Cancer Screening and Prevention **2024** vol. 3(2) | 106–112
DOI: 10.14218/CSP.2024.00012

Mini Review

The Current Status and Prospects of Early Diagnosis and Treatment of Esophageal Cancer in China

Yuan Ding, Lihua Ren, Yaqi Geng, Chenge Fu and Ruihua Shi*

Department of Gastroenterology, Zhongda Hospital, Medical School of Southeast University, Nanjing, Jiangsu, China

Received: April 20, 2024 | **Revised:** June 12, 2024 | **Accepted:** June 23, 2024 | **Published online:** June 25, 2024

Abstract

Esophageal cancer is one of the most common malignant tumors in the digestive tract in China. Due to late diagnosis and rapid progression, it leads to a poor survival prognosis. Early diagnosis and treatment are crucial for improving the prognosis of esophageal cancer. Implementing simple and efficient screening methods is more in line with China's healthcare economics and national conditions. This article mainly introduces the current status of esophageal cancer screening and new technologies for esophageal cancer screening in China, including endoscopic technology, biomarker detection, exhaled breath detection, and artificial intelligence assisted screening, and looks ahead to its future development trends.

Introduction

Esophageal cancer is a malignant tumor originating in the esophageal epithelium with extremely strong invasiveness and a low survival rate, making it one of the most common digestive tract malignant tumors. In China, esophageal cancer ranks 6th in incidence and 5th in mortality, significantly impacting public health.[1] Due to China's large population, the country accounts for more than 50% of the world's esophageal cancer cases and deaths, the highest in the world.[2] On the contrary, screening for esophageal cancer in China is relatively insufficient. Early-stage esophageal cancer often presents without obvious clinical symptoms, leading to diagnosis typically occurring in the middle or late stages. In order to improve the prognosis of esophageal cancer, early identification and diagnosis are therefore essential. In China, high-risk areas for esophageal cancer include southern side of the Taihang Mountains (bordering Henan, Hebei, and Shanxi provinces), the Dabie Mountains, the Qinling Mountains, northern Sichuan, Guangdong and Fujian, northern Jiangsu, and Xinjiang.[3] Since the national critical public health project's inception in 2005, endoscopic screening for upper gastrointestinal cancer has been conducted in more than 110 high-risk locations nationally, yielding notable outcomes.[4] In recent years, the incidence and mortality of esophageal cancer have shown an overall downward trend, although the decline is slow. This improvement is mainly due to the continuous implementation of the screening efforts for high-risk groups in the country, and the active intervention of esophageal cancer related risk factors. Stronger efforts are still needed to promote esophageal cancer screening, early detection, and treatment programs, along with stringent preventative and control measures.

Keywords: Screening; Carcinoma of esophagus; Cancer detection and diagnosis; Artificial intelligence; Exfoliation cytological examination; Laboratory tests.

***Correspondence to:** Ruihua Shi, Department of Gastroenterology, Zhongda Hospital, Medical School of Southeast University, No. 87 Ding Jia Qiao, Nanjing, Jiangsu 210009, China. ORCID: https://orcid.org/0000-0003-4977-8801. Tel: +86-025-83262835, Fax: +86-025-83262835, E-mail: ruihuashi@126.com

How to cite this article: Ding Y, Ren L, Geng Y, Fu C, Shi R. The Current Status and Prospects of Early Diagnosis and Treatment of Esophageal Cancer in China. *Cancer Screen Prev* 2024;3(2):106–112. doi: 10.14218/CSP.2024.00012.

The goals of screening for esophageal cancer

The goal of early esophageal cancer screening is to detect early-stage esophageal cancer or esophageal intraepithelial neoplasia. Early detection allows for timely intervention and treatment, significantly improving survival rates and quality of life for patients. With early diagnosis and treatment, the 5-year survival rate can exceed 95%.[5] Therefore, early diagnosis and treatment are key to improving the patient survival rates and reducing the social burden.[6] Research indicates that the screening programs for upper gastrointestinal cancer can reduce the incidence rate of the population by 23% and the mortality rate by 57%.[4] The development of esophageal cancer follows the general course of intraepithelial neoplasia to invasive carcinoma. Extensive research has shown that the likelihood of invasive esophageal cancer developing from intraepithelial neoplasia increases with its grade.[7,8] By preventing the spread of esophageal cancer while it is still in the stage of intraepithelial neoplasia or situ carcinoma, early identification and therapy can greatly enhance the prognosis of patients.

