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COLON CANCER

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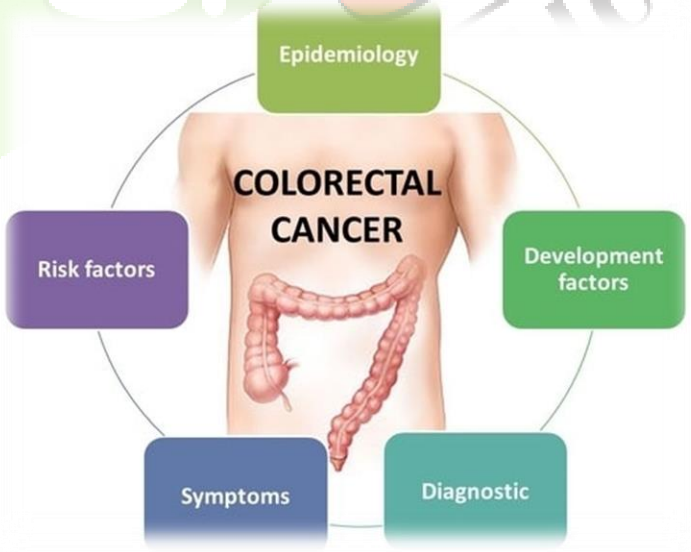
Abstract

The big intestine is where colon cancer typically first manifests itself. The digestive system ends with the colon. Colon cancer can strike any one at any age, but it often strikes older persons. Small, noncancerous clumps of cells called polyps that form on the inside of the colon. Over time some of these polyps can become colon cancers. Colon cancer are also known as colorectal cancer as well as rectal cancer. Which starts in the rectum, is another name for colon cancer.

The second most deadlist cancer in the united states and the third most frequently diagnosed is colon & rectal cancer. Unlike colon cancer has specific environmental connections and genetic risk factors. In recent years, significant advancements in the treatment of metastatic colorectal cancer have been noted.



Graphical Abstract

Key words: - Colorectal carcinoma, pathology, adenoma, molecular, MSI, KRAS, BRAF

Introduction

Cancer: Cancer is just an abnormal cell proliferation in the body. Growth may become out of control when a cell's or a group of cells' programming is compromised. This is related to a diet high in fat and poor in fibre. It is a disease of the wealthy and is more common in wealthy

nations. This cancer can cause diarrhoea, abdominal, lower back, or bladder pain, as well as changes in bowel patterns. [11]

Colon cancer, often known as CRC, is the first cancer that comes to mind when we think about common cancers that can be prevented. In fact, CRC is now diagnosed as the third most frequently in males with cancer and United States of America women [1] The World Health Organization (WHO) reports that 862,000 persons died from CRC in 2018, while 1.80 million new cases were detected worldwide.[2] Currently, it is the most frequent malignant cancer in the gastrointestinal system, comprising 13% of all malignant tumours, it is the second most prevalent cause of cancer-related death worldwide, affecting men and women equally in established and developing nations, and it is anticipated to surpass the mortality rate. heart disease incidence in the upcoming years. [3-5] It is a prevalent disease in those aged 65-74, with a higher prevalence in women. [6] Due to risk factors like obesity, sedentarism, poor eating habits (rich in fats and proteins), smoking, and population ageing, this pathology is found more commonly in younger people. The clinical presentation in patients with colorectal cancer varies on the tumor's size, location, and whether or not it has metastasized. Anorexia, abdominal distension, altered chronic bowel habits, altered bowel movements, nausea, vomiting, malaise, and involuntary weight loss are among the symptoms that characterise the clinical presentation. [4] Colorectal carcinogenesis is a lengthy, multistage process that takes place over many years. Most CRCs develop from adenomatous polyps that take between five and fifteen years to transform from dysplasia to malignancy. [7]

