past infection); 94.7 (current infection)	93.4
Nakashima *et al* [49], 2018	CNN	WLI	162 patients, 1944 images	60 patients, 60 images	0.66	66.7	60.0	NA
	CNN	BLI-bright	162 patients, 1944 images	60 patients, 60 images	0.96	96.7	86.7	NA
	CNN	LCI	162 patients, 1944 images	60 patients, 60 images	0.95	96.7	83.3	NA
Yasuda *et al* [21], 2020	SVM	LCI	32 patients, 128 images	105 patients, 525 images	NA	90.4	85.7	87.6%

AI: Artificial intelligence; AUC: Area under curve; BLI: Blue laser imaging; CNN: Convolutional neural network; *H. pylori*: *Helicobacter pylori*; LCI: Linked color imaging; ML: Machine learning; NA: Not applicable; RFSNN: Refined feature selection with neural network; SFFS: Sequential forward floating selection; SVM: Support vector machine; WLI: White-light imaging.

have adopted a retrospective method which could be subject to considerable selection bias. As it is, images of high quality or with distinct features of *H. pylori* infection may be preferred for inclusion in studies, which probably lead to exaggerated diagnostic performance of AI and overestimation of the accuracy.

In addition, researchers and endoscopists need to be aware of potential pitfalls and biases in AI research, such as overfitting, spectrum bias, data snooping bias, straw man bias, and P-hacking bias, which can be reduced or eliminated through rigorous research design and appropriate methods[53]. Overfitting occurs when the AI algorithm modulates itself too much on the training dataset and the developed prediction system does not generalize well to new datasets. The translation, rotation, scaling, and clipping of the original endoscopic images to enlarge datasets may be one of the causes of overfitting. Spectrum bias occurs when the training dataset does not adequately represent the range of patients who will be applied in clinical practice (target population)[54]. External validation using independent datasets for model development, collected in a way that minimizes the spectrum bias, is necessary to prove the real performance of an AI algorithm and is important in the verification of any diagnostic or predictive model[55,56]. It is a pity that there is no study that utilized external validation for the performance of an established AI system in this review. It is worth noting that AI has one unavoidable disadvantage that needs to be addressed: "Black box" nature (lack of interpretability), which means that AI technology cannot explain the decision-making processes. But precise interpretability, which can provide diagnostic evidence, assist reduce bias, and build social acceptance, is extremely important in clinical practice. Some methods, such as class activation map, can supplement the "black box" features, hoping to be applied to future research [57].

Besides, some studies only divided *H. pylori* infection status into infected and uninfected, without considering *H. pylori* post-eradication, which is not in line with the clinical reality. Some studies only used single diagnostic method as the gold standard to judge *H. pylori* infection, which will lead to a great loss of diagnostic accuracy. Some studies included a small quantity of subjects and images, which may cause large errors and affect the credibility of the conclusions. IEE has great potential to improve the diagnosis rate of *H. pylori* infection, but there are few studies on the construction of CAD system based on AI using IEE images. What's more, all of the studies in this review were conducted in Asia, and racial difference cannot be avoided.

Finally, before any new technology is introduced into medical practice, ethical problems cannot be avoided and need to be properly solved, including AI technology. AI is not perfect, making no perfect predictions. If a CAD system based on AI technology misdiagnoses or misses diagnoses, who will be held accountable — the endoscopist, medical institution, or manufacturer? What is the attitude of endoscopists towards the results of AI diagnosis? Question and reject the AI, learn from it, or accept the diagnosis indiscriminately? In the era of AI, how to build a harmonious doctor-patient relationship?

Anyway, in the future, we should expect a "perfect study", a multicenter, large sample, generalized, and prospective study, which has strict inclusion/exclusion criteria, a suitable gold standard for diagnosis and external validation of third-party independent datasets, using high quality datasets to establish a high diagnostic accuracy, and the stability of the CAD system based on AI technology to judge the *H. pylori* infection status. More importantly, ethical principles and laws and regulations related to AI technology need to be improved to protect everyone's legitimate interests. However, it should be pointed out that AI will not completely replace physicians, but will increase diagnostic accuracy, improve diagnostic efficiency, and reduce the burden on physicians. Health care workers need to consider patients' preferences, environment, and ethics before making decisions, which AI cannot replace[58].

CONCLUSION

The era of AI is coming, with both opportunities and challenges. AI is undoubtedly a greatly excellent assistant, which can help endoscopists to evaluate *H. pylori* infection status more quickly, accurately and easily under the endoscope. At the same time, there are some issues as well as ethical considerations that need to be addressed before AI is applied in clinical practice.

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MINIREVIEWS

Progress and prospects of artificial intelligence in colonoscopy

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Abstract

Artificial intelligence (AI) is a branch of computer science. As a new technological science, it mainly develops and expands human intelligence through the research of intelligence theory, methods and technology. In the medical field, AI has bright application prospects (for example: imaging, diagnosis and treatment). The exploration of robotic gastroscopy and colonoscopy systems is not only a bold attempt, but also an inevitable trend of AI in the development of digestive endoscopy in the future. Based on the current research findings, this article summarizes the research progress of colonoscopy, and looking forward for the application of AI in colonoscopy.

Key Words: Artificial intelligence; Colonoscopy; Application; Gastrointestinal; Endoscopy

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Core Tip: Artificial intelligence is a new technological science that studies and develops theories, methods, technologies and application systems for simulating and expanding human intelligence. This article will systematically review the exploration and application of artificial intelligence technology in colonoscopy, and look forward to the development direction of intelligent colonoscopy.

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INTRODUCTION

Artificial intelligence (AI) is a new technological science that studies and develops theories, methods, technologies and application systems for simulating and expanding human intelligence. It relates to many fields, for instance, computer science, cybernetics, information theory, and neuroscience. The first AI seminar at Dartmouth College in 1956 marked the birth of the AI, but the development of AI has experienced several ups and downs. AI has achieved results both theoretically and practically in these cycles. It has made solid progress in the world, especially when scientists made breakthrough progress in deep learning.

In its more than 60 years of development, AI has been used in computer vision, natural language processing, data mining, automatic speech recognition. The applications of intelligent robot, automatic programming, and expert systems are becoming increasingly mature, making AI one of the three cutting-edge technologies in the 21st century.

AI is hailed as the stethoscope of the 21st century[1]. With the strengthening of people's health awareness, preventive and precise treatments have been paid more attention at the same time. The improvement of medical standards and the improvement of medical equipment have made the process of patients' visits produce increasingly medical data. Image recognition, speech/semantic recognition, and expert system have received more and more attention in the medical field, smart medical products have gradually emerged[2-4]. A large amount of image data and diagnostic data are used to simulate the mind and diagnostic process of medical experts especially in the field of medical image recognition, AI is expected to partially replace traditional empirical diagnosis so as to provide a more reliable diagnosis and treatment plan.

AI HELPS BREAK THROUGH THE BOTTLENECK OF COLONOSCOPY

In recent years, the incidence of colorectal adenoma, colorectal cancer, and inflammatory bowel disease has increased significantly[5-7], causing great harm to human's health. Colonoscopy is the first choice for the diagnosis and treatment of colorectal diseases. It can not only intuitively judge the nature of the lesion, but also obtain biopsy specimens for pathological diagnosis. Colonoscopy is of great significance, especially in preventing and treating colorectal cancer, as it can be used to screen and follow up high-risk groups in patients who are asymptomatic. We can greatly reduce the incidence of colorectal cancer by adopting corresponding treatments according to the condition, and achieve the purpose of primary prevention. Even if colorectal lesions develop to the early stage of cancer, the 5-year survival rate of endoscopic treatment can still exceed 90%[6].

Studies have found that gradual expansion of colorectal cancer screening in asymptomatic populations and the early diagnosis promotion have extremely important socio-economic significance[8-10]. The popularization of colonoscopy screening among high-risk populations is restricted by the hard operation, excessive physical exertion, and limitation of technical inheritance, which has caused bottlenecks. At this time, the development and maturity of AI technology provides new ideas and possibilities for breaking through these bottlenecks.

RESEARCH ON THE MECHANISM OF COLONOSCOPY INTO LOOPS AND UNLOOPS

According to the anatomical characteristics of the intestine, the ascending colon, descending colon and upper rectum, which are straighter and smaller in extension, are generally easier to pass with colonoscopy. However, the transverse colon and sigmoid colon are in a free state, with longer mesentery and larger mobility, which can easily cause loops. Common types of loops in the sigmoid colon include N loops, α loops, reverse α loops, and atypical loops, while the common types of loops in the transverse colon include deep loops/dangling loops, deep large γ loops, and inverted splenic loops[11]. Usually, the time for a skilled endoscopist to enter the cecum is about 4-6 minutes, but someone who have difficulty in this process may not be able to reach it, even if the operation time is more than 1 h[12].

In view of the factors of patients who develop a loop during colonoscopy, experts have conducted many studies which found that factors including long-term constipation, abdominal surgery history, female, body mass index is lower or higher than normal, the volume of visceral fat tissue is low and the proficiency of colonoscopy directly affect the formation of intestinal loops[13] (Figure 1).