Risk factors and screening target population for esophageal cancer

Squamous cell carcinoma is the main type of esophageal cancer in China. Its occurrence is related to several risk factors, includ-

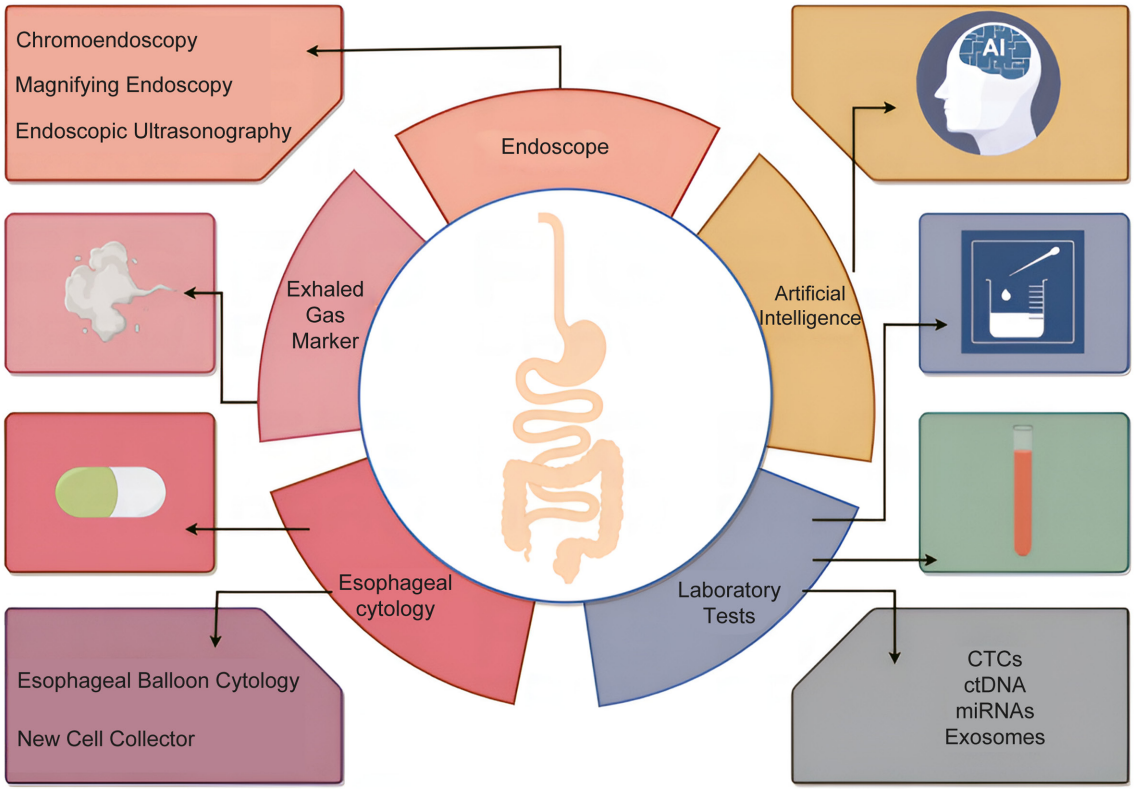

Fig. 1. Methods of screening for esophageal cancer. Methods of screening for esophageal cancer include endoscopy, esophageal cytology, exhaled gas markers, artificial intelligence-assisted systems, and laboratory tests. CTCs, circulating tumor cells; ctDNA, circulating tumor DNA; miRNAS, microRNAs.

ing smoking, alcohol consumption, intake of hot or red foods, consumption of red meat, poor oral hygiene, insufficient intake of fresh fruits and vegetables, edentulous diseases, and environmental pollution.[9–11] Additionally, family history of esophageal squamous cell carcinoma, human papillomavirus infection, gastric mucosal atrophy, and a history of head and neck squamous cell carcinoma further increase the risk.[12,13]

Esophageal adenocarcinoma, though less prevalent in China, is linked to smoking, obesity, gastroesophageal reflux disease, and Barrett's esophagus.[14,15] Early identification and treatment of esophageal cancer are challenging because symptoms such as substernal pain, worsening dysphagia, and gastrointestinal bleeding often appear in the tumor's middle or late stages. Therefore, relying on the onset of symptoms for screening is not effective. Given the high-risk factors and current national conditions for esophageal cancer, it is recommended to screen individuals aged forty and older. In addition, people from high-incidence esophageal cancer areas, those with upper gastrointestinal symptoms, a family history of the disease, precancerous conditions or esophageal lesions, and those with other high-risk characteristics should be included in the screening target population.[16] The current main screening methods are shown in Figure 1.

Current status of screening for early esophageal cancer

At present, early diagnosis and treatment of esophageal cancer in China remain relatively underdeveloped. Most early diagnosis and treatment programs are conducted in high-risk areas and have achieved some success, but there are significant limitations. The decrease in screening positivity rate and the issue of disproportionate screening costs and benefits become evident when the target population shifts from high-risk to lower-risk areas. Thus, one of the main goals of modern esophageal cancer screening is to increase the efficiency and accuracy of the screening process. Future efforts should focus on exploring and innovating screening methods and technologies. This includes optimizing and improving existing screening methods and actively seeking new strategies and technologies to achieve more accurate and efficient early screening of esophageal cancer.

