CME CREDIT

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Understanding current guidelines for colorectal cancer screening: A case-based approach

■ ABSTRACT

After a polyp or polyps are discovered on colonoscopy, many patients are being told to come back for repeat colonoscopy unnecessarily soon, thus diverting a scarce resource away from patients who may derive the most benefit—those with high-risk polyps and those who have never been screened.

■ KEY POINTS

All polyps do not pose the same risk. Small, left-sided hyperplastic polyps are nonneoplastic and require no increased follow-up. Adenomas are precancerous, and follow-up is determined by size, number, and histologic features.

The American College of Gastroenterology recommends that African Americans undergo screening under an average-risk strategy starting at age 45, as they have the highest incidence of colorectal cancer of any racial or ethnic group and present with it at a younger age.

People with a family history of colorectal polyps or cancer are recommended to start screening earlier—at age 40 or 10 years younger than the age of the relative that was affected (whichever is younger)—-and some of them should have colonoscopy more often than every 10 years

When deciding on the proper surveillance interval, one must take into account several details regarding the patient's colonoscopy. Patients who have had an inadequate preparation, incomplete examination, or large lesions removed piecemeal should be recalled sooner.

F EWER THAN HALF of all people in the United States who should be screened for colorectal cancer have actually been screened. But at the same time, many people who have no or low-risk polyps on colonoscopy may be returning unnecessarily soon. Utilizing current screening and surveillance guidelines to direct patient care can reduce the number of unnecessary colonoscopies and improve surveillance of patients who may be at greater-than-average risk of colorectal cancer.

In this paper, we use several case examples to clarify the current guidelines on who should be screened, why, how, and how often.

■ WHY SCREEN?

Approximately 6% of American men and women develop an invasive colorectal neoplasm in their lifetime. Colorectal cancer is the second-leading cause of cancer death in the United States. In 2007, an estimated 153,760 people were newly diagnosed with colorectal cancer, and 52,180 people died of it.[1]

Yet, colorectal cancer is one of the few preventable cancers. Screening has been advocated as a way of preventing deaths by removing precancerous adenomas and detecting colorectal cancer early.[2] Medicare has paid for screening colonoscopy since 1998, and since that time demand for this procedure has increased 112%.[3,4] (See "Colonoscopy is the preferred test" on page 444.[2,4–17])

■ START SCREENING AT AGE 50 FOR PEOPLE AT AVERAGE RISK

National society guidelines recommend that people at average risk of colorectal cancer be screened starting at age 50 (**TABLE 1**).[5,18–21] People are considered to be at average risk if they have no symptoms, do not have ulcerative colitis or Crohn's colitis, and do not have a personal or family history of colorectal neoplasia.

The US Multi-Society Task Force on Colorectal Cancer[19] suggests that people at average risk undergo one of the following:

- Colonoscopy every 10 years
- Flexible sigmoidoscopy every 5 years
- Fecal occult blood testing every year
- An air-contrast barium enema or computed tomographic (CT) colonography every 5 years
- Fecal DNA testing, interval uncertain.

Anyone who has a positive result with any test other than colonoscopy should subsequently undergo colonoscopy.

Start screening sooner in people at higher risk

African Americans should undergo screening for colorectal cancer under an average-risk strategy starting at age 45, according to a position paper from the American College of Gastroenterology.[4] Reasons for starting sooner are that African Americans have the highest incidence of colorectal cancer of any racial or ethnic group, and that they present with it at a younger age. In the years 1970–1994, 10.7% of cases of colorectal cancer in African Americans were detected before age 50 compared with 5.5% of cases in white people.[22] In addition, compared with other ethnic groups, African Americans have a more proximal distribution of colorectal neoplasms, present with later-stage disease, and have lower survival rates.[4]

People with a family history of colorectal polyps or cancer should also start screening earlier—as early as age 40, or 10 years younger than the age at which the relative was affected—and some should be tested more often than every 10 years (see below).

Patients with ulcerative colitis or Crohn's colitis. Current multisociety guidelines for colorectal cancer screening and surveillance in patients with ulcerative colitis or Crohn's colitis are based on expert consensus and recommend a systematic biopsy protocol in some patients. When to begin surveillance in these patients and the specifics of the biopsy protocol are beyond the scope of this paper but are discussed in detail elsewhere.[19]

■ FAMILY HISTORY INCREASES RISK

Case 1:
A woman with a family history of cancer
A 55-year-old woman comes in for a routine physical examination. Her medical history is not remarkable, but her family history is: her maternal grandmother was diagnosed with colon cancer at age 75, her sister was diagnosed with endometrial cancer at age 34, and her mother was diagnosed with colon cancer at age 60. The patient underwent colonoscopy 5 years ago, and a 1.2-cm villous adenoma was removed from her right colon. She had been advised to have her next colonoscopy in 3 years.

*   *   *

Current recommendations for screening and surveillance differ based upon the number, age, and relationship of relatives affected with colorectal neoplasia (**TABLE 1**). The patient described above began screening at age 50 in accordance with the guidelines for people at average risk, but her extended family history was not taken into account.

Hereditary nonpolyposis colorectal cancer
Our patient's family history meets the criteria for hereditary nonpolyposis colorectal cancer,[23] ie, she has three family members with hereditary nonpolyposis colorectal cancer-associated cancers (colorectal cancer or cancer of the endometrium, small bowel, ureter, or renal pelvis), and one family member (her mother) is a first-degree relative of the other two affected relatives. Two successive generations of her family are affected, and one family member (her sister) was diagnosed before the age of 50.