The successful removal of the loop is key for a colonoscopy to reach the cecum, and it is necessary for the endoscopist to be able to observe and monitor the shape of colonoscopy in order to overcome this technical difficulty. With the continuous advancement of colonoscopy accessories, magnetic endoscopic imaging (MEI), a real-time three-dimensional imaging colonoscopy-assisted positioning technology, has become an effective tool for observing the shape of the colonoscopy in human body [14]. There is a meta-analysis that summarizes 8 randomized controlled trials and contains 2967 patients which compares cecal intubation rates and times, sedation dose, abdominal pain scores and the use of ancillary maneuvers between MEI and standard colonoscopy. The conclusion is that compared with traditional technique, MEI has an advantages in cecal intubation rate, but MEI did not have any distinct advantages for cecal intubation time and lower pain scores[15] (DW1). The variable stiffness of the colonoscopy body, flexible tubing, and Responsive Insertion Technology (RIT)[16,17] make the inspection equipment more maneuverable. Prieto-de-Frías *et al*[17] and Pasternak *et al*[18] studied the application of RIT technology in reducing discomfort and pain during colonoscopy insertion. The results showed that the RIT group shortened the cecal intubation time, decrease intestinal loop formation, lower manual pressure of abdomen and decrease discomfort or pain of patients. Although RIT technology has shown good application prospects, it still relies on the experience of unwinding of endoscopists, some examinations are time-consuming and patients cannot achieve a good medical result.

MEI and RIT technology are an improvement of traditional colonoscopy in response to the actual problems in the endoscopy process. AI can explore the images of MEI technology in guiding colonoscopy. Applying deep learning to analyze a large number of unloop images, it is possible in the future to form a complete set of loop prediction and unlooping strategies system. The RIT technology can automatically adjust the bending angle of the intestinal cavity by sensing the degree of curvature of the endoscopic body, and minimize the formation of acute angles. These measures help to reduce the traction of the colonoscopy on the mesentery and the damage to the intestinal mucosa, and achieve the purpose of reducing the pain and injury of the patient during the colonoscopy. In general, MEI and RIT technologies provide useful explorations for the gradual migration of colonoscopy from artificial to intelligent (DW2).

COMBINATION OF COLONOSCOPY AND AI

Traditional research methods have limitations, such as multi-factors, complex variables, interrelationships, descriptive difficulties and quantitative mechanisms. It is urgent to introduce new ideas and methods to solve these problems. It can be described with a simplified model by demonstrating whether the colonoscopy is looped, and providing the corresponding unlooping strategy, as we mentioned above. The operation of the colonoscopy handle and insertion part by the endoscopist can be regarded as an input function. Analyze the correspondence between the data of the input function under the loop condition and the corresponding results of loop and unloop in a large number of cases, also fitting the unloop strategy function to assist the doctor in decision-making through the intelligent system. MEI and other technologies can display the posture of the colonoscopy in the intestine in real time, and wearable pressure sensor device can generate a series of mechanical data. A specific neural network model can be constructed to synthesize a loop-free strategy function by analyzing large amounts of data. We look forward to the AI-assisted system will be able to realize a loopless and painless colonoscopy in the future (DW3).

COLONOSCOPY FOR SMART MEDICINE

Smart medicine is the application of AI to improve the ability of medical services, which is the trend of future medical advancement. Smart medical care is to create a regional medical information platform for health records and use advanced Internet of Things technology to realize the interaction among patient-medical staff, institutions

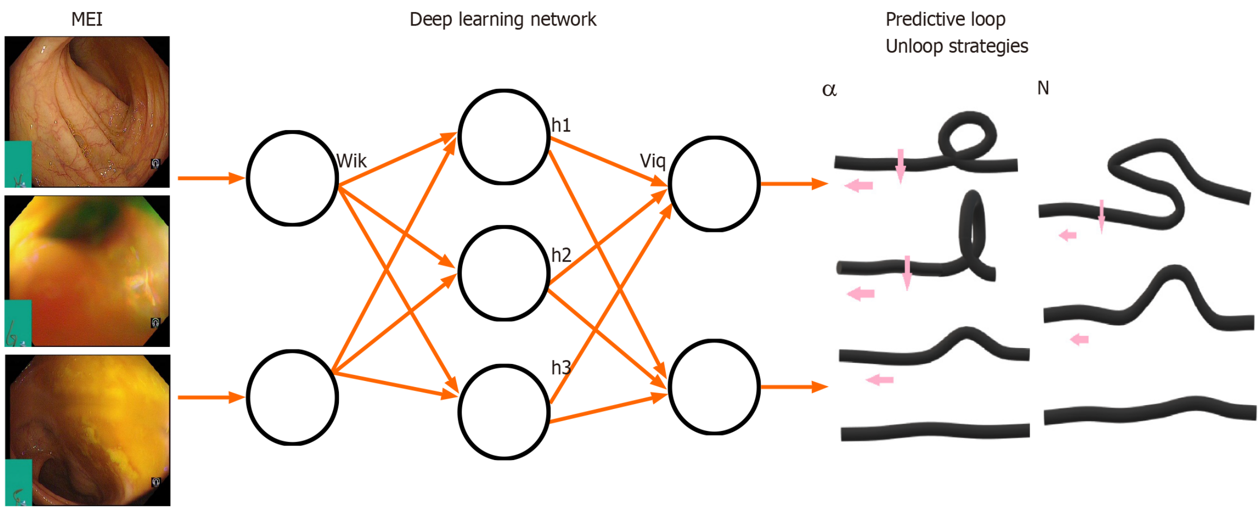

Figure 1 The idea of using magnetic endoscopic imaging to guide endoscopists in colonoscopy. MEI: Magnetic endoscopic imaging.

and equipment for achieving informatization gradually. Intelligent medicine cannot be separated from AI technology. On the basis of digital medicine, internet medicine and mobile medicine, smart medicine is gradually taking shape.

The emergence of smart medicine provides a new feasible path to solve the outstanding problems that restrict the medical development. Intelligent medical care plays an important role in science, it not only changes the traditional diagnosis and treatment methods but also improves the accuracy and efficiency, in addition, it relies on the advanced algorithms and powerful computing power of AI technology to significantly increase the success rate of medical innovation research and development and shorten time. In addition, smart medicine can also solve social problems, such as insufficient medical resources, unbalanced regional distribution, costs, personalized medical services, and respond to aging and chronic disease diagnosis and treatment needs. With the development of smart medical technology, AI can completely assist doctors in such arduous diagnoses in future, for example pathological diagnosis, laboratory test diagnosis, and imaging diagnosis.

COLONOSCOPY CONTINUUM ROBOT-ASSIST SYSTEM

Regarding the colonoscopy continuum robot-assisted system, some scholars have studied structural design, passability, compliance control based on force perception, and multi-motor control system design. Lee *et al*[19] proposed a caterpillar-like flexible self-propelled colonoscopy robot, which can effectively corner bends and conducted clinical trials, while Breedveld proposed a colonoscopy robot movement method based on a rollable doughnut[20]. Scholars research on the relevant working environment and clinical experiment results of the colonoscopy continuum robot assistance system, the flexible arbitrary bending of the colonoscopy assistance system, the exploration of the biomimetic and the continuum robot design, which are the most irreplaceable (DW4) part of the robot-assisted colonoscopy system, its structure and design provide an important reference.

FLEXIBLE ENDOSCOPY CONTROL ROBOT

In December 1998, the first Da Vinci Robot-Assisted Surgery System came out. In June 2000, the Da Vinci Robot-Assisted Surgery System became the first automatic mechanical system approved by the Food and Drug Administration for laparoscopic surgery. At present, the system is widely used. In 2017, the flexible endoscopy manipulation robot developed by the General Hospital of the Chinese People's Liberation Army successfully carried out clinical applications. It surpassed the traditional endoscopy operation method in terms of coordinated operation of multiple degrees of freedom of the endoscopy and quantitative display of operating parameters, and laid the foundation for high-quality standardized operation and internet medical treatment.

The research on small soft robots with multi-mode motion published by Hu has attracted widespread attention[21]. The article pointed out that the soft robot has bright prospects in the fields of bioengineering and minimally invasive treatment. They have greater potential to achieve high maneuverability through multi-channel motion because small soft robots have a higher degree of freedom than rigid robots. We can expect that these small flexible robots are equipped with camera devices to produce soft motion which is similar to worms that can move in the human digestive tract and has better control and operability than the magnetic-control capsule endoscopy.

At present, there are no reports on the use of flexible endoscopic robots for endoscopic treatment, and the author believes that the reason is that endoscopic treatment is different from examination. Endoscopic treatment have higher requirements for the operation technology, including horizontal and vertical joint movement of the endoscope handle to achieve rotation, control colonoscopy and handle strength during the treatment (DW5). The grasp of the patients' breathing and coordination with its movement are relatively subtle that are difficult to achieve at this stage. However, with the accumulation of quantitatively analyzed endoscopic operation data and the construction of software endoscopic operation strategy functions, combined with powerful algorithms and machine learning, AI will continue to improve the existing colonoscopy equipment, accessories and instruments in the future. At the same time, it may partly replace manual labor, reduce medical costs and improve efficiency.