Screening techniques for esophageal cancer

The standard screening method for esophageal cancer is upper gastrointestinal endoscopy combined with biopsy. In China, the most feasible and efficient screening technique currently involves combining indicator biopsy with endoscopic esophageal mucosal iodine staining. This approach uses staining, magnification, and other techniques to visually detect alterations in the esophageal mucosa. It allows for the assessment of the type, location, borders, and extent of lesions, enabling screening and early diagnosis in a single step.

The technology for combining pathological screening with endoscopy to detect early esophageal cancer has improved. However, due to China's large population and the high number of people at risk for the disease, there is a shortage of endoscopic equipment and trained endoscopists to meet the national demand. Even in areas with a relatively high incidence of the disease, only one case of early esophageal cancer is found for every 275 asymptomatic

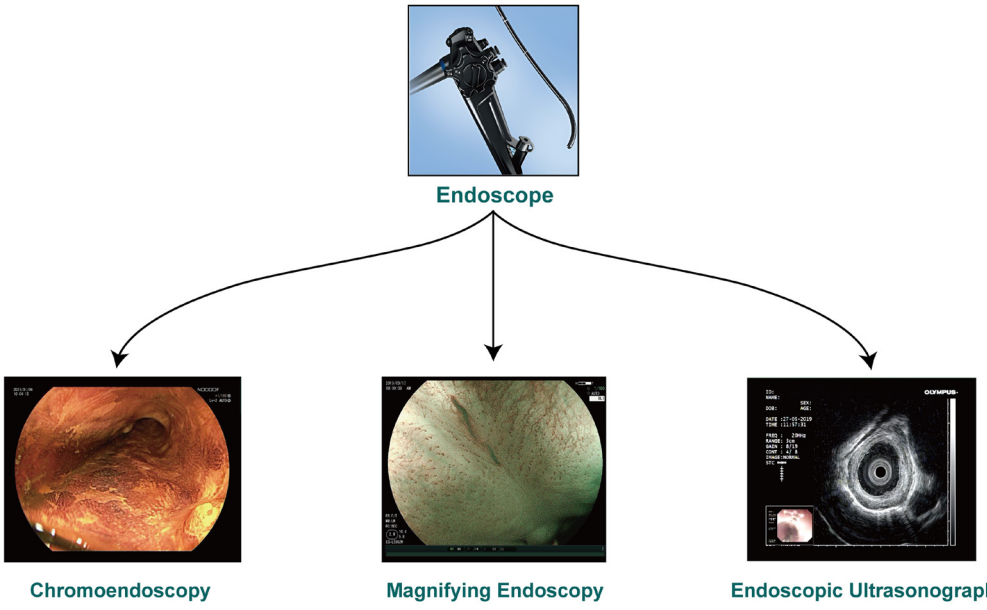

Fig. 2. Classification of endoscopy. At present, the mainstream endoscopy includes dyeing endoscopy, magnification endoscopy and ultrasound endoscopy.

people tested.[4]

Therefore, a practical and effective prevention and control plan for China would involve using a more practical, accurate, and cost-effective method to stratify the target population's risk, followed by endoscopic inspection of high-risk individuals. This stratified approach would optimize resources and improve the efficiency of the screening process.

Exfoliation cytological examination

During a particular historical period in China, esophageal balloon cytology played a significant role in the screening of numerous early cases of esophageal cancer prior to the widespread use of endoscopic technologies. However, it is no longer utilized for early esophageal cancer screening because of its poor diagnostic efficacy. To solve problems like poor cell collection efficiency, Chinese researchers have enhanced the design of the esophageal cell collector by using a novel sponge-like polymer material.

This improved cell collector is encapsulated in a tiny capsule that dissolves in water, expanding into a mushroom shape in the stomach. It can be removed within minutes, and upon examination, 6–10 million cells from the cardia, esophagus, and oropharynx can be collected. Artificial intelligence is used to assist in diagnosis, achieving sensitivity and specificity rates exceeding 90%.[17] Compared to endoscopic inspection, this technology is less expensive and easier to use, which makes it appropriate for population screening at an early stage.

The new esophageal cell collector represents a qualitative improvement over traditional mesh cytology examinations and has been applied to screening populations in high-risk areas, with broad application prospects nationwide.

Endoscopy

With the advancements in technology and increased funding for research and development, traditional white light endoscopy is no longer the only option for esophageal cancer screening. Newer endoscopic technologies, such as electronic staining endoscopy, chromoendoscopy, magnifying endoscopy, ultrasound endoscopy, and traditional white light endoscopy , have significantly enhanced the precision of esophageal cancer screening (Fig. 2).[18,19]

Chromoendoscopy mainly stains the esophageal mucosa to make the color contrast between the lesion and the normal mucosa more obvious. This makes small lesions, which are difficult to detect with ordinary endoscopy, more visible. It helps in early diagnosis, determines the surgical approach, and defines the scope of resection during surgery.

