ASGE guideline: colorectal cancer screening and surveillance

This article is one of a series of statements discussing the use of gastrointestinal endoscopy in common clinical situations. The Standards of Practice Committee of the American Society for Gastrointestinal Endoscopy prepared this text. In preparing this guideline, a MEDLINE literature search was performed, and additional references were obtained from the bibliographies of the identified articles and from recommendations of expert consultants. When little or no data exist from well-designed prospective trials, emphasis is given to results from large series and reports from recognized experts.

Guidelines for appropriate use of endoscopy are based on a critical review of the available data and expert consensus. Further controlled clinical studies are needed to clarify aspects of this statement, and revision may be necessary as new data appear. Clinical consideration may justify a course of action at variance to these recommendations. This guideline replaces and supplements our previous document on colorectal cancer screening and surveillance.[1]

INTRODUCTION

Colorectal cancer (CRC) is the fourth most commonly diagnosed cancer and the second leading cause of cancer-related deaths in the United States.2 Each year, approximately 140,000 individuals are diagnosed with CRC and more than 50,000 will die from this malignancy.[2] The 5-year survival rate for early-stage cancers is greater than 90%, whereas the 5-year survival rate for those diagnosed with widespread cancer is less than 10%.[3] There is indirect evidence that most cancers develop from adenomatous polyps and that on average it takes 10 years for a <1 cm polyp to transform into invasive CRC.[4,5] Given the finding that adenomatous polyps are precursors to cancer and that polyps and early cancers are usually asymptomatic, there is a strong rationale to support screening asymptomatic individuals for early cancer detection and prevention.

RISK STRATIFICATION

Approximately 30% of individuals harbor risk factors for CRC.[6] These risk factors include family or personal history of CRC or adenomatous polyps, personal history of inflammatory bowel disease, and familial polyposis syndromes (including familial adenomatous polyposis [FAP] and hereditary nonpolyposis colon cancer [HNPCC]). The other 70% of individuals are considered average risk.

Screening strategies for average-risk individuals

Average-risk individuals should be offered screening beginning at age 50 years.[7] The choice of modality for CRC screening along with the associated risks and benefits must be discussed between the practitioner and the individual patient[8] (Table 1).

Colonoscopy. Colonoscopy is the preferred modality for CRC screening. Both cancer and premalignant neoplasms can be accurately detected by colonoscopy. It offers the advantages of complete visualization of the entire colon, detection and removal of polyps, and diagnostic sampling of cancers. Colonoscopy with polypectomy has been shown to significantly reduce the expected incidence of CRC by 76% to 90% in multiple cohort studies.[9-11] In the National Polyp Study, patients who underwent colonoscopy with polypectomy had a 76% reduction in CRC incidence compared with a general population registry.[9] The CRC incidence after colonoscopic polypectomy was reduced by 90% compared with the incidence in a cohort of patients who did not undergo polypectomy.[9] In a European cohort study of 1,693 patients who underwent colonoscopy with the removal of at least 1 adenoma ≥5 mm in size, the cancer incidence ratio was 0.34 compared to the incidence in a reference population.[10] In a study from Norway, 400 patients who were identified as having colon polyps on flexible sigmoidoscopy underwent colonoscopy with polypectomy and were followed prospectively over 13 years.[11] A control group of 399 patients who did not have any form of CRC screening was also followed prospectively. At 13 years, both groups underwent colonoscopy; the relative risk of cancer was 0.2 in the group that had prior colonoscopic polypectomy compared with the control group.

There are currently no published studies specifically evaluating whether screening colonoscopy reduces

CRC-related mortality. There is indirect evidence from fecal occult blood testing (FOBT) trials that colonoscopy reduces CRC-related mortality.[12-14] Colonoscopy provides a more complete examination than sigmoidoscopy, for which there is direct evidence of reducing CRC-related mortality by up to two thirds.[15-18] We can extrapolate from this evidence that colonoscopy likely results in a significant reduction in CRC-related mortality; however, further studies are needed to establish a benefit in mortality.

There is recent evidence that advanced neoplasia (adenoma ≥1cm in size, villous adenoma, adenoma with high-grade dysplasia, or invasive cancer) in the proximal colon can occur in the absence of adenomatous polyps in the distal colon.[19,20] The overall prevalence of proximal advanced adenomas in patients without distal adenomas is approximately 2% to 5%.[19-21] Lieberman et al[19] and Imperiale et al[20] demonstrated that approximately 50% of patients with proximal advanced neoplasia have no distal polyps. In a prospective multicenter study of 116 average-risk patients with established colon cancer located proximal to the splenic flexure, 58.6% had no distal polyps.[22] This evidence favors the use of colonoscopy as the primary method of screening for CRC, given that a significant portion of proximal advanced neoplasia will not be detected with use of flexible sigmoidoscopy.