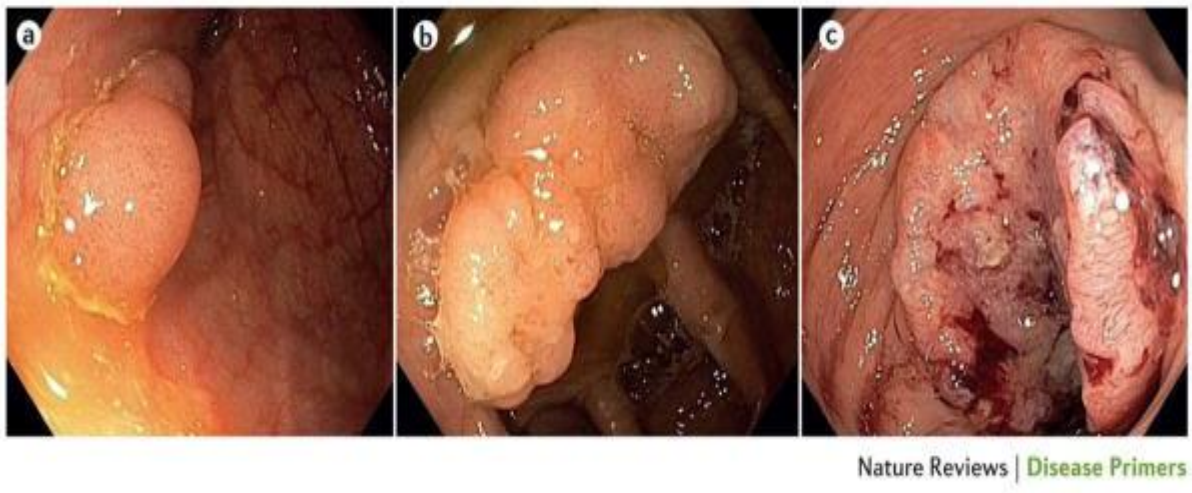


Figure Colorectal neoplasia at different stages

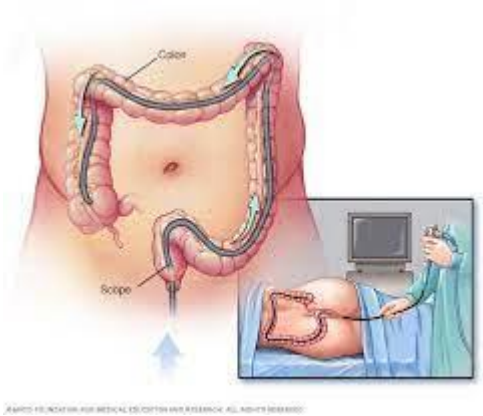
(a) A small sessile adenoma.

(b) An advanced, larger sessile adenoma.

(c) A large, dish-shaped, ulcerating sigmoid carcinoma.

The tumour covers most of the circumference, but has not yet led to substantial obstruction of the lumen. [31]

It creates a chance for early diagnosis and treatment. Early-stage CRC is easier to treat and has a lower mortality rate than advanced CRC, and it can be found by screening. Aside from that by identifying and removing premalignant polyps before they develop into carcinoma, screening helps prevent CRC. Due to the widespread use of screening, CRC incidence and mortality rates have been dropping in the United States. [8] Approximately 25% of false-negative outcomes from conventional colonoscopies are caused by flat or depressed precancerous lesions.[9] An analysis of colonoscopy studies found that the overall miss rate was 22% and the miss rate for polyps smaller than 5 mm was 26%.[10]



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Scope of the work

This scope is a thin tube with a tiny video camera at the tip that allows your doctor to see inside your rectum and colon to look for polyps or other abnormalities. Polyps are little clumps of cells that grow inside the colon. Most of them are harmless and benign, but sometimes they can lead to colorectal cancer

Epidemiology

Colon cancer has the fourth-highest incident rate of any cancer worldwide, whereas rectum cancer has the eighth-highest incidence rate, according to GLOBOCAN 2018 data. Together, CRCs make up the third most prevalent type of cancer diagnosed worldwide, accounting for 11% of all cancer diagnoses. [12] According to the Epidemiology and Final Results programme, there were 132,700 new cases of colorectal cancer in the United States in 2015. There were around 49,700 cancer-related deaths, which represents 8% of all new cancer cases. [13, 14]

The estimated number of new cases of colon cancer in 2018 is 576,000 in men and 521,000 in women. For men aged 0-74, this incidence represents a cumulative risk of 1.51%; for women, it represents a cumulative risk of 1.12%. It is anticipated that 274,000 women and 430,000 men will be given rectum cancer diagnoses. They each have lifetime cumulative risks of 1.2% and.65%, respectively. [15]