APPLICATION STATUS OF AI IN COLONOSCOPY IMAGE RECOGNITION

With the progress of colonoscopy operation technology and endoscopic imaging technology, especially magnifying endoscopy has achieved remarkable results in the detection of fine structure on the surface of colorectal tumors. It should be pointed out that the development of electronic staining endoscopy is extremely rapid, such as narrowband imaging technology (NBI), flexible spectral imaging color enhancement technology (FICE) and i-Scan digital contrast technology (iSCAN), *etc.* (DW6). These imaging technologies can highlight the mucosal surface structure or capillary morphology by switching between different wavelengths of light, clearly observe the boundary and scope of the lesion, and obtain a visual effect similar to chromoendoscopy.

Depth research for colonoscopy image recognition has already started, using specific data sets and special deep learning network structure models to establish a labeled colonic lesion image data set to provide technical support for intelligent image recognition of colonoscopy images. Computer-aided diagnosis analysis used for accurately classify neoplastic/hyperplastic, adenoma/non-adenomas colorectal polyps found that the system have a classification accuracy rate above 90%, and the diagnosis time required is decreased compared with endoscopy experts and non-experts[4,22-24].

The dynamic recognition system decomposes the real-time video of the colonoscopy into a continuous picture. The deep learning neural network is used for the recognition of the marked images, and the fine recognition of each image is carried out to realize the purpose of automatically discovering and classifying the lesions. Mori *et al*[25] used deep learning models to analyze colonoscopy videos to classify adenomatous and hyperplastic polyps in real time, the results find that the accuracy of the AI model is 94%, the sensitivity and the specificity is 98% and 83% respectively (Figure 2).

We expect that AI combined with white light, chromoendoscopy and magnifying endoscopy will greatly reduce the time spent on diagnosis and treatment in the future, thereby providing great help for the clinical and scientific research of gastrointestinal diseases.

APPLICATION OF AI IN CAPSULE ENDOSCOPY

In recent years, the rapid development of capsule endoscopy technology, especially the appearance of magnetron capsule endoscopy, which has realized the controllability of the capsule endoscopy on some extent. The emergence of capsule endoscopy has made up for the insufficiency of gastroscopy and colonoscopy, the patients acceptance is high because of the whole examination process is painless. Nowadays,

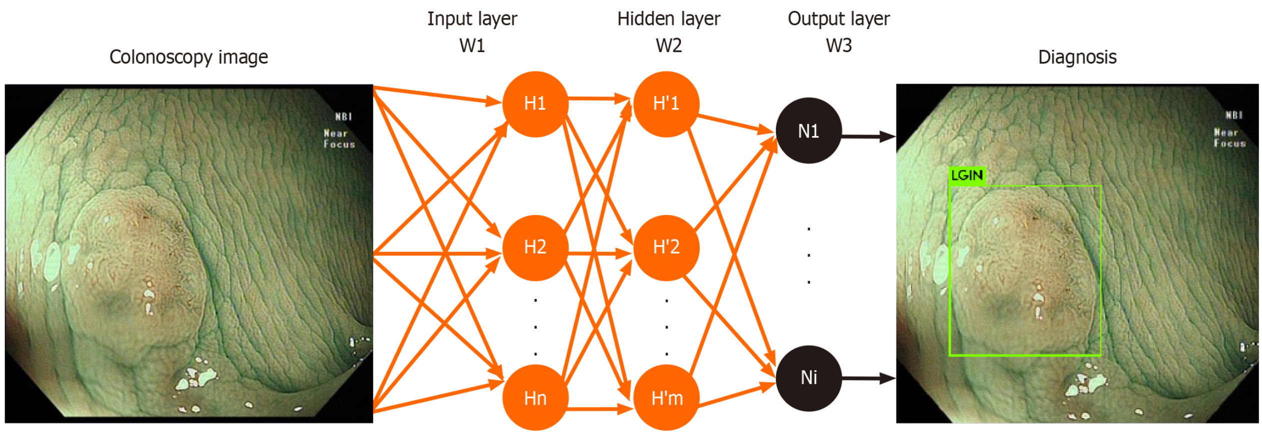

Figure 2 Artificial intelligence diagnosis system for colonoscopy lesions based on deep learning.

the application of capsule endoscopy is mostly focused on discovery of small bowel disease, for example bleeding.

AI is widely used in capsule endoscopy technology. The pixels are grouped by super pixel segmentation, the red ratio in the RGB space is used to extract the features of each super pixel, and these things are input into Support Vector Machines (SVM) for classification for intelligent recognition of capsule endoscopic bleeding. The specificity of the experimental results is 83%-98%, and the sensitivity is 94%-99%[26,27].

In order to identify polyps in capsule endoscopy images, Yuan and Meng[28] proposed a new complex feature learning method, which is a stacked sparse autoencoder with image manifold constraint. This method introduces multiple image constraints force images in the same category to share similar learning features and keep them, so the learned features retain a large number of differences and small internal differences in the images. The results show that the average overall recognition accuracy of this method is 98%, and could be further utilized in the clinical trials to help physicians from the tedious image reading work.

THE PROBLEMS FACED BY AI IN THE APPLICATION OF COLONOSCOPY

The development of depth research has enabled AI to achieve fruitful results in many aspects. However, there is no major breakthrough in the theory that AI follows, and the methods from supervised learning to unsupervised learning are still being explored. Therefore, looking for in-depth theoretical explanations is an important issue that must be solved in the development of the studies. In addition, deep learning generally requires a large amount of data, but not all applications have the conditions for it. Therefore, how to realize traditional knowledge expression and data-driven knowledge learning is an important research direction in the future. Furthermore, the neural network model needs to be adapted to transfer the learned knowledge to new conditions and environments in order to acquire the ability to solve many practical problems from a small number of learning samples. Finally, the method of machine learning is determined according to the functional relationship between the data and the target, a "deep forest" learning method, with a comparable setting proposed by Zhou and Feng[29], achieved a considerable or even better than deep neural networks.

In the field of colonoscopy image recognition, experts and scholars have made very useful explorations on the intelligent recognition of colorectal lesions, but most of them are limited to judge colorectal polyps. To achieve the integration of doctors and patients with auxiliary examination equipment, it is necessary to further expand the colorectal lesion image data set and the types of diseases involved. It must be pointed out that the endoscopic manifestations of colorectal diseases are various, the same disease often manifests differences in different periods and different diseases have very little difference in a specific period, and pathological diagnosis is still the gold standard.

CONCLUSION

In short, AI in colonoscopy has significant social benefits and bright application prospects, and it is foreseeable that smart medicine is an inevitable trend in medical development. Based on previous research, integrating colonoscopy's loop factors, unlooping strategies, active lesion capture and recognition, and assistive robotics technology, we have reason to believe that the future smart colonoscopy system will bring a revolution, and promote the diagnosis and treatment of colorectal diseases, especially the widespread development of colorectal cancer screening for the benefit of mankind.

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Application of convolutional neural network in detecting and classifying gastric cancer

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Abstract

Gastric cancer (GC) is the fifth most common cancer in the world, and at present, esophagogastroduodenoscopy is recognized as an acceptable method for the screening and monitoring of GC. Convolutional neural networks (CNNs) are a type of deep learning model and have been widely used for image analysis. This paper reviews the application and prospects of CNNs in detecting and classifying GC, aiming to introduce a computer-aided diagnosis system and to provide evidence for subsequent studies.

Key Words: Artificial intelligence; Convolutional neural network; Endoscopy; Gastric cancer; Deep learning

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Core Tip: With the development of new algorithms and big data, great achievements in artificial intelligence (AI) based on deep learning have been made in diagnostic imaging, especially convolutional neural network (CNN). Esophagogastroduodenoscopy (EGD) is currently the most common method for screening and diagnosing gastric cancer (GC). When AI was combined with EGD, the diagnostic efficacy of GC could be improved. Therefore, we review the application and prospect of CNN in detecting and classifying GC, aiming to introduce a computer-aided diagnosis system and provide evidence for following studies.

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INTRODUCTION

Gastric cancer (GC) is a globally prevalent cancer, and its incidence and mortality rank fifth and fourth, respectively, among cancers worldwide[1]. It is estimated that in 2020 there were over 1000000 new cases and 769000 deaths of GC globally. The lack of early detection and treatment contributes to the high mortality and poor outcomes of GC [2]. Esophagogastroduodenoscopy (EGD) is currently the most common method for screening and diagnosing GC. However, the efficacy of EGD varies significantly[3]. It has been reported that the false negative rate of EGD in detecting GC ranges from 4.6%-25.8%[4-6]. GC lesions are difficult to recognize due to the subtle changes in the gastric mucosa[7]. Additionally, the quality of EGD can be heavily influenced by the subjective determination of endoscopists[8]. Therefore, it is significant to develop an objective and reliable method to recognize possible early GC (EGC) lesions and blind spots.

With the development of new algorithms and big data, great achievements in artificial intelligence (AI) based on deep learning (DL) have been made for diagnostic imaging. Meanwhile, as one of the most representative network models in DL, convolutional neural network (CNN) contributes to enhancing the accuracy of image analysis. CCN is now being successfully applied in detecting the gastrointestinal tract [9-11]. CNNs have achieved tremendous successes and wide application in image recognition and classification[12,13]. Therefore, we applied CNN in endoscopic diagnosis, aiming to improve the diagnostic efficacy of EGC. In this review, we scrupulously elucidate the application and evolution of CNN in the detection and classification of GC.

