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Review Article

The application of artificial intelligence in gastrointestinal endoscopy: a state-of-the-art review

Chenxia Zhang, MA[1,2,3]**, Lianlian Wu, MD**[*1,2,3]

[1] Department of Gastroenterology, Renmin Hospital of Wuhan University, Wuhan 430060, Hubei Province, China
[2] Hubei Provincial Clinical Research Center for Digestive Disease Minimally Invasive Incision, Renmin Hospital of Wuhan University, Wuhan 430060, Hubei Province, China
[3] Key Laboratory of Hubei Province for Digestive System Disease, Renmin Hospital of Wuhan University, Wuhan 430060, Hubei Province, China

*Correspondence: wu_leanne@whu.edu.cn

Abstract: Endoscopy is an important tool for detecting and diagnosing digestive diseases. However, the performance of endoscopists varies, which significantly impacts the health outcomes of patients. In recent years, with the continuous development of science and technology, artificial intelligence (AI) has also set off a new wave. Nowadays, AI has been widely studied in the medical field and has shown great potential, especially in gastrointestinal endoscopy. The application of AI in endoscopy mainly includes the detection of lesions, classification of diseases, selection of best therapy, prognosis judgment, quality control, etc. What's more, the effectiveness and safety of the application of AI in gastrointestinal endoscopy have been confirmed in clinical trials. In this paper, we review the current research status and future development of AI in gastrointestinal endoscopy.

Keywords: Artificial intelligence, Deep learning, Gastrointestinal endoscopy, Digestive diseases, Quality control

Core Tips: Endoscopy is an important tool for detecting and diagnosing digestive diseases. However, the level of endoscopists varies, which significantly impacts the health outcomes of patients. In recent years, with the continuous development of science and technology, artificial intelligence (AI) has also set off a new wave. AI is increasingly widely used in the medical field nowadays and has shown great potential, especially in gastrointestinal endoscopy. The application of AI in endoscopy mainly includes the detection of lesions, classification of diseases, selection of best therapy, prognosis judgment, quality control, etc. Furthermore, the effectiveness and safety of the application of AI in gastrointestinal endoscopy have been confirmed in clinical trials. In this paper, we review the current research status and future development of AI in gastrointestinal endoscopy.

Introduction

Gastrointestinal cancer is one of the most common and deadly malignant tumors worldwide. According to the latest statistics (2020) [1], colorectal cancer and stomach cancer rank in the top five cancers amongst women; amongst men, they are the third and fourth most common cancers, respectively. In addition, nearly 2.5 million people die of gastrointestinal cancer every year. Among the leading causes of cancer-related deaths,

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colorectal cancer and gastric cancer rank second and fourth, respectively, causing a huge social and economic burden. The basic reason why malignant tumors are life-threatening is that they cannot be detected in the early stage [2]. Gastrointestinal tumors are generally treatable in their early stages [3, 4]. More importantly, the 5-year survival rate for early cancer of the digestive tract is higher than 90%. However, if cancer progresses to the middle and advanced stage, the 5-year survival rate will be less than 25% [5]. Therefore, early diagnosis and early treatment are the keys to improve the survival rate of patients with gastrointestinal cancer.

Endoscopy is the most commonly used method for screening and detecting gastrointestinal diseases. In recent decades, rapid progress in endoscopy has been seen worldwide. However, behind the vigorous development, some quality and safety concerns also exist. Mucosal changes in early gastrointestinal cancer are slight and difficult to identify, which requires endoscopists to be armed with rich experience and strong knowledge [6, 7]. However, there are great variations among the level and performance of endoscopists, resulting in a high rate of missed detection of lesions and the poor quality of gastrointestinal endoscopy, which seriously threatens the health and prognosis of patients [8, 9].

With the rapid development of computer technology and big data, artificial intelligence (AI) has gradually entered the public eye and the medical industry in recent years [10-12]. Nowadays, AI has made tremendous advances in medical fields such as radiology, pathology, and dermatology [13-15]. At present, numerous studies have shown the great potential of AI in endoscopy, which is expected to bring revolutionary changes to the diagnosis and treatment of digestive endoscopy [16]. This article summarizes the AI technology and its research in the field of digestive endoscopy, including (1) the introduction of AI and deep learning; (2) the application of AI technology in the field of endoscopy: diagnosis of cancer or pre-cancer diseases, diagnosis of other diseases, and quality control; (3) challenges and prospects of artificial intelligence.

1. Overview of artificial intelligence

1.1 Artificial intelligence and deep learning

Broadly speaking, artificial intelligence (AI) is a new technical science that enables computers to simulate certain thinking processes and intelligent behaviors of human beings, such as learning, reasoning, thinking, and planning [17, 18]. As an important branch of computer science, AI is one of the three cutting-edge technologies (space technology, energy technology, and artificial intelligence) in the world. The development of AI has experienced three waves [12]. The first two waves occurred in the 1970s and 1990s [19, 20], respectively. Due to the constraints of algorithms and computing power, AI did not achieve good results in the practical application of various industries at that time. With the deep learning technology proposed in 2006, AI ushered in the third wave [21]. In 2012, the ImageNet competition brought a breakthrough to the application of artificial intelligence in the field of image recognition and also made deep learning a widely used method in the field of image recognition. Different from the previous two waves, AI is not limited to academic theory but has entered into wide fields, showing extraordinary practical results and gradually changing our lives.

