



Early diagnosis of esophageal cancer: How to put “early detection” into effect?

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Abstract

This editorial comments on the article by Qu *et al* in a recent edition of *World Journal of Gastrointestinal Oncology*, focusing on the importance of early diagnosis in managing esophageal cancer and strategies for achieving “early detection”. The five-year age-standardized net survival for esophageal cancer patients falls short of expectations. Early detection and accurate diagnosis are critical strategies for improving the treatment outcomes of esophageal cancer. While advancements in endoscopic technology have been significant, there seems to be an excessive emphasis on the latest high-end endoscopic devices and various endoscopic resection techniques. Therefore, it is imperative to redirect focus towards proactive early detection strategies for esophageal cancer, investigate the most cost-effective screening methods suitable for different regions, and persistently explore practical solutions to improve the five-year survival rate of patients with esophageal cancer.

Key Words: Esophageal cancer; Early diagnosis; Early detection; Iodine staining; Five-year survival rate

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Core Tip: Despite technological advancements, the mortality rate for esophageal cancer remains high, with the five-year survival rate lagging behind that of other gastrointestinal cancers. This editorial highlights the importance of early esophageal cancer detection and delves into the current status, challenges, and potential solutions for enhancing esophageal screening efforts.

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INTRODUCTION

Esophageal cancer is a highly lethal malignancy with a poor prognosis due to its late presentation and rapid progression. For decades, esophageal cancer has consistently ranked among the top ten leading causes of cancer-related deaths globally[1]. Projections for 2040 suggest that there will be an estimated 957000 new cases of esophageal cancer worldwide, along with approximately 880000 deaths linked to the disease[2]. The persistently low five-year age-standardized net survival for esophageal cancer patients underscores the imperative of early detection and precise diagnosis for improving treatment outcomes[3]. Early detection of esophageal cancer is crucial in identifying cancers at a stage where curative treatments stand a greater chance of success. However, despite ongoing endoscopic advancements that have contributed to a decrease in mortality rates among esophageal cancer patients, the five-year survival rate for esophageal cancer remains disappointingly low, even in Japan, which boasts the highest five-year survival rates for esophageal cancer, the rate hovers at just 36%[3].

In contrast, other gastrointestinal cancers exhibit notably higher five-year survival rates, with some reaching 70% or above (for instance, 69% for gastric cancer, 72% for colon cancer, and 71% for rectal cancer in South Korea)[3]. Concurrently, in the research and treatment of esophageal cancer, there appears to be an excessive fixation among gastroenterologists and endoscopists on state-of-the-art endoscopic equipment and various endoscopic techniques. This disproportionate emphasis on equipment and technology may overshadow the importance of emphasizing practical early detection programs and enhancing education for esophageal cancer patients across diverse regions. This is especially true for strategies not reliant on the most advanced endoscopic equipment.

We are particularly intrigued by the original article, “Esophageal Cancer Screening, Early Detection and Treatment: Current Insights and Future Directions”, by Qu *et al*[4]. We regard this as a well-qualified and insightful study that underscored the significance of early screening, prompt diagnosis, and timely treatment as pivotal strategies for significantly reducing esophageal cancer incidence and mortality rates. The paper adeptly navigates the challenges and debates surrounding this topic. Moreover, while acknowledging the enhanced visualization of suspicious esophageal lesions made possible by advanced endoscopic equipment, the author emphasized the necessity of customizing esophageal cancer screening programs to fit the risk profiles and resource capacities of various populations to ensure that screening efforts are both feasible and sustainable[4]. We concur with the authors’ viewpoint and advocate that future endeavors should prioritize refining esophageal cancer screening strategies and augment educational programs for physicians and patients regarding esophageal cancer rather than over-reliance on high-end endoscopic equipment and advanced endoscopic expertise. In education initiatives, we suggest including gastroenterologists, endoscopists, primary care physicians, healthcare facility administrators, and health management professionals. This inclusive approach will incrementally heighten their awareness and understanding of esophageal cancer screening. It is promising that these measures will substantially bolster the currently suboptimal five-year survival rate for esophageal cancer. We extend our gratitude to Qu *et al*[4]. for their research, which raised attention to the early screening of esophageal cancer and the development of practical screening programs.