Magnifying endoscopy uses a zoom lens to magnify the mucosal tissue by 1.5 to 150 times, , allowing for a clearer observation of the fine structure of the mucosal surface of the digestive tract. By magnifying and observing the changes of glandular duct openings, microvessels, capillaries, and other microstructures on the mucosal surface, the pathological grade of mucosal lesions can be preliminary judged, the scope of lesion infiltration can be defined, and the accuracy of the biopsy can be improved.

Endoscopic ultrasound is a combination of endoscopy and ultrasound technology. By placing a miniature high-frequency ultrasonic probe at the top of the endoscope, real-time scanning is performed by ultrasound under the endoscopy to obtain the anatomical hierarchy of the esophageal mucosa and ultrasound images of neighboring organs. This helps judge the depth of lesion invasion, local lymph node metastasis and infiltration of surrounding organs. Endoscopic ultrasound can also assist in minimally invasive operations such as submucosal tumor resection, puncture biopsy, stent, or drainage catheter intervention.

Those advanced endoscopic techniques have not been widely adopted at the grass-roots level due to certain learning costs and relatively expensive equipment, but their importance in the screening and treatment of esophageal cancer cannot be ignored. Furthermore, a number of novel endoscopic technologies, including magnetic capsule esophageal endoscopy, confocal laser microscopy, volume laser microscopy, and transnasal endoscopy, have recently been implemented in clinical practice or are still in the re-

search and development phase. These technologies are anticipated to enhance patient acceptance and comfort while also improving the accuracy of esophageal cancer screening. However, many of these new technologies are currently difficult to apply to widespread screening due to high costs and a lack of comprehensive prospective studies. With the continuous progress of science and technology and the gradual reduction of research and development costs, it is believed that these new technologies will eventually be popularized and promoted, providing more effective and convenient means for the screening and treatment of esophageal cancer.

Laboratory tests

Furthermore, some academics are shifting the focus of esophageal cancer screening from physical examinations to laboratory tests. As a non-invasive examination method, laboratory examination is more acceptable to patients, and also has the potential to save labor and material costs. Detecting relevant tumor markers in serum before morphological changes occur in tissues and organs is a crucial method for identifying early asymptomatic lesions. This method is simple, economical, and rapid, making it an important tool for early tumor screening and auxiliary diagnosis. It can serve as a "pre-screening" mechanism to identify patients who may have esophageal cancer, allowing for further examination and treatment, such as endoscopy, for this group, thereby reducing screening costs.

However, the academic community has not yet formed a unified and persuasive view on pre-screening for esophageal cancer. Unlike gastric cancer, esophageal cancer lacks well-recognized serological indicators, making it difficult to increase the positive rate of screening. Nonetheless, with the advent of precision medicine, new esophageal cytology and novel biomarkers have shown potential in esophageal cancer screening, offering hope for future breakthroughs in screening methods.

Research has found that serum tumor markers related to esophageal cancer, such as cytokeratin 19 fragments, squamous cell carcinoma antigen, carcinoembryonic antigen, and P53 protein antibodies, have low sensitivity and specificity. As a result, these markers can only be used as auxiliary diagnostic tools and are not recommended for population screening.[20]

However, recent advancements in liquid biopsy technology have shown promising preliminary results in the field of esophageal cancer. Liquid biopsies, which detect circulating tumor cells (CTCs), circulating tumor DNA (ctDNA), microRNAs (miRNAs), and exosomes, are convenient and allow for real-time, repeatable monitoring of tumors. Studies have indicated a strong correlation between the level of CTCs in patients with esophageal squamous cell carcinoma and factors such as tumor cell differentiation, initial tumor invasion, lymph node metastasis, and clinical staging. Therefore, CTC levels may serve as good indicators of tumor progression and can support clinical diagnostic and prognostic assessments.[21,22]

Additionally, identifying ctDNA and miRNA in bodily fluids like blood or saliva can provide genomic information about the tumor, identify small tumor lesions at early stages, and even help create individualized treatment strategies. miRNA, a non-coding RNA composed of 18–25 nucleotides, regulates gene expression by binding to the 3′-UTR of mRNA, inhibiting RNA translation, and leading to RNA degradation. Since miRNA is widely present in blood and other body fluids, it may serve as a potential non-invasive biomarker. Scholars have developed a detection system based on miRNA for predicting early esophageal squamous cell carcinoma, and its accuracy has been validated in some retrospective or prospective multicenter cohorts.[23]

Although several liquid biopsy procedures are currently in clinical development, challenges such as inconsistent detection levels remain. With further research, liquid biopsy technology has the potential to become a widely utilized, non-invasive, real-time efficacy monitoring tool for esophageal cancer.

Exhaled gas marker

Exhaled gas marker analysis is a very promising screening technique that is affordable, straightforward, non-invasive, and easy to use. It is particularly suitable for grassroots primary screening.[24] While studies have shown that volatile aldehydes can effectively diagnose esophageal adenocarcinoma,[25] this method is not applicable for screening esophageal cancer in China, where most cases are esophageal squamous cell carcinoma.