Deep learning, whose principle is to establish a neural network that analyzes and interprets data by imitating the operation mechanism of the human brain, is an important branch of technology in the field of AI and the latest development trend of artificial neural networks [17]. By extracting more abstract features of the input data layer by layer from the lower level to the higher level, the deep learning model forms the most appropriate network weight structure of the required features, to achieve an accurate classification. Deep learning mainly includes Deep Neural Network (DNN), Convolutional Neural Network (CNN), Recurrent Neural Network (RNN), and so on [22]. Although various deep learning architectures have been explored to solve different tasks, convolutional neural networks (CNNs) remain the most popular type of deep learning architecture in medical imaging today. A typical CNN is mainly composed of the input layer, convolution layer, pooling layer, and output laye [23]. The input layer receives input values and passes them to the next layer, but does not perform operations on the input value. The first hidden layer is the nonlinear mapping of the input data, and the second hidden layer is also the nonlinear mapping of the previous layer. They get the maps that are easy to classify through weight updating and pass the values to the output layer, to get the ideal results within a reasonable range. The artificial neurons of CNN respond to the part of the surrounding units within the coverage, which helps with processing large images [24].

1.2 Deep learning in computer vision

Computer Vision (CV), a discipline that teaches machines to see, has a rich history of decades. Advances in neural networks and deep learning have greatly promoted the development of computer vision recognition systems [25]. Four types of tasks are commonly applied to computer vision using deep learning, namely image classification, object detection, semantic segmentation, and instance segmentation. Image classification is the most basic application in computer vision, and the purpose of it is to determine the classification of a given picture. The training data set contains a variety of different objects, and the objects included in a given picture are required to output. Object detection refers to further clarifying the specific positions of various objects in the picture with a rectangular frame based on image classification. The essence of semantic segmentation is to classify every pixel in the image to distinguish various objects in the image. For the positions of objects of different categories, each pixel should be distinguished, but not for different objects belonging to the same category. Instance segmentation is the combination of object detection and semantic segmentation. It not only uses object detection to box out different objects in the picture but also needs to use semantic segmentation to understand the given box at the pixel level. Compared with the boundary box given by object detection, instance segmentation can be further refined to the edge of the object. What's more, it can further annotate different objects of the same categories in the picture compared with semantic segmentation.

2. Application of AI in upper gastrointestinal endoscopy

2.1 Esophageal cancer

Esophageal cancer is one of the most fatal tumors. In 2020, more than 604,000 people were newly diagnosed with esophageal cancer worldwide, accounting for 3.1% of new cancer cases globally each year [1]. Furthermore, esophageal squamous cell carcinoma (ESCC) is the major subtype of Esophageal cancer, accounting for more than 90% of esophageal cancer in China [26]. However, in recent years, the incidence of esophageal adenocarcinoma has increased significantly. And it has surpassed the incidence of esophageal squamous cell carcinoma gradually in many western countries [27]. With early diagnosis and treatment, the 5-year survival rate of patients with esophageal cancer is up to 90% [28]. However, most esophageal cancers are in the middle and late stages at the time of diagnosis, and the overall 5-year survival rate is less than 20% [1]. There is no doubt that early diagnosis of esophageal cancer is crucial to improve the prognosis.

LinJie Guo et al. used 6473 NBI images, including dysplasia, early ESCC, and non-cancerous lesions from 549 patients to train the semantic segmentation model SegNet for real-time diagnosis of esophageal precancerous lesions and early ESCC [29]. The sensitivity, specificity, and the area under the curve (AUC) in predicting precancerous lesions and early ESCC in a test set consisting of 6,671 NBI images from 59 cancerous patients and 2004 non-cancerous patients were 98.04%, 95.03%, and 0.989, respectively. In the test set of 47 patients with cancer and 33 patients without cancer, the model achieved a per-case sensitivity of 100% and a per-case specificity of 90.9%. The authors conclude that the deep learning model achieved high sensitivity and specificity in images and videos, and has the potential to assist endoscopists in diagnosing precancerous lesions and ESCC in real-time. As we all know, Intrapapillary capillary loops (IPCLs) are an effective endoscopic marker for the detection of squamous dysplasia and esophageal squamous carcinoma. Everson MA et al. used 67,742 magnification endoscopy narrow-band(ME-NBI) images of 115 patients to construct a convolutional neural network that could classify IPCL patterns [30]. The model predicted dysplasia with an accuracy of 91.7% and sensitivity of 93.7%, which was preferable to previous studies [31]. In short, this kind of clinically interpretable CNN based on the IPCL model puts forward a new idea for our future research.

The key point of early esophageal cancer is not the diagnosis, but the judgment of invasion depth, which is very crucial for the selection of treatment [32]. Nevertheless, the current diagnostic theory of invasion depth is complex, and the judgment is often subjective. Kentaro et al. developed a deep learning system to evaluate invasion depth of esophageal superficial squamous cell carcinoma using 8660 non-ME images and 5678 ME images from 804 patients whose invasion depth was confirmed by pathology [33]. The system performed well in diagnosing the depth of invasion of superficial esophageal squamous cell carcinoma with a sensitivity of 90.1%, a specificity of 95.8%, and an accuracy of 91.0%, comparable to experienced endoscopists.

2.2 Barrett's esophagus

Barrett's esophagus (BE) refers to a pathological phenomenon in which the lamellar squamous epithelium of the lower mucosa of the esophagus is replaced by a single columnar epithelium. BE is the only known precancerous lesion of esophageal adenocarcinoma (EAC), and early detection and follow-up monitoring of patients with BE are conducive to the improvement of prognosis [34, 35]. However, the lesion of BE is relatively mild, which could be easily ignored or missed. Guidelines recommend an endoscopic biopsy of the four quadrants of BE at random intervals of 1-2cm to detect dysplasia in time [32], but this method is invasive, time-consuming, and difficult to adhere to in some cases. The use of deep learning to detect BE and distinguish BE from neoplasia is expected to improve detection efficiency.

