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Screening and Surveillance Colonoscopy

Rotimi R. Ayoola, Hamza Abdulla, Evan K. Brady, Muhammed Sherid and Humberto Sifuentes

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Abstract

Colorectal cancer is a major cause of worldwide morbidity and mortality. As such, there are many guidelines and recommendations set forth by various medical societies regarding colonoscopy for screening and surveillance. The universal goal of these guidelines is to reduce colorectal cancer prevalence and mortality. Recommendations for colorectal cancer screening and surveillance using colonoscopy vary slightly between medical society guidelines and are often dictated by some combination of age, known disease severity, length of time since last study, family history, and comorbid conditions.

Keywords: Screening, surveillance, colonoscopy, recommendations, colorectal cancer

1. Introduction

Colorectal cancer is the second leading cause of death from cancer in the United States, as well as the fourth most common cause of cancer-related death, and the third most diagnosed cancer worldwide.[1, 3] In 2008, there were an estimated 1.2 million newly diagnosed cases of colorectal cancer worldwide and an estimated 609,000 colorectal cancer-related deaths.[3] In 2014, it was estimated that there were 136,830 newly diagnosed cases of colorectal cancer and nearly 50,310 deaths associated with this disease in the Unites States alone.[4] The age-adjusted incidence of colorectal cancer in the United States was 43.7 cases per 100,000 population among men and women based on reported cases from 2007 to 2011.[4] In 2011, there were an estimated 1,162,426 people living with colon and rectum cancer in the United States.[4] Screening of those at average risk may result in lower mortality rates by detecting cancers at earlier and more curable stages. Also, detection of cancer-precursor lesions may reduce the incidence of colorectal cancer if removed on endoscopic screening tests.[5, 6] The incidence and mortality

of colorectal cancer have declined from 2002 to 2010 in the United States,[7] possibly due to improvement in the adherence to screening and surveillance guidelines.

2. Colorectal cancer screening

2.1. Prevention strategies

Recommended strategies for colorectal cancer screening can be divided into two categories: stool tests (occult blood and DNA tests) and structural examinations (flexible sigmoidoscopy, colonoscopy, double contrast barium enema, capsule endoscopy, and computed tomographic colonography). Each screening method has its own advantages and disadvantages, which are summarized in Table 1. Screening is currently recommended beginning at 50 years of age in average-risk populations, and varies in populations with increased risks.[6, 8]

Test	Advantages	Disadvantages
Sensitive guaiac fecal occult blood test	Inexpensive, easily done at home	Low sensitivity, annually repeated, lack of compliance
Fecal immunochemical test	Inexpensive, easily done at home	More expensive than guaiac fecal occult, annually repeated, unknown adherence, low sensitivity for advanced adenomas
Stool DNA	More accurate than blood detection; easily done at home	Expensive, sensitivity and specificity unknown, uncertain screening intervals
CT Colonography	High sensitivity of lesions >10 mm in diameter; not invasive	Not been proven to reduce incidence or mortality, bowel prep needed, unknown management of polyps <6 mm in diameter, radiation exposure
Sigmoidoscopy	Can be done in office without sedation, 60% reduction in mortality from cancer of the distal colon	Proximal colon cancer may be missed
Colonoscopy	90% sensitivity for lesions >10 mm in diameter, 53-72% reduction in incidence and 31% reduction in mortality from colorectal cancer, lesions can be detected and removed during one examination	Bowel preparation and expertise needed, expensive, invasive with possible complications

**Data from Lieberman[6], Baxter, et al.[9], Muller, et al.[10], and Singh, et al.[11]

Table 1. Advantages and disadvantages of screening tests

Strategies used to identify patients at an increased risk for developing colorectal cancer should be started early. Before determining the best screening tool, clinicians should determine a patient's level of risk. The most common indicator of increased risk is a first-degree relative with colorectal cancer. Diagnosis of colorectal cancer in a first-degree relative before 50 years of age is concerning for hereditary gastrointestinal cancer syndromes such as Lynch syndrome, familial adenomatous polyposis (FAP), attenuated familial adenomatous polyposis (AFAP), and MUTYH-associated polyposis (MAP). Patients with hereditary gastrointestinal cancer syndromes require a special timing for endoscopic screening and surveillance. Colonoscopy is the preferred screening test in these persons, which should be initiated at 40 years of age or 10 years younger than the age at which the family member was diagnosed with colorectal cancer, whichever comes first.[6, 8] Patients with chronic ulcerative colitis or colitis due to Crohn's disease are at increased risk for colorectal cancer and should undergo a screening colonoscopy after 8-10 years.[6, 8] Prior colorectal cancer or polyps also increases the risk of colorectal cancer, especially if polyps are large, or have villous architecture.[12]

