Trends, Risk Factors, and Preventions in Colorectal Cancer

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Definition of Cancer

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Thousands of new cells proliferate in our body every day as many cells die. New cells locate in organs and tissues when adapting to their normal structures. Normally uncontrolled proliferation is not seen. Multiple genes are affected in most tumors. This may result in loss of function of the tumor suppressor genes or activation of the oncogenes [1, 2].

Cancer tissue is characterized by uncontrolled and limitless cell proliferation. It does not resemble the properties of the tissues that it originated. Cancer cell proliferation continues by disrupting the original tissue structure. With this proliferation, cancer cells exceed the organ borders and destroy the organs beside or spread into distant areas and begin to proliferate in distant tissues. Cancer cells need blood vessels for growing. This vascularization provides oxygen and nutritional elements to cancer cells and also helps in eliminating metabolic waste from the area through systemic circulation. Angiogenesis is the basic rule of disease in tumor growth. Vascular endothelial growth factor A is an important factor in this process [3].

Tumor cells continue uncontrolled proliferation and invade the blood and lymph vessels by destroying their wall. If the tumor cells invade the blood vessels, they continue to move with venous circulation. Inferior mesenteric vein drains to liver via portal vein. After the liver, circulation continues through the inferior vena cava to the right atrium and right ventricle. Blood flows from the right ventricle to the lung through the right pulmonary artery and then to the left atrium and from the left ventricle to the whole body. Therefore, the first step for colon cancer cells on this path is the liver, and the next place is lungs and the other organs of the body. According to this knowledge, liver metastases are common in colon cancer because the liver is the first organ in the pathway of tumor cells. If cancer cells pass through

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liver, they come to the lungs and then spread to the entire body. In lymphatic spread, the cancer cell invades the lymphatic vessel first and then comes to the first lymph node in the path of that lymphatic drainage. There, while the lymph fluid infiltrates, most of the tumor cells attack and metastasize. Cancer cells that do not settle that lymph node can continue to settle in later lymph nodes. The lymph circulation continues like this and eventually enters the systemic circulation. These flow paths will be explained in detail in the anatomy section of the colon and rectum [4, 5].

Breast cancer is the cancer type which most causes death in women, whereas in men lung cancer is the cancer type which most causes death. In some countries, colorectal cancer (CRC) is the second leading cause of cancer-related deaths. Colorectal cancer occurs more frequently in Australia, New Zealand, Europe, and North America, but less frequently in Africa and South-Central Asia [6, 7].

Risk Factors for Colorectal Cancer Family history, inflammatory bowel diseases (crohn, colitis ulcerosis), diabetes, smoking, alcohol use, red meat consumption, processed meat consumption, presence of colon polyps, obesity, low physical activity, and low vegetable and fruit consumption are risk factors that increase CRC incidence.

Risk Decreasing Factors Acetyl cysteic acid and multivitamin use (supplemental folate and calcium), physical activity, and calcium and milk consumption can reduce the risk for colorectal cancer [8, 9].

We will explain these issues in detail in the following of this chapter.

Risk Increasing Factors for Colorectal Cancer

Family History

People with family history of CRC or who have colorectal adenoma (CRA) have a high risk of developing CRC. Colorectal adenomas will be discussed in detail in other sections. Relatives of patients diagnosed with CRC at a young age also have high risk [10].

First-degree relatives of patients with CRC have a high risk for CRC than the second and third degree relatives. Patients that have CRC in first-degree relatives double the risk of having CRC [11, 12].

It has been shown that the incidence of colorectal cancer is reduced by removing the polyps detected during colonoscopic scans in patients with a family history of colorectal cancer. According to our knowledge, the removal of adenomatous polyps reduces the risk of developing colorectal cancer. Therefore, adenomatous polyps must be removed in patients with or without family history [13, 14].

The American College of Gastroenterology (ACG) and the American Society of Gastrointestinal Endoscopy (ASGE) and the American Association of Gastroenterology (AGA) generally recommend colonoscopy screening every 5 years after the age of 40

for first-degree relatives of patients with colon cancer before the age of 60 years. While ASGE and AGA recommend colonoscopic screening after the age of 40 to first-degree relatives of patients diagnosed with colon cancer after age 60, ACG recommends colonoscopy after age 50 [15].

Hereditary Syndromes

The risk of colon cancer is high in patients with hereditary syndrome. These syndromes are named familial adenomatous polyposis and hereditary nonpolyposis coli [16, 17].