Hashimoto R et al. collected 916 images from 65 cases with early esophageal neoplasia in BE containing high-grade dysplasia or T1 cancer and 919 images from 119 cases of BE without high-grade dysplasia or T1 cancer, to train image classification and target detection nested model (Inception-ResNet-v2 as the main model to detect whether there is a target lesion in the image, and adding Yolo to locate the lesion), to identify and locate early tumors from BE images [36]. In the 458 test images (225 early tumors and 233 controls), the sensitivity, specificity, and accuracy of the model to detect early tumors were 96.4%, 94.2%, and 95.4%, respectively. The intersection over union (IOU) between the model and the endoscopist on the localization of the lesion was 0.3. The authors conclude that the model can detect early esophageal tumors in BE images with high accuracy and map a positioning box around the areas of early esophageal neoplasia with high accuracy. What's more, Ebigbo A et al developed a real-time deep learning artificial intelligence system based on their previous work [37]. The system differentiated and predicted normal BE and early oesophageal adenocarcinoma (EAC) accurately. This is the first real-time application of a deep learning AI system in the evaluation and diagnosis of early EAC in BE in a real-life setting.

The differentiation between Barrett's cancer mucosa (T1a) and submucosal invasion (T1b) is the key to the choice of treatment and prognosis [32]. Unfortunately, it is quite challenging [38]. Ebigbo A et al. trained a deep learning system to distinguish T1a from T1b Barrett's-related cancer using 230 white light endoscopy images (108 T1a and 122 T1b) from 116 patients with Barrett's cancer [39]. The sensitivity, specificity, and accuracy of the system were 0.77, 0.64 and 0.71, respectively. This suggested its diagnostic performance was comparable to that of experts. However, this study was based on static images, so it still needed further improvement to be put into the practical clinical application as soon as possible.

2.3 Esophageal protruded lesions

Nearly 30% of the protruded lesions of the upper digestive tract originate in the esophagus [40]. In clinical practice, it is important to distinguish esophageal protruded lesions, such as esophageal leiomyoma (EL), esophageal cyst (EC), and esophageal papilloma (EP). But it is difficult to judge by white light image alone, and endoscopic ultrasonography (EUS) is often required [41]. Unfortunately, EUS has a steep learning curve and remains a challenging task for endoscopists of all levels of experience [42]. Min Zhang et al. developed a CNN-based model using WLE and EUS images of 1217 patients with benign esophageal protruded lesions to identify and differentiate the three subtypes (EL, EC, EP) [43]. For the identification of esophageal benign lesions from healthy controls, the AUC of the CNN model was 0.751. The model achieved an AUC of 0.907, 0.897 and 0.868 for the identification of EP, EL, and EC under WL, while 0.739 and 0.724 for EL and EC under EUS. Compared with all endoscopists, the model achieved higher sensitivity and specificity than all endoscopists in correctly classifying EL and EC using EUS images.

2.4 Esophagogastric varices

Esophagogastric varices (EGV) are one of the main complications of cirrhosis, and the death rate of acute variceal rupture and bleeding can reach 15%-50% [44]. Early identification of patients with a high risk of variceal hemorrhage in cirrhosis is very important for the primary prevention of variceal hemorrhage. Esophagogastroduodenoscopy (EGD) is recommended in the Guidelines as a tool for assessing the risk of bleeding from esophageal and gastric varices, but this is often subjective in practical clinical practice [45]. Chen M et al. trained a DCNN system (ENDOANGEL) based on 8,566 endoscopic images of gastroesophageal varices in 3021 patients and 6,152 normal esophagus/stomach images in 3168 patients for the diagnosis of gastroesophageal varices and the prediction of rupture risk [46]. As a result, ENDOANGEL detected esophageal varices (EVs) and gastric varices (GVs) at the accuracy of 97.00% and 92.00%, respectively, comparable to that of experts. Moreover, it achieved excellent results in the detection of endoscopic risk factors for esophagogastric variceal bleeding. The authors point out that although this system still has some limitations in the judgment of treatment decisions, prospective studies are needed to further verify the performance of the model. As for patients with compensated advanced chronic liver disease, Agarwal S et al developed a machine learning model to predict bleeding in esophageal varices [47]. The model improved the performance of endoscopic stratification to predict VB with an accuracy of 98.7%.

2.5 Gastric cancer

More than 1 million new cases of gastric cancer occur globally each year, making it the fourth leading cause of cancer-related death [1]. The 5-year survival rate of advanced gastric cancer is 5%-25%, while early endoscopic diagnosis and treatment can improve the survival rate to more than 90% [5]. Early detection and treatment is critical to reduce mortality and improve survival rates. The recognition and diagnosis of EGC based on deep learning are expected to reduce the missed diagnosis of gastric cancer and enhance survival.