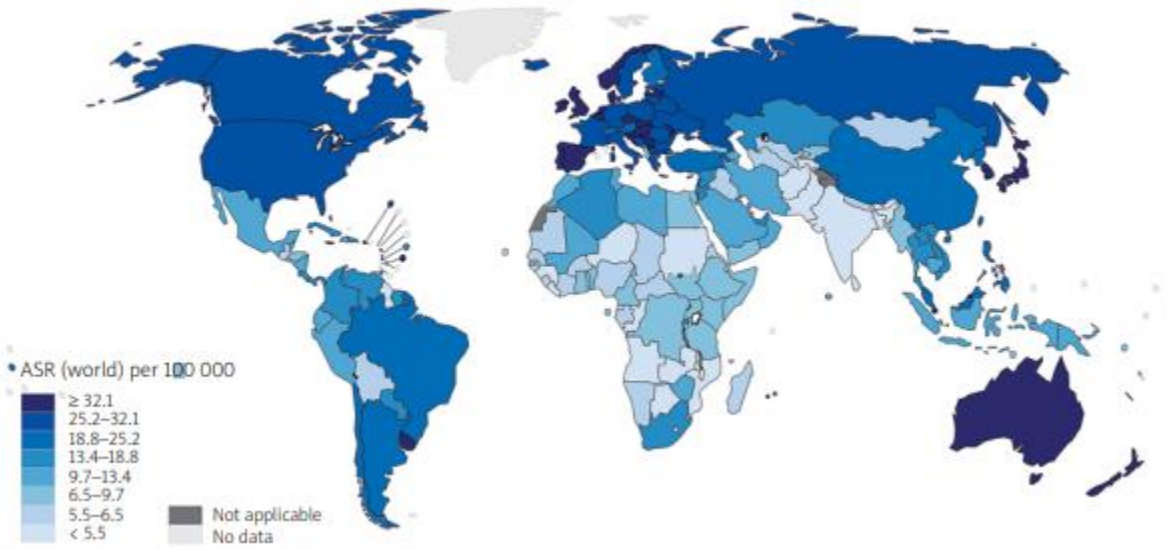
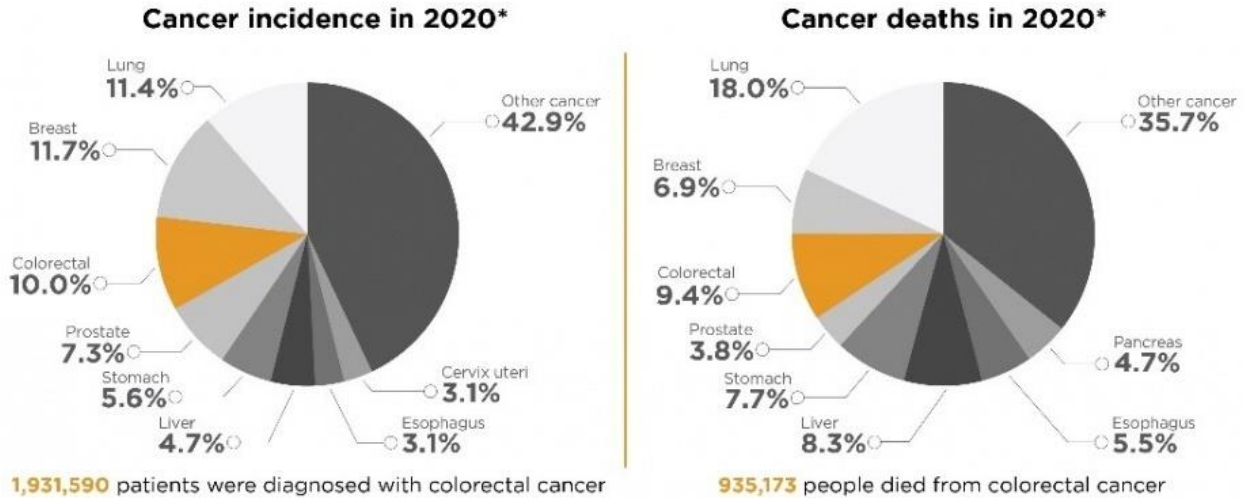


figure 1. Map showing estimated age-standardised incidence rates (world) in 2018, colorectum, both sexes, all ages (reproduced from http://globocan.iarc.fr/ [14])

