

Artificial Intelligence in *Gastroenterology*

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Artificial Intelligence in Gastroenterology

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ABOUT COVER

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AIMS AND SCOPE

The primary aim of *Artificial Intelligence in Gastroenterology* (AIG, *Artif Intell Gastroenterol*) is to provide scholars and readers from various fields of artificial intelligence in gastroenterology with a platform to publish high-quality basic and clinical research articles and communicate their research findings online.

AIG mainly publishes articles reporting research results obtained in the field of artificial intelligence in gastroenterology and covering a wide range of topics, including artificial intelligence in gastrointestinal cancer, liver cancer, pancreatic cancer, hepatitis B, hepatitis C, nonalcoholic fatty liver disease, inflammatory bowel disease, irritable bowel syndrome, and *Helicobacter pylori* infection.

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Application of artificial intelligence in the diagnosis and prediction of gastric cancer

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Abstract

Gastric cancer is the second leading cause of cancer deaths worldwide. Despite the great progress in the diagnosis and treatment of gastric cancer, the incidence and mortality rate of the disease in China are still relatively high. The high mortality rate of gastric cancer may be related to its low early diagnosis rate and poor prognosis. Much research has been focused on improving the sensitivity and specificity of diagnostic tools for gastric cancer, in order to more accurately predict the survival times of gastric cancer patients. Taking appropriate treatment measures is the key to reducing the mortality rate of gastric cancer. In the past decade, artificial intelligence technology has been applied to various fields of medicine as a branch of computer science. This article discusses the application and research status of artificial intelligence in gastric cancer diagnosis and survival prediction.

Key words: Artificial intelligence; Gastric cancer; Early diagnosis; Survival prediction

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Core tip: Much research has been focused on improving the sensitivity and specificity of diagnostic tools for gastric cancer, in order to more accurately predict the survival times of gastric cancer patients. Artificial intelligence technology has been applied to various fields of medicine as a branch of computer science. This article discusses the application and research status of artificial intelligence in gastric cancer diagnosis and survival prediction.

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INTRODUCTION

Gastric cancer is a common malignant tumor of the digestive system caused by the proliferation of malignant gastric cells. It can spread to every part of the stomach and other organs, especially the esophagus, lungs, and liver. Gastric cancer is the fourth most common cancer in the world after lung cancer, breast cancer, and intestinal cancer^[1], and the second leading cause of cancer deaths worldwide^[2]. The incidence and mortality rates of gastric cancer in China far exceed those of other countries, both developed as well as developing. By 2020, death due to gastric cancer will become the leading cancer death in China^[3]. Due to the lack of specific symptoms and signs of early gastric cancer, most patients are already in advanced stages when they are diagnosed with gastric cancer. Although the diagnosis and treatment of gastric cancer have made great progress, the mortality rate of gastric cancer is still very high. Determining how to improve the diagnosis rate of early gastric cancer and accurately predict the survival of gastric cancer patients is a major problem facing clinicians.

In November 2015, Google DeepMind's AlphaGo artificial intelligence (AI) software program played a best-of-five match against the European Go champion Fan Hui and won easily. Then in March 2016, AlphaGo played another best-of-five match against 18-time Go world champion Lee Sedol. The program won the first three games to win the match. This result made many people realize the impact that AI could have on real life. Today, AI is widely used in various fields of medicine, such as diagnosis and prediction of related diseases, medical image interpretation and classification, drug development, personalized medicine, and genomics. This article focuses on the application of AI in gastric cancer diseases and combines the actual cases to determine the application and research status of AI in the diagnosis and survival prediction of gastric cancer.

ARTIFICIAL INTELLIGENCE

AI is a branch of computer science devoted to enabling machines to perform complex tasks that normally require human intelligence. AI in a broad sense includes machine learning, robots, and computer vision. AI goes through four stages: Inference period, knowledge period, machine learning period, and deep learning period. Using artificial neural network (ANN), support vector machine (SVM), convolutional neural network (CNN), and fully convolutional networks are represented^[4,5]. This article focuses on the application of machine learning in the diagnosis and prediction of gastric cancer. Machine learning can be divided into three types of training methods: Supervised learning, unsupervised learning, and reinforcement learning^[6]. Supervised learning refers to the training of machines with annotated data and includes random forest, SVM, decision tree linear regression, logistic regression, naive Bayes, K-nearest neighbor, AdaBoost, and neural network. Unsupervised learning refers to directly submitting data lacking manual labeling to a computer for classification. Unsupervised learning includes the K-means method, mean moving method, cluster analysis method, Gaussian mixture modeling method, Markov random field method, and iterative self-organizing data method. Reinforcement learning refers to constructing a computer classifier using artificially labeled datasets and then providing a certain amount of unlabeled data training to the constructed system to optimize the performance of the model^[7].