CONVOLUTIONAL NEURAL NETWORK

With the development of neuroscience, researchers have attempted to build artificial neural networks to simulate the structure of the human brain by mathematically activating neuronal activity. DL has been the mainstream machine learning method in many applications. It is a type of representation learning method in which a complex neural network architecture automatically learns representative data by transforming the input information into multiple levels of abstractions[10]. Computer-aided diagnosis requires the extraction of extensive original image data and the application of a series of complex algorithms. DL has a strong modeling and reasoning ability that is superb in realizing computer output diagnosis.

CNNs are neural networks sharing connections between hidden units that feature a shortened computational time and translational invariance properties[14]. A typical CNN framework includes three main components: A convolutional layer, an activation function, and a pooling layer. The convolutional layer is composed of several small matrices. These matrices are convolved throughout the whole input image working as filters, and then a nonlinear transformation is applied in an element-wise fashion. Finally, the pooling layer aggregates contiguous values to one scalar. The common types of pooling in popular use are either average or max[15,16].

In the early 1990s, CNNs were used in many applications, such as object detection and face recognition. With the advances of technology, CNN was first applied to the analysis of medical images in 1993. Lo *et al*[17] reported the detection of lung nodules using a CNN in 1995. However, due to the limitation of computer language, CNNs have been underestimated in their value for a long time. In 2012, Krizhevsky *et al*[18] proposed a CNN with five convolutional layers and three fully connected layers (namely, AlexNet) and achieved breakthrough performances in the ImageNet Large Scale Visual Recognition Challenge. Since then, CNNs have been of great interest and widely applied. For example, CNNs have been applied to identify diabetic retinopathy from fundus photographs and distinguish benign proliferative breast lesions from malignant[19]. In 2020, Plaksin *et al*[20] estimated the possibility of diagnosing malignant pleural effusion from facies images of pleural exudates obtained by the method of wedge-shaped dehydration using CNNs.

Compared with the general neural network, CNN is superior in the adaptation of the image structure, extraction, and classification, and as a result it presents satisfactory work efficiency.

APPLICATION OF CNN IN GC

Automatic detection

At present, CNNs have been applied to detect GC, showing distinctive improvements. Hirasawa *et al*[10] created and trained a CNN-based diagnostic system containing 13584 endoscopic images. In this study, the constructed CNN was able to detect 92.2% of GC cases, including small intramucosal GC, through a quick analysis of an independent test set involving 2296 stomach images, which is extremely difficult even by experienced endoscopists. To achieve the real-time detection of EGD, Ishioka *et al*[21] tested their CNN system for identifying video images and achieved a high detection rate (94.1%). The detection rate in video images by CNN is similar to that of still images, demonstrating the great potential of CNN in the early detection of GC.

Magnifying endoscopy with narrow band imaging (M-NBI) has been used for the differential diagnosis of various focal, superficial gastric lesions. By observing the microvasculature and fine mucosal structure, M-NBI has a better accuracy in the diagnosis of early GC than ordinary white light endoscopy[22]. Li *et al*[23] developed a novel CNN-based system for analyzing gastric mucosal lesions observed by M-NBI. The test results showed that the sensitivity, specificity, and accuracy of the CNN system in diagnosing early GC were 91.18%, 90.64%, and 90.91%, respectively. Notably, the specificity and accuracy of CNN diagnostics are comparable to those of experts with more than 10 years of clinical experience.

Ikenoyama *et al*[24] compared the diagnostic ability of CNN and 67 endoscopists, and the results showed that CNN had a faster processing speed and 25% higher sensitivity than endoscopists [95% confidence interval (CI): 14.9-32.5]. The use of CNN can effectively urge endoscopists to re-examine and evaluate ambiguous lesions, which also helps reduce false negatives and false positives (Table 1).

Histological classification

An excellent endoscopist not only detects mucosal lesions but also distinguishes benign and malignant features. Cho *et al*[25] trained three CNN models, namely, Inception-v4, Resnet-152, and Inception-Resnet-v2, to classify gastric lesions into five categories: Advanced GC, EGC, high-grade dysplasia, low-grade dysplasia, and non-neoplasm. Among these systems, the Inception-Resnet-v2 model showed the best performance; the weighted average accuracy reached 84.6%, and the mean area under the curve (AUC) of the model for differentiating GC and neoplasm was 0.877 and 0.927, respectively.

To date, pathological diagnosis is still the gold standard to assess the presence or absence of cancerous lesions, cancer types, and degree of malignancy. Nevertheless, the accuracy of diagnosis and workload alleviation of pathologists are still challenging, and advanced computer-aided technologies are expected to play a key role in assisting pathological diagnosis. By optically scanning histologic tissue slides and converting them into ultrahigh-resolution digital images called whole slide images (WSIs), digital pathology is available for further investigations[26]. With the rapid development of EGD, the combination of DL models such as CNN and digital pathology is expected to greatly reduce the increasing workload of pathologists.

Sharma *et al*[27] explored two computerized applications of CNNs in GC, cancer classification and necrosis detection, based on immunohistochemistry of human epidermal growth factor receptor 2 and hematoxylin-eosin staining of histopathological WSIs. The overall classification accuracies that they obtained were 0.6990 and 0.8144, respectively. However, their study is limited by a small sample size with only 11 WSIs involved.

Iizuka *et al*[28] collected a large dataset of 4128 WSIs of stomach samples to train CNN and a recurrent neural network, and the evaluation results of CNN showed that the AUC for detecting gastric adenocarcinoma and adenoma was up to 0.97 and 0.99, respectively. They proposed that DL models can be used as a component in an integrated workflow alongside slide scanning, thus determining the top priority of the most valuable case, enhancing the accuracy of diagnosis, and speeding up the work efficacy.

Song *et al*[29] established a multicenter massive WSI dataset and tested slides collected from different hospitals that were detected with the histopathological diagnosis system for GC detection using DL. The results showed that the AUCs of the AI assistance system developed at the Chinese PLA General Hospital, Peking Union Medical College Hospital, and Cancer Hospital, Chinese Academy of Medical Sciences, were 0.986, 0.990, and 0.996, respectively, confirming its consistent stable performance. Their model-building approach may also be applied to identify multiple

Table 1 Detailed information on studies concerning automatic detection by convolutional neural network in gastric cancer

Ref.	Endoscopic images	Training dataset	Test dataset	Resolution	Sensitivity %	Specificity %	Accuracy/AUC %	PPV %	NPV %
Hirasawa *et al* [10] (2018)	WLI/NBI/chromoendoscopy images	13584	2296	300 × 300	92.2	NA	NA	30.6	NA
Ishioka *et al* [21] (2019)	Video images	NA	68	NA	94.1	NA	NA	NA	NA
Li *et al*[23] (2020)	M-NBI images	20000	341	512 × 512	91.18	90.64	90.91	90.64	91.18
Ikenoyama *et al*[24](2021)	WLI/NBI/chromoendoscopy images	13584	2940	300 × 300	58.4	87.3	75.7	26.0	96.5

AUC: Area under the curve; PPV: Positive predictive value; NPV: Negative predictive value; WLI: White-light imaging; NBI: Narrow-band imaging; M-NBI: Magnifying narrow-band imaging; NA: Not applicable.

cancers in different organ systems in the future (Table 2).

Prediction of depth of tumor invasion

EGC is categorized as a lesion confined to the mucosa (T1A) or the submucosa (T1B). An accurate identification of the depth of tumor invasion is the basis for determining the therapeutic schedule[30]. Endoscopic mucosal changes, such as irregular surfaces and submucosal tumors (*e.g.*, marginal elevation), have been suggested as predictors of the depth of tumor invasion[31].

Zhu *et al*[11] built a CNN computer-aided detection (CNN-CAD) system to determine the depth of tumor invasion, which is expected to avoid unnecessary gastrectomy. In this system, there was a development dataset of 790 images and a test dataset of 203 images. The final results showed that the AUC for the CNN-CAD system was 0.94 (95%CI: 0.90-0.97), and the overall accuracy was 89.16%, which was significantly higher than that determined by endoscopists (17.25%, 95%CI: 11.63-22.59). Yoon *et al*[32] proposed a novel loss function for developing an optimized EGC depth prediction model, called the lesion-based visual geometry group-16. Using this novel function, the depth prediction model is able to accurately activate the EGC regions during training and simultaneously measure classification and localization errors. After experimenting with a total of 11539 endoscopic images, including 896 images of T1A-EGC, 809 of T1B-EGC, and 9834 of non-EGC, the AUC of the EGC depth prediction model was 0.851. In this study, it was also demonstrated that histopathological differentiation significantly affects the diagnostic accuracy of AI for determining T staging.

Upper abdominal enhanced computed tomography (CT) is the main imaging examination for T staging of GC[33]. Zheng *et al*[34] retrospectively collected 3500 venous phase-enhanced CT images of the upper abdomen from 225 patients with advanced GC, aiming to predict the depth of GC invasion and extract different regions of interest. The dataset was then enhanced by cropping and flipping, and the Faster R-CNN detection model was trained using other data enhancement methods. They found that the AUC of the experimentally established CNN model was 0.93, and the recognition accuracies for T2, T3, and T4 GC were 90%, 93%, and 95%, respectively. The abovementioned findings may be helpful for radiologists to predict the progression and postoperative outcomes of advanced GC (Table 3).