Potential disadvantages of colonoscopy as a screening method include the inconvenience of bowel preparation, the risks of sedation, the risk of perforation, the risk of not identifying neoplasms, and the cost.[23] The risk of perforation associated with colonoscopy appears to be no more than 0.1% to 0.2%.[24,25] The miss rate of colonoscopy for polyps, on the basis of studies of back-to-back colonoscopies, is 27% for adenomas ≤5 mm and 6% for lesions ≥10 mm.[26] A recent study that used computed tomographic (CT) colography suggested that the miss rate for lesions ≥10 mm may be as high as 11%.[27] Colonoscopy miss rates appear to be associated with the skill and technique of the endoscopist, with higher quality of withdrawal technique resulting in lower miss rates.[23,28] Finally, colonoscopy represents a cost-effective means of screening for CRC compared with FOBT and flexible sigmoidoscopy.[29,30]

The role of endoscopy in the diagnosis, staging, and management of CRC is considered in another guideline.[31] After a good-quality colonoscopic examination without findings of colon cancer or adenomatous polyps is performed, further screening tests (eg, FOBT) should not be done for approximately 10 years. Currently, the American College of Gastroenterology endorses colonoscopy as the preferred screening method for CRC in average-risk patients.[32]

Recommendation. Colonoscopy is recommended approximately every 10 years for average-risk individuals. The completeness of the examination and the quality of the preparation should be taken into account for the timing of subsequent examinations.

FOBT. FOBT can be performed with use of a guaiac-based test, immunochemical test, or fluorometric quanti-

TABLE 1. Recommended tests for CRC screening in average-risk individuals beginning at age 50 years
Preferred modality
Colonoscopy every 10 y
Alternatives
FOBT yearly
Flexible sigmoidoscopy every 5 y
FOBT yearly and flexible sigmoidoscopy every 5 y
FOBT, Fecal occult blood test.

tative assay. Two samples from each of 3 consecutive stools should be tested. Patients with positive FOBT results are at increased risk of advanced neoplasia and should undergo a complete colonoscopy. Prospective randomized trials of FOBT have demonstrated a 15% to 33% reduction in CRC-related mortality when positive results were followed by colonoscopy.[12-14,33] Dietary restrictions are recommended when the more sensitive guaiac-based tests are used; these restrictions include the avoidance of red meat and peroxidase-containing foods for 1 to 3 days before and during stool collection, to reduce false positive rates.[12,13] However, dietary restrictions may not be needed if test development is delayed for 3 or more days.[34,35] Samples that are rehydrated or obtained by digital rectal examination have higher false-positive rates.[36] Immunochemical tests are more specific but have reduced sensitivity than do guaiac-based tests. They may be helpful in combination with guaiac-based tests to improve overall accuracy.[37,38]

Currently, the American Cancer Society[39] and the Multisociety Task Force on Colorectal Cancer[40] recommend yearly FOBT with any positive test result followed by colonoscopy. However, in a recent U.S. national survey of 1,147 primary care physicians, 32.5% of physicians used a single digital rectal examination as the primary method to obtain stool for FOBT.[41] Only 26.3% of physicians adhered strictly to the recommended home-based screening with 2 samples from 3 consecutive stools. Furthermore, approximately 30% of physicians recommended repeat FOBT to patients after a positive test result. Of the physicians who pursued workup of a positive FOBT result, only 52.8% recommended colonoscopy, with the rest ordering sigmoidoscopy, double contrast barium enema, or a combination of several tests. A recent study conducted in 13 Veteran Affairs medical centers found that the sensitivity of a single digital rectal examination FOBT for the detection of advanced colonic neoplasia is 4.9% compared with a sensitivity of 23.9% when the recommended home-screening protocol was performed.[42] The practice of a single digital rectal examination for FOBT, therefore, is

considered a poor screening method for CRC and should not be performed.

Recommendation. Yearly FOBT from 2 samples of 3 consecutive stools is recommended. A single digital rectal examination for FOBT is not recommended. Colonoscopy should be done if any sample has positive results.

Flexible sigmoidoscopy. Case-control studies of sigmoidoscopy (mostly using rigid sigmoidoscopes) have suggested a reduction in CRC incidence in the portion of the colon examined, and an associated decreased mortality between 59% to 80%.[15-18] The benefit persists for up to 10 years.[16] The risk of colon cancer in the area beyond the reach of the sigmoidoscope does not appear to be reduced. It is estimated that the overall reduction in CRC-related mortality from flexible sigmoidoscopy screening may be as high as 45% up until the age of 80 years.[43] There are currently no published prospective trials of screening flexible sigmoidoscopy showing a decrease in CRC-related mortality.

In a randomized prospective study, the detection rate for advanced neoplasia was 3 times higher after screening by sigmoidoscopy than by FOBT.[44] A recent study that used screening colonoscopy to estimate the sensitivity of sigmoidoscopy and FOBT for advanced neoplasia found that sigmoidoscopy identified only 70.3% of patients with advanced neoplasia.[45] Several studies have demonstrated that a significant number of advanced proximal adenomas occur in the absence of distal adenomas and therefore would be missed on flexible sigmoidoscopy.[19,20] In a study of 1,463 asymptomatic women undergoing colonoscopy, only 34.7% with advanced neoplasia had distal adenomas and would have been identified on flexible sigmoidoscopy.[46] Comparison with age-matched men from the Veterans Administration Cooperative Study showed that men were more likely to have advanced neoplasia than women (8.6% vs 4.5%). However, a higher percent of advanced neoplasia in men (66.3%) would have been detected by flexible sigmoidoscopy.[46] These data suggest that colonoscopy has advantages over flexible sigmoidoscopy for screening of colorectal cancer in women. Likewise, because the prevalence of proximal neoplasia increases with age, colonoscopy may be better suited for screening older patients (aged $\geq$60 years).[47]

