

Review article

Colorectal cancer screening: a minireview

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Abstract

Background: Colorectal cancer is increasing worldwide, especially in young populations. **Objective:** In this minireview, we discussed the different screening methods for colorectal cancer in the general population. **Conclusions:** screening colorectal cancer by other methods is an effective way to diagnose colorectal cancer early.

Keywords: screening, colorectal cancer, minireview.

1. Introduction

Rationale

Worldwide, colorectal cancer (CRC) is the third most commonly diagnosed cancer in males and the second in females. In 2018, the new cases were 1.8 million, and deaths were nearly 861,000. Rates are higher in males than in females. Australia and New Zealand have the highest incidence rates, while the lowest rates are in Africa and South-Central Asia(1,2). The CRC is the 7th most commonly diagnosed cancer in Egypt, representing 3.47% and 3% of all male and female cancers (3).

The incidence of CRC increases with age, beginning around the age of 40 with an approximate doubling with each successive decade reaching the age of 80(1,4).

The American Cancer Society (ACS) recommends the age of 45 to start screening for people at average risk of colorectal cancer. This can be done either by a sensitive test that looks for signs of cancer in the stool (a stool-based test) or by investigating the colon and rectum directly (a visual exam). People in good health should continue regular colorectal cancer screening through 75. For people ages 76 through 85, screening should be based on a doctor's preference, life expectancy, overall health, and the previous screening history. Older adults should be counseled before undergoing screening or surveillance colonoscopy due to the increased risk of colonoscopy (17). People over 85 should no longer get colorectal cancer screening; this is the proposed protocol for all people(5,6).

People at high risk of colorectal cancer might need to start colorectal cancer screening before age 45. This includes people with(1,5,6):

- A positive family history of colorectal cancer or certain types of polyps
- A previous personal history of colorectal cancer or certain types of polyps
- A personal history of inflammatory bowel disease (ulcerative colitis or Crohn's disease)
- A known family history of a hereditary colorectal cancer syndrome, such as familial adenomatous polyposis (FAP) or Lynch syndrome (also known as hereditary non-polyposis colon cancer or HNPCC)
- A previous history of radiation to the abdomen or the pelvic area to treat previous cancer.

Objectives

This minireview discussed the different screening methods for colorectal cancer in the general population.

2. Methods

We searched the web for any data related to screening colorectal cancer. Also, we extensively review the guidelines of different gastroenterological societies.

Search

We use an entire electronic search strategy for at least one database.

Screening Guidelines

Updated guidelines of the various societies regarding colorectal cancer screening

Test options for colorectal cancer screening

Several test options are available for colorectal cancer screening:

Stool-based tests

- Highly sensitive fecal immunochemical test (FIT) every year
- Highly sensitive guaiac-based fecal occult blood test (gFOBT) every year
- Multi-targeted stool DNA test (MT- sDNA) every three years

Visual exams of the colon and rectum

- **Colonoscopy every ten years**
- CT colonography (virtual colonoscopy) every five years
- Flexible sigmoidoscopy (FSIG) every five years (5,6)

Stool-based tests

These tests look for possible signs of colorectal cancer in the stool. Many people find these tests more comfortable than tests like a colonoscopy, which could be done at home. However, these tests need to be done more often.

Moreover, if the result from one of these stool tests is positive, we still need a colonoscopy to ensure the presence of CRC; this means that these tests are helpful negative tests while the visual exams of the colon and rectum are the gold standard for sure diagnosis. Three types of stool tests are available – FIT, guaiac-based FOBT, and fecal DNA test (5,6).

1- Fecal immunochemical test (FIT)

It is used for hidden blood in stool or occult as it reacts to part of the hemoglobin protein of humans that is found in RBCs. The blood vessels in the larger colorectal polyps & cancers are often fragile and easily damaged by the passage of stool. Usually, there is bleeding into the colon or the rectum due to the damaged blood vessels, but rarely seen in the stool because the bleeding is not enough to be seen(5).

