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Biomarkers for Esophageal Cancer Early Detection, Prognosis and Therapy

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Abstract

Esophageal cancer is the deadliest cancer in the world, with a 92% annual mortality rate per incidence. The two major types of ECs are esophageal squamous cell carcinoma and esophageal adenocarcinoma, with EAC having one of the worst prognoses in oncology. Limited screening techniques and a lack of molecular analysis of diseased tissues have resulted in late-stage presentation and extremely short survival times. The five-year survival rate of EC is less than 20%. Thus, early detection of EC may increase survival and improve clinical outcomes. Cellular and molecular biomarkers are used in diagnosis. However, this is an invasive method that does not produce a molecular profile of the diseased compartment. To reduce the invasiveness of diagnostic procedures, researchers are proposing non-invasive biomarkers for early diagnosis and point-of-care screening options.

Keywords: Esophageal carcinoma • Esophageal adenocarcinoma • Saliva • Blood

Introduction

Because of its poor prognosis and high mortality rate, esophageal cancer is one of the deadliest cancers in the world. EC is the world's eighth most common cancer and the sixth leading cause of cancer deaths. More than 90% of ECs are the two most common histological types, namely esophageal squamous cell carcinoma and esophageal adenocarcinoma. The conversion of normal squamous esophageal epithelium to ESCC is characterised by basal cell hyperplasia, dysplasia, and invasiveness. ESCC can affect any part of the oesophagus. The most common risk factors, alcohol and tobacco use, cause cellular DNA damage and contribute to ESCC.

Early detection of ESCC and EAC is required to improve survival and reduce morbidity and mortality. For early detection and diagnosis, esophageal endoscopy with biopsy and histological analysis is the gold standard. Chromoendoscopy, virtual chromoendoscopy, magnification endoscopy, and other advanced endoscopic imaging techniques may improve the sensitivity of early-stage carcinoma detection. However, the difficulty in defining a well-characterized screening population, the lack of an accurate, cost-effective, and widely accepted screening tool, and the lack of data on the costs of non-invasive screening are all associated challenges. Furthermore, because of the invasive and costly procedures involved, endoscopic screening is not practical for mass screening. Chemotherapy, radiotherapy, chemoradiation, laser therapy, electrocoagulation, immunotherapy, and targeted therapy are treatment strategies for advanced and nonresectable lesions [1].

Literature Review

Poor prognosis due to late detection of ECs warrants the development of early detection methods using non-invasive biomarkers so that timely intervention can be started to improve outcomes. Tissue histology after endoscopy has limitations for mass screening and serum tumour markers including squamous cell carcinoma antigen and carcinoembryonic antigen are insufficiently specific and sensitive for early EC diagnosis. Inter and intra-observer variability impedes lesion recognition during endoscopy. The specificity and accuracy of blood biomarkers/liquid biopsy are higher. Proteomic profiling has promise but is limited by higher costs in routine use, whereas epigenetic markers are promising due to their ease of detection in tissue and body fluids such as blood, plasma, and urine. In the case of metastatic tumours that are difficult to sample using a core biopsy, liquid biopsy is advantageous.

The detection of a panel of non-invasive biomarkers in blood, urine, and saliva may improve diagnostic sensitivity and specificity, as well as have clinical implications for improving outcomes. Non-invasive biomarkers will be useful in clinics because they use readily available clinical and laboratory information to non-invasively detect tumours early in the course of disease in at-risk populations and can be used for mass screening. Other benefits of using non-invasive strategies include the absence of side effects and the reduced risk of sampling error. This will improve the interpretation's objectivity and allow it to overcome the limitations of endoscopy for mass screening. Furthermore, non-invasive biomarkers are useful not only in early diagnosis, but also in predicting treatment outcome, disease progression, and relapse.

Discussion

Circular RNAs, which play a role in cell proliferation, migration, death, tumour invasion, and metastasis, may also be used as ESCC biomarkers because dysregulated expression of circRNA is associated with the pathogenesis of ESCC and can be detected not only in tumour tissue but also in nearby tissue. The detection of circRNAs using techniques such as RNA sequencing and bioinformatics analysis allows for the detection of both known and unknown circRNAs, which is superior to the microarray technique, which detects only known circRNAs. In addition to circRNA, miRNAs, and ctDNAs, transcription factors, which regulate gene expression, may also be used as biomarkers for early detection [2-6].

Although the incidence of esophageal adenocarcinoma is one of the fastest rising in the United States, the prognosis is poor because many patients present to their oncologists at advanced stages of disease progression. One reason for this could be the poor standard of care for EAC monitoring. Patients are currently subjected to endoscopy, in which a tissue sample from a pinch biopsy is stained for antibody detection and examined under a microscope. However, it has been demonstrated that the current method is insufficient for identifying patients at risk for EAC. This is happening because pre-cancerous tissues with different morphologies are sometimes labelled as having the same level of cancerous

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marker expression.

When determining which patients should be placed on ICIs, histopathology presents technical and clinical challenges. The testing sample must be taken from a slice of primary tumour tissue that has not been chemoradiated. The interpretation is heavily influenced by the type of cancer, the indication for treatment, the IHC scoring method, and the pathologist's level of experience. The antibody clone, staining platform, fixation time, and fixation type all have a significant impact on technical performance. The method is dependent on antibody binding and epitope integrity, proper tissue fixation is subject to inter- and intra-observer disagreement, and inconsistent results have been reported across clinical trials. Furthermore, defining a high TMB across various cancers is currently impossible.

Conclusion

Although tissue biopsy during esophageal endoscopy is the standard diagnostic method for ESCC and EAC, the need for non-invasive early markers for mass screening is obvious. This is due to the fact that tissue biopsy during endoscopy is not appropriate for mass screening. As previously discussed, recent research suggests that liquid biopsy, urine, and saliva may be used as non-invasive methods for investigating biomarkers for ESCC and EAC. The advantage is that these samples will be suitable for mass screening. Furthermore, in advanced ESCC, longitudinal serial monitoring of the liquid biopsy is important in terms of treatment response, relapse prediction, and prognosis for CT responses.

Acknowledgement

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Conflict of Interest

There are no conflicts of interest by author.

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