Currently, the Multisociety Task Force on Colorectal Cancer,[40] the American College of Gastroenterology,[32] and the American Cancer Society[39] all recommend that, if flexible sigmoidoscopy is used for CRC screening, it should be performed every 5 years. The U.S. Preventive Services Task Force also recommends this procedure for screening but does not specify a time interval.[48] Several studies have demonstrated a low risk of development of adenomas and advanced neoplasms within the first 3 years of negative results from flexible sigmoidoscopy.[49-51] A recent large cohort study from Kaiser Permanente showed low age-adjusted incidence rates of CRC within the first 4 years after a negative sigmoidoscopy results compared with the incidence in the general population.[52] This study supported maintaining the time interval between screening sigmoidoscopies at 5 years.

Recommendation. Flexible sigmoidoscopy is recommended every 5 years. See below for management of findings on flexible sigmoidoscopy.

FOBT and flexible sigmoidoscopy. There is no evidence that the combination of annual FOBT and flexible sigmoidoscopy every 5 years reduces CRC mortality. A recent study showed that 70.3% of patients with advanced neoplasia were identified by use of sigmoidoscopy alone,[45] and the addition of FOBT minimally increased the detection rate to 75.8%.[45] However, a randomized trial has shown that the performance of one-time FOBT detected fewer neoplasms than did use of FOBT plus sigmoidoscopy.[53]

Recommendation. The combination of yearly FOBT and flexible sigmoidoscopy every 5 years may be considered, although the added benefit of FOBT appears to be minimal. If both tests are planned together, recommend performing FOBT first because a positive test would be an indication for colonoscopy.

Double-contrast barium enema. Although double-contrast barium enema (DCBE) offers the evaluation of the entire colon, its diagnostic sensitivity is inferior to colonoscopy and it lacks therapeutic capability.[54] In a prospective study comparing DCBE with colonoscopy, DCBE detected 53% of adenomatous polyps 6 to 10 mm in size and 48% of those >1 cm in size compared with colonoscopy.[55] Another study found that the sensitivity for detecting CRC was 83% for barium enema versus 95% for colonoscopy.[56] There are no prospective studies demonstrating the efficacy of screening DCBE in reducing CRC incidence or mortality. The addition of flexible sigmoidoscopy with DCBE is not recommended because the incremental detection rate achieved is uncertain and probably small.[40] Currently, the U.S. Preventive Services Task Force[48] and the American College of Gastroenterology[32] do not support DCBE as the primary form of CRC screening, given the lack of data demonstrating its efficacy and sensitivity for identifying colonic lesions.

Recommendation. DCBE is not recommended. If it is used, it should be performed every 5 years. Colonoscopy should be performed if the DCBE results are abnormal.

Virtual colonoscopy. Virtual colonoscopy (VC), also known as CT colonography, involves helical CT scanning of the colon after bowel preparation and colonic distention. The technique for VC is considered in another guideline.[57] Studies of VC have reported a sensitivity of 55% to 100% and a specificity of 94% to 98% for the detection of polyps measuring $\geq$10 mm and a sensitivity of 39% to 94% and a specificity of 79% to 92% for polyps at least 6 mm in size compared to colonoscopy.[58-62] One prospective study of 614 patients with fecal occult blood, hematochezia, iron-deficiency anemia, or family history of colon cancer compared DCBE, VC, and colonoscopy.[54]

For lesions measuring ≥10 mm, the sensitivity of DCBE, VC, and colonoscopy was 48%, 59%, and 98% respectively.

Higher patient acceptance of VC compared with colonoscopy has been suggested as a potential advantage of this procedure[63]; however; comparative studies show no consistent patient preference.[58,64] There are no studies demonstrating the efficacy of VC in reducing CRC incidence or mortality. There is also a concern regarding the associated radiation exposure,[65] although VC may detect clinically important extracolonic findings.[66] Virtual colonoscopy is not endorsed for CRC screening by multidisciplinary societal guidelines and is not covered by Medicare or private insurers. Cost-effectiveness analyses indicate that under most assumptions colonoscopy is more cost-effective than VC.[67,68] Improvement in technology, training, and standardization of the technique are required before VC can be recommended for widespread screening. However, it may be useful for patients who refuse colonoscopy or who have had an incomplete colonoscopic examination.[69] In general, patients with polyps detected on VC should undergo a complete colonoscopy. Although some authors advocate colonoscopy for any polyp identified on VC,[70] others suggest that colonoscopy should be selected for patients with polyps greater than 0.5 to 10 mm.[71]

Recommendation. Virtual colonoscopy is an evolving technique and is not currently recommended as the primary method of screening for CRC.