APPLICATION OF AI IN THE DIAGNOSIS OF GASTRIC CANCER

The prognosis of patients with gastric cancer depends on the stage of the cancer at the time of diagnosis^[8,9]. Due to the lack of specific symptoms and signs of early gastric cancer, most patients with gastric cancer are already in advanced stages at the time of diagnosis. Although the prognosis for patients with advanced gastric cancer is poor,

the 5-year survival rate of patients diagnosed with early gastric cancer is greater than 90%^[8-11]. Therefore, improving the diagnosis rate of early gastric cancer is the most effective measure to reduce the mortality rate of the disease. Because early gastric cancer lacks characteristic morphological changes, its diagnosis generally depends on the subjective judgment of doctors. The development of AI technology has brought about opportunities to solve these problems.

Application of AI in endoscopic images of gastric cancer

In recent years, CNNs have made great progress in AI image recognition for deep learning and as a result are increasingly used in diagnostic imaging in the medical field (Table 1). Hirasawa *et al*^[12] developed a CNN diagnostic system that can automatically detect gastric cancer in endoscopic images and used 13584 gastric cancer endoscopic images as a training set for the CNN diagnostic system. Then, 2296 gastric cancer images were used as a testing set to evaluate the accuracy of the diagnosis. The results showed that CNN analyzed 2296 test images in only 47 s and correctly diagnosed 71 of 77 gastric cancer lesions, with an overall sensitivity of 92.2%. The missing lesions were surface depressions and differentiated intramucosal cancers. Even experienced endoscopists have difficulty distinguishing these from gastritis. The system classified 161 non-cancerous lesions as gastric cancer, with a positive predictive value of 30.6%. The reason for the low positive rate could be that the morphological characteristics of early gastric cancer are fewer and are similar to gastritis.

To solve the above problems, Sakai *et al*^[13] proposed a transfer CNN model, using two types of image datasets for transfer learning. A data enhancement method was used to intercept 9587 cancer images and 9800 normal images from the cancer images and the normal images as the training set. Similarly, 4653 cancer images and 4997 normal images obtained from the unused cancer images and normal images were used as the testing set. The network accuracy after training was 87.6%, the detection accuracy was 82.8%, the sensitivity and specificity achieved a good balance, and the candidate regions of early gastric cancer could be presented as heat maps of unknown images to reveal the approximate position.

Zhu *et al*^[14] used the most advanced pre-trained ResNet 50 CNN model to construct a set of AI-based CNN computer-aided detection systems to analyze the depth of cancer cell invasion in endoscopic images, with 790 images as the training set of the system and 203 images as the test set. The researchers compared the analysis results of the CNN model with the analysis results of the endoscopy doctor. The CNN model specificity was 95.56%, and the overall accuracy rate was 89.16%. The specificity of the endoscopist was 32.21%, and the accuracy was 17.25%. The study showed that the CNN model performs better than the human eye in judging the depth of cancer cell infiltration in endoscopic images. Because early gastric cancer lacks specific morphological features, even an experienced endoscopist has trouble distinguishing it from chronic gastritis. The diagnosis rate of inexperienced young endoscopists will be even lower, which will easily lead to missed diagnoses and misdiagnoses.

To more accurately determine early gastric cancer and non-cancerous lesions, Li *et al*^[15] developed a CNN system based on narrow-band magnifying endoscopy. By observing the microvessels and microsurface structures of the gastric mucosa, the narrow-band magnifying endoscopy-based system was able to establish an average 0.02s/picture speed to screen for early gastric cancer. Comparing the results of CNN with those of experts and nonexperts, the sensitivity of the CNN system in the diagnosis of early gastric cancer was 91.18%, the specificity was 90.64%, and the accuracy was 90.91%. Although there was no significant difference in the specificity and accuracy of diagnosis between CNN and the experts, the diagnosis sensitivity of the CNN system was higher than that of the experts. In addition, the sensitivity, specificity, and accuracy of CNN system diagnosis were significantly higher than those of nonexperts. Horiuchi *et al*^[16] conducted a similar study to identify early gastric cancer and chronic gastritis and obtained higher sensitivity and accuracy. The reason may be that researchers have different interpretations and naming rules for histology.