Familial adenomatous polyposis (FAP) is an autosomal dominant disease. In this disease, there are many adenomatous polyps, and if these polyps are not detected and managed early, they can progress to colorectal cancer. Extraintestinal symptoms (osteomas, dental anomalies, etc.) may be present in 70% of the cases. In patients with the diagnosis of FAP or in family members with high-risk factors, annual sigmoidoscopy at 10–12 years of age is recommended for screening the lower gastrointestinal tract. If polyp is detected in sigmoidoscopy, total colonoscopy is recommended [18–20].

Hereditary nonpolyposis coli is also known as Lynch syndrome, and it is an autosomal dominant disease. It is a disease which many malignancies can accompany. The most common malignancy is presented as colorectal cancer. Other malignancies can be sorted as ovary cancer, endometrium cancer, intestinal cancer, hepatobiliary tract cancer, stomach cancer, urinary tract cancer, etc. In this disease, high-quality surveillance colonoscopy is recommended starting from the age of 20–25 every 1–2 years. Or screening colonoscopy is recommended to be performed 2–5 years before the earliest age of diagnosis in the family [21–26].

Gender

Advanced colorectal neoplasia is more common in men than in women [27]. Right colon cancer is more common in women than in men [28].

Previous Treatment for Certain Cancers

It is reported that the risk of colorectal cancer is increased in patients having radiotherapy due to testicular cancer. It is also reported that the risk of cancer is increased in men with prostate cancer. This may be due to radiotherapy given for prostate cancer. There is a relative risk for colorectal cancer development in women having pelvic radiation due to gynecological cancer. During radiotherapy, the rectum is exposed to radiation due to being nearer to gynecological organs. The American Cancer Society and other medical organizations recommend earlier screening for these patients with increased risk of colorectal cancer. Radiotherapy given directly to the abdomen is another risk factor that increases colon cancer [16, 29, 30].

Night Shift Work

There are researches that working on night shifts three times a month for 15 years may increase colon cancer in women. Studies have shown that melatonin levels may be effective in the risk of developing colorectal cancer. More clinical research is needed on this subject. Night shift work is also reported to increase risk for breast cancer, prostate cancer, and endometrial cancer [29, 31–33].

Presence of Multiple Primary Cancers

There are reports that approximately 10% of patients may develop a second primary tumor within the first 10 years after primary tumor development [34].

Multiple primary tumors can develop in the same patient at the same time or at a different time. It is reported to be between 0.7% and 11.7% of all carcinomas. Multiple primary tumors are more common in age older than 65. Although multiple primary cancers are rare, nowadays we see more common. The development of diagnostic techniques and longer survival than previous times has been shown to be factors in this increase in frequency. Multiple primary tumors can be divided as synchronous and metachronous. If the second primary tumor is detected within 6 months after the diagnosis of the first primary tumor, it is called synchronous tumor. If the second primary tumor is diagnosed after 6 months, it is called a meta-chronous tumor [35, 36].

Age

Although colon cancer may be seen at a young age, its incidence increases with age. It is very rare in pediatric ages. Annual incidence in pediatric age is approximately 1 case per million individuals. It is most commonly seen between the ages 60 and 75. In colorectal cancers, 90% of new cases and 94% of deaths occur in people older than 50 years [37, 38].

Inflammatory Bowel Diseases (Crohn, Colitis Ulcerosa)

The coexistence of chronic inflammation and cancer has been demonstrated by studies between inflammatory bowel disease and colon cancer. People with inflammatory bowel disease have a higher risk of developing colorectal cancer. Especially if the disease persists for a long time, if there is extensive colonic involvement, if the patient has pseudopolyps, and if the disease is associated with primary sclerosing cholangitis, patients have a higher risk for colorectal cancer. People with chronic ulcerative colitis or Crohn's disease have a five- to sevenfold increased risk of developing colon cancer compared to healthy individuals. It is generally accepted that this risk develops after 8 years of illness. Initial screening for colon cancer is

recommended in patients with inflammatory bowel disease 8 years after the onset of the disease [39–41].

The lifetime risk of developing colorectal cancer in patients with ulcerative colitis is between 5% and 13.5% [42, 43].

There is an increased risk for colorectal cancer and dysplasia in patients with Crohn's colitis and primary sclerosing cholangitis [44].

