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Review Article

Esophageal cancer: Epidemiology, risk factors and screening

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Abstract

More than 600,000 people are diagnosed with esophageal cancer (EC) every year globally, and the five-year survival rate of EC is less than 20%. Two common histological subtypes of EC, esophageal squamous cell carcinoma (ESCC) and esophageal adenocarcinoma (EAC), have great geographical variations in incidence rates. About half of the world's EC was diagnosed in China and a majority of which belong to ESCC. Globally, the overall incidence rate of EC is decreasing. In some high-risk Asian regions, such as China, the incidence rate of ESCC has generally declined, potentially due to economic growth and improvement of diet habits. In some European high-income countries and the United States, the decline is mainly attributed to the decrease in smoking and drinking. The risk factors of EC are not well understood, and the importance of environmental and genetic factors in the pathogenesis is also unclear. The incidence and mortality of advanced EC can be reduced through early diagnosis and screening. White light endoscopy is still the gold standard in the current screening technology. This article reviews the epidemiology, risk factors, and screening strategies of EC in recent years to help researchers determine the most effective management strategies to reduce the risk of EC.

Keywords: Esophageal cancer; esophageal squamous cell carcinoma; epidemiology; risk factors; screening

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Introduction

Most of the esophageal cancer (EC) is esophageal squamous cell carcinoma (ESCC) or esophageal adenocarcinoma (EAC), which is a malignant tumor originating from the esophageal epithelium. Global epidemiological data in 2020 showed that EC ranks seventh in terms of incidence (604,100 new cases) and sixth in the overall mortality (544,076 deaths) (1). The incidence rate of EC has shown a general downward trend in recent years. However, its mortality remains high, and the 5-year relative survival rate is only 20%, which is the second lowest survival rate after pancreatic cancer (10%) (2,3). According to global cancer statistics 2020, China has a high incidence rate of EC, and new cases and deaths account for 53.70% and 55.35% of the global total, respectively (1,4).

The composition of histologic subtypes and the incidence rate of EC vary significantly across different countries and regions. In those with the highest EC rates, such as Eastern Asia, Southern and Eastern Africa, 90% of the cases are ESCC (5). The lowest rates were found in Central America, Western and Middle Africa, where the main pathological type is EAC.

The etiology for EC is poorly understood. Because early EC has no specific clinical symptoms, a majority of patients missed the opportunity of early diagnosis are often diagnosed in advanced stage, resulting in low quality of life and poor prognosis (6). The British and American Society of Gastroenterology has developed a series of guidelines for screening and surveillance of Barrett's esophagus (BE) and EAC (7-10), and China has also issued consensus for the screening of early EC and precancerous lesions (11-14). The release of these guidelines and consensus facilitated standardization of management strategy of ESCC and EAC. The screening of EC and precancerous lesions has received large attention due to the progress of screening technology and the development of a series of high-quality studies. The epidemiology, etiology, and screening strategy of ESCC and EAC will be reviewed in this article.

Epidemiology of EC

EC is the seventh most common cancer and sixth most common cause of death in the world (1,15). The Global Burden of Diseases Study (GBD) provides a systematic scientific assessment of published, publicly available, and contributed data on disease incidence, prevalence, and mortality (16). Based on the GBD visualization database, we analyzed the burden and trend of EC from 1990 to 2019 both in domestic China and across the globe (*Figure 1*). The number of patients diagnosed with EC worldwide increased from 489,194 in 1990 to 960,610 in 2019. Correspondingly, the number of patients diagnosed with EC in China increased from 254,169 in 1990 to 498,410 in

