Artificial Intelligence in

Gastrointestinal Endoscopy

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AIMS AND SCOPE

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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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

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.

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 histopatho-logical 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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