Early Colorectal Cancer Detection, Prediction, and Diagnosis Techniques and Biomarkers

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Abstract

One of the most frequent digestive illnesses worldwide is Colorectal Cancer (CRC). In terms of incidence and death, it has steadily risen to become one of the top three malignancies. The main contributing factor is the delay in diagnosis. As a result, early diagnosis and detection are crucial for preventing colorectal cancer. Despite recent advancements in surgical and multimodal therapy as well as a variety of approaches for CRC early diagnosis, the disease's poor prognosis and late discovery remain important. Therefore, it is crucial to research cutting-edge technology and biomarkers to enhance the specificity and sensitivity of CRC detection. We hope that this review will encourage the adoption of screening programmes and the clinical use of these promising molecules as biomarkers for CRC early detection and prognosis. Here, we highlight some popular techniques and biomarkers for early detection and diagnosis of CRC.

Keywords: Colorectal cancer • Early detection• Diagnosis • Biomarkers

Introduction

A serious threat to human life and health is Colorectal Cancer (CRC), one of the most common tumours of the digestive tract in the world with one of the highest rates of morbidity and mortality of all malignancies. The population's standard of living has significantly increased in recent years as a result of economic growth, but because of dietary incontinence, the number of CRC patients has been steadily increasing, and CRC is now the second leading cause of cancer-related death worldwide, accounting for about 600,000 deaths. According to the study's statistical findings, the incidence of colorectal cancer ranked third globally in 2020, accounting for about 10% of all cases globally and for about 11% in Asia, and the fatality rate was around 9% both internationally (ranking second) and in Asia. As the prevalence of the disease continues to climb year after year, the age distribution of colorectal cancer patients is currently shifting younger and younger. In addition, Yue Xi et al. predict that China would have the highest rate of new cancer cases and cancer-related fatalities worldwide in 2040. The percentage of new cases and deaths globally and in Asia in 2020, as well as the quantity of new CRC cases and fatalities in the nations with the greatest incident instances in 2020 and forecasts for 2040. Global and Asian estimates of the number of new cancer cases in 2020. Estimated death toll from cancer globally and in Asia in 2020. Source from GLOBOCAN 2020. (Estimated global cancer incidence in 2020 and forecasts for 2040. Global estimates of the number of deaths in 2020 and 2040 predictions.Elsevier Inc. is the publisher. 5-year survival rates for various CRC stages. Artificial Intelligence (AI) uses in medicine for CRC. The four major clinical components of CRC are shown by the outer circle, which also represents the main data types used in CRC research. For each clinical component, AI has divided and particular tasks, which are displayed in boxes outside the circle.Because the prognosis of colorectal cancer is strongly correlated with the timing of diagnosis and the stage at which the disease is detected—stage I disease has a five-year survival rate as high as 90%, but stage IV disease has a survival rate of less than 10%—almost all cancer-related organisations advise early screening for CRC after the age of fifty. Early colorectal cancer has a very long incubation time, frequently longer than 10 years, with no obvious signs. The majority of CRC are in stages III or IV when they are discovered and have spread to other tissues; the five-year survival rate for CRC is less than 10%.Furthermore, only around 25% of patients with liver metastases are suitable for surgery, despite the fact that they are the most common type of colon cancer organ metastases. Radiation or chemotherapy is the primary form of treatment for colorectal cancer, which has a significant negative impact on the patient's quality of life and is frequently accompanied by infection, nerve damage, and/or skin damage. More and more molecules have recently been discovered to be biomarkers for the diagnosis of colorectal cancer as a result of the development of high throughput omics analysis techniques, such as the next-generation sequencing and microarray analysis, comprehensive association and bioinformatics analyses. In this work, we compiled the most important techniques for colorectal cancer early detection and prediction, and we summarised the genomics, transcriptomics, proteomics, and metabolomics biomarkers that can be used to diagnose colorectal cancer, accordingly. The 5-year survival rate for colorectal cancer is almost 90% if it is found early; however, the rate is lower when the cancer has spread outside the colon or rectum. Therefore, to increase the length of time that patients with colorectal cancer live, early identification is crucial. Imaging and stool-based testing are now the main modalities for colorectal cancer screening. Colonoscopy, stool-based testing, cologuard (stool DNA), flexible sigmoidoscopy, and computed tomographic colonography are the five different categories of imaging and stool-based tests. Each test has a unique set of benefits and risks. Prior to the onset of colorectal cancer, adenomas or rectal polyps may appear, and some adenomas larger than 10 mm in diameter will advance to colorectal cancer. Rectal polyps or adenomas can successfully prevent the development of CRC if they are found and removed at an early stage.Endoscopy procedures include colonoscopies, flexible sigmoidoscopies, and Computed Tomographic (CT) colonography. Since colonoscopy has long been regarded as the gold standard for detecting adenomas and CRC, it is a crucial step in the diagnosis of CRC. Because of this, colonoscopy can be used to detect colorectal cancer either directly or as a review of other prior tests, and there is currently a wealth of data showing that colonoscopy screening reduces colorectal cancer morbidity and death. Additionally, the only technique that combines testing and prevention is the colonoscopy. The flexible sigmoidoscopy examines the rectum and the lower end of the colon using a short, thin, flexible tube with a tiny camera on the end. CT colonography is a procedure that takes pictures of a person's rectus muscle and colon using a specialised machine. While polyps and other abnormalities can be found with flexible sigmoidoscopy or CT colonography, a colonoscopy is required for a more thorough inspection. However, colonoscopy just serves to reflect the precancerous lesions' inherent risk index; it is not a preventative. However, this method of checking still has a significant clinical impact because it can help people identify their colorectal cancer risk early and ensure that they have a long period of time with a decreased risk of contracting the illness. Endoscopy is a crucial inspection technique, yet it can also cause patients' pain and harm. Endoscopic procedures are more likely to result in bleeding and perforation, and the risk of such accidents rises with age, according to studies on patients who are asymptomatic and those whose screening has been approved. Due to the increased danger to patients, high cost, and difficulty for many patients in detecting colorectal cancer in its early stages, endoscopic compliance is low. Meanwhile, research has shown that right colorectal cancer is not always correctly diagnosed by