Application of AI in gastric cancer pathology images

The rapid development of AI in the field of pathological images is also a hot topic in current research. Yoshida *et al*^[17] first attempted to screen gastric biopsy specimens using an automated image analysis software system called e-Pathologist. They analyzed 3062 gastric cancer pathological images and compared the results of the automatic image analysis software with those of human pathologists. Classification as third grade (positive cancer or suspected cancer; adenoma or suspected neoplastic lesion; or negative neoplastic lesion) had a total coincidence rate of 55.6%. A biopsy negative specimen had a coincidence rate of 90.6%, and a biopsy positive specimen

Table 1 Application of artificial intelligence in endoscopic images of gastric cancer

Ref.	Images	Sensitivity	Specificity	Accuracy
Hirasawa <i>et al</i> ^[12]	Endoscopic images with NBI imaging	92.20%	-	30.60 %
Zhu <i>et al</i> ^[14]	Endoscopic images	76.47%	95.56%	89.16%
Li <i>et al</i> ^[15]	ME-NBI images	91.18%	90.64%	90.91%
Horiuchi <i>et al</i> ^[16]	ME-NBI images	95.40%	71.00%	85.30%

NBI: Narrow band imaging; ME-NBI: Magnifying endoscopy with narrow band imaging.

had a coincidence rate of less than 50%. The sensitivity of the two-level (negative or non-negative) classification of electronic pathology experts was 89.5%, and the negative predictive value was 90.6%. However, the specificity (50.7%) and positive predictive value (47.7%) were low. The results were encouraging at the time. However, at this stage, the tissue slices created by the pathologist cannot be directly used for AI analysis. The lack of well-annotated pathological image data has become a major limitation to the development of AI in the field of pathological images.

To solve this problem, Qu *et al*^[18] proposed a gradually fine-tuned new deep learning CNN for gastric pathological image classifications and introduced the concept of target-related intermediate datasets. The research results showed that the use of target-related intermediate datasets significantly improves the classification performance of CNNs. We hope that the effectiveness of the target-related intermediate data applied to deep neural networks can be specifically evaluated in future work.

Lymph node metastasis of gastric cancer has always been regarded as the most important factor affecting the prognosis of patients, which therefore plays a key role in guiding the selection of postoperative treatment options^[19]. Traditional pathological examination methods are time-consuming and expensive, and it is easy to miss tiny lesions. In response to this problem, Wang *et al*^[20] evaluated the clinical application value of CNN in the pathological diagnosis of gastric cancer metastatic lymph nodes. They divided 124 patients undergoing radical gastrectomy and D2 lymph node dissection into training set (80 cases) and testing set (44 cases). The test group verification results showed that the accuracy rate was 100% in terms of slice-level classification, that 40 normal slices and 38 tumor slices were correctly classified, and that the classification results were completely consistent with the pathologist. In terms of identifying block-level transfers, the accuracy rate was 0.989, the specificity 0.995, the positive predictive value 0.822, and the area under the curve 0.89, which is basically consistent with the diagnosis level of the pathologist.

Application of AI in noninvasive examination of gastric cancer

Endoscopy and pathological examination are the gold standard for the diagnosis of gastric cancer. Because of their invasiveness, high cost, and low compliance, they are generally only suitable for high-risk groups. This is why it is so important to carry out early gastric cancer risk screening and find practical gastric cancer biomarkers. Compared with invasive examinations, these noninvasive examinations have the advantages of simple operation, low cost, and high comfort, and the patient's compliance is relatively high. Huang *et al*^[21] made full use of the advantages of machine learning to find a set of microRNA combinations with high accuracy and high sensitivity for noninvasive prediction of gastric cancer in the serum of patients with gastric cancer. From the published miRNA map (GSE23739), we selected miR-21-5p, miR-22-3p, and miR-29c-3p as the training sets to train the three classifiers. The areas under the characteristic curve were 0.9437, 0.9456, and 0.9563, respectively, and the positive predictive value and negative predictive value were both more than 80%. Then it was verified in two maps (GSE26595, GSE28700) of the Gene Expression Omnibus database and the patient's serum. Finally, similar results were obtained. Quantitative reverse transcription polymerase chain reaction confirmed that the level of serum miR-21 in gastric cancer patients was higher than that in healthy controls, whereas the levels of miR-22 and miR-29c were opposite. The results of this study indicate that miR-21-5p, miR-22-3p, and miR-29c-3p can be used as potential biomarkers for detecting gastric cancer. However, the sample size of this study was small, and therefore its predictive value requires more research to be confirmed.