2.2. Identifying high-risk individuals

The risk of developing colorectal cancer is largely multifactorial. The factors associated with an increased risk of colorectal cancer include lack of physical activity, obesity, high-fat and low-fiber diets, tobacco use, gender, ethnicity, and genetics. There is limited evidence to suggest that lifestyle modification alone in adults will reduce the risk of this cancer.[6, 13] Aspirin, nonsteroidal anti-inflammatory drugs, and hormone-replacement therapy can decrease the risk of adenomas or colorectal cancer but are not recommended in prevention of colorectal cancer because the possible adverse effects are higher than the potential benefits.[6, 14, 15]

2.3. Screening modalities

Multiple tests are used as options for colorectal cancer screening. Stool-based tests can improve disease prognosis by detecting early cancers. Endoscopic or radiologic tests can visualize the bowel mucosa and detect polyps that can be removed before malignant transformation. Sensitivities of various screening modalities (Table 2) and screening guidelines (Table 3) can be very useful when choosing the most appropriate screening test.

Test	Sensitivity		References
	Cancer Detection	Advanced Adenoma* Detection	
Standard guaiac fecal occult blood test (three stool samples)	33-50%	11%	Mandel et al.[16], Hardcastle et al.[17], Kronborg et al.[18], Imperiale TF.[19], Ahlquist.[20]

Test	Sensitivity		References
Sensitive guaiac fecal occult blood test (three stool samples)	50-75%	20-25%	Allison et al.[15], Levin et al.[21], Whitlock et al.[22], Ahlquist et al.[20]
Immunochemical fecal occult blood test (one-three stool samples)	60-85%	20-50%	Levin et al.[21], Whitlock et al.[22]
Old stool DNA test (one stool sample)	51%	18%	Imperiale et al.[19]
New stool DNA test (one stool sample)	≥80%	40%	Allison et al.[15], Itzkowitz et al.[23]
CT Colonography	Uncertain; probably >90%	90% (if ≥10 mm diameter)	Johnson et al.[24]
Sigmoidoscopy	>95% (for distal colon)	70%	Lieberman[6], Shelby et al.[25]
Colonoscopy	>95%	88-98%	Lieberman[6], Imperiale et al.[19], Schoenfeld et al.[26], Lieberman et al.[27], Pickhardt et al.[28], Cotton et al.[29], Rockey et al.[30]

*Advanced adenoma is defined as tubular adenoma that is ≥10 mm in diameter or with villous histologic features or high-grade dysplasia.

Table 2. Sensitivity of one-time colorectal cancer screening tests

Screening Test	ACS-MSTF-ACR	USPSTF	Recommended Interval for Rescreening
Sensitive guaiac fecal occult blood test	Recommended if "/>50% sensitivity for colorectal cancer	Recommended	1 yr
Fecal immunochemical test	Recommended if >50% sensitivity for colorectal cancer	Recommended; high-sensitivity test only	1 yr
Stool DNA test	Recommended if >50% sensitivity for colorectal cancer	Not Recommended (insufficient evidence to assess sensitivity and specificity of fecal DNA)	Uncertain

Screening Test	ACS-MSTF-ACR	USPSTF	Recommended Interval for Rescreening
Flexible sigmoidoscopy	Recommended if sigmoidoscope is inserted to 40 cm of the colon or to the splenic flexure	Recommended; with guaiac fecal occult blood test every 35 yr yr	
Barium enema Examination	Recommended, but only if other tests not available	Not recommended	5 yr
CT colonography	Recommended, with referral for colonoscopy if polyps ≥6 mm in diameter detected	Not recommended (insufficient evidence to determine risk-benefit ratio)	5 yr
Colonoscopy	Recommended	Recommended	10 yr

* Data from Lieberman[6], Preventive Services Task Force[14], Levin et al.[21], Preventive Services Task Force[14], and Whitlock et al.[22]; ACS-MSTF-ACR denotes American cancer Society, US Multisociety task force on Colorectal Cancer, and American College of Radiology; and USPSTF denotes US Preventive services Task Force.