CURRENT EXISTING PROBLEMS

Limitations of studies

Selection bias: In most studies, researchers tend to select clear, typical, high-quality endoscopic images for training and testing image sets[10,35]. Because low-quality images with air, postbiopsy bleeding, halation, blurs, defocusing, or mucus secretion have been excluded, the results of retrospective clinical tests are often superior to actual ones. Therefore, prospective studies that are less affected by biases should be thoroughly analyzed to improve the accuracy and specificity of clinical trials, thus ensuring the reliability of the results.

Table 2 Detailed information on studies concerning histological classification by convolutional neural network in gastric cancer

Ref.	Training dataset	Test dataset	Resolution	Group	AUC %
Cho *et al*[25] (2019)	4205	812	1280 × 640	Five-category classification	84.6
				Cancer *vs* non-cancer	87.7
				Neoplasm *vs* non-neoplasm	92.7
Sharma *et al*[27] (2017)	231000 for cancer classification	NA	512 × 512	Cancer classification	69.9
	47130 for necrosis detection			Necrosis detection	81.4
Iizuka *et al*[28] (2020)	3628	500	512 × 512	Adenocarcinoma	98
				Adenoma	93.6
Song *et al*[29] (2020)	2123	3212 from PLAGH	320 × 320	Benign and malignant cases and tumour subtypes	98.6
		595 from PUMCH			99.0
		987 from CHCAMS			99.6

PLAGH: Chinese PLA General Hospital; PUMCH: Peking Union Medical College Hospital; CHCAMS: Cancer Hospital, Chinese Academy of Medical Sciences; AUC: Area under the curve.

Table 3 Detailed information on studies concerning prediction of depth of tumor invasion by convolutional neural network in gastric cancer

Ref.	Dataset	Resolution	Sensitivity %	Specificity %	Accuracy/AUC %	PPV %	NPV %
Zhu *et al* [11] (2019)	Development datasets: 5056; Validation datasets: 1264; Test dataset: 203	299 × 299	76.47	95.56	89.16	89.66	88.97
Yoon *et al* [32] (2019)	11539 images were randomly organized into five different folds, and at each fold, the training: validation: testing dataset ratio was 3:1:1	NA	79.2	77.8	85.1	79.3	77.7
Zheng *et al* [34] (2020)	Totally 5855, training:verification dataset ratio was 4:1	512 × 557	NA	NA	T2 stage: 90; T3 stage: 93; T4 stage: 95	NA	NA

AUC: Area under the curve; PPV: Positive predictive value; NPV: Negative predictive value; NA: Not applicable.

Single-center studies: Most of the testing images are obtained from a single-center institution using the same type of endoscope and endoscopic video system, which may result in potential biases. In future studies, images obtained from multicenter institutions using different types of endoscopic devices should be collected for analysis.

Lack of endoscopic video images: Still images are used for the training and test dataset in most studies, which may limit the extensive clinical application[36]. Using video images may improve the performance of the CNN and represent real-life scenarios[21].

Limitations of CNN

False positive and false negative results: The specificity and sensitivity of automatic detection are very important to determine the choice of therapeutic schedule. False positive and false negative results directly lead to improper treatment. For example, gastritis with pathological manifestations of redness, atrophy, and intestinal metaplasia is easily confused with EGC, which increases the false positive rate[10]. In addition, early-stage cancer lesions are often too small to be found, which increases the false negative rate. The main reason for false positive and false negative results may be attributed to the limited quantity and quality of learning samples. Therefore, it is necessary to collect a large number of high-quality endoscopic images for training algorithms, thus enhancing the detection accuracy.

Ethical and moral issues: AI will not completely replace doctors. Who should be responsible for the safety of patients if misdiagnosed? Patient consent should be obtained before using AI to determine who should be responsible for misdiagnosis or incorrect treatment that can possibly occur[37].

CONCLUSION

As a classical and widely used DL model, CNN has been widely used in the medical field, especially for EGD detection. In remote or crowded areas, CNNs can be used to assist early cancer screening to prevent misdiagnosis due to a lack of experience and professional knowledge of endoscopists. Additionally, CNN is a promising method to provide online professional training for improving the professional skills of young endoscopists. Most importantly, CNN helps endoscopists detect, classify, and even predict the invasion depth of EGC.

At present, most of studies are still in the early stages of system development. More powerful, efficient, and stable algorithms, and more prospective studies are urgently required in the future to make AI more sensitive, specific, and accurate in cancer detection and classification.

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MINIREVIEWS

Utility of artificial intelligence in colonoscopy

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Abstract

Colorectal cancer is one of the major causes of death worldwide. Colonoscopy is the most important tool that can identify neoplastic lesion in early stages and resect it in a timely manner which helps in reducing mortality related to colorectal cancer. However, the quality of colonoscopy findings depends on the expertise of the endoscopist and thus the rate of missed adenoma or polyp cannot be controlled. It is desirable to standardize the quality of colonoscopy by reducing the number of missed adenoma/polyps. Introduction of artificial intelligence (AI) in the field of medicine has become popular among physicians nowadays. The application of AI in colonoscopy can help in reducing miss rate and increasing colorectal cancer detection rate as per recent studies. Moreover, AI assistance during colonoscopy has also been utilized in patients with inflammatory bowel disease to improve diagnostic accuracy, assessing disease severity and predicting clinical outcomes. We conducted a literature review on the available evidence on use of AI in colonoscopy. In this review article, we discuss about the principles, application, limitations, and future aspects of AI in colonoscopy.

Key Words: Artificial intelligence; Colonoscopy; Colorectal cancer; Inflammatory bowel disease; Adenoma detection rate; Adenoma

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Core Tip: Artificial intelligence (AI) pertains to performance of intelligent tasks like human beings by computer-controlled machines. Machine learning, one of the most important and fundamental principles of AI, essentially means automatically using the available data to learn and make decisions without human intervention. AI based detection models have been developed for polyp detection and to differentiate

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malignant from nonmalignant lesions. It has been also utilized to analyze endoscopic images for inflammatory bowel disease diagnosis, grading its severity and predicting treatment response.

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INTRODUCTION

What is artificial intelligence

The capability of human brain to perceive, analyze and react is defined as intelligence. Gottfredson[1] described it as ability of a human beings to reason, plan, solve problems, think abstractly, comprehend complex ideas, learn quickly and learn from experience. It has been a long desire of human beings to build machines which can think and act autonomously to ease human work. Several complex computer algorithms and models have been developed to provide automation to these machines. The famous Turing test invented by Alan Turing in 1950 demonstrated that it may be difficult for a blinded investigator to distinguish humans from intelligent machines[2]. However, intelligence of these machines is still way below human intelligence which is based on logic, reasoning, and adaptive learning. In 1997 International Business Machines's artificial intelligence (AI) driven chess playing system defeated world chess champion Garry Kasparov. Although this victory of computer programs over human beings in chess was criticized by many, and it was argued that machines can only be as good as the programs developed for them by human beings, nevertheless it remains an important landmark in the history of AI.

There is no one formal definition of AI. It is vaguely defined as ability of computer-controlled machines to perform intelligent tasks like human beings. There are two basic subtypes of AI- weak or soft and strong or hard AI[3]. Weak or soft AI is also called as narrow AI and as the name suggests it specializes in a very specific task like face recognition, voice recognition capabilities. On the other hand, strong or hard AI which is also known as general AI has more broad application due to its capability to understand, think and act like human beings. It is at the core of advanced robotic systems.

Machine learning (ML) is one of the most important and fundamental principles of AI. ML is at the heart of any AI system and essentially means automatically using the available data to learn and make decisions without human intervention. It is an adaptive technology which is continuously learning and hence gets better with each use. ML utilizes three fundamental methods which include supervised learning, unsupervised learning, and reinforcement learning. Artificial neural network (ANN) is a ML algorithm adapted from model of biological neurons in humans. ANN is an information processing technology, also considered as mathematical models utilized to analyze data.

AI IN THE FIELD OF GASTROENTEROLOGY

In the last two decades, substantial progress has been made in the use of AI driven algorithms in the field of medical science. Use of AI in the field of medical practice can be categorized in two broad categories-virtual and physical[4]. The virtual category of AI pertains to its use in electronic health record. It is based on ML and deep learning *via* mathematical algorithms to identify individuals at risk of some specific disease and help in clinical decision making. The physical category of AI includes use of medical devices and robotics for delivering medical care.

AI operated systems have been utilized to monitor patient's medical conditions remotely. More specifically in gastroenterology, AI based detection models have been developed to differentiate malignant from nonmalignant lesions, detect gastrointestinal bleeding using wireless video capsule endoscopy, detecting pancreatic cancer, and detecting liver fibrosis. In the subsequent sections, we have detailed progress of AI and its application during colonoscopy.

AI AND COLON POLYPS

Colorectal cancer (CRC) is the third most common form of the cancer worldwide and is the 2nd most common cause of cancer related mortality globally[5]. Colonoscopy is the primary method for detection and removal of polyps and thus for prevention of CRC. It has been shown in the study that with every 1% increase in the adenoma detection rate (ADR), the risk of CRC decreases by 3%[6]. However, colonoscopy is not the perfect tool as polyps can be missed during colonoscopy mainly because of two factors: Blind spot and proceduralist error. The error due to blind spot can be overcome by using wide-angle camera, but the error due to proceduralist cannot be overcome easily. Small polyps (1-5 mm) are prone to be missed regardless of experience of proceduralist. Some studies have shown improvement in the rate of polyp detection with the help of second observer[7,8]. The factors responsible for proceduralist error could be fatigue, distraction, visual perception, impaired level of alertness, recognition error and poor bowel preparation. The application of AI in endoscopic field has shown improvement in ADR in recent studies and it helps in overcoming proceduralist error. Computer-aided detection and characterization of colorectal polyps is now getting popular among endoscopists.