The importance of early diagnosis cannot be emphasized enough, as it has the potential to improve the current landscape, where most newly diagnosed esophageal cancers are in advanced stages. Early diagnosis can minimize the need for invasive treatments and significantly enhance survival prospects[1]. By strongly emphasizing early detection, we can pivot the management of esophageal cancer from a model heavily reliant on advanced therapeutic interventions to one that precedes prevention and early diagnosis. This strategic shift promises to improve individual patient outcomes and alleviate the overall burden of this devastating disease on healthcare systems and society at large[5,6]. The global challenge lies in effectively achieving “early detection” in population-based contexts. It requires exploring the most cost-effective screening methods suitable for diverse regions, considering prevalence rates, healthcare policies, medical infrastructure, and economic factors.

In this editorial, we aim to highlight the importance of early diagnosis of esophageal cancer and explore strategies for effectively implementing early detection. We will examine the current status of early detection efforts, identify the barriers to their implementation, and propose potential solutions that could enhance early detection and survival rates for patients with esophageal cancer.

CURRENT LANDSCAPE OF ESOPHAGEAL CANCER SCREENING

Analyzing the current screening methods is essential for understanding the landscape of early detection efforts for esophageal cancer. Endoscopic visualization of the esophagus is the preferred method for screening, as it allows for an immediate and detailed examination and also enables targeted pathological biopsies during the same procedure. While innovative screening technologies, such as esophageal capsules, confocal laser endomicroscopy, non-invasive cell collection devices, circulating tumor DNA as part of blood-based testing, and artificial intelligence-assisted image

recognition and risk prediction algorithms have emerged in recent years, none have succeeded in supplanting the leading role of endoscopic examination and esophageal biopsies in the screening for esophageal cancer[7-10]. However, esophageal endoscopy can be invasive and incur significant costs in certain areas where there may also be a shortage of skilled endoscopists to conduct extensive screening programs. Moreover, screening for esophageal cancer demands considerable skill and experience from the practitioners. After all, endoscopists without the requisite expertise cannot diagnose early esophageal cancers they do not recognize. An alternative, albeit somewhat time-consuming, method involves using the pink and silver signs after esophageal iodine staining to assist in distinguishing esophageal lesions and guide targeted esophageal biopsies[11,12]. A prospective endoscopic surveillance study has found that negative iodine staining is associated with the progression of esophageal lesions[13]. However, the rigorous application of esophageal iodine staining according to guidelines has not been universally adopted in many endoscopic centers, particularly for every high-risk individual undergoing esophageal endoscopy. This discrepancy is attributed to the inexperience of some junior endoscopists, a shortage of endoscopists in certain areas, and limited examination time per patient. Nonetheless, this current state should not continue to be overlooked.

Esophageal cancer remains a significant health challenge due to its typically late presentation and the lack of effective screening programs across numerous regions. Devising screening protocols for various areas requires careful consideration of genetic predisposition and environmental risk factors. As Qu *et al*[4] have underscored, it is essential to tailor screening methods according to the predominant histological subtypes of esophageal squamous cell carcinoma (ESCC) and esophageal adenocarcinoma within a specific area. High-incidence regions have shown promise in implementing targeted screenings with endoscopy or Lugol's chromoendoscopy, which are more adept at identifying early lesions. For instance, in some areas of China, such programs have led to a notable increase in the detection of ESCC. However, this progress is juxtaposed with the challenges faced in low-incidence areas, where a lack of standardized screening protocols and limited resources result in delayed diagnosis. The feasibility of implementing comparable screening approaches in these regions is contingent upon multiple factors, including the local incidence of esophageal cancer, the availability of trained personnel, and financial considerations.

BARRIERS TO IMPLEMENTING EARLY DETECTION STRATEGIES

Reference Citation Analysis (RCA, <https://www.referencecitationanalysis.com/>) is a unique artificial intelligence system for citation evaluation of biomedical literature. RCA has been employed to analyze previous studies of screening strategies for esophageal cancer up to February 2024. Qu *et al*[4] noted that the path to effective early detection is fraught with challenges. Despite the ongoing evolution in both the volume and quality of upper gastrointestinal endoscopy in many developed and developing countries, the five-year survival rate of patients with esophageal cancer has not seen the same improvement as other gastrointestinal cancers, a disparity that warrants our thorough consideration[14-16]. Surprisingly, even in certain developed nations or regions, there is also a shortage of endoscopists and endoscopic equipment to varying degrees, akin to the situation in developing countries[17]. Consequently, the extended waiting time for esophageal screening, along with the limited screening time and examination quality, will inevitably impact the early diagnosis of esophageal cancer and the five-year survival rate of patients.