So, cards or tubes are used to collect a small amount of stool; we must ensure that there are no drug or dietary restrictions before the test (vitamins and food do not affect the test). It is not common for this test to react to bleeding from any part of the digestive tract other than the colon or the rectum. The FIT test targets the hemoglobin in the lower part of the GI tract, so it is less likely to react to bleeding in the stomach. That is because hemoglobin of the upper digestive tract will be degraded when it reaches the lower GI tract. This character allows us to detect any disease with bleeding in the lower GI tract; therefore, the FIT test is specific for lower GI tract bleeding (7).

Depending on the FIT test, if the result is positive, we will need a colonoscopy for further investigation. As cancer and polyps are not the only causes of blood in the stool, for example, hemorrhoids, ulcers, and other conditions causing bleeding, the blood in the stool can be found. In addition, the FIT test may not detect blood from further up the digestive tract (e.g., the stomach), which means it is more specific for finding blood coming from the lower gastrointestinal tract than the FOBT(8).

2- Guaiac-based fecal occult blood test (gFOBT)

The guaiac-based fecal occult blood test (gFOBT) detects occult (hidden) blood in the stool through a chemical reaction rather than a FIT. However, like the FIT, this test cannot tell if the blood is from the colon or other parts of the digestive tract(5). Its sensitivity and specificity for CRC detection are lower than

the FIT test. The gFOBT relies on peroxidase-like activity between heme and guaiac, which can be affected by many factors in the daily diet without distinguishing between upper and lower gastrointestinal (GI) tract bleeding. Therefore, this test cannot tell if the blood is from the colon or other parts of the digestive tract(5,9).

Before the test: Some foods or drugs can affect the results of this test, so the patient should be instructed to avoid the following before this test:

- Non-steroidal anti-inflammatory drugs (NSAIDs) for seven days before testing (They can cause bleeding, leading to a false-positive result).
- Vitamin C above 250 mg daily from either supplements or citrus fruits and juices for three days before testing can affect the chemicals in the test and make the resulting negative, even if blood is present.
- Red meats (beef, lamb, or liver) for three days before testing because the blood components in the meat may cause a positive test result(9,10).

3-Fecal DNA test

We can detect the abnormal DNA or the epigastric markers from colorectal lesions by detecting them based on the natural shedding of cancerous or precancerous cells into the colorectal tract. The fecal DNA test aims at detecting the DNA mutations, microsatellite instability, impaired DNA mismatch repair, and abnormal methylation(5,11). For example, DNA tests are based on methylation and mutation analysis, the detection of long-chain DNA, and microsatellite instability. In addition, we can use the single or the multiple DNA markers to optimize performance in individual tests(11).

A case-control series involving 252 patients with CRC, 133 with adenomas ≥ 1 cm in diameter, and 293 with average colonoscopy results, reported specificities for detecting cancer of $>85\%$ and sensitivity of $>50\%$ for large adenomas using the best-performing tests, with a focus on four methylated genes (NDRG4, BMP3, VIM, and TFPI2), a mutant form of KRAS, and the α -actin gene ACTA1 as a reference(12).

Similarly, RNA markers, including MMP7 (encoding matrix metalloproteinase-7, also known as matrilysin) and PTGS2 (encoding prostaglandin G/H synthase 2), have been assessed in smaller case-control studies, alone or in combination with each other, based on the assumption that these markers are differentially expressed in cancer and healthy tissues(13).

Visual (structural) exams

These tests look at the structure of the inside of the colon and rectum for any abnormal areas that might be cancer or polyps. These tests can be done less often than stool-based tests, but they require more preparation ahead of time and can have some risks not seen with stool-based tests.

1- Colonoscopy

Colonoscopy is considered the gold standard for the diagnosis of colorectal cancer. It has a very high diagnostic value and therapeutic accuracy and can quickly assess the tumor's location. In addition, the technique enables us to take a biopsy and so confirm the diagnosis. Colonoscopy is the only screening technique that provides both a diagnostic and a therapeutic effect (1).