Fecal DNA testing. The molecular genetics of CRC provides the basis for fecal DNA testing. Adenomas and CRC arise from at least 3 different genetic pathways: chromosomal instability, microsatellite instability, and CpG island methylation.[72] Previous studies that used fecal-based DNA testing in individuals with advanced, symptomatic lesions have reported sensitivities between 62% to 91% for cancer and 27% to 82% for advanced adenomas, with specificities between 93% and 96%.[73-76] A large prospective study comparing fecal DNA testing with FOBT for CRC screening in average-risk individuals showed that the sensitivity of fecal DNA testing was 4 times that of FOBT (Hemoccult II; Beckman Coulter, formerly SmithKline Diagnostics) for detecting invasive cancer and more than double for adenomas containing high-grade dysplasia.[77] The sensitivity of fecal DNA testing compared with colonoscopy in detecting invasive cancers was 51%.[77] There are currently no studies demonstrating a reduction in CRC-related mortality from fecal DNA testing, and the technique for the test has not been standardized. The use of this test is still in development and under study and, therefore, cannot be recommended at this time for CRC screening.

Recommendation. Fecal DNA testing is not recommended.

Screening for high-risk individuals

FAP. Individuals with a diagnosis of FAP have an almost 100% risk for development CRC by age 40 to 50 years. FAP is an autosomal dominant syndrome caused by mutations in the adenomatous polyposis coli (APC) gene, which phenotypically presents with >100 adenomas throughout the colon. A variant of FAP is the attenuated form in which individuals have a variable number of adenomas (usually 20-100), a proximal distribution of adenomas, and relatively delayed onset of CRC that is approximately 10 years later than for FAP. Several germline mutations in the 3′ and 5′ ends of the APC gene have been identified in individuals with the attenuated form of FAP.[78,79]

Genetic testing accompanied by specialized counseling should be offered to patients with FAP and to family members at risk.[80,81] The actual benefits and impact of genetic testing have not been studied. Testing is first performed on the affected kindred with known FAP to identify the disease-producing mutation. The current commercially available genetic test is positive in approximately 80% of patients with FAP.[82] Once a mutation is identified, other individuals in the family, aged 10 years or older, should be tested for the mutation. Individuals with positive test results should be followed by annual sigmoidoscopy beginning at age 10 to 12 years. In a study of all FAP patients recorded in the Finnish Polyposis Registry, overall mortality resulting from CRC was significantly reduced in FAP patients undergoing screening sigmoidoscopy compared with those patients with a new diagnosis of CRC.[83] When multiple adenomas are identified on screening sigmoidoscopy, colectomy is indicated. If no polyps are identified, annual sigmoidoscopy should be offered up to age 40 years and then every 3 to 5 years thereafter.[1] Family members with negative genetic test results are assumed not to be affected; however, they can be offered sigmoidoscopy every 7 to 10 years to account for any potential error in genetic testing.[84] If genetic testing is not available, or the affected kindred has a negative test result for a mutation, annual sigmoidoscopy should be performed in all family members beginning at age 10 to 12 years. Colonoscopy should be performed yearly in those patients with attenuated FAP beginning in the late teens or early 20s given the proximal distribution of polyps and the later onset of disease.

Patients with FAP are at increased risk for upper gastrointestinal neoplasia, which is considered in a separate guideline.[85]

HNPCC. HNPCC is an autosomal dominant disorder characterized by the early development of colorectal cancer. In patients with HNPCC, CRC develops at a younger age (average 44 years) and tumors are predominantly located proximal to the splenic flexure. Affected patients carry a germline mutation in one of several DNA mismatch repair genes.[86] In those cases with defective mismatch repair, approximately 90% have mutations in the MLH1 or MSH2 genes.[86] Diagnostic clinical criteria for HNPCC have been outlined in detail elsewhere[40,87] and include the Amsterdam and Bethesda classifications. These clinical criteria are highly predictive of a mismatch repair gene

TABLE 2. Recommendations for individuals with genetic cancer syndromes

Family history	Screening recommendation
FAP with positive genetic test result in proband	Offer genetic testing with counseling. In relatives with positive genetic testing, annual flexible sigmoidoscopy beginning at age 10-12 y with colectomy when polyps develop. If no polyps are detected, annual flexible sigmoidoscopy until age 40 y, then every 3-5 y. Relatives with negative genetic test results are assumed not to be affected; however, they can be offered sigmoidoscopy every 7-10 y until age 40 y then colonoscopy every 5 y.
FAP with negative genetic test result in proband	Annual flexible sigmoidoscopy in all potentially affected relatives beginning at age 10-12 y as outlined above.
HNPCC	Colonoscopy every 1-2 y beginning at age 20-25 y, or 10 y younger than the earliest age of diagnosis of CRC in the family, whichever is earlier. Annual colonoscopy should be performed after age 40 y.

mutation. However, some families that do not meet these criteria may carry mismatch repair mutations and thus have HNPCC.