Diabetes Mellitus

Studies have shown that patients with type 2 diabetes have a 27% higher risk of colorectal cancer than non-diabetic patients. The risk of developing colorectal cancer in patients with diabetes is both validating for men and women. Type 2 diabetes creates risk factors such as hyperinsulinemia, insulin resistance, hyperglycemia, or hypertriglyceridemia for colorectal carcinogenesis. Insulin can stimulate cell proliferation. This stimulation can be directed with the insulin receptor or insulin like growth factor (IGF)-I receptor. Studies have shown that high levels of insulin, C-peptide (a marker of insulin secretion), or IGF-I may increase the risk of colorectal cancer. As intestinal transit time is prolonged in diabetes, it may lead to an increased risk of colorectal cancer. With prolonged bowel transit time, colon mucosa contacts potential carcinogenesis and fecal bile acids for longer periods. Even fecal acids have been shown to promote colorectal cancer in animal models. Some studies have reported increased colorectal cancer mortality in patients with diabetes, whereas some studies have not identified this risk. In a study, the risk of colon cancer recurrence is reported as similar in patients with and without diabetes at the time of diagnosis. There are studies reporting that type 2 diabetes is a potential risk for CRC to start at an early age in patients with type 2 diabetes, and early screening might be appropriate in patients with type 2 diabetes [45–50].

Smoking

There are many carcinogens in cigarette smoke. These carcinogens can cause changes in DNA, and they can even cause irreversible damage and colon cancer in the colon mucosa. Carcinogens in cigarette smoke can come to the colon mucosa through the blood circulation or they may come to mucosa because of ingestion of smoke-contaminated saliva [51].

Some studies showed that smoking duration is associated with colorectal polyps. Smokers have an 18% greater risk of developing colorectal cancer than nonsmokers. Proximal colon cancer risk is reported to be higher in these patients than distal colon cancer risk. However, other studies reported no significant difference between proximal and distal colon cancer risks. Therefore, colorectal cancer screening may be recommended more frequently in smokers. American College of Gastroenterology supports screening for colorectal cancer in older smokers at an age of 45 instead of 50 [7, 51–56].

Smoking is the cause of microvascular disease that leads tissue ischemia. Tissue ischemia may pose a risk for anastomosis. There are also clinical studies reporting that the risk of anastomotic leakage after colon surgery is higher in smokers than in other patients. Therefore, caution should be exercised against the risk of postoperative fistula [57, 58].

Alcohol Use

Individuals using alcohol have a modest increased risk for colon cancer. There is a connection between alcohol use and oral cavity cancer, pharynx cancer, larynx cancer, esophagus cancer, liver cancer, female breast cancer, and colorectal cancer. The risk of colorectal cancer associated with alcohol consumption is similar in both men and women. Alcohol consumption is divided into three groups as mild, moderate, and severe in the meta-analysis published by Fedirko et al. Heavy consumers are defined as who consume 50 g/day or more of alcohol, and there are 52% more likely to develop colorectal cancer than nonalcohol users. Moderate alcohol users are defined as those who consume 12.6–49.9 g/day ethanol, and the risk is 21% higher in these people. Those who consume mild alcohol are those who consume 12.5 g/day or less ethanol, and the risk is 0–7% compared to those who do not consume alcohol. These results show that the risk of colorectal cancer depends on alcohol consumption dose. In correlation with the amount of alcohol consumption, the risk of developing colorectal cancer increases. It has been reported that alcohol consumption is a risk factor for anastomotic leakage in patients who underwent anastomosis after resection due to colorectal cancer [58–62].

In a study, it was found that increased risk of disease recurrence and shorter time to disease recurrence was higher in patients who used alcohol in early-stage rectum cancer than those who did not use alcohol. Ethanol intake is associated with poor prognosis and lower overall survival counts in cases of CRC [63, 64].

Red Meat and Processed Meat Consumption

High rate red meat consumption is associated with a high risk of colon cancer occurrence. Higher green leafy vegetable (GLV) consumption may reduce this risk [65].

Possible biological mechanisms that may explain the increased risk of colorectal cancer associated with consumption of red meat and processed meats are indicated. Potential mutagenic effects of heterocyclic amines present in highly cooked meat may be a reason. The second mechanism is the endogenous formation of N-nitroso compounds in the gastrointestinal tract. Depending on the dose of red meat intake, endogenous formation of nitroso compounds occurs in humans. Nitrites or nitrates are used as additives to prevent spoilage of meat. These form exogenous nitrites which work just like endogenous nitrites. The risk of cancer caused by taking cured

meats and red meats is a moderate risk (20–30%). It is recommended not to eat more than 500 g of red meat per week and avoid processed meat [66–70].