Another critical and frequently overlooked challenge is the shortage of awareness among the general population and healthcare providers regarding the importance of early detection. This lack of knowledge can lead to delayed or missed screenings, a critical factor for low survival rates. Moreover, this knowledge gap, coupled with cultural beliefs and stigmas associated with cancer, deters individuals from seeking timely medical attention, thereby missing the critical window for early intervention. The issue of low screening compliance due to the public's lack of awareness about esophageal cancer screening has garnered considerable attention and research in recent years. Studies have revealed that endoscopic screening compliance among urban populations in China is below 24%. Researchers suggest that improving the public's understanding of cancer prevention and control, prioritizing outreach to vulnerable groups with lower adherence to endoscopic screening by community health workers, and optimizing the screening process to minimize waiting times for endoscopic screening may help address poor compliance with esophageal cancer screening[18]. Additional research indicates that to improve screening attendance rates, individuals undergoing esophageal cancer screening prefer the procedure to cause minimal or no discomfort[19]. From this perspective, the screening challenge also encompasses the current shortage of anesthesiologists and the inadequate proportion of painless gastrointestinal endoscopies conducted in many regions or medical institutions.

In resource-constrained environments, inadequate healthcare infrastructure disproportionately impacts the ability to screen and diagnose esophageal cancer at an early stage. A scarcity of skilled healthcare professionals, particularly in endoscopic techniques, exacerbates this issue. The high cost of advanced endoscopic equipment, which may be beyond the financial reach of many healthcare systems, presents another substantial barrier. Additionally, the requirement for trained personnel creates financial and educational hurdles, particularly in low-resource settings with the highest disease burden. Meanwhile, even in endoscopy centers with a relatively high number of endoscopists and endoscopic equipment capabilities, establishing quality control indicators for endoscopic screening may still be in its nascent stages.

POTENTIAL SOLUTIONS FOR ENHANCING EARLY DETECTION

Addressing the challenges of early detecting esophageal cancer necessitates a multifaceted approach. The ultimate goal is to enhance early detection rates of esophageal cancer while factoring in the accessibility and cost-effectiveness of the

methods in diverse regions. From this standpoint, although various innovative screening techniques have been introduced, such as unsedated transnasal endoscopy, which offers a less invasive option compared to traditional endoscopy, and methods to detect biomarkers in body fluids that could expand the pool of individuals undergoing screening, many of these novel screening technologies are still in the early stages of exploration or have been applied to only small populations in clinical trials, and are not more cost-effective than esophageal endoscopy[20]. These new methods may benefit regions with well-established esophageal screening programs. However, for many other areas in the early stages of endoscopic technology, it may take longer for novel screening methods to yield improved five-year survival rates for esophageal cancer patients. For instance, in some areas of China and many other developing countries, where economic conditions, equipment, or professionals required for routine esophageal endoscopy screening are not guaranteed, the anticipated impact of implementing the aforementioned new technologies to enhance early screening for esophageal cancer and the five-year survival rate of patients may currently be unrealistic. Thus, bolstering the implementation of fundamental and practical esophageal endoscopy screening, which is currently underutilized, could represent a more cost-efficient and viable strategy.

Tailoring endoscopic screening of esophageal cancer within the constraints of limited health and sanitation funding across different regions is a topic that warrants dedicated study and discourse. Identifying high-risk populations for esophageal cancer and determining optimal screening intervals could be universally acknowledged as effective solutions. Numerous guidelines have already defined high-risk groups that require screening for esophageal cancer. A recent study from the Cancer Screening Office of the Chinese National Cancer Center has revealed that universal endoscopic screening is the optimal strategy for individuals over 55 in high-risk areas in China[21]. In its current efforts in esophageal cancer endoscopic screening, China has employed a strategy of universal endoscopy screening for high-risk areas and risk-stratified endoscopic screening for high-risk populations in non-high-risk areas, achieving preliminary results[18]. Concurrently, a tailored or varied cost-effectiveness threshold, rather than a single one, may be more practical for implementation in real-world scenarios[22]. Building on this, a study from a high-risk area for upper gastrointestinal tumors in China suggested that endoscopic screening for esophageal and gastric cancer among the Chinese population aged 40-69 offered good cost-effectiveness, recommending biennial screening as the optimal strategy[23]. Research to determine high-risk groups for esophageal cancer and optimal screening intervals in different countries or regions merits research investment and attention from local health departments and cancer screening centers.