Our previous work used a total of 3,170 gastric cancer and 5,981 benign images to train the vgg-16 and resnet-50 for the detection of EGC [48]. Based on the image classification model, a class-like activation map was further developed to automatically cover suspicious cancerous areas. One hundred EGC and one hundred non-cancerous images were used as a test set to evaluate and compare the diagnostic capabilities of the model and endoscopists. The results showed that the accuracy, sensitivity, specificity, positive predictive value, and negative predictive value of the model were 92.5%, 94.0%, 91.0%, 91.3%, and 93.8%, respectively, which were better than that of endoscopists. At the same time, the study of real-time monitoring of EGC in early cancer and non-cancer videos demonstrated a good effect. Li L et al. collected 386 images of non-cancerous lesions and 1702 images of early gastric cancer to train the classification model Inception-v3 to distinguish early and non-cancer by magnifying endoscopy with narrow-band imaging (ME-NBI) [49]. The model showed comparable accuracy (90.9%) and superior sensitivity (91.2%) to that of experts. In addition, Tang D et al. used 3407 endoscopic images from 666 patients with gastric cancer to construct a deep convolutional neural network model to differentiate intramucosal GC from advanced GC [50]. With the help of this model, novice endoscopists(84.6%) achieved the same level of accuracy as specialists(85.5%).

With the development of endoscopic treatment for EGC, endoscopic submucosal dissection (ESD) is becoming more and more popular [51]. However, whether ESD can be performed depends to a large extent on the depth of invasion, degree of differentiation, and boundary of gastric cancer [52, 53]. Zhu Y et al. developed a CNN-CAD system for judging the depth of gastric cancer invasion, which can effectively distinguish early gastric cancer from deep submucosal invasion and minimize the overestimation of the depth of invasion to avoid overtreatment [54]. Ling T et al. retrospectively collected 2217 images of differentiated gastric cancer and 11,870 images of undifferentiated gastric cancer to establish a model to evaluate the degree of differentiation of gastric cancer [55]. In addition, 694 images of differentiated cancer and 234 images of undifferentiated cancer labeled by experts were used to train and test the gastric cancer boundary delineation model to accurately identify the differentiation state and delineate the edge of EGC under ME-NBI endoscopy. The accuracy of the model to identify the differentiation degree of EGC reached 83.3%. At the overlap rate of 0.80, the accuracy rate for differentiated and undifferentiated EGC was 82.7% and 88.1%, respectively, which was better than that of endoscopy experts and had potential clinical practical value. The system performed excellently in a multicenter, prospective, real-time, competitive comparative, diagnostic study [56].

2.6 Precancerous lesions

Chronic inflammation of gastric mucosa induces a series of precancerous conditions (gastric atrophy and intestinal metaplasia) and lesions (dysplasia), leading to the occurrence and development of gastric cancer [57]. In patients with extensive atrophy of gastric mucosa, the 5-year incidence of gastric cancer can reach 1.9%-10%, while in patients with intestinal metaplasia, the incidence is as high as 5.3%-9.8% [58]. Therefore, early identifying and monitoring the precancerous conditions is beneficial to the healthy outcome of patients. Zhang Y et al. collected 3042 images of atrophic gastritis and 2428 images of non-atrophic gastritis from the gastric antrum of 1470 patients, aiming to construct a classification model to diagnose chronic atrophic gastritis [59]. The authors conclude that the deep learning model has high sensitivity (94.5%) and accuracy (94.2%) in the diagnosis of atrophic gastritis, which can improve the diagnostic ability of endoscopists on atrophic gastritis. Based on 6250 endoscopic images from 760 patients with precancerous gastric cancer and 98 videos from 77 patients who underwent image-enhanced endoscopy (IEE), Xu M et al. constructed ENDOANGEL, a deep convolutional neural network system, for the detection of precancerous gastric cancer [60]. The system showed high accuracy, sensitivity, and specificity in detecting precancerous lesions, and the diagnostic accuracy (GA 0.901; IE 0.908) was close to the expert level, which provided the possibility of being widely used in the diagnosis of precancerous lesions of gastric cancer.

2.7 Helicobacter pylori (Hp) infection

Helicobacter pylori (Hp) is a ubiquitous microbe, which can be found in 50% of the world's population [61]. Chronic infection with Hp can lead to gastric atrophy and even metaplasia. The International Agency for Research on Cancer (IARC) of the World Health Organization (WHO) believes that 78% of gastric cancers can be attributed to chronic infection caused by Hp and has classified it as a class I carcinogen [62]. Timely diagnosis and eradication of HP are considered to be an important strategy to prevent gastric cancer. With the continuous progress of endoscopic technology, more and more studies have found that morphological changes of esophageal and gastric mucosa under endoscopy (such as atrophy, punctured redness, mucosal swelling, erosion, etc.) are related to Hp infection [63, 64]. However, there are no objective indicators for these endoscopic features, which greatly limits their clinical application. Shichijo S et al. constructed a convolutional neural network that could diagnose Hp infection [65]. The sensitivity and accuracy of the model in determining Hp infection through gastroscopic images reached 81.9% and 83.1%, showing excellent performance. Zheng W et al. collected 11,729 gastric images from 1,507 patients (847 of whom were infected with Hp) to train classification model ResNet-50 and tested the model in 3,755 images from 452 patients (310 of whom were infected with Hp) [66]. The results showed that the AUC per image and per patient was 0.93 and 0.97, respectively. with sensitivity, specificity, and accuracy of 91.6%, 98.6%, and 93.8%, which indicated a high diagnostic accuracy. To evaluate the infection status of Helicobacter pylori (not infected, past infection or current infection), Yoshii S et al. recruited 498 subjects and developed a predictive model by evaluating their gastritis endoscopic results based on the Kyoto classification [63]. The overall diagnostic accuracy of the model for gastritis was 82.9%. With further improvement, this model might be very helpful to novice endoscopists.