Microsatellite instability (MSI) is found in >90% of CRCs in patients with HNPCC.[87] In contrast, MSI is found in only 15% of sporadic CRCs. MSI is characterized by the expansion or contraction of short repeated DNA sequences caused by the insertion or deletion of repeated units.[80] The finding of MSI within CRC tissue is associated with defects in the DNA mismatch repair genes, as found in HNPCC.[88] In addition, low levels of expression of the protein products of the MLH1 or MSH2 genes in CRC tissue are also associated with a mutation in one of these mismatch repair genes.[89] Currently, MSI testing and immunohistochemical staining for MLH1 and MSH2 gene products on CRC tissue are recommended for screening patients clinically suspected to have HNPCC.[80,90-92] The finding of MSI and low gene protein expression in a tumor should then prompt genetic testing of the affected individual for germline mutations in the mismatch repair genes. If a mutation is identified, the first-degree relatives should then undergo genetic testing. If tumor tissue is not available, genetic testing should be performed in the affected individual. In a prospective cohort study of 11 families with HNPCC, genetic testing and the detection of germline mutations in asymptomatic relatives led to increased colonoscopic screening and surveillance.[93] Genetic testing should be done along with expert genetic counseling.

Colonoscopy should be performed in all persons potentially affected with HNPCC every 1 to 2 years starting at age 20 to 25 years or 10 years younger than the age of the earliest diagnosis in the family, whichever is earlier.[39,40] Beginning at age 40 years, colonoscopy should be performed annually. Patients with HNPCC are also at increased risk for development of upper gastrointestinal neoplasia, which is considered in a separate guideline.[85]

See Table 2 for a summary of recommendations for screening and surveillance in individuals with genetic cancer syndromes (FAP and HNPCC).

Individuals with a family history of CRC or adenomatous polyps. Individuals with one or more first-degree relatives with sporadic CRC or adenomatous polyps have a 2- to 4-fold increased risk for CRC. A meta-analysis of 27 case-control and cohort studies was performed to determine the familial risk of CRC.[94] The relative risk of CRC was 1.99 with a first-degree relative with adenomatous polyps, 2.25 with a first-degree relative with CRC, 3.87 with a first-degree relative with CRC before age 45 years, and 4.25 with more than one first-degree relative with CRC. It is recommended that individuals with a first-degree relative with CRC regardless of age should have colonoscopy beginning at age 40 years or 10 years younger than the affected relative, whichever is earlier,[40,95] although the benefit of earlier colonoscopy for patients with one first-degree relative diagnosed with CRC at an advanced age is unclear. Follow-up colonoscopy should be performed every 3 to 5 years if the relative was <60 years old and 10 years if the relative was ≥60 years old.[40] Individuals with a first-degree relative aged <60 years with adenomatous polyps should undergo colonoscopy screening beginning at age 40 years or 10 years younger than the affected relative.[40] Follow-up colonoscopy should be performed every 5 years. If the first-degree relative was greater than age 60 years at the time of diagnosis of adenomas, screening colonoscopy should be performed; however, the timing of initial colonoscopy has not been established and should be individualized. The interval timing for follow-up colonoscopy in these individuals should be the same as for average-risk persons. Patients with a second- or third-degree relative with colonic neoplasia should adhere to average-risk screening recommendations.[32,40] See Table 3 for a summary of recommendations.

SURVEILLANCE STRATEGIES FOR INDIVIDUALS WITH SIGNIFICANT PERSONAL HISTORY

Personal history of inflammatory bowel disease

Individuals with long-standing ulcerative colitis (UC) and extensive Crohn's colitis are at increased risk for development of dysplasia and CRC, and they should undergo colonoscopic surveillance. The risk of CRC increases with

the duration and extent of colitis, family history of CRC, continuing active colitis, young age at onset of disease, presence of backwash ileitis, and personal history of primary sclerosing cholangitis.[96-100] The presence of proctitis alone does not appear to increase the risk for CRC. In UC, patients with left-sided colitis or more extensive disease are at increased risk. In Crohn's colitis, those patients with extensive disease involving more than a third of the colon also have an increased risk of CRC, similar to that of patients with UC.[101,102] The extent of colonic involvement should be based on both endoscopic and histologic criteria, whichever reveals more extensive disease.[103] The role of colonoscopy in the management of inflammatory bowel disease is discussed in another guideline.[104]

Currently, there are no prospective, randomized trials evaluating the efficacy of surveillance colonoscopy in UC or Crohn's colitis. In a case-control study of patients with UC undergoing colonoscopic surveillance, there was a reduction in mortality from CRC in those patients in surveillance programs.[105] Patients with UC or extensive Crohn's colitis (greater than one third colonic involvement) should undergo surveillance colonoscopy every 1 to 2 years beginning 8 to 10 years after disease onset. Biopsy specimens of the colon in patients with documented pancolitis should be obtained in all 4 quadrants every 10 cm from the cecum to the rectum, to obtain a minimum of 32 biopsy samples.[103] In patients with less extensive colitis, biopsy specimens can be limited to the microscopically involved segments.[103] The presence of high-grade dysplasia or multifocal low-grade dysplasia in flat mucosa is an indication for colectomy. The management of unifocal low-grade dysplasia is controversial as to whether colectomy should be performed. Biopsy specimens should be obtained of strictures, mass lesions, and macroscopic abnormalities other than pseudopolyps.[106,107] Adenomatous-appearing polyps should be completely removed by polypectomy and biopsy specimens should be obtained from the adjacent flat mucosa to determine the presence of dysplasia. If a dysplastic polyp is identified outside an area of inflammation and there is no evidence of dysplasia in the adjacent mucosa, it can be managed as a sporadic polyp, similar to polyps in individuals without UC or Crohn's colitis.[103] If a dysplastic polyp is in an area of active inflammation (dysplasia associated lesion or mass) and there is evidence of dysplasia in the adjacent mucosa, colectomy is indicated.[103]