Table 3. US colorectal cancer screening guidelines, 2008*

2.3.1. Fecal screening tests

Fecal screening tests use small stool samples to help determine the presence of colorectal cancer. Fecal screening tests include Guaiac-based fecal occult blood test, immunochemical-based fecal occult blood test, also known as fecal immunochemical test (FIT), and Cologuard (fecal DNA testing, combined with hemoglobin and DNA methylation assays). These tests are easily performed at home or in a clinical office, are noninvasive, inexpensive, without direct adverse health effects, and require few specialized resources. One disadvantage of fecal testing is that positive results require colonoscopy evaluation to confirm or exclude the diagnosis of colorectal cancer.

Guaiac fecal occult blood tests detect hemoglobin peroxidase activity and turn guaiac-impregnated paper blue, but are not specific for human blood. Three separate stool samples per test are preferred for better sensitivity.[21] The fecal occult blood test is associated with significant false-positive results, which may lead to unnecessary follow-up colonoscopies. In the Minnesota trial, false-positive test results were found in almost 9% of fecal occult blood testing.[3] The cost-effectiveness of colorectal cancer screening with an annual or biennial fecal occult blood test varied from US\$ 5,691 to US\$ 17,805 per life-year gained.[31] Randomized, controlled trials in which standard guaiac tests were administered annually or biennially have shown that cancers are detected at an earlier and more curable stage when compared with no regular screening. Over a period of 10-13 years, regular guaiac screening tests result in a reduction of colorectal cancer mortality by 15-33%.[6, 8, 32]

FIT uses antibodies specific to hemoglobin to screen for colorectal cancer. It is more accurate than the guaiac test.[33, 37] As a result, FIT is now recommended as the first-choice fecal occult blood test in colorectal cancer screening.[38] FIT has sensitivity for detecting cancer of 60-85%

with the use of one to three stool samples.[4, 6, 22] Cologuard is a screening modality that tests stool DNA for specific mutations that are associated with colorectal cancer. These specific segments of cellular DNA are excreted in stool and can be detected with the use of polymerase chain reaction (PCR) amplification. Newer versions of the test are currently being developed; however, overall performance, utility, and cost-effectiveness has not been well studied.

2.3.2. Structural examinations of the colon

Colorectal cancers can be detected through physical exams with a digital rectal examination, but there is little evidence to support the effectiveness of digital rectal exam in the detection of colorectal cancer and, therefore, it is not recommended in the current screening guidelines (Table 3).

Anatomical examination of the colon is effective in detection of early cancer and precancerous lesions. Radiography imaging such as barium enema and computed tomographic (CT) colonography can be used to detect lesions. In clinical studies of CT colonography for polyp detection with expert radiologists, 90% of polyps 10 mm or larger in diameter were identified correctly, with a false-positive rate of 14%.[6] CT colonography is not as sensitive for polyps less than 6 mm. There are currently no conclusive studies supporting appropriate screening intervals for negative results or suitable next steps for polyps less than 6 mm. While radiation exposure during CT colonography is considered minimal, the cumulative radiation exposure puts people at increased risk for developing other types of radiation-related cancers. Additionally, cost-effectiveness of CT colonography has not been thoroughly studied in comparison to other modalities.

Before colonoscopy became available, barium enema was the primary means of detecting polyps, and their removal required surgical colostomy.[39] Barium enema examination is not the best test for identifying precancerous lesions and is rarely used for colorectal-cancer screening in current practice.[6] Double-contrast barium enema is another screening modality that involves the patient drinking contrast, which coats the intestinal mucosa with barium. Then, the colon is insufflated with air and multiple radiographs are taken under fluoroscopy. Double-contrast barium enema detects about half of adenomas larger than 1 cm and 39% of all polyps.[40] Retrospective studies have found that double-contrast barium enema failed to diagnose 15-22% of colorectal cancers.[41] If an abnormality is found, then colonoscopy evaluation should follow. False-positives or inconclusive results can be a result of stool, mucosal irregularities, or air. Barium enemas are safe and typically do not require sedation, but may cause the patient discomfort during the procedure. The usage rates of double contrast barium enema for colorectal cancer screening recently declined with improved screening tools, but may be useful where colonoscopy is not readily available.[42]