Gallbladder Diseases

Cholecystectomy is a moderate risk factor for colon cancer. This risk has not been shown for distal colon and rectal cancer. Biological mechanisms associated with intestinal exposure of bile may be responsible for this risk. The presence of gallstone increases the risk of colonic adenoma. Chiong et al. reported in their meta-analysis that cholelithiasis increases the risk of rectal cancer. There are also studies reporting that reflux of bile into the stomach may be a risk factor for gastric cancer in patients with cholecystectomy [71–76].

Presence of Adenomatous Polyp

The presence of adenomatous polyps is a risk factor for colon cancer. Colonic adenomatous polyps may show malignant transformation. These risk factors can be classified as high risk and low risk.

Large size (especially >1.5 cm), sessile or flat formation, severe dysplasia, presence of squamous metaplasia, villous architecture, and polyposis syndrome (multiple polyps) are defined as high-risk factors for polyps. On the other hand, small size (especially <1.0 cm), pedunculated formation, mild dysplasia, no metaplastic areas, tubular architecture, and single polyp are identified as low-risk factors.

The cancer focus within the adenomatous polyp will progress and lead to invasive cancer; therefore, polyp excision prevents this risk [77–80].

Obesity

Obesity has been implicated as a risk factor for colorectal cancer. Obesity has also been shown to be a risk factor for postmenopausal breast cancer, endometrial cancer, kidney cancer, and esophageal cancer. In a study conducted in postmenopausal women showed that the existence and duration of obesity are risk factors for cancer development. In addition, there are also studies that reported this risk can be decreased with regression of the obesity [81, 82].

Obesity increases the risk of colon cancer in men more than in women. According to clinical studies, it is reported that the presence of abdominal obesity is more risky than subcutaneous fat tissue in colorectal cancer etiology [83–86].

Leptin secreted from adipose tissue controls the body fat storage and stimulates cell proliferation. Circulatory leptin levels increase as adipose tissue mass increases. Studies have reported that leptin may be responsible for the development of colorectal adenoma [87].

There are also studies that make obesity responsible for colorectal cancer recurrence, treatment outcomes, and survival [88].

Metabolic Syndrome

The condition consisting of three or more components is called metabolic syndrome. These components are defined as high blood pressure, increased waist circumference, hypertriglyceridemia, low level of HDL cholesterol, and diabetes. The risk of colon cancer, liver cancer, pancreas cancer, breast cancer, and endometrial cancer increases in metabolic syndrome [89–91].

Infections

Helicobacter pylori can settle in the stomach and cause gastritis, ulcers, and gastric neoplasia. Helicobacter pylori infection should be considered in the risk of colonic adenomatous polyps and colon cancer [92–95].

Schistosomiasis is a common parasitic disease in underdeveloped and developing countries. Contaminated water can cause infection. Chronic schistosomiasis can cause cystitis and fibrosis. It can also be a risk factor for bladder cancer, liver cancer, colonic adenomatous polyps, and colorectal cancer [39, 96].

Human papilloma virus infection is associated with cervical cancer. In clinical studies, association between human papillomavirus infection and colorectal cancer has been identified. The risk of colon cancer increases tenfold in people with human papillomavirus infection than in healthy individuals [97–99].

Human cytomegalovirus (HCMV) is a beta-herpes virus and can be found endemically. It can lead to life-threatening diseases in immunosuppressive individuals. Studies have shown that CMV nucleic acids and proteins can be found in neoplastic cells in colorectal polyps and adenocarcinomas. It is informed that this virus infection may have an important role in colon cancer [100, 101].

There are also studies that indicate an increased risk of colorectal cancer in people with HIV infection [102, 103].

Organ Transplantation

Organ transplantation increases the risk of cancer in other organs. Adami et al. reported the risk of colorectal cancer fourfold higher in patients undergoing organ transplantation. In addition, in a study, it was reported that proximal colon cancer increased in patients who underwent organ transplants, whereas there was no increase in distal colon cancer [104, 105].

Nonalcoholic Steatohepatitis

Nonalcoholic fatty liver disease is a risk factor for colorectal neoplasm and colorectal cancer. Also nonalcoholic fatty liver disease has an additive effect on the development of colorectal cancer. In a study published in 2011, Wong et al. reported that nonalcoholic steatohepatitis was highly associated with colorectal adenoma and advanced neoplasm. They also reported that these adenomas were more common in the right colon, and they recommended colorectal cancer screening for these highly risked patients [106, 107].

Gallbladder Polyps

There are studies suggesting the association between gallbladder polyps and proximal colon polyps [108].