PRINCIPLES AND APPLICATION OF AI IN COLONOSCOPY FOR POLYP DETECTION

AI has been a part of medical field since early 1950s. The concept and use of basic technology of computer-aided diagnosis (CAD) for colonoscopy has been explored since past one decade[9]. Use of CAD system in detection of colon polyps was first demonstrated by Karkanis *et al*[10]. Although the sensitivity of detecting adenomatous polyps demonstrated by these authors was 90%, this system was not used in clinical practice as it relied on static images rather than live endoscopic videos. In 2011, Bernal *et al*[11] introduced how intelligent systems can help in colonoscopy. Bernal *et al*[12] later introduced window median depth of valley accumulation (WM- DOVA) energy maps as a tool for automatic polyp detection in colonoscopy images. Fernández-Esparrach *et al*[13] for the first-time reported use of CAD system based on WM-DOVA maps and utilized colonoscopy videos in assisting colon polyp detection. With significant advancements in computer power and emergence of deep learning algorithms over past decade, it is being realized that CAD assistance during colonoscopy can be used in real time[14]. The inclusion of CAD for colonoscopy can help by automatic detection of polyps in real time which could be easily overlooked by endoscopists visually, thus resulting in higher ADR. Additionally, it helps in characterization of polyps in real time that in turn would help in reducing unnecessary biopsies of non-neoplastic polyps significantly[15].

There have been multiple studies to prove the advantage of inclusion of AI in the field of colonoscopy (Table 1). Most of these studies are of retrospective design, however few of them done recently were conducted prospectively. Luo *et al*[16] conducted a prospective, randomized cohort study using 150 participants to explore whether a high-performance, real-time automatic polyp detection system could improve the polyp detection rate in the actual clinical environment. The results showed that a real-time automatic polyp detection system can increase the ADR, especially for small polyps which are usually easily missed by conventional colonoscopy technique. Furthermore, Misawa *et al*[17] developed a 3-D convolutional network model for automated polyp detection which worked nearly in real time. They demonstrated sensitivity of 90% and a specificity 63% using 50 polyp videos and 85 non-polyp videos as test sets. Subsequently, Urban *et al*[18] developed a CAD model to improve polyp detection rate and they tested the model for its diagnostic capability on 8641 hand-labeled colonoscopy images collected from more than 2000 patients and on 20 colonoscopy videos. The results showed diagnostic accuracy of 96.4% and an area under the receiver operating characteristic curve of 0.991. However, the false positive rate was 7%. Additionally, Wang *et al*[19] developed the deep-learning algorithm which provided > 90% sensitivity and specificity for video-based analysis after testing their model on many polyp images and colonoscopy video recordings from patients.

Table 1 List of studies evaluating role of artificial intelligence in the detection of colon polyps during the colonoscopy

Ref.	Country of origin	Study design	Results
Fernandez-Esparrach *et al* [13], 2016	Spain	Retrospective	Sensitivity 70%, Specificity 72 %
Geetha *et al*[36], 2016	India	Retrospective	Sensitivity 95%, Specificity 97%
Misawa *et al*[37], 2017	Japan	Retrospective	Accuracy higher than trainees (87.8 *vs* 63.4%; P = 0.01), but similar to experts (87.8 *vs* 84.2%; P = 0.76)
Zhang *et al*[38], 2017	China	Retrospective	Accuracy 86%
Yu *et al*[39], 2017	China	Retrospective	Sensitivity 71%, PPV 88%
Billah *et al*[40], 2017	Bangladesh	Retrospective	Sensitivity 99%, Specificity 98.5%, Accuracy 99%
Chen *et al*[23], 2018	Taiwan	Retrospective	Sensitivity 96.3%, Specificity 78.1%
Urban *et al*[18], 2018	United States	Retrospective	Accuracy 96.4%
Misawa *et al*[17], 2018	Japan	Retrospective	Sensitivity, Specificity, and Accuracy were 90%, 63%, and 76%, respectively
Wang *et al*[19], 2018	China	Retrospective	Sensitivity 94.38%, Specificity 95.92%
Su *et al*[41], 2019	China	Prospective	Polyp detection rate was 38.3% as compared to 25.4% in control group (P < 0.001)
Wang *et al*[42], 2019	China	Prospective	Polyp detection rate was 45% as compared to 29% in the control group (P < 0.001)
Klare *et al*[43], 2019	Germany	Prospective	Larger polyp detection, Odds ration 2.71, P = 0.042
Figueiredo *et al*[44], 2019	Portugal	Retrospective	Sensitivity 99.7%, Specificity 84.9%, Accuracy 91.1%
Yamada *et al*[45], 2019	Japan	Retrospective	Sensitivity 97.3%, Specificity: 99%
Lee[46], 2020	South Korea	Retrospective	Accuracy 93.4%, Sensitivity 89.9%, Specificity 93.7%
Luo *et al*[16], 2020	China	Prospective	Polyp detection rate for diminutive polyps increased (38.7% *vs* 34%, P < 0.001). No difference was found for larger polyps
Gong[47], 2020	China	Prospective	Polyp detection rate was 47% as compared to 34% in control group (P = 0.0016)
Liu *et al*[48], 2020	China	Prospective	Polyp detection rate was 44% as compared to 28% in control group (P < 0.001)
Ozawa *et al*[49], 2020	Japan	Retrospective	Sensitivity 92%, PPV 86%, Accuracy 83%
Wang *et al*[50], 2020	China	Prospective	Polyp detection rate was 52% as compared to 37% in control group (P < 0.0001)
Hassan *et al*[51], 2020	Italy	Retrospective	Sensitivity 99.7%
Repici *et al*[52], 2020	Italy	Prospective	Adenoma detection rate was 54.8% as compared to 40.4% in control group (P < 0.001)

PPV: Positive predictive value.

In a recent meta-analysis[20] from the researchers in Norway, who included five randomized control trials, AI aided colonoscopy had a ADR of 29.6% as compared to 19.3% without AI. In another recent meta-analysis involving 5 randomized control trials including 4354 patients, ADR was 36.6% with AI aided colonoscopy as compared to 25.2% in the standard control group (P < 0.01)[21].

In addition to improvement in colorectal polyp detection, AI has also been shown accuracy in polyp characterization in several studies. Byrne *et al*[22] developed an AI model for real-time characterization of colorectal polyps. They assessed their model using 125 unaltered endoscopic videos containing diminutive polyps. The AI model did not generate sufficient confidence to predict the histology of 19 out of 125 diminutive polyps which was about 15% of the polyps. For the remaining 106 diminutive polyps, the accuracy of the model was 94%, the sensitivity for identification of adenomas was 98%, specificity was 83%, negative predictive value (NPV) was 97%, and positive predictive value (PPV) was 90%. On the other hand, Chen *et al* [23] assessed their model using 284 diminutive polyps. The model identified neoplastic or hyperplastic polyps with 96.3% sensitivity, 78.1% specificity, NPV of 91.5% and PPV of 89.6%. There have been several other studies from across the world analyzing capacity of AI to characterize colon polyps (Table 2).

Table 2 List of studies evaluating role of artificial intelligence in characterization of colon polyps during the colonoscopy

Ref.	Country of origin	Study design	Results
Misawa *et al*[53], 2016	Japan	Retrospective	Sensitivity 84.5%, Specificity 98%
Mori *et al*[54], 2016	Japan	Retrospective	Accuracy 89%
Kominami *et al*[55], 2016	Japan	Prospective	Sensitivity 93%, Specificity 93.3%
Komeda *et al*[56], 2017	Japan	Retrospective	Accuracy 75%
Takeda *et al*[57], 2017	Japan	Retrospective	Sensitivity 89.4%, Specificity 98.9%, Accuracy 94.1 %
Chen *et al*[23], 2018	Taiwan	Retrospective	PPV of 89.6%, and a NPV of 91.5%
Renner[58], 2018	Germany	Retrospective	Sensitivity 92.3% and NPV 88.2%
Mori *et al*[59], 2018	Japan	Prospective	Accuracy 98.1%
Blanes-Vidal *et al*[60], 2019	Denmark	Retrospective	Accuracy 96.4%
Min *et al*[61], 2019	China	Prospective	Sensitivity 83.3%, Specificity 70.1%
Byrne [22], 2019	Canada	Retrospective	Accuracy 94%
Sánchez-Monteset al[62], 2019	Spain	Retrospective	Sensitivity 92.3%, Specificity 89.2%
Horiuchi *et al*[63], 2019	Japan	Prospective	Sensitivity 80%, Specificity 95.3%
Lui *et al*[64], 2019	China	Retrospective	Sensitivity 88.2%, Specificity 77.9%
Ozawa *et al*[49], 2020	Japan	Retrospective	Sensitivity 97%, PPV 84%, NPV 88%
Jin *et al*[65], 2020	South Korea	Prospective	Sensitivity 83.3%, Specificity 91.7%
Rodriguez-Diazet al[66], 2020	United States	Prospective	Sensitivity 96%, Specificity 84%
Kudo *et al*[67], 2020	Japan	Retrospective	Sensitivity 96.9%, Specificity 100%

NPV: Negative predictive value; PPV: Positive predictive value.