Currently, exhaled gas indicators for esophageal squamous cell carcinoma are poorly understood, but the potential for their use in screening is significant and warrants further investigation. If the detection of exhaled gas biomarkers for esophageal squamous cell carcinoma becomes feasible, it could significantly reduce screening costs and enhance the accessibility and effectiveness of early diagnosis and treatment programs for esophageal cancer.

Artificial Intelligence

Medicine evolves with technological advancements, and deep learning-based artificial intelligence (AI) has rapidly been integrated into the medical industry. Many large medical centers have developed auxiliary systems by combining AI with gastroscopy. These systems are primarily used in five areas: endoscopic image recognition, time monitoring, reducing blind spots during the examination process, image recording, and gastrointestinal preparation scoring. AI has shown exceptional performance in esophageal cancer screening, with convolutional neural networks (CNN) models trained on 8,428 images of esophageal cancer in several studies. These models can detect lesions with a diameter of less than 10 millimeters and analyze 1,118 test photos in just 27 seconds, achieving a sensitivity of up to 98%.[26] This indicates that AI technology can analyze a large number of endoscopic images of esophageal cancer with high sensitivity in a short period of time, reducing the missed diagnosis rate of small lesions.

Yuan *et al.*[27] combined AI with the endoscopic system and built an AI system that can automatically detect early esophageal squamous cell carcinoma in real time using a large number of images based on the commonly used white light examination and narrow band spectral imaging endoscopic modes in clinical practice. This system evaluated the effect of the AI system in real-time assisted diagnosis of early esophageal squamous cell carcinoma in real clinical practice for the first time in the world. And it is also the largest number of reports of artificial intelligence-assisted diagnosis of early esophageal cancer in the world.

Zhang *et al.*[28] has developed an an AI-assisted diagnosis system using magnifying endoscopy to predict the invasion depth of esophageal squamous cell carcinoma. Multi-center verification showed that the sensitivity, specificity, and accuracy in image verification were 85.7%, 86.3%, and 86.2%, respectively. In continuously collected videos, the sensitivity, specificity, and accuracy of differentiating the depth of lesion infiltration were 87.5%, 84%, and 84.9%, respectively, significantly improving the diagnostic accuracy of endoscopists.[28]

There is no denying that junior endoscopists have different ex-

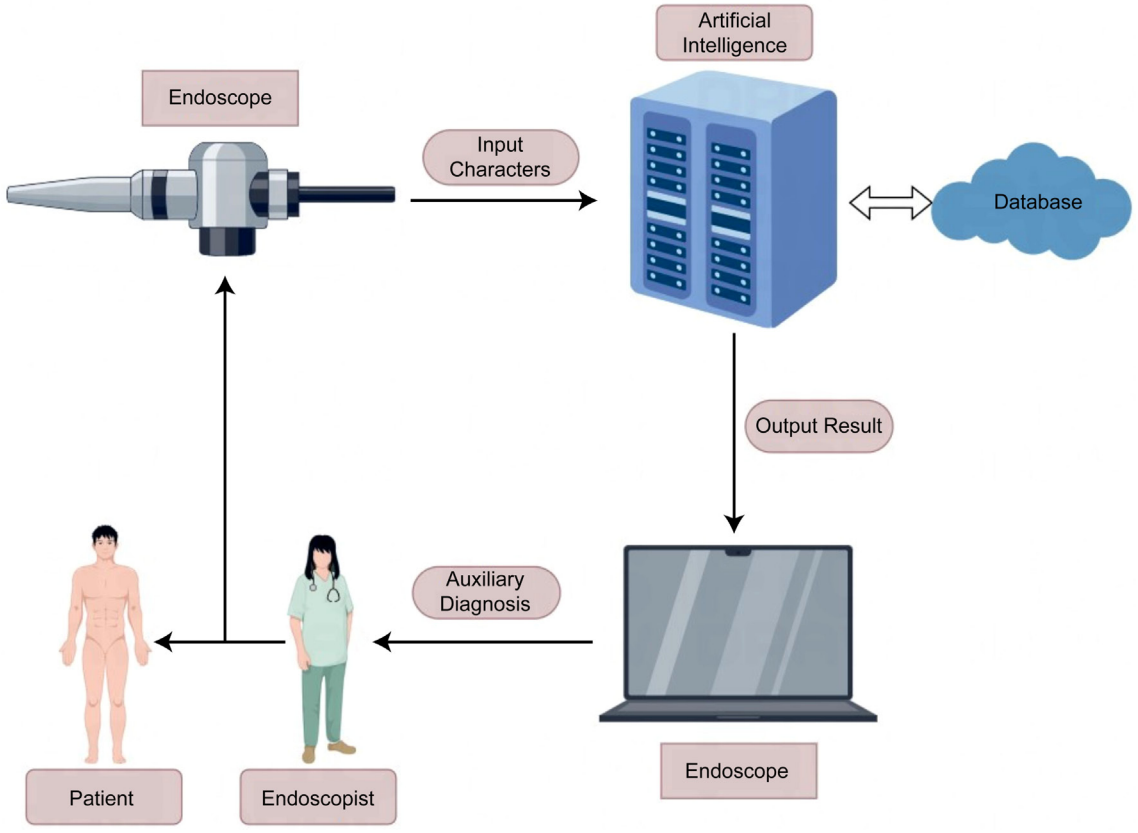

Fig. 3. Flow chart of AI-assisted endoscopist. Endoscopists perform gastroscopy on patients with endoscopes, and transmit images to the AI-assisted diagnosis system in real time. The system accurately identifies high-level lesions through the training of a large number of databases, and displays them on the screen. The endoscopists focus on high-risk lesions for further examination according to instructions.