Risk-Reducing Factors for Colorectal Cancer

Acetylsalicylic Acid

The use of prophylactic aspirin is currently recommended for the possible risk of thromboembolism. On the other hand, aspirin use can cause bleeding complications and hemostasis problems [109].

The use of aspirin also reduces the recurrence of adenomatous polyps. The mechanism on this issue is not fully known. There are studies reporting that low-dose (75–300 mg/day) aspirin use reduces colon cancer incidence by 76% and mortality by 65% in the long term (median time 18 years). Aspirin is known to reduce the incidence and mortality of colorectal cancer. In another study, it was suggested that the use of intermittent aspirin or naproxen inhibits the progression of colon adenomas to colonic invasive adenocancer [109–113].

Statins

Statin is used in the treatment of hypercholesterolemia. Some studies have reported that statin use reduces proximal colon cancer in men and rectal cancer risk in both genders. Another case-control study has shown that statin reduces the risk of colorectal cancer. However, in most cohort studies, the benefit of statin could not be found [114, 115].

Bisphosphonates

Bisphosphonates are often used in treatment of osteoporosis. Some studies have reported that the use of bisphosphonates for more than a year reduces the risk of colorectal cancer by 59% [116].

Calcium and Vitamin D

It was suggested that calcium combined with secondary bile acids and ionized fatty acids reduced the risk of colon cancer by forming insoluble soap in the colon lumen. It is also reported that colon cancer is associated with vitamin D deficiency. Studies showed that vitamin D deficiency increases the risk of colorectal cancer, whereas vitamin D intake reduces the risk of colorectal cancer [117–120].

Physical Activity

Physical activity has a risk-reducing effect for many types of cancer (e.g., breast cancer, endometrial cancer, prostate cancer, colon cancer). Physical activity can prevent about 15% of colon cancers. For cancer prevention, 30–60 min of moderate-vigorous intensity physical activity is recommended 5 days in a week. Since physical activity increases bowel movements, it may be effective in reducing the risk of colon cancer by reducing the passage duration of the carcinogenic substances [121–126].

Fish Consumption

Some studies showed that consuming more than two servings of fish each week may reduce the risk of colorectal cancer recurrence [127].

Serum Cholesterol Level

In a clinical study, it was reported that high concentration of serum HDL reduces the risk of colon cancer [128].

Dietary Fiber

There are studies reported that meals with fiber-rich grain reduce the risk of colorectal cancer. Especially the cereal fibers and whole grains are mentioned to reduce the risk of colorectal cancer. The contact time of toxic substances with the colon mucosa is reduced by reducing the intestinal passage time and constipation with taking fibrous foods [129–131].

Postmenopausal Hormone Therapy

It is reported that hormone therapy given to postmenopausal women reduces the risk of colorectal cancer [132–135].

Screening Program

Screening programs have an important role in decreasing the incidence and mortality of CRC. There is a generally accepted opinion that the age of onset of CRC screening should be 50 years. However nowadays, some groups advise that CRC screening starts from 45 years old. The side effects of colonoscopy are rare, but these side effects may increase in the elderly individuals due to their comorbidities. For this reason, some guidelines recommend the screening program to terminate at the age of 75, while others recommend it to end at the age of 80. Major risk factors for CRC are defined as family history, medical history, presence of colorectal polyps, and chronic inflammatory bowel disease history. Also familial adenomatous polyposis and hereditary nonpolyposis colorectal cancer (Lynch syndrome) are determined as high-risk factor for CRC. Smoking increases the development of adenomatous polyps, and smokers have a higher incidence of rectal cancer. The success of screening programs may increase with the increase of the general population education [8, 136].

In addition, colorectal cancer can be prevented by removing adenomatous polyps which can cause cancer with screening colonoscopy. Another advantage of the screening program is the early recognition of CRC. Early diagnosis of CRC has a higher chance for treatment. Colorectal cancers usually develop in 10–15 years. It typically begins as a noncancerous polyp; then, the polyp may become cancerous. Such polyps are called adenomatous polyps or adenomas. Ten percent of adenomas can develop to cancer. Adenomas are quite common and one third or half of individuals can have one or more adenomas. Ninety-six percent of colorectal cancers are adenocarcinomas, and most of these cancers develop from adenomatous polyps. When cancer occurs, it begins to grow in the colon wall and tries to invade blood and lymph vessels. The tumoral cells make lymph node, liver, and spleen metastasis due to these vascular and lymphatic invasions. On the other hand, tumor can invade the organs in abdominal cavity according to its localization [137–140].