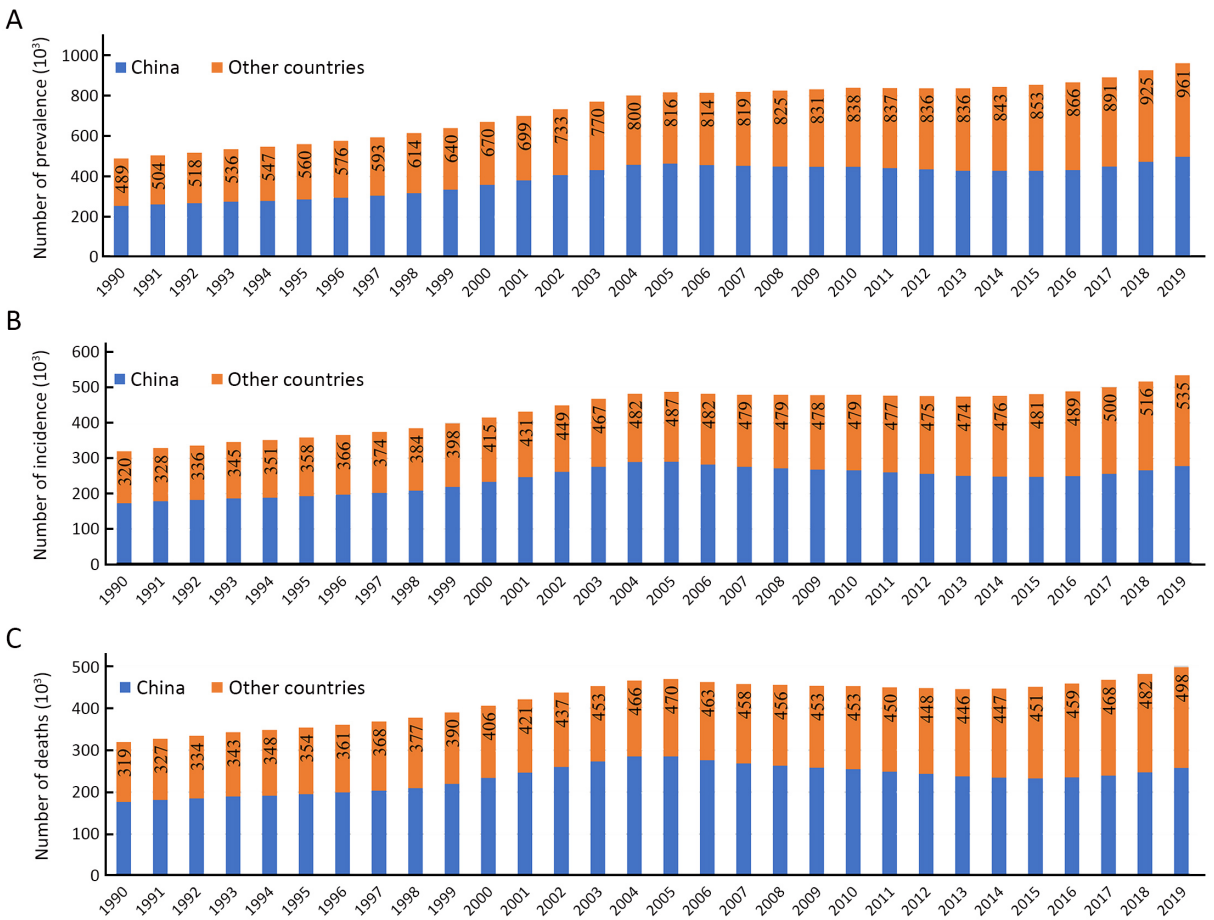

Figure 1 Global burden of esophageal cancer. Number of prevalence (A), incidence (B), and deaths (C), respectively.

2019, accounting for half of the cases in the world. The number of EC cases worldwide increased from 319,969 in 1990 to 534,563 in 2019, with a relative increase of 67.07%. The number of incident cases of EC in China increased from 173,687 in 1990 to 278,121 in 2019. The number of incident cases has continued to increase in recent years, and the global data have now climbed to 600,000. The number of EC deaths worldwide increased from 319,332 in 1990 to 498,067 in 2019, and the EC mortality in China increased from 176,602 in 1990 to 257,316 in 2019, a relative increase of 55.97% and 45.70%, respectively. From 1990 to 2019, the crude prevalence, incidence, and mortality of EC are on the rise both in worldwide and in China. This indicates that prevention and control of EC is still grim, which will depend largely on the efforts made by China, focusing on developing new strategies for more effective screening and surveillance. *Table 1* shows the estimated age-standardized rates (ASR) of EC in 2020, and only countries & regions with the highest prevalence were shown. Complete worldwide data could be found in the GLOBOCAN 2020 produced by the International Agency for Research on Cancer (http://www.iarc.fr/) (1). China's crude incidence rate was 22.4 in 2020, and the ASR incidence rate was 13.8, with a mortality rate of 20.8 and an ASR mortality rate of 12.7. The ASR prevalence rate, incidence rate, and mortality rate of EC showed a significant downward trend, which is related to increasing proportion of elderly population in recent years. It also indicates the important influence of population aging trend on the burden of EC (4,17).