The Technique

For this test, we look at the colon and rectum with a colonoscope with a flexible tube about a finger's width with a light and tiny video camera at the end. It is put through the anus and then into the rectum and colon. We use special instruments that pass through the colonoscope to take a biopsy or remove any suspicious areas such as polyps(5).

Before the test: The doctor must know any patient's medicines (including daily aspirin, vitamins, or supplements). The patient might need to change how he handles them before the test. The colon and rectum must be empty and clean to see the entire inner lining during the trial. This can be done by different means such as pills, fluids, and enemas or may be combinations of these. We tell the patient to drink large amounts of a liquid laxative solution the night before the procedure. Also, this leads to taking much time in the bathroom. Therefore, some people may not want to do this test because the process is not pleasant. However, newer kits are now available to evacuate the bowel and are better tolerated than the previously mentioned ones. The patient arranges for someone to take him home after finishing the test because of the sedative; he will take before the procedure. So, that is why we see so many centers that do colonoscopies, do not discharge people to go home in a cab. If transportation might be a problem, talk with the health care provider about the hospital or surgery center policy. Depending on the situation, other resources may be available to get back home (5,6).

During the test: The test takes 30 minutes, but if one or more polyps are removed, it can take longer. Before the test starts, the patient will be given a sedative to relax him during the procedure, and for some people, this medicine makes them forget about the process afterward. The patient will wake up after the test is over, but they might not be fully awake until later in the day. During the trial, we will ask him to lie on his side with his knees pulled up and a drape covering him, and we should monitor his heart rate, blood pressure, and respiratory rate during and after the procedure. At first, insert a gloved finger into the rectum to examine it before putting in the colonoscopy, and it should be lubricated to be easily inserted into the rectum. Once inside the rectum, it is introduced to the beginning of the colon (the caecum). If the patient wakes up, he might feel an urge to have a bowel movement when the colonoscopy is inserted or pushed further up the colon. We also put air into the colonoscopy through the colonoscopy to quickly see the colon's lining.

Moreover, to ease any discomfort, we ask the patient to breathe deeply and slowly through his mouth. We will look at the inner walls of the colon while slowly removing the colonoscopy. If a small polyp is found, it may be removed and then sent to the lab to check if it turned into cancer. If a giant polyp or tumor is seen, a small piece of it will be removed through the colonoscopy, and this biopsy is taken to the lab to check if it is a benign growth or something else(1,5).

Possible side effects and complications: Preparing the bowel before starting the test can be an unpleasant event. Also, the test is slightly uncomfortable, that is why the sedative usually helps with this, and most people feel normal again once the effects of the sedative go away. Some patients may complain of gas pains, bloating, or cramping after the test because the gas introduced into the colon and rectum during the operation will take some time until the air passes out. Others may suffer from low blood pressure or heart rhythm changes from the sedation during the test, but it is rarely severe. Besides, patients may notice some blood in their stool because of the polyp removed, or the biopsy was taken during colonoscopy. It can take two days after the test. Severe bleeding is uncommon, but in rare cases, bleeding needs to be treated or can even be life-threatening. Colonoscopy is a safe procedure, but in rare cases, perforation can occur(1,5).

2- CT colonography (virtual colonoscopy)

We direct our use of CT colonography because of its advantages of needing minimal bowel preparation and detecting most of the advanced tumors detected by colonoscopy (70:100%). In addition, it is not invasive(10).

For primary screening, the usage of CT colonography (34%) was higher than CT colonoscopy (22%), whereas the detection rate of advanced neoplasia among participants was higher with colonoscopy (6.1 versus 8,7 per 100 participants)(14).