Descriptive epidemiology

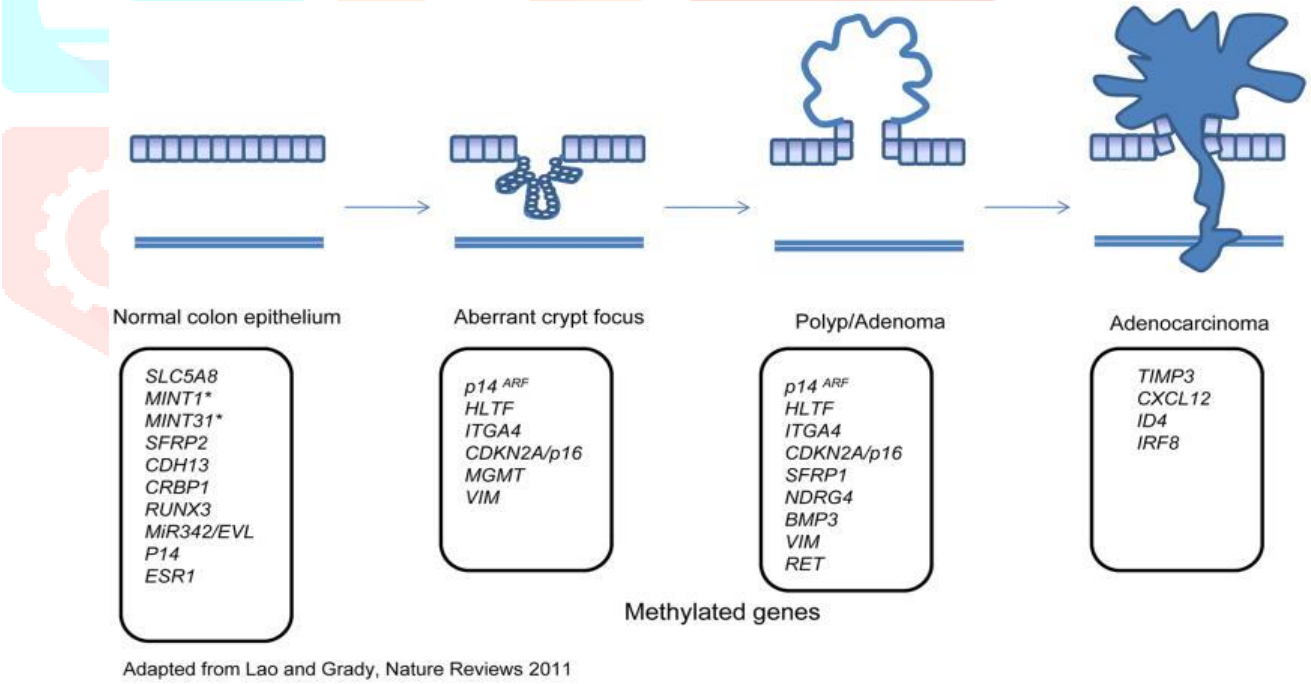
A projected 134,490 new instances of colorectal cancer (70,820 in men and 63,670 in women) and 49,190 deaths from the disease will occur in 2016. (26,020 and 23,170 in males and females, respectively). For new instances in men (8% of all new cancer cases), colorectal cancer is third only to lung and prostate cancer; for new cases in women (8% of all new cancer cases), colorectal cancer is third only to breast and lung cancer. Similar to this, only lung cancer and prostate cancer are anticipated to kill more American lives than colorectal cancer in 2016 for both men and women (representing 8% of all cancers).[16] As a result, colorectal cancer continues to be a serious burden on the population of the United States, with 1,177,556 expected to have the disease in 2013.[17] However, the incidence of colorectal cancer in the United States has been declining over the past few decades. According to national statistics, incidence and death rates have decreased, while 5-year survival rates have progressively increased. All races and both sexes combined, the age-adjusted colorectal cancer death rate in the United States decreased by 50% between 1975 and 2012. (28.58 deaths per 100,000 in 1976 to 14.45 deaths per 100,000 in 2013) [18]

However, the incidence of colorectal cancer in the United States has been declining over the past few decades. According to national statistics, incidence and death rates have decreased, while 5-year survival rates have progressively increased. The age-adjusted colorectal cancer death rate in the United States decreased by 50% between 1975 and 2012, affecting both sexes and all races (from 28.58 deaths per 100,000 in 1976 to 14.45 deaths per 100,000 in 2013) [6]. Similar to this, age-adjusted incidence rates for both sexes and all races in the U.S. decreased from the low- to mid-sixties per 100,000 in the 1970s and 1980s to 37.20 new cases per 100,000 in 2013 [7]. Furthermore, in the United States between 1975 and 2011 (again, for both races and both sexes)[19]



Molecular Pathogenesis

The accumulation of acquired genetic and epigenetic alterations that convert healthy glandular epithelial cells into invasive adenocarcinomas is one of the key factors in the development of colorectal cancer (CRC). The polyp to cancer progression sequence was put forth in the seminal and classic tumour progression model of Fearon and Vogelstein and entails a step that promotes the progression to more histologically advanced neoplasms (adenomas and sessile serrated polyps), followed by a step that transforms the tumours into invasive carcinoma (Figure 3). 1 The original Vogelstein and Fearon model has undergone multiple adjustments as a result of significant advancements in our understanding of the molecular aetiology of CRC since it was first put forth. For example, the initial model suggested [20, 21]