Table 1 Worldwide ASR per 100,000 person-years for esophageal cancer in 2020*

Population	Prevalence**	Incidence	Mortality
Japan	25.4	7.2	2.8
China	24.0	13.8	12.7
The Netherlands	20.5	6.8	5
United Kingdom	17.9	6.4	5
Bangladesh	14.2	14.8	13.9
Ireland	13.4	5.7	5
Mongolia	12.6	17.1	16.2
Belgium	12.2	4.6	3.5
Germany	12.1	4	3
Denmark	11.6	4	3.2

ASR, age-standardized rate; *, only countries & regions with the highest prevalence were shown. Data source: GLOBOCAN 2020; **, estimated number of prevalent cases (5-year) as a proportion per 100,000 in 2020.

The two main histological types of EC showed dramatic difference in terms of incidence rate and spatial variation. During most of the 20th century, ESCC constituted the vast majority of EC globally. Although ESCC is decreasing overall, most current cases in the world are ESCC now and the incidence rate is still rising in some areas (18,19). Another change in recent years is that the incidence of EAC has increased significantly, showing anatomical specificity (20).

ESCC is still the most common histology of EC in the world (21). The incidence of ESCC and EAC can vary internationally by 16-fold. In high-risk areas commonly known as EC belt, starting from northern Iran, passing through the republics of Central Asia, extending to central and northern China, the incidence of EC is high and more than 90% are ESCCs (1,15). The main risk factors in these areas are not well understood. Yet, the preliminary evidence shows that potential factors might include poor nutritional status, low intake of fruits and vegetables, and drinking at high temperature (22,23). In contrast, in low-risk areas of ESCC, such as the United States and some Western countries, smoking and excessive alcohol consumption account for about 90% of the total cases of ESCC. According to the latest GLOBALCAN data, China accounts for half of the world's total in terms of both incidence and mortality of EC (1). With the development of surveillance, screening and prevention awareness in high-risk areas of ESCC in China, the overall incidence of ESCC is decreasing. However, in some areas, such as Taiwan, China, ESCC still shows an increasing trend, which may result from increased consumption of tobacco and alcohol (19). The most typical epidemiological characteristics of EC include histological differences and obvious regional differences in incidence. Even in central and northern China, the high-incidence area is in sharp contrast with the surrounding areas with relatively low-incidence (24,25). Even in the two adjacent counties, there are sometimes significant differences in EC incidence rate. The most concentrated area of EC in China is located on the south side of Taihang Mountain at the junction of Hebei, Henan and Shanxi provinces, especially in Cixian County, with an age-standardized incidence rate of more than 100/10,000. Generally speaking, there are relatively concentrated high-incidence areas in Qinling Mountains, Ta-pieh Mountains, northern Sichuan, Fujian, Guangdong, northern Jiangsu, and Xinjiang, respectively (26-28).

In contrast, in low-risk areas of ESCC, such as the

United States and some Western countries, the histology is mostly EAC and the overall incidence is low. In the United States, an estimated 19,260 cases of EC are diagnosed each year, and 15,530 people die of EC (1,29). In these areas, the incidence rate of EAC has increased dramatically, partly due to increased risk factors such as higher body mass index (BMI). When stratified by anatomical sites, the increased incidence rate mostly involved esophagogastric junction and gastric cardia tumors (30). BE has become the main focus of esophageal precancerous lesions in these areas. This epidemiological change has been found in Western countries in the past 30 years, and recently in some Eastern countries as well (31).