AI AND INFLAMMATORY BOWEL DISEASE

Inflammatory bowel disease (IBD) comprises of mainly ulcerative colitis and crohn's disease. It results from complex interplay of environmental, immunological, microbial, and genomic factors[24]. The prevalence of IBD has exceeded 0.3% in the Western countries, and its incidence is rising in newly industrialized countries all over the world[25].

Over the last decade, role of AI has been explored in the field of inflammatory bowel disease (IBD). It has been utilized to analyze endoscopic images for disease diagnosis, grading of severity of disease and predicting treatment response. It has been also utilized to build risk prediction models based on integration of clinical, laboratory as well as gene expression data[26]. There are limited studies exploring the utility of AI aided colonoscopy in the field of IBD. Mosotto *et al* employed machine learning mathematical model of endoscopic and histologic data to distinguish different types of pediatric IBD and found 83.3% accuracy[27]. Similarly, a study from China found AI through machine learning model to be a promising approach specially for unexperienced endoscopists for subtyping of IBD[28].

There are clinical scores available for grading the severity of IBD. AI assisted models have been applied to improve accuracy and precision in assessing the disease severity. In a prospective study from Japan, deep neural network was utilized for evaluating endoscopic images from patients with ulcerative colitis and it showed 90.1% accuracy for endoscopic remission and 92.9% accuracy for histologic remission[29]. In another study from Belgium, computer algorithm for pattern recognition from endoscopic images had significantly better accuracy in determining endoscopic and histologic inflammation in patients with ulcerative colitis[30]. In a retrospective study involving 777 patients with ulcerative colitis, deep learning aided assessment of Mayo endoscopic sub-score for the automated grading of disease yielded 72.4% sensitivity, 85.7% specificity, 77.7% PPV, 87% NPV[31]. Ozawa *et al*[32] constructed a CAD system using convolutional neural network and the results showed better performance for identification of normal mucosa in patients with ulcerative colitis. In a prospective trial, Gottlieb *et al* showed that deep learning algorithm can be used effectively in predicting ulcerative colitis disease severity[33].

Currently, these AI aided algorithms are mainly used in research setting. Further studies are needed to explore their utility in clinical practice and management of patients with IBD.

LIMITATIONS

One of the possible limitations for the use of CAD could be significantly large number of false positive results[34]. Sometimes CAD system may flag frames which usually endoscopists may never have considered as suspicious area. Thus, the endoscopists may have to spend some extra time to go through all those flagged frames to differentiate between actual false positives and possible false negatives[35]. Additionally, false positive results may lead to unnecessary biopsy and thus related complications which could have been avoided. Hassen *et al*[34] conducted a post hoc analysis of randomized trial comparing colonoscopy with and without CAD to assess relative distribution of false positives in real life setting. During this analysis, two main reasons were found as causes of false positive results, such as artifacts from either mucosal wall or bowel content. Out of total false positives, 88% were due to artifacts from bowel wall, while 12% were due to artifacts from bowel content. However, most of the false positives were rejected by endoscopists right away and there was only 1% increase in the total withdrawal time due to false positives. Another limiting factor is cost effectiveness of the use of AI in colonoscopy, and it needs to be established. Also, the impact of the use of AI in colonoscopy on long-term clinical outcomes, such as decrease in CRC rate or increase in surveillance interval for colonoscopy is not known [35]. We require long-term prospective cohort studies to address these issues.

FUTURE DIRECTIONS

Food and Drug Administration has recently approved the first real-time CAD system for colonoscopy in April 2021, known as gastrointestinal (GI) Genius. It can identify the regions of the colon within the endoscope’s field of view where a colorectal polyp might be located, allowing for a more extended examination in real time during colonoscopy. After getting the alert from the device, it is up to the clinician to decide whether the identified region contains a suspected lesion, and how the lesion should be managed and processed per standard clinical practice and guidelines. However, GI Genius is not intended to characterize or classify a lesion, nor to replace lab sampling as a means of diagnosis. The device does not provide any diagnostic assessments of colorectal polyp pathology, nor does it suggest to the clinician how to manage suspicious polyps.

Although many studies have shown good results but most of these studies were retrospective studies which could be subject to considerable selection bias. On the other hand, only few prospective studies are available till date which are more statistically significant than retrospective studies. Thus, we need to design more prospective studies and should be directed towards polyp characterization during real-time colonoscopy. Additionally, future studies can explore AI assisted identification of polyps with submucosal invasion. The prospect of a fully automated independent colonoscopy system is still too premature at this stage. Furthermore, trials to build more cost-effective models should be conducted in near future before considering use of CAD assisted colonoscopy widespread in daily practice.

CONCLUSION

In conclusion, utility of AI methods and algorithms have significantly evolved over the last decade. AI technology provides us a very robust tool to improve the accuracy and precision during the colonoscopy. ML models of AI technology provide us a valuable tool to transform the healthcare. Further larger and prospective studies are needed to see if these positive outcomes can be replicated in a cost-effective manner in clinical practice.

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MINIREVIEWS

Use of artificial intelligence in endoscopic ultrasound evaluation of pancreatic pathologies

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Abstract

The application of artificial intelligence (AI) using deep learning and machine learning approaches in modern medicine is rapidly expanding. Within the field of Gastroenterology, AI is being evaluated across a breadth of clinical and diagnostic applications including identification of pathology, differentiation of disease processes, and even automated procedure report generation. Many pancreatic pathologies can have overlapping features creating a diagnostic dilemma that provides a window for AI-assisted improvement in current evaluation and diagnosis, particularly using endoscopic ultrasound. This topic highlight will review the basics of AI, history of AI in gastrointestinal endoscopy, and prospects for AI in the evaluation of autoimmune pancreatitis, pancreatic ductal adenocarcinoma, chronic pancreatitis and intraductal papillary mucinous neoplasm.

Key Words: Artificial intelligence; Deep learning; Machine learning; Convolutional neural network; Endoscopic ultrasound; Autoimmune pancreatitis; Pancreatic ductal adenocarcinoma; Chronic pancreatitis; Intraductal papillary mucinous neoplasm

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Core Tip: Artificial intelligence is an emerging diagnostic tool that may further aid clinicians in the current evaluation of diseases of the pancreas.

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INTRODUCTION

Artificial intelligence (AI) has emerged as a mechanism to assist clinicians, particularly in the analysis and interpretation of clinical data such as radiologic images and pathology. In general, AI encompasses the use of computer algorithms and learning models designed to complete undertakings that typically require conscious human processing[1]. For pattern recognition in images, a deep neural network learns multiple representations of the input images at different levels of abstractions. Subsets of AI include machine learning (support vector machine algorithms, artificial neural networks) and direct learning (convolutional neural networks, recurrent neural networks[1-3]. Deep learning has shown great promise in healthcare applications ranging from early detection of cancers to predicting disease survivability. The overarching goal of AI in medicine has been to decrease inter-operator variability while improving diagnostic accuracy and real-time decision making[4]. The application of AI in Gastroenterology has largely been focused on endoscopy, ranging from the detection and classification of colon polyps, to the diagnosis of esophageal and gastric cancer[1,3]. However, more recently there has been further evaluation of the role of AI in biliopancreatic endoscopy, including improved endoscopic ultrasound (EUS) differentiation between pancreatic ductal adenocarcinoma (PDAC) and other pancreatic pathologies such as autoimmune pancreatitis (AIP), chronic pancreatitis (CP) and cystic pancreas lesions such as intraductal papillary mucinous neoplasm (IPMN). This "topic highlight" will focus on the potential use of AI in the EUS evaluation of pancreatic conditions.

HISTORY OF AI IN GASTROINTESTINAL ENDOSCOPY

Early studies on the application of AI in GI endoscopy dating back to the 1990s-2000s were focused on aiding the detection and classification of colorectal polyps to improve adenoma detection rates and decrease interval colon cancers[5-8]. Additional studies have used AI to help diagnose inflammatory bowel disease and predict histologic inflammation during colonoscopy evaluation[9,10], as well as grade bowel preparation [11]. The use of AI in upper endoscopy has been assessed in the identification and labeling of basic anatomic structures with automatic image capture[12], diagnosis of Helicobacter pylori infection[13], identification of gastric and esophageal cancer[14], as well as diagnosis of dysplasia in Barrett's esophagus[15]. With regards to capsule endoscopy, existing technology within current software platforms allows for removal of redundant or uninformative images and identifies potential images of bleeding through color detection, while more recent studies are looking into the use of AI to identify other small bowel pathologies[16]. PDAC and AIP are diseases with a highly analogous visual presentation that are difficult to distinguish by imaging. AI systems have been developed to aid EUS evaluation of pancreatic lesions with the particular goal of distinguishing pancreatic cancer from other pancreatic pathologies including CP and AIP[17-19].