Endoscopic screening is more sensitive than fecal testing for the detection of adenomatous polyps.[37, 43, 45] In the United Kingdom, one-time screening with flexible sigmoidoscopy significantly reduced the incidence of colorectal cancer by 23% and cancer-related mortality by 31%.[45, 46] Studies, with the use of screening colonoscopy, have shown that more than 30% of patients with advanced neoplasia have proximal lesions that would not be identified with sigmoidoscopy alone.[47, 48]

The most performed indication for colonoscopy in the United States is for screening and surveillance purposes. Colonoscopy can detect a wide range of colon pathologies including polyps, angiodysplasias, hemorrhoids, and cancer. Colonoscopy also permits therapeutic interventions. The procedure is highly feasible and relatively safe. The quality of the procedure depends on an adequate bowel preparation. The patient is typically sedated throughout the procedure. Colonoscopy can reduce the incidence and the mortality of colorectal cancer.[9, 27, 49] Endoscopic procedures may be uncomfortable for patients and carry the risks of perforation and bleeding, especially when polypectomy is performed. The risk of serious adverse events is 3-5 events per 1000 colonoscopies.[6]

Capsule endoscopy has the potential to become a useful screening tool. A camera, in the size and shape of a pill, is swallowed to help visualize the gastrointestinal tract. Reductions of incidence and mortality have not yet been studied using this modality. Capsule endoscopy does not require sedation or radiation. However, accuracy data show inferior screening performance compared to colonoscopy.[3] Despite all these available methods, colorectal cancer screening rates are still suboptimal. In a National Health Interview Survey in 2010, the rate of screening was only 58.6%.[39]

2.4. Screening guidelines

Two major guidelines, from the US Preventive Services Task Force (USPSTF) and a joint guideline from the American Cancer Society, the US Multi-Society Task Force on Colorectal Cancer, and the American College of Radiology (ACS-MSTF), were released in 2008 regarding colorectal cancer screening in the United States (Table 3). The joint guidelines recommend structural examinations for cancer prevention. The ACS-MSTF recommends offering screening beginning at age 50 years for average-risk patients, and continued surveillance every 10 years, if negative. In average-risk patients, CT colonography should be performed every 5 years, flexible sigmoidoscopy every 5 years, and double-contrast barium enema every 5 years. The joint guidelines recommend fecal occult blood testing with sensitive guaiac method or fecal immunochemical-based test every year for screening. Screening should be terminated if a patient's life expectancy is less than 10 years.[21] Prior to screening, patients should understand that a positive test indicates a need for colonoscopy. There are no specific guidelines regarding colorectal cancer screening for sex or ethnicity but the American College of Gastroenterology supports initiation of screening in African Americans at 45 years of age.[8]

The US Preventive Services Task Force does not recommend CT colonography or stool DNA testing. The USPSTF recommends three screening options for adults 50-75 years old: sensitive fecal occult blood testing annually, flexible sigmoidoscopy every 5 years with sensitive fecal occult blood test every 3 years, and colonoscopy every 10 years. Screening for patients older than 75 is not routinely recommended by the USPSTF, and recommends against screening over the age of 85 years.[14] Colorectal cancer screening in older patients who have never undergone formal screening is controversial and there are currently no guidelines regarding appropriate screening in these scenarios. The risk of colorectal cancer and advanced polyps continues to increase in age even after 75 years. Thus, the decision to screen between the ages of 75 and 85

years should be discussed with and individualized to each patient depending on health status and other comorbidities.