Risk factors of EC

There is existing evidence suggesting some potential risk factors of ESCC, although the main risk factors and etiology are not fully understood yet. For example, a study identified several major risk factors and evaluated their relative importance from a public health perspective (32). As mentioned above, in the high-risk areas of EC belt, including central and northern China, current research suggests that low intake of fruits and vegetables, smoking and drinking, poor nutritional status, and the use of hot beverages may be the main risk factors contributing to the high incidence of ESCC (23,33). Other factors may also affect the occurrence of ESCC, such as the existence of basic gastrointestinal diseases, head and neck cancer, human papilloma virus (HPV) infection, Tylosis, low socioeconomic status, and poor oral hygiene. The relative importance of specific risk factors may also vary across different geographic locations in the globe (34,35).

Dietary factors

The existing research in Asia has identified several dietary factors associated with ESCC. For a long time, foods containing N-nitroso compounds, such as pickled vegetables and meat, have been considered to be associated with ESCC. These compounds are carcinogenic and can exert their mutagenic potential by inducing alkyl adducts in DNA. Aflatoxin producing fungi have also been found in raw food materials in some Chinese areas where ESCC is prevalent. To some extent, these fungi can exert their mutagenic potential by reducing nitrate to nitroso compounds.

In China and some areas of South Asia where areca nuts chewing is prevalent, relevant studies have revealed an association between ESCC and the areca nut chewing behaviors (36). The underlying mechanism may be that the released copper ions induce fibroblasts to synthesize collagen and eventually lead to carcinogenesis.

High temperature tea and foods can cause heat damage to esophageal mucosa, thus increasing the risk of EC. Few studies have reported the results related to ESCC and EAC, respectively (37-39). In a systematic review of 59 studies (37), more than half of the studies found a statistically significant correlation between intake of high-temperature liquids and increased risk of EC. There is no evidence suggesting that the intake of tea beverage is associated with the risk of EC, or the chemicals in the beverages can affect the association between high-temperature liquid and EC risk as an independent factor (40).

However, a population cohort study from China does suggest a correlation between drinking hot tea and EC incidence rate. Moreover among smokers and alcoholics, the excessive risk of EC caused by drinking hot tea will be relatively more salient (39). A study from northern Iran also showed that drinking hot tea was significantly associated with an increased risk of ESCC (41).

Other dietary factors may also affect the risk of EC. A meta-analysis of observational studies showed that the intake of fruits and vegetables was negatively correlated with the risk of ESCC (42). Red meat intake is positively correlated with the risk of ESCC (43,44). Low selenium levels can increase the risk of EC, while selenium supplementation can reduce the risk (45). Low zinc levels may increase the risk of EC by enhancing the carcinogenic effects of nitrosamines and the overexpression of cyclooxygenase (COX)-2 (46). It has been reported that a low-folic acid diet can also increase the risk of EC (47,48).

Smoking and alcohol

Despite some variations of the relative importance across different geographic locations, the consumption of cigarette and alcohol is found to be a consistent predictor of ESCC (25,49-51). Both smoking and drinking have a synergistic and positive interaction effect, which induces normal tissue cancerization (52). Due to the existence of regional carcinogenesis, smoking and drinking are also risk factors for other respiratory and digestive cancers (including head and neck cancer and lung cancer).

Both pipe and cigar smoking increase the risk of ESCC, although being seemingly lower than that of cigarettes (53).

The type and amount of alcohol consumed also have different effects on increasing the risk of ESCC. For example, the risk of cancer caused by spirits may be higher than that of wine or beer. That is, the effect of cumulative alcohol intake may be more important. In addition, individual differences in the sensitivity and tolerance of alcohol may also have an impact. For example, some studies have reported that mutations in the alcohol dehydrogenase gene can prevent the occurrence of respiratory and digestive tract cancer (54,55).