Liu *et al*^[3] used data mining methods to establish four classification models for

screening early gastric cancer risk. A questionnaire entailing serological examination and endoscopy plus pathological biopsy was given to 618 patients with gastric disease, with the patients divided into high risk and low risk groups. The accuracy rates of the three data mining models were higher than the logistic regression model. The study also found that 16 factors, such as occupation, *Helicobacter pylori* infection, and drinking hot water can have a significant impact on the risk of early gastric cancer. The discovery of these risk factors helps to evaluate the occurrence of gastric cancer in patients and reminds them of the importance of early prevention and detection. The study also helps clinical researchers select and implement optimal prediction models.

Mortezag *et al*^[2] conducted a similar study using data mining methods, using SVM, decision tree, naive Bayes model and k-nearest neighbor to classify gastric cancer patients. A total of 11 features and risk factors were examined, and research showed that the SVMs achieved the highest accuracy in the classification results. Dividing patients into high-risk and low-risk groups, as done in the above research, can help clinicians target high-risk patients for early gastric cancer screening, which can not only lead to the use of fewer medical resources but also reduce the workload of clinicians.

APPLICATION OF AI IN SURVIVAL PREDICTION OF GASTRIC CANCER

The human body is a complex biological system, and most clinical features exhibit a multidimensional, nonlinear relationship. It is difficult to predict the prognosis of gastric cancer patients using traditional statistical methods. AI offers a unique advantage in evaluating the prognosis of gastric cancer patients. Biglarian *et al*^[1] used the Cox proportional hazard model and an ANN to predict the survival rate of gastric cancer patients. The accuracy of the ANN model was 83.1%, and the accuracy of the Cox regression model was 75.0%. Another study obtained similar results. The prediction accuracy of the ANN was 85.3%, and the prediction accuracy of the Cox model was 81.9%^[22]. Both of the above studies indicate that the neural network model is a better statistical tool for predicting the survival rate of gastric cancer patients. Because the current tumor, nodes, and metastases (TNM) staging system cannot provide enough information to predict the prognosis of gastric cancer and the effect of chemotherapy, we need to build a more accurate classifier to predict the prognosis of gastric cancer patients.

Oh *et al*^[23] used ANNs to establish a predictive model for the survival outcome of gastric cancer patients. The survival curve of the prediction model is better than the survival curve of the American Joint Committee on Cancer stage 8, which can differentiate the survival results of gastric cancer patients. The predicted lifetime of the model is in agreement with the actual lifetime. The immune marker SVM classifier established by Jiang *et al*^[24] is more accurate than traditional TNM staging in predicting the survival rate of gastric cancer patients and can supplement the prognostic value of the TNM staging system. Furthermore, the classifier can predict which patients with stage II and III gastric cancer can benefit from adjuvant chemotherapy. Therefore, these gastric cancer survival prediction models can be used to classify high-risk gastric cancer patients and allocate necessary treatment and health resources to them. At the same time, it enables patients with gastric cancer to have more effective consultations after surgery. It also helps clinicians design treatment strategies and arrange follow-ups.

CONCLUSION

The mortality rate of gastric cancer in China is high. Due to the lack of specific morphological characteristics and clinical manifestations of early gastric cancer, its early diagnosis mainly depends on the personal experience of the doctor, meaning that it lacks objectivity and is highly time-consuming. In the diagnosis of early gastric cancer, AI has high sensitivity and specificity. Not only can the use of AI reduce misdiagnosis and variability among observers, but it can also save clinicians a great deal of time. It can also help inexperienced doctors. With AI, clinicians can divide patients into high-risk and low-risk groups according to risk factors related to the incidence of gastric cancer and certain serological markers so that the clinicians can focus on the high-risk patients. Compared with traditional TNM staging, AI is more accurate in predicting the survival of gastric cancer patients. This can guide clinicians to formulate follow-up treatment strategies and arrange follow-up times, which can

help to prolong the survival time of patients with advanced gastric cancer.

However, there are still few articles on the use of AI to guide chemotherapy treatment for advanced gastric cancer. We hope that more scholars will engage in related research in the future. Of course, the development of AI in the medical field also faces many challenges. The training of AI models in order to achieve accuracy requires a great deal of manually annotated medical data. Although many scholars have abandoned many poor-quality data to obtain high performance of AI models, it is still impossible to capture many details of AI for feature extraction and the decision-making process. However, we believe that with the development of AI in the world of medicine, this will soon change.

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