Personal history of CRC

Patients diagnosed with colorectal cancer are at risk of having synchronous lesions or for development of metachronous lesions. Synchronous colon cancers occur in 3% to 5% of patients.[108,109] A complete colonoscopy should be performed at the time of CRC diagnosis to rule out synchronous mass lesions and to remove any additional adenomatous lesions. If a complete colonoscopy

TABLE 3. Recommendations for individuals with family history of CRC or adenomatous polyps		
Patient category	Screening	Surveillance
First-degree relative(s) with colorectal cancer diagnosed at age <60 y	Colonoscopy at age 40 or 10 y younger than affected relative (whichever is younger)	If normal, repeat every 3-5 y
First-degree relative(s) with colorectal cancer diagnosed at ≥60 y	Colonoscopy at age 40 y	If normal, repeat every 10 y
First-degree relative(s) with adenomatous polyp <60 y	Colonoscopy at age 40 y or 10 y younger than affected relative	If normal, repeat every 5 y
First-degree relative with adenomatous polyp >60 y	Colonoscopy for screening, age individualized	If normal, same as average risk
Second- or third-degree relative with cancer or polyps	Colonoscopy as average-risk individuals	If normal, same as average risk

cannot be performed because of malignant obstruction, CT colonography, DCBE, or intraoperative colonoscopy can be performed to exclude proximal neoplasms. Otherwise, postoperative colonoscopy within 6 months of complete surgical resection should be performed.

Postoperative colonoscopy is also performed for the detection of cancer recurrence or metachronous lesions in patients with stage I-III and selected patients with stage IV cancer. Frequent, repeat colonoscopy starting at 1 year after resection of nonrectal colon cancer has not been shown to improve patient survival or increase resectability of recurrent disease.[110-112] Currently, the American Cancer Society recommends colonoscopy within 1 year of curative-intent resection of CRC.[39] The American Society of Clinical Oncology recommends colonoscopy 3 to 5 years after surgery, whereas the American Society of Colon and Rectal Surgeons recommends periodic colonoscopy at 3-year intervals.[113,114] The rationale for intensive colonoscopic follow-up soon after curative resection for colon cancer is based on the recent finding that the incidence of metachronous cancers is higher in this group of patients compared with the general population and with patients with adenomatous polyps.[115] Furthermore, the yield of surveillance colonoscopy for the detection of metachronous cancers and adenomatous polyps appears to be highest during the first 24 months after surgery.[116,117] On the basis of these data, we recommend that surveillance colonoscopy be performed at 1 year after surgical resection of colon cancer. If results are normal, the next

TABLE 4. TNM staging classification of CRC	
Primary tumor (T)	
TX	Primary tumor cannot be assessed
T0	No evidence of primary tumor
Tis	Carcinoma in situ: intraepithelial or invasion of lamina propria
T1	Tumor invades submucosa
T2	Tumor invades muscularis propria
T3	Tumor invades through the muscularis propria into the subserosa or into non peritonealized pericolic or perirectal tissues
T4	Tumor directly invades other organs or structures or perforates visceral peritoneum
Regional lymph nodes (N)	
NX	Regional lymph nodes cannot be assessed
N0	No regional lymph node metastasis
N1	Metastasis in 1 to 3 regional lymph nodes
N2	Metastasis in 4 or more regional lymph nodes
Distant metastasis (M)	
MX	Distant metastasis cannot be assessed
M0	No distant metastasis
M1	Distant metastasis

colonoscopy should be in 3 years. If that colonoscopy has normal results, the next colonoscopy should be performed in 5 years.

Conversely, the optimal surveillance of patients with surgically resected rectal cancer is not known. Local recurrence of rectal cancer occurs in 2% to 30% of patients, depending on stage and therapy; it is usually detectable within 30 months of the initial surgical resection.[116] Several large studies have demonstrated a significant decrease in local cancer recurrence associated with preoperative radiation therapy in advanced locoregional disease[31] (defined as tumors with extension to the perirectal fat, stage T3 N0 or T4 N0 or involvement of mesorectal or pelvic lymph nodes, stage TX N1 or TX N2.) See Table 4 for TNM staging classification of CRC established by the American Joint Committee on Cancer and the International Union Against Cancer.[118] The rate of local recurrence also depends on the surgical approach, and it significantly decreases with the use of total mesorectal excision. The combination of preoperative radiation therapy and total

mesorectal excision reduces the rate of recurrence of locally advanced disease to 2.4% within 2 years after resection compared with 8.2% with surgery alone.[119] Given the decreased likelihood of local cancer recurrence in patients treated with pelvic radiation, the American Society of Clinical Oncology does not recommend postoperative surveillance sigmoidoscopy in patients treated with preoperative radiation.[113] The American Society of Colon and Rectal Surgeons recommends periodic endoscopic evaluation of the surgical anastomosis in patients who have undergone resection but does not, however, specify the preferred method or timing of the evaluation.[114] There are no prospective trials demonstrating a significant survival benefit or improvement in resection rates of recurrent rectal cancers as a result of frequent sigmoidoscopy; however, most studies to date have been underpowered to detect a significant difference.[110,111] Patients who did not receive neoadjuvant radiation therapy for locally advanced disease or those who did not undergo total mesorectal excision should undergo sigmoidoscopy every 3 to 6 months postoperatively for the first 2 or 3 years. All patients should undergo a complete colonoscopy at 1 year.