Basic underlying gastrointestinal diseases and upper gastrointestinal cancer

The presence of specific esophageal diseases such as achalasia and corrosive esophageal stricture can increase the risk of ESCC. A population study involving 1,062 cases of achalasia showed that the risk of ESCC increased by more than 16 folds within 1–24 years after diagnosis, and patients have detected EC an average of 14 years after the diagnosis of achalasia. Another retrospective study analyzed 2,414 cases of ESCC patients with previous complications. Among them, 63 cases of esophageal corrosion caused by ingestion of lye in childhood, the average diagnosis time of ESCC was 41 (range: 13–71) years after ingestion of lye. Atrophic gastritis and other conditions that cause stomach atrophy can increase the risk of ESCC to approximately twice the original (56). A number of studies have reported that head and neck cancers, including oral cancer, nasopharyngeal cancer, hypopharyngeal cancer, and laryngeal cancer, are related to simultaneous or metachronous ESCC (56-58). This may reflect the existence of similar risk factors, such as smoking or drinking. In several prospective studies on head and neck cancers, the probability of EC occurring at the same time or at different times was 3%–14% (57,58).

HPV

HPV infection is thought to be related to the pathogenesis of ESCC, especially serotypes 16 and 18. There are more than 100 meta-analyses about the correlation between HPV and ESCC. Thus, umbrella analysis and overview of systematic review are needed to summarize the relevant evidence and evaluate the quality of the evidence. A systematic review and meta-analysis of 66 case-control studies showed that HPV infection was significantly associated with ESCC (59). However, the detection rate of HPV and HPV-16 was only 22.4% and 11.4%, respectively. The obvious heterogeneity among the included studies also affected the credibility of the combined results. Another systematic review and meta-analysis with 124 studies from six continents involving 13,832 ESCC patients evaluated the HPV detection rate (60). The results showed that less than 40% of EESC patients have been infected by HPV before.

Genetic factors

The role of genetic factors in the pathogenesis of EC is still uncertain. That is, it is still unclear whether the familial aggregation of EC is induced by common environmental risk factors or genetic factors. The inherited type of Tylosis (Howell-Evans syndrome) is an autosomal dominant genetic disease caused by *RHBDF2* gene mutation, which is highly associated with ESCC (61). In a case series study, 70% of patients with ESCC had this gene deletion. It is also reported that Peutz-Jeghers syndrome and autosomal dominant genetic disease caused by germline mutations of the tumor suppressor gene *PTEN* may also increase the risk of EC (62,63).

Among patients with EAC, about 80% had the history of gastroesophageal reflux disease (GERD), smoking, obesity and low intake of fruits and vegetables (32,64). As an independent risk factor of EAC, the role of GERD has not been fully understood yet. More than half of patients with EAC have no history of symptomatic GERD. A meta-analysis that included five studies showed that weekly symptoms of GERD at least increased the odds of EAC fivefold [OR=4.92, 95% confidence interval (95% CI), 3.90–6.22], while daily symptoms increased the odds sevenfold (OR=7.40, 95% CI, 4.94–11.11) (65). Even in patients after anti-reflux surgery, the risk of esophageal and gastric cardia developing EAC still showed an increasing trend (66). Patients with BE have an increased risk of developing EC with a 30-fold rate above that of the general population (67). However, patients with BE have a relatively low absolute risk of developing EC. Obesity seems to be an indirect risk factor for EAC and BE (68,69). A meta-analysis including case-control and cohort studies found that the relative risk of EAC and gastric cardia EAC was 1.71 (95% CI, 1.50–1.96) for patients with BMI of 25–30 kg/m^2, and 2.34 (95% CI, 1.95–2.81) for patients with BMI≥30 kg/m^2 (70). At the same time, it seems that obesity does not increase the risk of ESCC (68,71). Increased esophageal acid exposure may increase the risk of EAC for patients with acid hypersecretion (71), such as Zollinger Ellison syndrome. Moreover, for potential factors

such as lower esophageal sphincterotomy, balloon dilatation, or scleroderma, they will not only increase risks for gastroesophageal reflux, but also may increase risk for esophageal acid exposure. Taking drugs that reduce the pressure of the lower esophageal sphincter, such as nitroglycerin, anticholinergic drugs, β-adrenergic agonists, aminophylline and benzodiazepines, may increase the risk of adenocarcinoma, but the strength of this association remains unclear (72). There are many differences in risk factors between ESCC and EAC due to their different pathological characteristics. EAC mostly were diagnosed among male Caucasians, and the etiology of BE and EAC has been investigated comprehensively (73). As this is not the focus of the present article, we will not review it in depth here.