A subset of hyperplastic polyps, most likely microvesicular hyperplastic polyps, develop into serrated neoplasms (SSP or TSA), and a portion of these serrated neoplasms develop into colorectal cancer (CRC). [22] The condition known as the CpG Island Methylator Phenotype (CIMP), which is characterised by possessing an extremely high frequency of aberrantly methylated CpG dinucleotides, is linked to premalignant serrated polyps that more typically develop in the proximal colon 5. Contrarily, conventional tubular adenomas exhibit chromosome instability (CIN), a type of genomic instability that is characterised by aneuploidy and gains and losses of significant chunks of

chromosomes or entire chromosomes, and appear to be more frequently caused by biallelic inactivation of the APC tumor-suppressor gene. [23-25]

Risk Factor

It is estimated that genetic factors can account for 35% of the risk factors for getting colorectal cancer. The risk of colorectal cancer, as well as colon or rectal cancer, hereditary disorders like familial adenomatous polyposis, and hereditary colon cancer without polyposis, which is known as Lynch syndrome, are all significantly influenced by a person's family history. [26] It is linked to mutations in the MLH1, MSHS2, MSH6, and PMS2 genes, which are involved in the MMR, or mismatch repair, pathway for repairing improper DNA coupling and mating.

About 90% of the mutations reported in families with hereditary colon cancer, whether or not they have polyposis, are in MLH1 and MLH2 genes. APC germinal online mutations, repair MTHYU, SMAD4, BMPR (Alq3), and STK11, however, only account for fewer than 5% of all colorectal cancer cases. [27]

Factors that may increase your risk of colon cancer include:

- **Older age.** Colon cancer can be diagnosed at any age, but a majority of people with colon cancer are older than 50. The rates of colon cancer in people younger than 50 have been increasing, but doctors aren't sure why.
- **African-American race.** African-Americans have a greater risk of colon cancer than do people of other races.
- **A personal history of colorectal cancer or polyps.** If you've already had colon cancer or noncancerous colon polyps, you have a greater risk of colon cancer in the future.
- **Inflammatory intestinal conditions.** Chronic inflammatory diseases of the colon, such as ulcerative colitis and Crohn's disease, can increase your risk of colon cancer.
- **Inherited syndromes that increase colon cancer risk.** Some gene mutations passed through generations of your family can increase your risk of colon cancer significantly. Only a small percentage of colon cancers are linked to inherited genes. The most common inherited syndromes that increase colon cancer risk are familial adenomatous polyposis (FAP) and Lynch syndrome, which is also known as hereditary nonpolyposis colorectal cancer (HNPCC).
- **Family history of colon cancer.** You're more likely to develop colon cancer if you have a blood relative who has had the disease. If more than one family member has colon cancer or rectal cancer, your risk is even greater.
- **Low-fiber, high-fat diet.** Colon cancer and rectal cancer may be associated with a typical Western diet, which is low in fiber and high in fat and calories. Research in this area has had mixed results. Some studies have found an increased risk of colon cancer in people who eat diets high in red meat and processed meat.
- **A sedentary lifestyle.** People who are inactive are more likely to develop colon cancer. Getting regular physical activity may reduce your risk of colon cancer.
- **Diabetes.** People with diabetes or insulin resistance have an increased risk of colon cancer.
- **Obesity.** People who are obese have an increased risk of colon cancer and an increased risk of dying of colon cancer when compared with people considered normal weight.

- **Smoking.** People who smoke may have an increased risk of colon cancer.
- **Alcohol.** Heavy use of alcohol increases your risk of colon cancer.
- **Radiation therapy for cancer.** Radiation therapy directed at the abdomen to treat previous cancers increases the risk of colon cancer.

Protecting factor

Non-steroidal anti-inflammatory medicines (NSAIDs) lower the incidence of colorectal cancer, but it has been shown that their molecular foundation controls the overexpression of the EGFR, which is overexpressed in 80% of cases of colorectal cancer as an early event in the development of the tumour. Selective COX-2 inhibitors can be utilised as a chemopreventive strategy against colorectal cancer because the overexpression of cyclooxygenase 2 (COX-2) activates the transcription factor of the c-Jun dependent protein activator 1 (AP-1) that binds to the EGFR promoter.