2.8 Quality control

Gastroscopy is a key step in the diagnosis of upper gastrointestinal diseases. However, endoscopists vary in their performance levels, which affects the detection of gastric cancer and precancerous lesions. At present, most of published articles focus on the diagnosis or detection of lesions, while a few studies focus on the quality of endoscopic examination.

Our previous work used more than 60,000 EGD images and divided them into training set and test set at the ratio of 9:1. Endoscopists studied the guidelines of the European Society of Gastrointestinal Endoscopy (ESGE), the Japanese systematic screening protocol and independently labeled EGD images into 26 different sites [67]. Then VGG-16 was trained to realize the function of classifying gastric sites [68]. The model monitored blind spots with an accuracy of 90.40% in real EGD videos. What's more, the blind spot rate of the patients in AI-assisted group (5.9%) was significantly lower than that of the control group (22.5%) in our clinical trial, which suggested that this system had the potential to improve the quality of daily endoscopic examination. In our most recent prospective randomized controlled study, the number of blind areas during gastroscopy was reduced from 9.82% to 5.39% with the aid of AI [69].

Table 1 Examples of the application of artificial intelligence in digestive endoscopy

Lesions	Diagnostic or predictive modality	AI model	Number of images/cases in training dataset	Number of images/cases in test dataset	Result
Esophageal cancer					
Guo L et al.	narrow-band imaging (NBI)	SegNet	6473 NBI images	6670 NBI images 80 videos	Sensitivity Image dataset:93.6% Nonmagnifying video dataset:46.9% Magnifying video dataset:85.8%
Everson MA et al.	magnification endoscopy	CNN	54,193 magnification endoscopy narrow-band images	13,548 magnification endoscopy narrow-band images	F1 score: 94% Sensitivity:93.7% Accuracy:91.7%
Nakagawa K et al.	upper GI endoscopes	CNN	8660 non-magnified endoscopic (non-ME) and 5678 ME images from 804 superficial esophageal SCCs	405 non-ME images and 509 ME images from 155 patients	SM1, SM2/3： Sensitivity:90.1% Specificity: 95.8% Accuracy :91.0%
Barrett's esophagus					
Hashimoto R et al.	Wchromoendoscopy	CNN	960 images from 65 patients	458 images (225 dysplasia and 233 non-dysplasia)	Sensitivity: 96.4% Specificity:94.2% Accuracy:95.4%
Ebigbo A et al.	upper GI endoscopes	CNN	230 white-light endoscopic images (108 T1a and 122 T1b)		Sensitivity: 0.77 Specificity:0.64 Accuracy:0.71
Esophageal protruded lesions					
Zhang M et al.	white-light endoscopy EUS	CNN	(1)identification of esophageal benign lesions from healthy controls: 17279 WLI images from 598 patients (2)differentiation esophageal leiomyoma, esophageal cyst, esophageal papilloma: 3226 WLI images from 619 patients (3) discrimination between EL and EC Wusing EUS images: 3411 EUS images from 248 patients		(1)AUC: 0.751 (2)AUC: EP:0.907 EL:0.897 EC:0.868 (3)AUC: EL:0.739 EC:0.724
Esophagogastric varices					
Chen M et al.	upper GI endoscopes	DCNN	8566 images (gastroesophageal varices) 6152 images (normal esophagus/stomach)	-	Accuracy: esophageal varices (EVs):97.00% gastric varices (GVs):92.00%
Gastric cancer					
Wu L et al.	esophagogastroduodenoscopy	DCNN	24,549 images of different parts of the stomach were taken to train the model to monitor the blind spot 3170 images of gastric cancer and 5981 images of benign lesions were used to train the model to recognize early cancer		Accuracy: 10 parts classification: 90% 26 parts classification: 65.9% early cancer in WL images: 92.4%
Li L et al.	magnifying endoscopy	CNN	386 images of non-cancerous lesions and 1702 images of early gastric cancer	341 endoscopic images (171 non-cancerous lesions and 170 early gastric cancer)	Sensitivity:91.18% Specificity:90.64% Accuracy:90.91%

Tang D et al.	esophagogastroduodenoscopy	DCNN	3407 endoscopic images from 666 gastric cancer patients	228 images from 62 patients	AUC:0.942 Sensitivity:90.5% Specificity:85.3%
Zhu Y et al.	esophagogastroduodenoscopy	CNN ResNet50	790 images	203 images	Ensitivity:76.47% Specificity:95.56% Accuracy:89.16%
Ling T et al.	magnifying narrow-band imaging (ME-NBI) endoscopy	CNN	1131 images of differentiated and 1086 images of undifferentiated gastric cancer	1526 images from 105 differentiated gastric cancers and 344 images from 34 undifferentiated gastric cancers	Accuracy:83.3 %
Wu L et al.	magnifying narrow-band imaging endoscopy	-	-	37 EGCs and 63 noncancerous lesions	Sensitivity:Detect neoplasms 87.81% Diagnose EGCs100% Accuracy: Predict EGC invasion depth78.57% Differentiate status 71.43%
Precancerous lesions					
Zhang Y et al.	esophagogastroduodenoscopy	CNN	5470 images of the gastric antrums of 1699 patients		Diagnose atrophic gastritis Accuracy:0.942 Sensitivity:0.945 Specificity: 0.940
Xu M et al.	image-enhanced endoscopy (IEE)	DCNN	3,049 images of precancerous states and 2,149 images of chronic inflammation	1052 images 98 videos	Accuracy: gastric atrophy:0.901 intestinal metaplasia:0.908
Helicobacter pylori (Hp) infection					
Shichijo S et al.	esophagogastroduodenoscopy	CNN	32,208 images either positive or negative for H. pylori	11,481 images from 397 patients	CNN1:sensitivity 81.9% specificity83.4% accuracy83.1% CNN2: sensitivity 88.9% specificity87.4% accuracy87.7%
Zheng W et al.	upper endoscopy	ResNet-50	11,729 gastric images	3,755 images	Sensitivity:81.4% Specificity:90.1% Accuracy:84.5%
Yoshii S et al.	upper endoscopy	CNN	498 patients		Accuracy: Kyoto classification of gastritis:82.9% without H. pylori eradication history: 88.6% with eradication history:93.4%
Quality control					
Wu L et al.	esophagogastroduodenoscopy	VGG-16 DenseNet	DCNN1:12 220 in vitro, 25 222 in vivo and 16 760 unqualified EGD images DCNN2:34 513 qualified EGD images	DCNN1:3000 images (1000 per category) DCNN2:2160 images (80 per site)	monitor blind spots with an average accuracy of 90.02%
Wu L et al.	esophagogastroduodenoscopy	-	ENDOANGEL groups: 498 patients Control groups:504 patients		The number of blind spots: ENDOANGEL group: 5.39% Control group: 9.82%
Application of AI in capsule colonoscopy					
Aoki T et al.	wireless capsule endoscopy	CNN	5360 WCE images of erosions and ulcerations	440 images of erosions and ulcerations	Ensitivity:88.2% Specificity:90.9% Accuracy:90.8%