Screening of EC

As the main pathogenic factors of EC are not yet clear, there is lack of effective intervention for this disease in present. Secondary prevention is to achieve the goal of early diagnosis and early treatment through screening, and it has become a practical means to reduce the risk of advanced EC as well as its mortality rate. There are obvious regional and ethnic differences in the incidence of ESCC and EAC. The gastroenterology societies of the United Kingdom, the United States, and China have developed a series of guidelines for the screening and surveillance of BE and EAC (7-11). The incidence of EC in China is mainly consist of ESCC, and EAC accounts for only about 5%. Although the incidence of EAC has increased in recent years, the screening process for BE and EAC is still not costly efficient in China (74). Given the negative impact of population screening, its benefits in low-risk areas do not seem to be satisfactory (75). Even for most of the people who participate in the screening, the screening might be harmful rather than beneficial due to invasive tests, additional invasive procedures caused by false positive diagnosis, psychological burden, as well as time and economic costs.

Since the 1960s, China has conducted a series of population-level screenings in areas with high ESCC prevalence. As of the end of 2018, more than 2.16 million people had undergone upper gastrointestinal endoscopy at 194 project implementation sites across China, and more than 34,000 cases of malignant lesions were diagnosed, with an early diagnosis rate exceeding 70% (76). Overall, China has made great contributions to the early prevention and treatment of ESCC, as the first randomized controlled trial study on screening for ESCC is also being carried out in China (77). In response to the high incidence of ESCC, China has formulated a series of consensus on the screening and surveillance of early EC and precancerous lesions in 2014, 2015, and 2019 (12-14). Based on these consensuses, recommendations have been made to the target population of EC screening, regarding of screening age, screening intervals, screening technology, and endoscopic procedures. The release of the relevant consensus further standardizes the process and management of ESCC screening in China, making the screening more targeted, as well as enabling people in high risk to obtain greater benefits despite limited resources.

Although the rising incidence of EC is of concern, screening is limited to a very specific group of patients. While the screening is encouraged among the target population, it is not recommended to use endoscopic or non-endoscopic methods to screen the general population. The definition of high-risk population of ESCC is quite different from that of high-risk population of EAC. The target population of the guideline for EAC screening mainly includes male, Caucasians, patients with family history of BE, patients with increased duration of reflux symptoms, smoking, obesity and other risk factors, while the target population of ESCC are from high-risk areas (78). For the starting and ending age of the target population, the guidelines for BE and EAC recommend that the high-risk population should start routine screening at the age of 50 years, and the latest guidelines for ESCC recommend that the high-risk population should start routine screening at the age of 40 years until the age of 75 years, except for those who have life expectancy less than five years (7,9,12). The definition of high-risk population for EC screening in different guidelines is provided in *Table 2*. In the consensus on ESCC screening published in China in 2019, the classification criteria of target population were defined (12). The last item about the definition of target population in this consensus, that is, the combination of other high-risk factors of EC, is relatively nonspecific. This necessitates making the definition of high-risk population more inclusive, correspondingly expanding the scope of screening population. There is a lack of clear evidence regarding whether this part of the population will benefit from screening and the cost-effectiveness of screening also remains uncertain.