periences compared to senior endoscopists. Additionally, when faced with a large screening population, the state of endoscopists can fluctuate, which may lead to differences in the quality of endoscopic screening and result in certain missed diagnoses. AI-assisted diagnostic systems have progressed from static picture analysis to real-time video processing, from conventional machine learning techniques to deep learning based on neural networks. AI can improve the accuracy of beginner endoscopists and assist senior experts in making more detailed and accurate diagnoses of lesions in complex cases, effectively correcting possible mistakes (Fig. 3).[29]

AI-assisted diagnostic systems have demonstrated performance comparable to that of expert endoscopists while also having the ability to continuously learn and optimize. By constantly learning and accumulating new medical data, AI-assisted diagnosis systems can continuously improve their diagnostic level and gradually adapt to various complex and special cases. This self-evolving property gives AI great potential and broad prospects in the medical field.[30] AI-assisted systems have shown performance comparable to that of skilled endoscopists, and the future trend of integrating AI with digestive endoscopy is anticipated to bring significant changes to the medical industry. Currently, AI use is primarily restricted to narrowband imaging, ultrasound endoscopy, and white light endoscopy. Future research on AI-assisted systems combined with novel endoscopic technologies like volume laser microscopy, confocal laser microscopy, and optical enhanced endoscopy is imperative.

The creation and training of more accurate and efficient artificial intelligence models are somewhat hampered by the closed and non-shared nature of current AI databases. Moreover, AI models trained in a single or a few centers have certain limitations in terms of population and region, and cannot be used for screening large-scale populations temporarily. With the construction of standardized big sample databases, AI assistance systems suitable for many locations, models, and people will soon emerge, enhancing the popularity of early detection and treatment programs for esophageal cancer.

Prospect

The early detection and treatment project for upper gastrointestinal cancer in China began in the 1970s and has grown quickly in the current century. In 2005, China initiated a cancer early detection and treatment project in rural areas with a high incidence of malignant tumors, with esophageal cancer being one of the primary screening targets. The urban cancer early diagnosis and treatment project, which includes esophageal cancer, was officially incorporated into the national key public health service initiatives in 2012.[31]

China continues to invest in early diagnosis and treatment projects for esophageal cancer, as proposed by the “Healthy China” plan and the 14th Five Year Plan. New screening technologies and methodologies are continually emerging, and screening initiatives are becoming more popular and accepted year after year. Detecting a case of early cancer means saving a life and saving a family.

Conclusions

In the future, China will need to aggressively develop new technologies for esophageal cancer screening, investigate related biomarkers, and employ artificial intelligence to increase screening efficiency and accuracy, optimize screening strategies, and avoid overscreening. Differences between urban and rural areas, regional disparities, and variations in medical resources necessitate higher standards for early detection and treatment projects across the country. Efforts should focus on standardizing esophageal cancer screening programs, boosting screening quality, and raising public awareness about the importance of screening. Many new technologies, such as AI image recognition, biomarker detection, and exhaled air detection, are still in the research stage and not yet ready for clinical application. Therefore, accelerating the deep integration of industry, universities, and research institutions, along with the transformation of innovative results, is essential. Only through standardized, scientific, and widespread screening efforts, combined with the continuous deepening of basic research and the exploration of new technologies, can we effectively reduce the incidence and mortality of esophageal cancer and improve the overall health of the population.

Acknowledgments

None.

Funding

No funding was received for the study.

Conflict of interest

One of the authors, Prof. Ruihua Shi has served as an associate editor of Cancer Screening and Prevention since February 2022. All other authors have no conflict of interests related to this manuscript.

Author contributions

YD contributed to study concept and design; YD, LHR, CGF and YQG performed the acquisition of data for the references; YD drafted the manuscript; LHR and RHS performed the critical revision of the manuscript; and RHS supervised the study.

References

[1] Qiu H, Cao S, Xu R. Cancer incidence, mortality, and burden in China: a time-trend analysis and comparison with the United States and United Kingdom based on the global epidemiological data released in 2020. Cancer Commun (Lond) 2021;41(10):1037–1048. doi:10.1002/cac2.12197, PMID:34288593.

[2] Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, *et al*. Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. CA Cancer J Clin 2021;71(3):209–249. doi:10.3322/caac.21660, PMID:33538338.