colonoscopy. The Stool-based tests are easy and affordable at-home methods for finding concealed and undetectable blood in human faeces. Stool testing and stool DNA tests are the two different forms of faeces-based tests. The two types of stool tests were faecal Occult Blood Tests (FOBT) and Faecal Immunochemical Tests (FIT). Blood in the stool can be found using both the FIT and FOBT tests.Due to the special properties of gold, Gold Nanoparticles (GNP) are among the most studied nanoparticles and have a significant application value in the portable test strip-based diagnosis of numerous diseases. One crucial method utilised in the FIT is the colloidal gold immunoassay. DNA and antibodies can be combined in three dimensions using colloidal gold particles as a connecting scaffold. The sensitivity of this connection strategy is substantially higher than that of traditional ELISA procedures.The primary antibody pair and the associated secondary antibody, which have a sensitivity and specificity of more than 80% for the detection of colorectal cancer, are primarily needed for the colloidal gold approach. As a result, the colloidal gold technique emerges as a key technique for the diagnosis of colorectal cancer. While being less sensitive and specific than the FIT, the FOBT can provide speedy findings. The method that uses Tetramethylbenzidine (TMB) as a chromogenic reagent to detect occult blood in faeces is the most used chemical method used today. Many patients find the FOBT method more convenient because it can be used at home, is non-invasive to the patient, and produces results in less than five minutes. There are several limitations, such as limiting the patient's diet because food-based peroxide active ingredients can result in false-positive tests. A stool DNA test that looks for aberrant DNA and concealed blood in the faeces is a tool for the early detection of colorectal cancer along with the FIT method. There are no food or pharmaceutical limitations before the stool DNA test, in contrast to the FIT. It doesn't require bowel preparation or a trip to the hospital; it can be taken at home. Although FOBT is a simple and affordable approach for CRC screening, due to its low selectivity and sensitivity, it is not typically advised to detect early lesions. Due to their sensitivity and specificity, colonoscopy and comparable methods cannot be used on all patients on a regular basis. As omics technologies advance, more and more biomarkers are being discovered and evaluated for the diagnosis of colorectal cancer, including genomic biomarkers (oncogene and tumour suppressor mutations), epigenetic biomarkers (DNA methylation), transcriptomic biomarkers (non-coding RNAs), proteomic biomarkers, and metabolomic biomarkers. Colorectal cancer is a heterogeneous tumor and relatively common malignant tumor in clinical practice. Previous studies demonstrated that the CRC can be categorized into three types according to the pathogenesis of CRC. First, Chromosomal Instability (CIN), which is mainly manifested in structural chromosome and aneuploidy structural abnormalities, as well as chromosomal deletion and rearrangement. Chromosomal aberrations and numerous gene mutations, including Adenomatous Polyposis Coli (APC), Kirsten rat sarcoma viral oncogene (KRAS), Phosphatidylinositol-4,5-Bisphosphate 3-Kinase Catalytic Subunit Alpha (PIK3CA), loss of heterozygosity of the long arm of chromosome 18 (LOH 18q), and tumour protein CpG Island Methylation Phenotype (CIMP) is the last category. The main location for methylation in CpG dinucleotides is the fifth carbon position of the cytosine residue.DNA methyltransferases (DNMTs) initiate methylation, which inhibits tumour suppressor genes and encourages the growth of colorectal cancer, particularly in tumours. Subcategories of CIMP-related processes include CIMP high MSS and CIMP high MSI linked to the BRAF gene, as well as CIMP low MSS linked to the KRAS gene.

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