Ding Z et al.	small bowel capsule endoscopy (SB-CE)	CNN	158,235 SB-CE images from 1970 patients	5000 patients	Sensitivity of identifying abnormalities per-patient analysis: 99.88% per-lesion analysis:99.90%
Yamada A et al.	colon capsule endoscopy	Single Shot MultiBox Detector	15 933 CCE images of colorectal neoplasms	4784 images(1850 images of colorectal neoplasms and 2934 normal colon images)	Sensitivity:79.0 % Specificity: 87.0 % Accuracy: 83.9 %
Leenhardt R et al.	small-bowel capsule endoscopy	CNN	-	-	sensitivity : 90.3 % Specificity: 83.3 % Accuracy: 89.7 %
Colorectal cancer					
Luo X et al.	white-light colonoscopy	CNN	7734 nonmagnified white-light colonoscopy (WLC) imagesfrom 657 lesions	1634 WLC images from 156 lesions	Accuracy: 91.1% Sensitivity: 91.2% Specificity: 91.0%
Ichimasa K et al.	colonoscopy	SVM	590 patients	100 patients	Sensitivity:100 % Specificity:66% Accuracy:69%
Polyps and adenomas					
Kudo SE et al.	colonoscopy	CNN	69,142 endocytoscopic images	100 lesions from 89 patients	Sensitivity:96.9% Specificity:100% Accuracy: 98%
Wang P et al.	colonoscopy	-	1,290 patients	612 polyp-containing images	per-image-sensitivity, 88.24%
Wang P et al.	colonoscopy	-	standard colonoscopy group:536 patients computer-aided group:522 patients		ADR standard colonoscopy group:29.1% computer-aided group:20.3%
Inflammatory bowel disease					
Takenaka K et al.	colonoscopy	DNUC	40,758 images of colonoscopies	4187 endoscopic images and 4104 biopsy specimens	The DNUC identified patients in histologic remission with 92.9% accuracy
Gottlieb K et al.	colonoscopy	-	795 prospectively recorded full-length endoscopy		quadratic weighted kappa (QWK): eMS :0.844 UCEIS:0.855
Quality control					
Zhou J et al.	colonoscopy	CNN	5583 clear colonoscopic images	120 images (30 in each classification)	BBPS four classification scoring accuracy: 93.33%

3. Application of AI in capsule colonoscopy

Capsule endoscopy (CE) entered the domain of small intestine disease diagnosis in 2001 [70]. As a non-invasive deglutition diagnostic device, CE can not only reduce patients' discomfort during the examination but also clearly observe various types of intestinal mucosal abnormalities [71]. However, the major limitation is that CE is time-consuming and has a high risk of missed detection [72]. Aoki T et al. collected 5,360 CE images of erosion and ulcer to train the detection model SSD and tested it in 10,440 CE images (including 440 erosion and ulcer) [73]. The deep learning model can automatically detect erosion and ulcers with an accuracy of 90.8% in the CE image, thus reducing the burden on endoscopists. Furthermore, Ding Z et al. collected 113,426,569 CE colonoscopy images from 6970 patients who had undergone small bowel capsule endoscopy in 77 medical centers to conduct a classification model ResNet which could distinguish between normal and abnormal images [74]. With the assistance of AI model, endoscopists identified abnormalities with a higher sensitivity(99.88%) and in a shorter time(5.9±2.23 min per case) with the assistance of AI. Recently, Yamada A et al. used 15 933 colon capsule endoscopy (CCE) images of colon tumors, such as polyps and cancers, to develop a deep convolutional neural network based on a Single Shot MultiBox Detector for the automatic detection of colorectal tumors [75]. Leenhardt R et al. also developed a neural network-based algorithm that can automatically evaluate the cleanliness of the small intestine during capsule endoscopy with a high sensitivity of 90.3% [76]. What's more, Saraiva MM et al developed a Convolutional Neural Network model using a database of CCE images to detect protruding lesions [77]. This model performed well in detecting protruding lesions with sensitivity and specificity of 90.7% and 92.6%, respectively.