The role of endoscopic ultrasound in the postoperative surveillance of rectal cancer has not been clearly defined and is discussed in another guideline.[31] EUS can be useful in the detection of tumor recurrence presenting extraluminally, which can be missed by routine surveillance with digital rectal examination and sigmoidoscopy. Several studies on the use of EUS in the surveillance of patients with resected rectal cancer have demonstrated that it can accurately detect and diagnose regional recurrence; however, its impact on long-term survival is not known.[31]

Personal history of adenomatous polyps

Colonoscopy is the recommended method of surveillance after the removal of adenomatous polyps because it has been shown to significantly reduce subsequent CRC incidence.[9,10] The timing of follow-up colonoscopy should be tailored to the number, size, and pathologic findings of the adenomatous polyps removed. Patients with 1 to 2 small (<1 cm) tubular adenomas with only low-grade dysplasia should undergo follow-up colonoscopy no earlier than 5 years later. Patients with advanced adenomatous lesions (defined above) or ≥ 3 adenomas should have repeat colonoscopy in 3 years as long as all visualized polyps were completely removed, the colonoscopy was completed up to the cecum, and the colonic preparation was adequate. A shorter interval of follow-up is recommended in those patients with numerous adenomatous (>10) polyps and in those in whom the colonoscopy was incomplete or the preparation was inadequate. After a surveillance colonoscopy has normal results, repeat examinations should be done at 5-year intervals. Patients with large, sessile adenomatous lesions removed in a piecemeal fashion should have a repeat examination within 2 to 6 months to exclude and remove

any remnant polypoid tissue. See Table 5 for summary of recommendations.

MANAGEMENT OF COLONIC POLYPS DURING FLEXIBLE SIGMOIDOSCOPY

The decision to perform colonoscopy after the detection of a small adenoma on flexible sigmoidoscopy is controversial and should be individualized.[40] Colonoscopy is the preferred method of examination of the colon after a flexible sigmoidoscopy with at least one adenoma found because it allows both the detection and removal of synchronous polyps. Controversy remains regarding whether individuals with small tubular adenomas (<1 cm) should undergo colonoscopy.[120,121] Factors associated with an increased risk of proximal advanced neoplasia include age >65 years, villous histologic findings in distal adenomas, adenomas ≥1 cm, and multiple distal adenomas.[19-21] Patients with any of these factors should undergo colonoscopy. Although there is some controversy as to the clinical significance of hyperplastic polyps, there does not appear to be an increased risk of proximal neoplasia or proximal advanced neoplasia in asymptomatic individuals undergoing screening.[122] Therefore, the discovery of hyperplastic polyps on screening flexible sigmoidoscopy is not an indication for colonoscopy, with the exception of patients with a hyperplastic polyposis syndrome, which is associated with an increased risk of colorectal cancer.[123]

For small polyps <1 cm in size encountered on flexible sigmoidoscopy, endoscopic biopsy specimens can distinguish inflammatory or hyperplastic polyps from adenomatous polyps. Biopsies of polyps >1 cm can miss significant adenomatous elements of the lesion and, therefore, may not reliably determine the true pathology of the lesion. Patients found to have one or more polyps ≥1 cm in size on flexible sigmoidoscopy should undergo complete colonoscopy. The cold snare technique is safe for sampling small polyps.[124] Application of cautery should be avoided in an unprepped colon because of the potential for explosion.

MANAGEMENT OF COLON POLYPS DURING COLONOSCOPY

Most polyps seen during colonoscopy can be completely removed. The safety of polypectomy has been substantiated by the low incidence of complications reported in numerous series.[25] The endoscopist should be prepared to perform a total examination and remove all polyps found at the time of the first colonoscopy, although technical factors encountered during colonoscopy may limit completion of the procedure. Every effort should be made to avoid repetitive procedures. Although controversy still exists regarding the degree of malignant potential of polypoid lesions of the colon, current opinion is

TABLE 5. Surveillance recommendations for individuals with significant personal history of colorectal neoplasia