There is a lack of high-quality evidence to support the surveillance intervals of EC screening. The Chinese consensus on ESCC screening in 2019 for the first time

Table 2 Definition of target population in current guidelines and consensus for screening of EC

Guidelines or consensus (year published)	Subtypes	Target population
Chinese expert consensus on screening and endoscopic management of early EC (2014) (14)	ESCC; EAC	Primary: older than 40 years, and at least one risk factors including: 1) from a high-incidence area of EC; 2) symptoms of the upper gastrointestinal tract; 3) family history of EC; 4) precancerous diseases or precancerous lesions of the esophagus; and 5) other high-risk factors for EC (smoking, heavy drinking, head and neck tumors, and respiratory squamous cell carcinoma)
Chinese consensus: Screening, diagnosis and treatment of early esophageal squamous cell carcinoma and precancerous lesions (2015) (13)	ESCC	Long-term residence in a high-risk area of ESCC; family history of ESCC; previous history of esophageal lesions (esophageal intraepithelial neoplasia); personal history of cancer; long-term smoking history; long-term drinking history; poor eating habits such as eating too fast, blanching diet, high-salt diet, and eating pickled vegetables
Chinese expert consensus on screening of early EC and precancerous lesions (2019) (12)	ESCC	Primary: older than 40 years, and at least one risk factors including: 1) born or living in an area with a high incidence of EC for a long time; 2) family history of EC; 3) precancerous diseases or precancerous lesions of the esophagus; 4) head and neck tumors; and 5) combined with other high-risk factors for EC: blanching diet, alcohol consumption (15 g/d), smoking, eating too fast, indoor air pollution, and missing teeth
American Gastroenterological Association medical position statement on the management of Barrett's esophagus (2011) (8)	EAC	Male sex, older than 50 years, Caucasian, chronic GERD, hiatal hernia and obesity
ASGE guideline on screening and surveillance of Barrett's esophagus (2019) (9)	EAC	Male sex, older than 50 years, Caucasian, family history of BE, increased duration of reflux symptoms, smoking and obesity
British Society of Gastroenterology guidelines on the diagnosis and management of Barrett's oesophagus (2014) (7)	EAC	Primary: patients with GERD, and at least three risk factors including: 1) male; 2) older than 50 years; 3) Caucasian; and 4) obesity. Family history of BE or EAC would lower included threshold
ACG clinical guideline: Diagnosis and management of Barrett's esophagus (2016) (10)	EAC	Primary: male patients with either >5 years of GERD or with more than weekly GERD symptoms, and at least two other risk factors including: 1) age >50 years; 2) central obesity; 3) smoking history; 4) Caucasian; and 5) first-degree relatives with BE or EAC
The Chinese consensus for screening, diagnosis and management of Barrett's esophagus and early adenocarcinoma (2017) (11)	EAC	1) Older than 50 years; 2) male; 3) family history of BE; 4) long-term GERD (>5 years); 5) history of heavy smoking; and 6) obesity (BMI>25 kg/m^2 or abdominal obesity)

EC, esophageal cancer; ESCC, esophageal squamous cell carcinoma; EAC, esophageal adenocarcinoma; GERD, gastroesophageal reflux disease; BE, Barrett's esophagus; BMI, body mass index.

recommended the frequency of ESCC screening (12). Given China's population base, financial investment, endoscopic equipment and the accessibility of endoscopists, it is recommended that mass endoscopic screening should be carried out once every five years in areas with extremely high incidence. For other areas with relatively low incidence of EC, the limitations of screening for the general population include the lack of accurate and widely applicable risk assessment tools, the lack of cost-effective screening methods, and the lack of beneficial impact on mortality. Therefore, only the high-risk population should be screened once every five years. In addition, for some economically underdeveloped areas with a lack of medical resources, a 10-year intervals endoscopic screening of surveillance could be considered (79,80). British Society of Gastroenterology (7) and American Gastroenterological Association (8) suggest that patients with BE shorter than 3 cm or without dysplasia should receive endoscopic screening every 3–5 years.

The key to EC screening is to find a screening tool that is minimal or non-invasive, cost-effective, widely applicable, safe and accurate for the diagnosis of EC (81). The research prospects in this field are broad, mainly focusing on improving optical technology and advanced sampling technology (82,83).