4. Application of AI in colonoscopy

4.1 Colorectal cancer

Colorectal cancer is the second most deadly malignancy in the world [1], and new cases of colorectal cancer are expected to rise to 2.5 million worldwide by 2035 [78] which will place huge health and economic burden on society. Screening for colorectal cancer, early detection and treatment of precancerous lesions and asymptomatic early cancer are essential to delay progression and reduce mortality. Colonoscopy is an important means for early diagnosis and treatment of lower gastrointestinal diseases and is the gold standard for colorectal cancer screening [79]. Unfortunately, the current application of AI in colonoscopy mainly focuses on the detection and classification of polyps [80, 81]. However, once colorectal cancer is diagnosed, evaluation of the depth of invasion is our first task, which is crucial for the selection of treatment strategy [52]. Luo X et al. constructed a deep convolutional neural network with tumor localization branches based on GoogLeNet architecture to evaluate the invasion depth using 7734 white light colonoscopy images of 657 lesions [82]. Pathological results were the gold standard. Consequently, the model achieved an accuracy of 91.1% in the prediction of non-invasive and superficial invasive tumors. In addition, the model could distinguish between superficial submucosal invasive tumors and deep invasive CRC with an accuracy similar to that of experienced endoscopists. Some studies also focus on the treatment and prognosis of patients with colorectal cancer, trying to use AI to select the optimal treatment plan for patients. Ichimasa K et al. developed a machine learning model to predict the risk of lymph node metastasis. Consequently, it showed that AI could significantly reduce unnecessary additional surgery after the endoscopic resection of T1 colorectal cancer [83].

4.2 Polyps and adenomas

Removal of adenomas found by colonoscopy can significantly reduce the incidence and mortality of colorectal cancer [84, 85]. Each 1.0% increase in the adenoma detection rate is associated with a 3.0% decrease in the risk of cancer [86]. However, the level of endoscopists varies, and polyps may be missed during colonoscopy. In one study, the missed rate of adenomas is as high as 26% [87]. At the same time, it is important to distinguish between non-neoplastic and neoplastic lesions for the treatment and prognosis of patients. The traditional method is to take biopsy to identify neoplastic lesions [88], but this method is invasive and time-consuming. Accurate optical diagnosis of colorectal polyps can decrease the cost of colonoscopy and reduce the complications related to polyp biopsy.

Kudo SE et al. collected 69,142 images of endoscopy from patients with colorectal polyps in 5 academic centers in Japan to train the system EndoBRAIN [89]. Compared with 30 endoscopists (20 trainees and 10 specialists), EndoBRAIN showed a better performance in the diagnosis of neoplasia in stained endocytoscopic images with a sensitivity of 96.9%. Furthermore, the sensitivity and accuracy of EndoBRAIN in narrow-band images were 96.9% and 96.0%, which were significantly better than that of non-experts and comparable with that of experts.

To improve the detection rate of colorectal polyps, early detection and removal of colorectal polyps is of great significance for the prevention of colorectal cancer. Wang P et al. conducted a segmentation model SegNet to detect colorectal polyps, which performed well with the sensitivity of 94.38% and specificity of 95.92% [90]. Subsequently, a randomized, controlled and single-blind clinical trial, of which 536 received conventional colonoscopy and 522 received AI-assisted colonoscopy was conducted [91]. The results showed that the AI system could significantly improve the adenoma detection rate (ADR) from 20.3% to 29.1% and the mean number of adenomas detected per patient (MNA) from 0.31 to 0.53. Recently, to study the influence of artificial intelligence system on ADR after eliminating the operational bias, Wang P et al. further designed and conducted a randomized double-blind clinical trial involving 1,010 patients [92]. The AI-assisted group simulates the alarm box on polyps; while the sham control group simulates the alarm box on the polypoid non-polyp mucosas. Only the observer can see the output of the systems on a second monitor and report the alert to endoscopists. Only when the area predicted by the AI system is not thought to be a polyp by the operating endoscopist and is about to leave the field of vision, will the observer point at the area to alert the endoscopist. The results showed that the ADR of the AI-assisted group(34%) was significantly higher than that of the sham control group(28%), which indicated that the AI system could help endoscopists detect more polyps and adenomas in real time. Furthermore, Sinonquel P et al also used a second observer in a non-RCT setting to assess the miss rate of AI system and endoscopists [93]. Both the system and the endoscopists performed well with a real-time accuracy of 96.5% and 98.2%, which suggested the system was non-inferior in terms of sensitivity and might aid in guaranteeing quality in colonoscopy.

4.3 Inflammatory bowel disease

At present, the prevalence of inflammatory bowel disease (IBD) is on the rise, and it has become a global disease [94]. As we all know, delayed diagnosis of IBD significantly increases the risk of surgical resection and complications [95, 96]. Objective endoscopic evaluation of inflammatory bowel disease is of great significance in promoting the treatment of patients and improving the prognosis [97]. However, endoscopic assessment requires training for endoscopists, and there are usually differences in the assessment among different endoscopists [98]. It is difficult to diagnose IBD, misdiagnosis and missed diagnosis are widespread in the world. Takenaka K et al. collected 40,758 colonoscopy images from 2,012 patients with ulcerative colitis (UC) to train the classification model to assess the severity of UC and validated it prospectively with 4187 endoscopic images from 875 patients with UC [99]. Endoscopic remission was defined as the ulcerative colitis endoscopic, the index of severity (UCEIS) score is 0. Histological remission was defined as Geboes score ≤ 3. The deep learning model is highly accurate in assessing UC with an accuracy of 90.1% and 92.9% in predicting endoscopic remission and histological remission, and is expected to help endoscopists identify remission in UC patients without biopsy. What's more, Bossuyt P et al also developed an operator-independent computer-based tool to determine UC activity based on endoscopic images, which provided an objective computer-based score that accurately assessed disease activity in UC [100]. In their validation study, they tested the correlation between the algorithm RD score and clinical, endoscopic and histological features. Consequently, RD was correlated with endoscopic and histological disease activity. To identify the endoscopic disease activity scoring in UC in the video, Gottlieb K et al. collected 795 endoscopy videos prospectively and constructed a system based on convolutional neural network and recurrent neural network to evaluate UC endoscopy Mayo score(eMS) and Ulcerative Colitis Endoscopic Index of Severity (UCEIS) score [101]. Quadratic weighted kappa (QWK), which was used to evaluate the model, was 0.844 and 0.855 for eMS and UCEIS respectively. Soffer S et al. was encouraged by this innovative research and believed that it would be a stepping stone for the future development of AI in Esophagogastroduodenoscopy [102].