Personal History	Surveillance Recommendation
Prior colon cancer	High quality clearance of remainder of the colon at or around time of resection, followed by colonoscopy at 1 y after curative resection, then at 3 y and then 5-y intervals if results are normal
Prior rectal cancer	Colonoscopy: clearance of remainder of colon at or around time of resection, followed by colonoscopy at 1 y and 4 y after resection, then at 5-y intervals
	Flexible sigmoidoscopy: after low anterior resection, if no pelvic radiation or no mesorectal excision every 3-6 mo for 2-3 y
Prior colonic adenomas ≤2 small tubular adenomas (<1 cm) and only low-grade dysplasia	No earlier than 5 y
Advanced neoplasia or 3-10 adenomas	3 years
>10 adenomas	Within 3 y
Large sessile polyp with potentially incomplete excision	2-6 mo
Negative surveillance colonoscopy	No earlier than 5 y
Ulcerative colitis or extensive Crohn's colitis of 8-10 y duration	Surveillance colonoscopy every 1-2 y with systematic biopsies to detect dysplasia

that most cancers arise in preexisting neoplastic polyps.[125] It is impossible to tell grossly which lesions are or will become malignant. The prevalence of malignancy in a polyp rises as the size and villous component of the polyp increase.[126] In general, all polypoid lesions ≥0.5 cm in diameter should be totally excised and recovered for histologic examination. Although the occurrence of carcinoma in a polyp <0.5 cm is rare, it is reasonable to remove all such diminutive lesions when they are encountered during colonoscopy performed for any indication.[127,128] Representative biopsy samples may be obtained when these lesions are too numerous for all of them to be removed.

Large, sessile polyps have a high malignant potential and tend to have microscopic foci of residual polyp after excision.[129] Therefore, a patient who has colonoscopic excision of these lesions should have repeat evaluation

of the polyp site within 2 to 6 months to document complete removal. If residual polyp tissue is found, it should be removed if possible, and the completeness of excision checked once again within another 6-month period. If complete removal of the lesion has been verified at the first or second follow-up interval, then subsequent surveillance colonoscopy should be individualized. If a large benign-appearing sessile polyp cannot be completely or safely removed endoscopically within 1 to 3 examinations, surgical resection should be strongly considered. The management and follow-up of patients with polyps removed endoscopically found to have high-grade dysplasia or cancer are discussed in another guideline.[31]

SUMMARY

- Colonoscopy is the preferred modality for CRC screening in average risk patients *(B)*.
- Alternative methods for CRC screening in average-risk patients include yearly fecal occult blood testing *(A)*, flexible sigmoidoscopy every 5 years, combined yearly FOBT and flexible sigmoidoscopy every 5 years *(B)*.
- Single digital rectal examination FOBT has a poor sensitivity for CRC and should not be performed as a primary screening method *(A)*.
- Studies evaluating virtual colonoscopy and fecal DNA testing for CRC screening have yielded conflicting results and therefore cannot be recommended *(A)*.
- Genetic testing along with counseling is recommended for individuals with hereditary forms of CRC, including FAP and HNPCC *(C)*.
- Individuals at risk for FAP should undergo screening flexible sigmoidoscopy yearly starting at age 10 to 12 years. The development of multiple, diffuse adenomas in the colon is an indication for total colectomy *(B)*.
- Individuals at risk for HNPCC should undergo colonoscopy every 1 to 2 years starting at age 20 to 25 years or 10 years younger than the age of the earliest diagnosis of cancer in the family, whichever is earlier *(B)*.
- Individuals with a family history of 1 or more first-degree relatives with sporadic CRC regardless of age should have a colonoscopy beginning at age 40 years or 10 years younger than the affected relative, whichever is earlier. If the index colonoscopy has normal results, repeat colonoscopy should be performed on the basis of the age of the affected relative *(B)*.
- Individuals with a first-degree relative age <60 years with adenomatous polyps should undergo colonoscopy beginning at age 40 years or 10 years younger than the affected relative, whichever is earlier. If the index examination is normal, recommend repeat colonoscopy every 5 years *(B)*.
- In patients with a first-degree relative more than 60 years old at diagnosis of adenomatous polyps, the timing of screening colonoscopy should be individualized.

The interval timing between follow-up examinations should be the same as for average-risk patients *(C)*.
- The risk for development of CRC is increased in individuals with extensive UC and Crohn's colitis. Surveillance colonoscopy with multiple biopsy specimens should be performed every 1 to 2 years beginning after 8 to 10 years of disease *(B)*.
- A complete colonoscopy should be performed in all patients diagnosed with CRC to rule out synchronous cancers or adenomatous lesions. If a complete examination cannot be performed at the time of CRC diagnosis, a colonoscopy should be performed within 6 months after surgical resection *(B)*.
- Surveillance colonoscopy after surgical resection of CRC should be performed 1 year after surgery and, if results are normal, every 3 to 5 years thereafter *(B)*.
- The risk of rectal cancer recurrence is dependent on stage, surgical management, and the administration of radiation therapy. Patients who did not receive pelvic radiation for locally advanced disease or those who underwent nonmesorectal resection should undergo sigmoidoscopy every 6 months for the first 2 years postoperatively *(B)*.
- Patients with a personal history of adenomatous polyps should undergo surveillance colonoscopy, the timing of which should be individualized depending on the number, size, and pathologic diagnosis of the adenomatous polyps removed, as well as the quality and completeness of the examination *(B)*. When feasible, all polyps ≥0.5 cm should be removed *(B)*.

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ERRATUM

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