High-definition (HD) upper gastrointestinal endoscopy is currently being used as the gold standard for screening target populations. The image resolution of HD can exceed

1 million pixels, which enhances the ability to identify small mucosal changes, so that more accurate biopsies can be performed (84). In the past few years, HD endoscopy has gradually replaced standard definition endoscopy (85). Cost is still the main factor restricting the use of HD upper gastrointestinal endoscopes as a screening tool for the general population. In addition to cost, there are several other concerns about the false negative rate of hyperplastic or neoplastic lesions. In a study that used standard protocols to evaluate the efficiency of biopsy, the missed diagnosis rate was as high as 57%. Advanced imaging technologies continue to emerge to improve the screening, monitoring and treatment of EC patients (85,86).

Dye-based chromoendoscopy improves the detection of abnormalities and target biopsies by enhancing the visualization of mucosal and vascular absorption patterns (87,88). Common stains include indigo carmine, methylene blue, acetic acid and Lugol's solutions. Lugol's solution is a composite stain containing iodine and potassium iodide, which stains brown once being absorbed by the squamous mucosa of the esophagus. By staining the squamous epithelium brown, Lugol's chromoendoscopy (LCE) highlights any metaplastic columnar epithelium in the esophagus (89). In general, the advantages of chromatography endoscopy are that it is relatively cheap, and chemical solutions are easy to use, provide wide-angle imaging, and are conducive to mucosal enhancement. However, the use of dye-based chromoendoscopy has several disadvantages. For example, the ability to identify abnormal mucosa varies greatly among observers, additional steps in the procedure are time-consuming, and some people are worried about the harm of contrasts.

Virtual chromoendoscopy such as narrow-band imaging (NBI), Fujinon intelligent chromoendoscopy, i-SCAN, blue-light imaging, and linked-color imaging usually enhances the mucosal surface and blood vessels through contrast agent enhancement (87,90). The difference between NBI, which is relatively widely used in clinical practice, and color endoscope is that it does not use any dyes. In contrast, NBI improves the resolution of the mucosal surface by limiting the wavelength range of light. A number of meta-analysis studies have shown that NBI performs well in detecting high-grade dysplasia, with sensitivity and specificity reaching 96% and 94%, respectively (91). At the same time, compared with white light endoscopy, several studies have shown that there is no difference between the two in detecting neoplastic tumors (92,93). The advantage of NBI is its minimal toxicity risk in comparison with dye-based chromoendoscopy. Moreover, NBI is relatively cheap and has been integrated in most standard equipment with better applicability.

There are a wide variety of optical technologies available for diagnosis, including white light endoscopy, dye-based chromoendoscopy, virtual chromoendoscopy, auto fluorescence imaging, microscopic endoscopy, optical coherence tomography/volumetric laser endomicroscopy, tethered capsule endomicroscopy, and spectroscopy. Some other advanced technologies as potential alternatives include wide area transepithelial sampling with 3-dimensional tissue analysis, Cytosponge™, transnasal endoscopy, biomarker panels, and breath testing using an electronic nose device (82,94-96). When it comes to choosing screening method, the most effective way to be recommended is the endoscopic monitoring combined with histopathological assessment, regardless of ESCC or adenocarcinoma. Among multiple options for endoscopic monitoring method, white light endoscopy is the first choice (97-99). Dye-based or virtual chromoendoscopy can be used as auxiliary screening methods in combination with white light endoscopy to increase the accuracy of diagnosis. At the present time, neither individual biomarkers nor panels of markers are ready for clinical practice can be recommended.

Conclusions

The epidemiological and pathological characteristics of EC vary significantly between the Eastern and the Western world, Moreover, the reference value of prevention and screening management for EAC in Western countries, China and other high-risk areas of ESCC is limited. Since the risk factors of EC are still unclear and not specific, it is a powerful preventive measure to carry out population screening of EC in high-risk areas. In light of poor prognosis of advanced EC, especially when the precancerous lesions are known to be monitored by endoscopy, it is important to determine an efficient and economic method for accurate screening of EC. Chinese experts are working together to solve this major health problem in the next few decades, and to provide Chinese experience for the prevention and control of ESCC worldwide.

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Footnote

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