AI IN PANCREATICOBILIARY ENDOSCOPY

The use of AI in pancreaticobiliary endoscopy is still in its infancy, therefore there is a paucity of literature related to EUS evaluation of pancreatic conditions using AI-based systems. However, the need for improved diagnostic evaluation of pancreatic conditions including AIP, PDAC, CP and pancreatic cystic lesions, provides an exciting niche for further research. AI has previously been applied in EUS differentiation of pancreatic cystic lesions and pancreatic tumors, thereby offering the capability of earlier and more accurate diagnosis. Both conventional machine learning and deep learning architectures have been used. A convolutional neural network (CNN) is a deep learning algorithm developed based on the concepts of visual tasks and signaling. In building a CNN for EUS, initial image data is collected and labeled based on the findings, these images are then entered as input and filtered through a multi-layer deep learning program which allows the system to learn key features of the provided EUS images. Multiple rounds of this process allow for the formation of a neural network where the system can then apply the previously learned features in analyzing novel images (Figure 1).

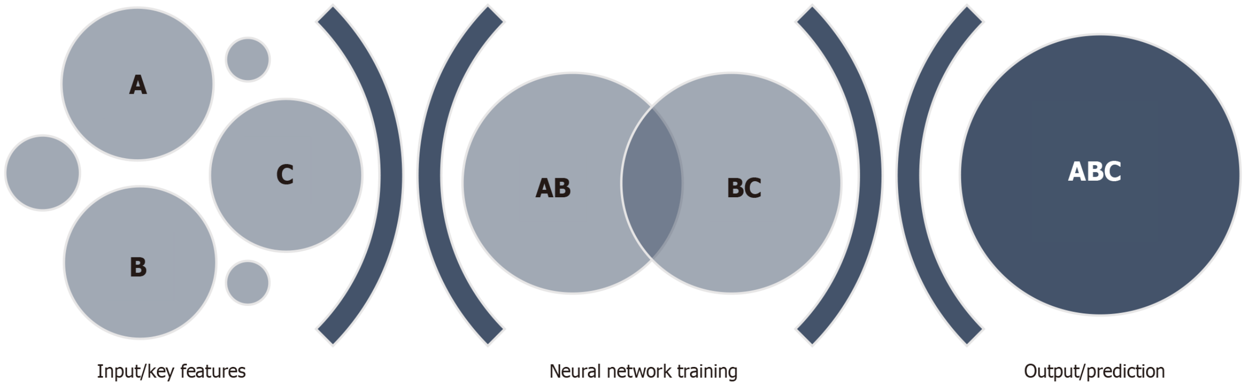

Figure 1 Example of neural network design.

LITERATURE SEARCH

To identify relevant literature on this topic, we searched the PubMed database through our institution's library for articles combining the terms "autoimmune pancreatitis", "pancreatic adenocarcinoma", "chronic pancreatitis", "intraductal papillary mucinous neoplasm", "artificial intelligence", and "endoscopic ultrasound".

AI IN THE EVALUATION OF AUTOIMMUNE PANCREATITIS

Autoimmune pancreatitis is an inflammatory condition of the pancreas commonly associated with a constellation of findings referred to as immunoglobulin G4-related disease. AIP is characterized radiologically/endoscopically by diffuse or focal enlargement of the pancreas parenchyma and diffuse irregular narrowing of the main pancreatic duct, histologically by pancreatic fibrosis and lymphoplasmacytic infiltration, and serologically by increased levels of serum gamma globulin, including immunoglobulin G4 (IgG4)[20,21]. The diagnosis of AIP can be challenging due to the overlap of clinical, laboratory and imaging findings with those of PDAC[22-24]. Studies have shown that 2%-5% of patients who undergo pancreatic resection of suspected cancer are found to have AIP on histopathologic evaluation, and instead of receiving highly effective immunosuppressive therapy such as corticosteroids, these patients are left to manage the morbidity associated with an invasive surgery[25,26]. While EUS remains the preeminent diagnostic tool in evaluating pancreatic diseases, the yield of needle aspiration/biopsy techniques can be inconclusive or non-specific, creating a diagnostic dilemma that may ultimately delay or compromise patient care [25-28].

In late 2020, Marya *et al*[22] published novel research on the development of EUS-based AI to improve the diagnosis of AIP. Using a CNN built from a large collection of EUS images and videos (583 patients: 146 AIP, 292 PDAC, 72 CP, 73 normal pancreas), their team sought to develop a reliable, real-time method of distinguishing AIP from PDAC on EUS evaluation. Going one step further, they also used occlusion heatmapping to identify key sonographic features of AIP compared to PDAC, further strengthening the utility of their model. On combined still image and continuous video image analysis, the developed CNN was able to distinguish AIP from PDAC with 90% sensitivity and 87% specificity; and distinguish AIP from all other studied diagnoses (PDAC, CP, normal pancreas) with 90% sensitivity and 78% specificity. On continuous video image analysis, the developed CNN was able to successfully differentiate AIP from PDAC with a sensitivity of 90% and specificity of 93%; and differentiate AIP from all other studied diagnoses with a sensitivity of 90% and specificity of 85%. Furthermore, occlusion heatmap evaluation showed that "enhanced hyperechoic interfaces between pancreas parenchyma and pancreas duct/vessels" were predictive of AIP, and "post-acoustic enhancement deep to a dilated pancreas duct" was more commonly associated with PDAC. In addition, the study evaluated the accuracy of diagnosis between the CNN and a group of expert endosonographers, showing that the CNN correctly diagnosed AIP with a sensitivity of 88.2% and specificity of 82.5%, while expert endosonographers correctly diagnosed AIP with a sensitivity of 53.8% and specificity of 86.7%. Overall, this study serves as a model for the application of AI in the EUS evaluation of pancreatic pathologies including AIP.

AI IN THE EVALUATION OF CHRONIC PANCREATITIS

CP is an irreversible fibro-inflammatory condition caused by recurrent or persistent pancreatic parenchymal injury[29]. The diagnosis of CP is often made by analyzing a patient's risk factors, radiographic imaging results and direct/indirect pancreatic function laboratory tests. EUS-guided tissue acquisition still serves as the gold standard for CP diagnosis when less invasive tools are inconclusive, however, studies have found similar sensitivities and specificities in the diagnosis of CP using EUS, MRI or CT[30]. This again identifies another diagnostic dilemma for which AI may serve a role to improve diagnostic accuracy, thereby improving patient care and outcomes.

Computer aided diagnosis based on digital image analysis (DIA) was initially utilized in a small study attempting to differentiate between focal, pseudotumorous pancreatitis and pancreatic malignancy with an overall diagnostic accuracy of 89% [31]. In 2008, Săftoiu *et al* developed a neural network to differentiate between CP and pancreatic malignancy through imaging features of EUS-elastography, further expanding to include the evaluation of contrast-enhanced EUS images in 2015[19]. Their initial system was able to differentiate between malignant and benign pancreatic masses with a sensitivity of 91.4%, specificity of 87.9% and accuracy of 89.7%. Das *et al* [32] used DIA of the spatial distribution of pixels on EUS images to create a neural network that could differentiate PDAC and CP with a 93% accuracy. In 2013, Zhu *et al* [33] published data on the use of a support vector machine predictive model to differentiate PDAC and CP based on EUS images which achieved a diagnostic accuracy of 94%. Overall, these studies provide positive reinforcement to the notion that AI can improve EUS differentiation of pancreatic malignancy from other pathologies including CP.

AI IN THE EVALUATION OF INTRADUCTAL PAPILLARY MUCINOUS NEOPLASMS

With the increasing detection of pancreatic cystic lesions on cross-sectional imaging, IPMNs have become an important pancreatic pathology given their potential for malignant transformation[34]. Early resection of IPMNs, particularly those with high grade dysplasia limit the progression to PDAC. International consensus guidelines for IPMN management have identified high risk stigmata (*i.e.*, obstructive jaundice) and worrisome features (size > 3 cm, enhancing mural nodule < 5 mm, thickened cyst wall, MPD > 5-9 mm, abrupt change in MPD diameter) of malignancy associated with IPMN[34]. However, the use of these features alone to differentiate benign *vs* malignant IPMN leaves room for improvement, particularly through the use of AI-assisted EUS evaluation. In 2019, Kuwahara *et al*[35] performed a retrospective single-center study that developed an EUS-based CNN to differentiate benign *vs* malignant IPMNs. Their model identified malignant IPMNs with a diagnostic accuracy of 94%, compared to the human pre-operative diagnosis control group based on consensus guidelines which had an accuracy of 56%. While further research in this area is needed, the overarching theme of improved diagnostic accuracy when AI is applied to EUS evaluation of pancreatic disease appears to be evident.

CONCLUSION

The diagnosis of pancreatic lesions can be difficult, often stemming from the overlap of features found in benign lesions with those found in PDAC. The development of improved diagnostic tools to differentiate PDAC from other pancreatic lesions presents an opportunity for significant impact on the overall care of patients with pancreatic disease. More robust studies are needed to validate the current available research, namely in the form of prospective, multicenter studies which may further determine the generalizability of current models and the overall, real-time clinical application of these AI systems. It should be noted that standardization of endoscopic image capture and reporting may better help facilitate future interdisciplinary work in this field[36,37]. While the use of AI to evaluate the pancreas appears to be in its early stages, the potential for AI-assisted EUS assessment provides an exciting and promising future for the diagnosis and management of pancreatic lesions.

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