Green Tea Consumption

There is a weak relationship between more green tea consumption and a reduced risk of male colon cancer [141].

Prevention of Colorectal Cancer

Colonoscopy screening reduces colorectal cancer risk by 90%. Screening colonoscopy can prevent cancer by detecting precancerous polyps. There are studies reporting that the prevalence of adenomatous polyps at the age of 50 is 25% in men and 15% in women. The majority of these polyps are found as asymptomatic, and the excision of these polyps during colonoscopy is important in preventing colon cancer [142, 143].

Some studies report that changing lifestyle reduces the risk of colorectal cancer [144].

It has been reported that consumption of fiber-rich fruit and vegetables reduces the risk of colorectal cancer. It has been suggested that the fibers contained in our food absorb or dilute fecal carcinogens, modulate colonic transit time, even alter acid metabolism, decrease colonic pH, and increase short-chain fatty acid production. High intake of fiber or vegetables is reported to reduce the risk of colon cancer by 40–50%. Red meat consumption is also known to increase the risk of colorectal cancer. Instead of red meat, alternative animal proteins such as fish can be taken. Reduction or discontinuation of alcohol intake will reduce the risk of colorectal cancer. Smoking is strictly forbidden. Also, obesity should be avoided, visceral fat mass should be reduced, and regular sports should be done. There are studies reporting that colorectal cancer can be reduced by 24% by doing physical activity. Calcium is thought to reduce the risk of colon cancer by binding to toxic secondary biliary acids [117, 145–149].

The most important risk in colon cancer is older ages. The greatest success in preventing colorectal cancer depends on screening tests. Precancerous lesions such as adenomatous polyps can be detected by screening tests before the cancer appearance, and the cancer can be prevented by polypectomy.

Colorectal cancer screening tests can be divided into two groups:

1. Stool tests: occult blood and exfoliated DNA tests
2. Structural examinations: colonoscopy and virtual colonoscopy

Stool tests for occult blood test are known as guaiac test and fecal immunochemical test (FIT) [150].

Guaiac Test

The Guaiac test is a test that measures occult blood in the stool. Some foods may affect this test result. Therefore, before 3 days of the test, patients must stop eating red meat, cantaloupe, uncooked broccoli, turnip, radish, and horseradish. Nonsteroidal anti-inflammatory drugs, vitamin C, aspirin, ibuprofen, and naproxen may also affect the test result. A negative test means that there is no blood in the stool, whereas a positive result indicates that there is too little blood to be seen in the stool. There are studies reporting the false-positive rate as 11% with normal diet. Also false-negative results can reach up to 48% [151, 152].

Fecal Immunochemical Test (FIT)

This test is known as a new fecal occult blood test. This test is performed with monoclonal antibodies that produced against human hemoglobin beta subunit. If the test result comes normal, it means that there is no blood in the stool. The sensitivity of this test is high, and FIT is seen more sensitive to colorectal cancer than guaiac test [153, 154].

Exfoliated DNA Test

Stool DNA test can detect colorectal cancer and large adenomas with high sensitivity. This enables the patient's early diagnosis and curability. Serrated sessile polyps greater than 1 cm can be recognized by this method [155, 156].

Colorectal screening is recommended in women and men. However, colonoscopy should be performed within the indications mentioned in Chap. 3.

Screening options may vary depending on risks, patient preference, and access. FOBT and FIT can be done once a year. The stool DNA test is a newly recommended test, and the interval for this test is uncertain. If adenomatous precancerous condition is detected in colonoscopy, colonoscopy must be performed more frequently (see Chap. 3) [157–160].

For positive results, indirect tests, such as the occult blood test, require the lesions in the colon to bleed and to pass this blood with feces. Therefore, it is not possible to identify non-bleeding lesions with these tests. For this reason, colonoscopic examination is thought to be more effective in detecting bleeding and non-bleeding colonic lesions early.

American Cancer Society Guideline for Colorectal Cancer Screening recommends people at average risk of colorectal cancer to start regular screening at age 45. For screening, people are considered to be at average risk if they do not have one of the following criteria:

- A personal history of CRC or certain types of polyps
- A family history of CRC
- A personal history of inflammatory bowel disease (ulcerative colitis or Crohn's disease)
- A confirmed or suspected hereditary colorectal cancer syndrome, such as familial adenomatous polyposis (FAP) or Lynch syndrome
- A personal history of getting radiation therapy to the abdomen or pelvic area to treat for a prior cancer [161]

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