[3] Lin Y, Totsuka Y, He Y, Kikuchi S, Qiao Y, Ueda J, *et al*. Epidemiology of esophageal cancer in Japan and China. J Epidemiol 2013;23(4):233–242. doi:10.2188/jea.je20120162, PMID:23629646.

[4] Chen R, Liu Y, Song G, Li B, Zhao D, Hua Z, *et al*. Effectiveness of one-time endoscopic screening programme in prevention of upper gastrointestinal cancer in China: a multicentre population-based cohort study. Gut 2021;70(2):251–260. doi:10.1136/gutjnl-2019-320200, PMID:32241902.

[5] Merkow RP, Bilimoria KY, Keswani RN, Chung J, Sherman KL, Knab LM, *et al*. Treatment trends, risk of lymph node metastasis, and outcomes for localized esophageal cancer. J Natl Cancer Inst 2014;106(7):dju133. doi:10.1093/jnci/dju133, PMID:25031273.

[6] Ciocirlan M, Lapalus MG, Hervieu V, Souquet JC, Napoléon B, Scoazec JY, *et al*. Endoscopic mucosal resection for squamous premalignant and early malignant lesions of the esophagus. Endoscopy 2007;39(1):24–29. doi:10.1055/s-2006-945182, PMID:17252456.

[7] Wang GQ, Abnet CC, Shen Q, Lewin KJ, Sun XD, Roth MJ, *et al*. Histological precursors of oesophageal squamous cell carcinoma: results from a 13 year prospective follow up study in a high risk population. Gut 2005;54(2):187–192. doi:10.1136/gut.2004.046631, PMID:15647178.

[8] Wen DG, Wang SJ, Zhang LW, Zhou W, Yu WF, Wang XL. Natural history of esophageal and gastric cardia precursor by repetitive endoscope screening with 425 adults in a high-risk area in China. Cancer Epidemiol 2009;33(2):108–112. doi:10.1016/j.canep.2009.06.002, PMID:19679056.

[9] Akhtar S, Sheikh AA, Qureshi HU. Chewing areca nut, betel quid, oral snuff, cigarette smoking and the risk of oesophageal squamous-cell carcinoma in South Asians: a multicentre case-control study. Eur J Cancer 2012;48(5):655–661. doi:10.1016/j.ejca.2011.06.008, PMID:21733677.

[10] Pandeya N, Williams G, Green AC, Webb PM, Whiteman DC, Australian Cancer Study. Alcohol consumption and the risks of adenocarcinoma and squamous cell carcinoma of the esophagus. Gastroenterology 2009;136(4):1215–1224.e1-e2. doi:10.1053/j.gastro.2008.12.052, PMID:19250648.

[11] Guha N, Boffetta P, Wünsch Filho V, Eluf Neto J, Shangina O, Zaridze D, *et al*. Oral health and risk of squamous cell carcinoma of the head and neck and esophagus: results of two multicentric case-control studies. Am J Epidemiol 2007;166(10):1159–1173. doi:10.1093/aje/kwm193, PMID:17761691.

[12] Islami F, Sheikhattari P, Ren JS, Kamangar F. Gastric atrophy and risk of oesophageal cancer and gastric cardia adenocarcinoma—a systematic review and meta-analysis. Ann Oncol 2011;22(4):754–760. doi:10.1093/annonc/mdq411, PMID:20860989.

[13] Katada C, Muto M, Nakayama M, Tanabe S, Higuchi K, Sasaki T, *et al*. Risk of superficial squamous cell carcinoma developing in the head and neck region in patients with esophageal squamous cell carcinoma. Laryngoscope 2012;122(6):1291–1296. doi:10.1002/lary.23249, PMID:22674532.

[14] Zhai R, Chen F, Liu G, Su L, Kulke MH, Asomaning K, *et al*. Interactions among genetic variants in apoptosis pathway genes, reflux symptoms, body mass index, and smoking indicate two distinct etiologic patterns of esophageal adenocarcinoma. J Clin Oncol 2010;28(14):2445–2451. doi:10.1200/JCO.2009.26.2790, PMID:20385987.

[15] Larghi A, Lightdale CJ, Ross AS, Fedi P, Hart J, Rotterdam H, *et al*. Long-term follow-up of complete Barrett's eradication endoscopic mucosal resection (CBE-EMR) for the treatment of high grade dysplasia and intramucosal carcinoma. Endoscopy 2007;39(12):1086–1091. doi:10.1055/s-2007-966788, PMID:17701854.

[16] He J, Chen WQ, Li ZS, Li N, Ren JS, Tian JH, *et al*. China guideline for the screening, early detection and early treatment of esophageal cancer (2022, Beijing) (in Chinese). Zhonghua Zhong Liu Za Zhi 2022;44(6):491–522. doi:10.3760/cma.j.cn112152-20220517-00348, PMID:35754225.