4.4 Quality control

In recent years, the incidence and mortality of colorectal cancer have been increasing and it has become one of the major malignant tumors threatening human health. Colonoscopy is the gold standard for CRC screening, and high-quality colonoscopy is the basis for the early detection of lesions. Studies have shown that adenoma detection rate (ADR), as an important indicator of colonoscopy quality control [86], can decrease the risk of interphase colon cancer by 3% and the mortality of colorectal cancer by 5% with an increase of 1%. The key indicators to evaluate the quality of colonoscopy mainly include intestinal preparation, cecal intubation rate, ADR, etc [88]. However, the existing number of endoscopists cannot meet the increasing demand for colonoscopy, and the level of endoscopists varies, which will lead to the uneven quality of colonoscopy. Therefore, we should further strengthen the quality control of colonoscopy, and reduce the rate of missed diagnosis of the lower gastrointestinal tract during colonoscopy.

Inadequate intestinal preparation is associated with a reduced adenoma detection rate (ADR). Our previous work used 4,764 colonoscopy images, which were graded from 0 to 3 according to the Boston bowel score (BBPS) by endoscopies to train the classification model DenseNet [103]. In predicting the bowel preparation in real-time, the model achieved an accuracy of 93.33% in a test set of 480 colonoscopy images (120 for each category) and 89.04% in 20 colonoscopy videos. We have recently developed an intestinal preparation assessment system for calculating automatic BBPS (E-BBPS) scores (range 0-20) [104]. The system classified colonoscopy video images into qualified and unqualified images, and then calculated the proportion of unqualified frames in real-time to reflect intestinal preparation. In addition, the correlation between the proportion of intestinal unqualified preparation and the

ADR was explored based on 616 prospective colonoscopy screening videos. We were pleasantly surprised to find that there was a significant negative correlation between the proportion of intestinal preparation unqualified frames and the ADR (ρ= -0.976, P<0.01), and ADR was significantly lower in patients with scores greater than 3 than in patients with scores less than 3 (15.93% vs 28.03%, OR 0.43). This suggests that our system has the potential to provide more objective and refined thresholds for the quantification of adequate intestinal preparation.

It is well known that the withdrawal time is significantly associated with the incidence of interval colorectal cancer [105]. As is recommended in the guidelines, it should not be less than 6 minutes [88]. Our previous work used more than 20,000 images of colonoscopy to construct a real-time quality improvement system through VGG-16 and perceptual hashing algorithm to monitor real-time withdrawal speed, withdrawal time and remind endoscopists of blind spots caused by scope slipping [106]. Subsequently, 791 patients were recruited for a randomized controlled clinical trial. The results showed that the ADR of the AI-assisted group (16.34%) was significantly higher than that of the control group (7.74%). We conclude that the system has greatly improved the detection of adenomas and polyps by improving the quality of colonoscopy, and it is expected to be a powerful tool to narrow the skill gap among endoscopists.

5. Summary and prospect

With the rapid development of computer technology, the application of AI in the field of digestive endoscopy has mushroomed. Needless to say, the future of artificial intelligence is promising. However, it is also full of challenges. Behind the rapid development of technology, there are still many problems and difficulties to be solved. Firstly, the sample data set is important to the deep learning model, and the quantity and quality of the data set directly affect the accuracy and generalization ability of the model. How to evaluate the quality of the data set, how to improve the quality of sample labeling, and how to ensure that there is no cross contamination between training and testing sets, etc., are problems worth further discussion. In addition, there are "black boxes" in the logic of deep-learning algorithms' decision-making processes that are difficult for humans to understand, preventing doctors from discovering potential confounding factors. More importantly, AI is still in the development stage, and there are no relevant rules or the formation of industry norms yet. In future practical applications, AI cannot know the comprehensive situation of patients, nor does it understand the laws and responsibilities except the picture information read. If misdiagnosis occurs, how to solve the ethical problem and who should bear the corresponding responsibility?

The free and open-source sharing of algorithms ensures us to use the most advanced deep learning model to study and explore the application of deep learning in medical imaging. We need to start from the actual clinical needs, take the basic theory as the starting point, and form a set of independent digestive endoscopy AI technology development mechanism with the accumulation of time experience. Hope we could see that AI brings revolutionary changes to digestive endoscopy and even the whole medical field, contributes to improving patients' outcome worldwide.

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Author contributions

CXZ analyzed the research data and drafted the manuscript; LLW revised the manuscript. All the authors discussed, reviewed and edited its content before submission.

Disclosure

There are no financial conflicts of interest to disclose.

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