In Europe, fecal occult blood testing is implemented at higher rates than in the United States. The fecal occult blood test for individuals aged 50-74 years at average-risk has been recommended to date by the European Union guidelines for colorectal screening, annually or biennially.[15]

The British Society of Gastroenterology (BSG) and the Association of Coloproctology for Great Britain and Ireland (ACPGBI) aimed to provide guidance on the appropriateness, method, and frequency of screening for people at moderate- and high-risk for colorectal cancer.[50]

3. Colorectal cancer surveillance

Surveillance colonoscopy refers to colonoscopy examination performed in asymptomatic individuals with previously identified cancerous or precancerous lesions. Colonoscopy surveillance is used to identify any recurrent or new neoplasia in these individuals.[51] High adenoma detection rate on follow-up colonoscopy (30-50%) provides the rationale for surveillance colonoscopy.[52, 56] There is strong evidence that surveillance colonoscopy decreases colorectal cancer incidence and colorectal cancer-related mortality.[57]

The timing of subsequent surveillance is crucial. Studies demonstrate both the protective effect and cost-effectiveness of performing surveillance colonoscopy on high-risk populations.[58] The overall impact of surveillance is not well defined and may be decreased by an inappropriate utilization of resources and nonadherence to published guidelines.[59]

3.1. Recommendations for surveillance colonoscopy

Guidelines from Gastrointestinal societies in the United States, the United Kingdom, and the European Union follow a risk stratification policy to time their surveillance intervals.

The US Multisociety Task Force (US MSTF) guidelines were published in 2008 and categorize patients into two major risk groups based on the likelihood of development of advanced neoplasia (Table 4). In 2012, the US MSFT updated their guidelines to address the role of serrated polyps, risk of interval colorectal cancer, and proximal colorectal cancer (Table 5).

The European Society of Gastrointestinal Endoscopy (ESGE) updated their guidelines in 2013 and formulated a risk stratification and surveillance strategy similar to the United States (Table 4 and Table 5). A new recommendation was to increase the interval from 3 years to 5 years after a normal follow-up colonoscopy in the high-risk group (3-4 adenomas, villous features or high-grade dysplasia, or ≥10 mm in size).

The UK guidelines are based on adenoma size and number without incorporating histological findings. It stratifies patients into low-, moderate-, and high-risks groups. It also recommends a "single clearing examination" at 1 year for high-risk patients (≥5 small adenomas or ≥3 adenomas, at least 1 of which is ≥1 cm).

	United States Multisociety Task Force (US MSTF)	European Society of Gastrointestinal Endoscopy (ESGE)	British Society of Gastroenterology (BSG)
Risk			
Low	1-2 tubular adenomas <10 mm	1–2 tubular adenomas <10 mm with low-grade dysplasia; serrated polyps < 10 mm and no dysplasia	1–2 adenomas <10 mm
Moderate	-	-	3–4 adenomas <10 mm or at least one adenoma >1cm
High	Adenoma with villous histology or high-grade dysplasia or ≥10 mm or ≥3 adenomas	Adenoma with villous histology or high-grade dysplasia or ≥ 10 mm in size, or ≥3 adenomas; serrated polyps ≥ 10 mm or with dysplasia	>5 small adenomas or at least 3 adenomas >1cm

Table 4. Risk stratification criteria

	United States Multisociety Task Force (US MSTF)	European Society of Gastrointestinal Endoscopy (ESGE)	British Society of Gastroenterology (BSG)
Risk			
Low	5-10 years	10 years	No surveillance or 5 years
Moderate	-	-	3 years
High	**3 years**	3 years	1 years

Table 5. Surveillance interval recommendation

A recently published study, which analyzed 3226 post-polypectomy patients, compared the US MSTF guidelines with the British Society of Gastroenterology (BSG) guidelines. The study showed that the application of the UK guidelines into the US population reclassified 26.3% of patients from high-risk to a higher-risk category and 7% to a lower-risk category.[60] The study also showed a net 19% of patients benefiting from detection 2 years earlier without substantially increasing rates of colonoscopy.[60]

3.2. Sessile serrated adenomas/polyps and surveillance colonoscopy

Sessile serrated adenoma/polyp (SSA/P) is a term used to describe polyps or adenomas characterized by the presence of a sawtooth appearance to crypt contour with prominent dilatation, serrations, and lateralization at the crypt base.[51] The discovery of the serrated adenoma/polyp pathway and the development of colorectal cancer has led to increased interest

and focus on the understanding of the histological and molecular changes that lead to CRC. Hypermethylation of genes in serrated lesions leads to microsatellite instability and rapid development of colorectal cancer.[61]