[17] Gao Y, Xin L, Feng YD, Yao B, Lin H, Sun C, *et al*. Feasibility and Accuracy of Artificial Intelligence-Assisted Sponge Cytology for Community-Based Esophageal Squamous Cell Carcinoma Screening in China. Am J Gastroenterol 2021;116(11):2207–2215. doi:10.14309/ajg.0000000000001499, PMID:34546186.

[18] di Pietro M, Canto MI, Fitzgerald RC. Endoscopic Management of Early Adenocarcinoma and Squamous Cell Carcinoma of the Esophagus: Screening, Diagnosis, and Therapy. Gastroenterology 2018;154(2):421–436. doi:10.1053/j.gastro.2017.07.041, PMID:28778650.

[19] Iglesias-Garcia J, Lariño-Noia J, de la Iglesia-García D, Dominguez-Muñoz JE. Endoscopic ultrasonography: Enhancing diagnostic accuracy. Best Pract Res Clin Gastroenterol 2022;60-61:101808. doi:10.1016/j.

bpg.2022.101808, PMID:36577529.
[20] Plum PS, Bollschweiler E, Hölscher AH, Warnecke-Eberz U. Novel diagnostic and prognostic biomarkers in esophageal cancer. Expert Opin Med Diagn 2013;7(6):557–571. doi:10.1517/17530059.2013.843526, PMID:24093836.
[21] Ujiie D, Matsumoto T, Endo E, Okayama H, Fujita S, Kanke Y, *et al*. Circulating tumor cells after neoadjuvant chemotherapy are related with recurrence in esophageal squamous cell carcinoma. Esophagus 2021;18(3):566–573. doi:10.1007/s10388-021-00829-x, PMID:33661456.
[22] Gallerani G, Fabbri F. Circulating Tumor Cells in the Adenocarcinoma of the Esophagus. Int J Mol Sci 2016;17(8):1266. doi:10.3390/ijms17081266, PMID:27527155.
[23] Okuda Y, Shimura T, Iwasaki H, Fukusada S, Nishigaki R, Kitagawa M, *et al*. Urinary microRNA biomarkers for detecting the presence of esophageal cancer. Sci Rep 2021;11(1):8508. doi:10.1038/s41598-021-87925-1, PMID:33879806.
[24] Miyoshi J, Zhu Z, Luo A, Toden S, Zhou X, Izumi D, *et al*. A microRNA-based liquid biopsy signature for the early detection of esophageal squamous cell carcinoma: a retrospective, prospective and multicenter study. Mol Cancer 2022;21(1):44. doi:10.1186/s12943-022-01507-x, PMID:35148754.
[25] Antonowicz S, Bodai Z, Wiggins T, Markar SR, Boshier PR, Goh YM, *et al*. Endogenous aldehyde accumulation generates genotoxicity and exhaled biomarkers in esophageal adenocarcinoma. Nat Commun 2021;12(1):1454. doi:10.1038/s41467-021-21800-5, PMID:33674602.
[26] Horie Y, Yoshio T, Aoyama K, Yoshimizu S, Horiuchi Y, Ishiyama A, *et al*. Diagnostic outcomes of esophageal cancer by artificial intelligence using convolutional neural networks. Gastrointest Endosc 2019;89(1):25–32. doi:10.1016/j.gie.2018.07.037, PMID:30120958.
[27] Yuan XL, Liu W, Lin YX, Deng QY, Gao YP, Wan L, *et al*. Effect of an artificial intelligence-assisted system on endoscopic diagnosis of superficial oesophageal squamous cell carcinoma and precancerous lesions: a multicentre, tandem, double-blind, randomised controlled trial. Lancet Gastroenterol Hepatol 2024;9(1):34–44. doi:10.1016/S2468-1253(23)00276-5, PMID:37952555.
[28] Zhang L, Luo R, Tang D, Zhang J, Su Y, Mao X, *et al*. Human-Like Artificial Intelligent System for Predicting Invasion Depth of Esophageal Squamous Cell Carcinoma Using Magnifying Narrow-Band Imaging Endoscopy: A Retrospective Multicenter Study. Clin Transl Gastroenterol 2023;14(10):e00606. doi:10.14309/ctg.0000000000000606, PMID:37289447.
[29] Luo H, Xu G, Li C, He L, Luo L, Wang Z, *et al*. Real-time artificial intelligence for detection of upper gastrointestinal cancer by endoscopy: a multicentre, case-control, diagnostic study. Lancet Oncol 2019;20(12):1645–1654. doi:10.1016/S1470-2045(19)30637-0, PMID:31591062.
[30] Zhang YH, Guo LJ, Yuan XL, Hu B. Artificial intelligence-assisted esophageal cancer management: Now and future. World J Gastroenterol 2020;26(35):5256–5271. doi:10.3748/wjg.v26.i35.5256, PMID:32994686.
[31] Lyu B, Jin XL. Status of Endoscopic Screening Strategies for Upper Gastrointestinal Tract Cancer. Cancer Screen Prev 2023;2(1):70–76. doi:10.14218/CSP.2022.00007.