In specific endoscopic screening procedures for high-risk patients, inexpensive esophageal iodine staining does not necessitate advanced endoscopic equipment, and its results are more accessible to interpret, making this method easier to teach and master. Additionally, the combination of esophageal iodine staining with electronic chromoendoscopy can further elevate the quality of esophageal cancer screening, especially in screening performed by less experienced endoscopists[11,24]. However, even in Asian regions where esophageal iodine staining is more prevalent compared to Europe and America, due to constraints such as the number of endoscopists and time per examination, iodine staining has not been universally adopted in esophageal cancer screening at some endoscopic centers. Hence, esophageal iodine staining warrants increased attention and should be recommended for inclusion in the quality control indicators of endoscopic screening for esophageal cancer. Enhancing the implementation rate of esophageal iodine staining in high-risk patients is crucial to improving the screening quality of esophageal cancer. It necessitates the establishment of practical endoscopic quality control standards for esophageal screening, increasing the number of endoscopists, and more time dedicated to screening each patient. There must also be a focus on enhancing the examined population's tolerance to iodine staining[25,26].

Furthermore, educational campaigns aimed at heightening awareness of esophageal cancer risk factors and the advantages of early diagnosis are essential to ensure that more individuals at high risk undergo endoscopic screening within the recommended timeframe. Without such initiatives, even the most advanced screening technologies or guidelines will not enhance the five-year survival rate of patients with esophageal cancer. Among these measures, educating primary care providers is crucial, as they can initiate early referrals to specialists when necessary. Current delays from symptom onset to referral underscore the necessity for further education of the public and general practitioners on symptoms warranting urgent referral[27]. At the same time, multidisciplinary assessments are crucial for the early diagnosis of esophageal cancer, which can help reverse the current trend of most cases being diagnosed at an advanced stage with poor prognosis[1]. In addition, multidisciplinary diagnosis, treatment, and care are instrumental in reducing the mortality risk for patients with esophageal cancer. Therefore, these practices deserve ongoing promotion to enhance the five-year survival rate of esophageal cancer patients[28].

It is also critical to acknowledge that healthcare systems and policymakers play a pivotal role in the allocation of resources towards esophageal cancer screening and facilitating early detection efforts for esophageal cancer. Governments and health organizations, particularly those in low- and middle-income countries or regions, should consider implementing measures to mitigate financial barriers to screening, such as providing subsidies or insurance for esophageal cancer screening for individuals at higher risk and gradually alleviating oncology healthcare professionals' moral distress and burnout due to resource constraints and systemic inequalities[29]. Collaboration between healthcare providers, policymakers, and community leaders is indispensable in creating an environment that supports early detection and timely treatment of esophageal cancer. Such concerted efforts can lead to a significant improvement in survival rates and quality of life for patients with esophageal cancer.

Lastly, it is worth mentioning that there is an increasing demand to leverage current mobile health technologies and telemedicine platforms to enhance disease management and life quality for patients with esophageal cancer[30]. Remote medical technologies facilitate remote assessment and monitoring of patients, thereby extending the reach of screening initiatives. They also enable improved education and awareness among high-risk populations or those at increased risk for esophageal cancer. These methods provide more equitable access to education and screening opportunities for high-risk patients across different regions and optimize the use of relatively scarce medical resources, particularly in areas

lacking specialist services or where transportation is less accessible. Furthermore, these technologies may improve esophageal cancer screening status quo and enhance postoperative recovery and self-management, thereby improving postoperative quality of life and survival rates for patients with esophageal cancer[30,31].

CONCLUSION

Despite the acknowledgment of the significance and cost-effectiveness of esophageal endoscopic screening over a decade ago, esophageal cancer still has one of the lower five-year survival rates among patients with gastrointestinal cancers. The solution to this current situation may also be multifaceted due to complex and multidimensional reasons in different regions. Emphasizing early diagnosis is crucial for improving the five-year age-standardized net survival rate for patients with esophageal cancer. Early detection involves considering novel screening technologies and their cost-effectiveness and accessibility across various regions. Within the constraints of limited resources, identifying high-risk populations, determining optimal screening intervals, and refining current endoscopic screening methods are critical strategies that warrant further investigation and attention. Concurrently, increasing the allocation of health resources for esophageal cancer screening, enhancing education for the general public and primary care providers, promoting multidisciplinary assessments and care, and gradually integrating telemedicine and mobile health technologies are instrumental in improving early detection rates and elevating patients' five-year survival rates and quality of life. Now is the time to convene healthcare policymakers, endoscopists, oncologists, surgeons, and community health workers to collaboratively explore the most effective and cost-efficient screening strategies and esophageal cancer management approaches across different regions. This alliance has the potential to elevate esophageal cancer patients' stagnant five-year survival rates.

FOOTNOTES

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