The technique

This test is an advanced computed tomography (CT) scan for the colon and rectum. The CT scan is an advanced technique of x-ray. An X-ray takes one picture while the CT scan takes many pictures as it rotates

around the patient while lying on the bed. Then the computer combines these pictures to give a more detailed image for the part of the body to be studied. For CT colonography, specialized computer programs create both the 2-dimensional x-ray pictures and a 3-dimensional view of the inside of the colon and rectum, which let the doctor look for polyps or cancer. The best advantage of this test, it is not invasive like colonoscopy, so it is beneficial for people who do not want an invasive test. Also, it can be done quickly, without sedation. However, we cannot depend only on it because any polyps or other suspicious areas are seen by it; we still need a colonoscopy to remove it or explore them fully. Although it is not invasive as a colonoscopy, the same type of bowel preparation is required. A small flexible tube is put into the rectum for this test to fill the colon and rectum with air(5,14).

Before the test: the colon must be empty before this test too. The patient should follow a clear liquid diet for at least a day before the test. The night before the procedure, the patient takes a liquid laxative solution. On the morning of the trial, enemas may be needed to ensure the bowels are empty. Newer kits are available to clean out the gut and may be better tolerated than previous ones(5,10,14).

During the test: the test takes about 10 minutes. The patient may need to drink a contrast solution before the test, which helps the doctor look at the test images and have a small, flexible tube put into the rectum. Air is pumped through the tube into the colon to expand to provide better images. The table then slides into the CT scanner, and the patient will be asked to hold his breath for about 15 seconds while the scan is done. The patient will likely have two scans: lying on his back and one on his stomach or side (5,10,14).

Possible side effects and complications: few side effects are reported. The patient may feel bloated or have cramps, but this should go away once the air passes from the body. There is a minimal risk that inflating the colon with air could injure or puncture it. Like other CT scans, this test also exposes the patient to a small amount of radiation(5,6).

3- Flexible sigmoidoscopy

Flexible sigmoidoscopy is judged a more suitable tool for population screening than a colonoscopy because it is safer, cheaper, quicker, and more convenient, and the uptake rates are much higher. In addition, two-thirds of adenomas and cancers are in the rectum and sigmoid colon, which is within reach of the flexible sigmoidoscope. The procedure takes only 5 min, requiring no sedation and only a self-administered enema to clear the bowel(15).

The Technique

The doctor looks at a part of the rectum and colon with a sigmoidoscope. It is put through the anus, passing through the rectum until reaching the colon's lower part. Images from the scope are seen on a video camera. This technique enables the doctor to detect any abnormalities in the rectum and lower part of the colon. If any polyps are found during the test, the doctor can remove them with a small instrument passed through the scope. This polyp will be examined in the lab. Then, if found precancerous or colorectal cancer patient will need to have a colonoscopy later on, to look for polyps or cancer in the rest of the colon. Sigmoidoscopy usually takes 10 to 20 minutes only. Most patients do not need to be sedated for this test(5,15).

Before the test: The doctor must know about any medication's patient takes, as these medications may be needed to be changed before the test. In addition, the insides of the patient must be empty and clean. So, the patient may be asked to follow a special diet, use enemas, or use strong laxatives to clean out his colon and rectum. This helps the doctor see the colon and rectum (6,15).

Advantage

Flexible sigmoidoscopy is considered a more suitable tool for population screening than colonoscopy as it is safer, quicker, and more convenient. In addition, it requires no sedation in most cases, just only a self-administered enema to clear the bowel. As a result, the incidence of colorectal cancers in people doing

flexible sigmoidoscopy screening was reduced by 33%, and mortality was reduced by 43%. In addition, the incidence of distal colorectal cancer was reduced by 50% (15,16).

Possible complications and side effects: This test may be uncomfortable because of air put into the colon and rectum, but it is usually not painful. The patient may see some blood in his bowel movements for a day or two after the test. Massive bleeding and puncture of the colon and rectum are rare but possible (5,15).

3. Conclusions

There are multiple available ways for the screening of colorectal cancer. Some of them are non-invasive, and the others are invasive. The sensitivity of these tests differs but, in general, is competent to diagnose colorectal cancer early. Screening colorectal cancer by different methods is an effective way to diagnose colorectal cancer in its early stages. The early-stage treatment of colorectal cancer had a remarkable long-term improvement in morbidity and mortality.

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