However, it has been shown that consuming a diet high in fibre, along with eating a lot of fruits and vegetables, is a factor in the prevention of colorectal cancer and other malignancies. [28-30]

Sign & Symptoms

Signs and symptoms of colon cancer include:

- ✓ A persistent change in your bowel habits, including diarrhea or constipation or a change in the consistency of your stool
- ✓ Persistent abdominal discomfort, such as cramps, gas or pain
- ✓ A feeling that your bowel doesn't empty completely
- ✓ A change in bowel habits, such as diarrhea, constipation, or narrowing of the stool, that lasts for more than a few days
- ✓ A feeling that you need to have a bowel movement that's not relieved by having one
- ✓ Rectal bleeding with bright red blood
- ✓ Blood in the stool, which might make the stool look dark brown or black
- ✓ Cramping or abdominal (belly) pain
- ✓ Weakness and fatigue
- ✓ Unintended weight loss

Many people with colon cancer experience no symptoms in the early stages of the disease. When symptoms appear, they'll likely vary, depending on the cancer's size and location in your large intestine.

Treatment

Stage 0 cancer can be treated by removing cancer cells by colonoscopy. For stage I, II and III Cancer, it is necessary to perform surgery. A diagnosis of colorectal cancer is made either as a consequence of screening or after a patient presents with symptoms. A wide range of symptoms, including blood in the stools, changes in bowel habits, and stomach pain, might be linked to the condition. Other signs include exhaustion, weight loss, and signs of anaemia like a pale complexion and shortness of breath. These symptoms have a limited ability to predict the presence of colon cancer in an elderly patient, but they nonetheless demand additional clinical investigation. Numerous people are now receiving pre-clinical colorectal cancer diagnoses as a result of the widespread use of population screening. Although colonoscopy is the recommended method of inquiry in symptomatic patients, alternative endoscopic approaches are either available or being developed (Box 2). [32] Over the last 20 years, videochip endoscopes have significantly outperformed the original fiber-optic endoscopes in terms of colonoscopy image quality. Over time, videochip endoscopes continued to advance, resulting in higher resolution and a larger field of view. The current standard produces high-definition white light endoscopy by fusing high-power endoscopes with high-resolution videoscreens (hWLE). Although other methods for further image improvement in colonoscopy have been developed over the past ten years, white light colonoscopy continues to remain the gold standard for the detection of polyps and colorectal cancer. [33] T1 lesions with cancer cells are known as malignant polyps. have entered the submucosa from the muscularis mucosa. They make up 12% of the polyps removed in polypectomy series[34]. If the histology reveals that the patient has a malignant polyp, we must determine whether endoscopic resection is sufficient or whether the patient requires segmental colonic resection, endoscopic submucosal dissection, or endoscopic mucosal resection. Snare polypectomy is thought to be curative for pedunculated (Ip in Paris classification) malignant polyps if the resection margin is 2 mm or greater, the histology is not poorly differentiated, and there is no lymphovascular involvement. [35]

Diagnostic workup

For healthy individuals who do not exhibit any symptoms, doctors advise a number of screening tests to look for non-cancerous colon polyps or indicators of colon cancer. The probability of curing colon cancer is highest when it is discovered in its earliest stages. It has been demonstrated that screening lowers your risk of dying from colon cancer.

Doctors typically advise starting colon cancer screenings around age 45 for persons with an average risk of the disease. However, those who are at a higher risk, such as those who have a family history of colon cancer or are of African-American background, ought to think about screening earlier.

There are several screening options, each having advantages and disadvantages of its own. Together, you can select which tests are right for you after discussing your options with your doctor. In case a colonoscopy

Future perspective

The high incidence and mortality rate of colorectal cancer (CRC) has made it a major public health issue on a global scale. In order to give researchers and clinicians an updated picture of the most important insights into this disease, we have examined the most recent findings in the study of CRC research as well as the most recent findings in diagnostic and treatment approaches in this article.

Similar to this, the creation and application of novel, more accurate, and sensitive biomarkers will enhance diagnostic approaches in the near future, enabling physicians to identify CRC cases in the early stages of the disease

and so improve the prognosis for thousands of patients. Only the detection of MSI and KRAS mutations in tumour samples is utilised at this time for diagnostic and treatment planning reasons. Different tests based on miRNA expression and gene microarrays are being evaluated for the early diagnosis of CRC, and while they have a bright future, more research with bigger populations is required for their validation.

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