Endoscopically, serrated lesions have a similar appearance to hyperplastic polyps and are often misdiagnosed as such. A recent study showed that as high as one-third of recently diagnosed hyperplastic polyps ≥5 mm were reclassified into SSA/P after a second pathology review.[62] The CARE study found that serrated lesions were five times more likely to be incompletely resected by polypectomy compared to conventional adenomas.[63] Serrated polyps larger than 1 cm or with a dysplastic component are considered advanced polyps.[63]

Surveillance recommendations for serrated adenomas/polyps are inconsistent among researchers and gastrointestinal societies and long-term studies evaluating SSA/P are limited. US MSTF and ESGE classifies serrated polyps <10 mm with no dysplasia as low-risk and serrated polyps ≥10 mm or those with dysplasia as high-risk. Both societies recommend surveillance colonoscopy in 3 years in high-risk. For low-risk lesions, ESGE recommends 10-year follow-up, whereas US MSTF recommends 5-year follow-up.[14, 50, 64]

3.3. Serrated polyposis syndrome

The World Health Organization defines serrated polyposis syndrome by either the presence of five or more serrated polyps proximal to the sigmoid colon (at least two of which must be ≥10 mm) or 20 or more serrated polyps of any size distributed throughout the colon.[65] US MSFT and ESGE recommend one-year follow-up surveillance in this patient population. [14, 66] ESGE also recommends referral for genetic counseling.[14, 66]

3.4. Effect of positive family history on surveillance intervals

Patients with a family history of colorectal carcinoma are at higher risk of developing high-risk adenoma and colorectal carcinoma. US MSTF recommends shortening the surveillance interval from 10 years to 5 years in patients with low-risk findings on colonoscopy and a first-degree relative with colorectal cancer prior to the age of 60.[14] US MSTF also recommends surveillance with colonoscopy as the preferred method.[14]

3.5. Surveillance colonoscopy in the elderly

There is a significant increase in incidence of both CRC and adenomas with increasing age.[14] The age at which screening colonoscopy should be performed remains controversial. Studies that examined the role of age in surveillance colonoscopy found no association with increasing age and polyp recurrence and concluded it was not necessary to tailor surveillance guidelines by age.[5, 67, 70] Retrospective studies have also shown that comorbidities reduce the benefits of CRC screening. The US MSTF does not give a specific age at which screening can be ceased, but recommends that competing comorbidities and life expectancy should be considered before ordering cancer screening at any age.[14]

3.6. Surveillance colonoscopy and physician nonadherence to guidelines

Nonadherence to guidelines remains a major problem in healthcare policy. The overuse of resources could lead to increased demand for colonoscopy, shifting resources from screening, and thus decreasing the cost-effectiveness of CRC screening program by increasing the unnecessary costs and possibility of adverse events. Alternatively, underuse of colonoscopy in surveillance may lead to suboptimal prevention of colorectal cancer. Schohen, et al. retrospectively evaluated 3,627 screening patients with a history of adenoma removal and found overuse of endoscopy in low-risk patients and underuse in high-risk patients.[71] The reasons for guideline nonadherence include lack of strong evidence to support the surveillance intervals, having multiple guidelines with inconsistent recommendations, lack of awareness of current evidence, fear of legal implication, suboptimal bowel preparation, financial incentive for performing the procedure, and miscommunication between gastroenterologist and primary care providers.[72] Measures to improve adherence to guidelines include continued medical education; written recommendations by endoscopist regarding the follow-up interval after the pathology report; quality improvement interventions such as reminder devices; improvement of bowel preparation quality; automated electronic alerting system[72, 73]; and continuous quality improvement process for colonoscopy (education, monitoring, audits, and financial incentives/penalties).[74]

4. Conclusion

Colorectal cancer screening and surveillance have been shown to provide many benefits. The associated risks are relatively minor and vary greatly on the particular screening test, and surveillance regimen. Patients should be informed that screening and surveillance reduce the risk of colorectal cancer, but may require additional tests and/or procedures to diagnose and manage the pathologic findings. Colorectal cancer screening rate is still suboptimal in the United States and this rate could be improved by dedicated patients and clinician reminders, patients' education, outreach, and follow-up. Screening and surveillance must be targeted to appropriate patients and occur at recommended intervals to ensure proper prevention.

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