People in families like this have an 80% lifetime risk of colorectal cancer, so it is imperative to review every patient's family history. Patients who meet the criteria should be referred for genetic counseling and possibly genetic testing. In addition, they should begin screening—with colonoscopy, not the other tests—between the

African Americans have the highest incidence of colorectal cancer of any racial or ethnic group

Recommendations for screening for colorectal cancer according to family history

FAMILY HISTORY	RECOMMENDATION
One first-degree relative with colorectal cancer or adenomatous polyp at age 60 or over, or Two second-degree relatives with colorectal cancer	Use an average-risk screening strategy starting at age 40 (See text)
Two or more first-degree relatives with colorectal cancer, or Two second-degree relatives with colorectal cancer or adenomatous polyp before age 60	Colonoscopy at age 40, or 10 years younger than the age the earliest case in the family was diagnosed, whichever is earlier If normal, repeat every 5 years
Hereditary nonpolyposis colorectal cancer (See text)	Colonoscopy and endometrial biopsy at age 21–25, or 10 years younger than the age the earliest case in family was diagnosed Repeat every 2 years until age 40, then annually Refer to specialty center for genetic counseling and consideration of genetic testing
Familial adenomatous polyposis	Sigmoidoscopy or colonoscopy at age 10–12 Esophagogastroduodenoscopy at age 20 Refer to specialty center for genetic counseling and consideration of genetic testing

ages of 21 and 25 or at an age 10 years younger than when the youngest family member was diagnosed with colorectal cancer, whichever is earlier. They should subsequently undergo colonoscopy every 1 to 2 years.

These patients also have an increased risk of certain extracolonic cancers, including a 40% to 60% lifetime risk of endometrial adenocarcinoma. They and their physicians need to be aware of consensus screening recommendations for ovarian, endometrial, and transitional cell cancers.[24]

Familial adenomatous polyposis

Patients with familial adenomatous polyposis develop hundreds to thousands of adenomatous colorectal polyps, usually in their teens, and have a 100% risk of developing colon cancer if the colon is not removed. Patients with a family history of this disorder should undergo screening at 10 to 12 years of age.

■ OVERCOMING BARRIERS TO SCREENING

In 2004, an estimated 70.1 million Americans were 50 years of age and older and at average risk of colorectal cancer.[25] Of these, only 28.3 million (40.4%) had undergone screening, and 41.8 million had not.

We could view this as an opportunity to make a significant impact on the disease, but resources are limited. Seeff et al[25] estimated that it would take 10 years to perform screening colonoscopy on unscreened Americans if one-half of all current endoscopic capacity were used for screening alone.

Barriers to screening also exist on an individual level. A recent study[26] found that only 50% of patients referred for screening colonoscopy actually underwent the procedure; patients were significantly less likely to make an appointment and keep it if they were younger or female or if they were on Medicaid. Reasons cited by patients for not following through with colonoscopy after referral included fear of pain or perforation, dislike of the bowel preparation, and misperceptions about colorectal cancer risk.

Understanding these barriers and improving patient-physician communication about the procedure and the risk of colorectal cancer in the general population, even in the absence

Colonoscopy is the preferred test

Colonoscopy is the preferred screening test for colorectal cancer, according to the American College of Gastroenterology,[5] as it has been shown to reduce the rate of death from this disease. The National Polyp Study Group prospectively followed 1,418 patients with one or more colorectal adenomas who underwent polypectomy.[6] All told, 1,210 patients were followed for the duration of the study (average follow-up 5.9 years), and five new cases of colorectal cancer were detected. Compared with the anticipated number of cases,[7–9] the actual incidence was 76% to 90% lower, which the investigators attributed to the effectiveness of colonoscopic polypectomy for colon cancer prevention (**FIGURE 1**).

Alternatives to colonoscopy for screening people at average risk are air-contrast barium enema studies, fecal occult blood testing, flexible sigmoidoscopy, and computed tomographic (CT) colonography. These have been carefully investigated, and their advantages and limitations are reviewed in detail elsewhere.[2]

Air-contrast barium enema studies may have a limited role in screening. Rockey et al[10] performed a prospective, multicenter trial comparing the accuracy of air-contrast barium enema studies, CT colonography, and colonoscopy. Air-contrast barium enema studies were significantly less sensitive than colonoscopy for detecting lesions larger than 10 mm (48% vs 98%) and lesions 6 to 9 mm (35% vs 99%).

Fecal occult blood testing once a year or every 2 years has been shown in randomized, controlled trials to reduce the number of deaths due to colorectal cancer by 15% to 33%,[11–13] but its sensitivity for detecting colonic adenomas is low and varies from 9% to 36% based on test characteristics and compliance with annual testing.[14–16]

Flexible sigmoidoscopy has excellent accuracy for detecting distal colonic neoplasms, but 50% of neoplasms are beyond the reach of the sigmoidoscope.[4,16,17] The percentage of people who have high-grade proximal lesions (which sigmoidoscopy cannot detect) seems to be higher in women than in men, so that colonoscopy may be the preferred method of screening for colorectal cancer in women.

CT colonography is an evolving radiologic tool. Although variable accuracy has been found, the largest study has shown it to be as accurate as colonoscopy, and it is endorsed by the Multi-Society Task Force as a screening method.[19] However, most insurers do not pay for it.

of a family history, may help improve adherence to screening colonoscopy.

■ POST-POLYPECTOMY SURVEILLANCE: OFTEN TOO SOON, TOO FREQUENT

After a polyp or polyps are discovered on colonoscopy, many patients are being told to come back for repeat colonoscopy unnecessarily soon,[27,28] thus diverting a scarce resource away from patients who may derive the most benefit—ie, those with high-risk polyps, those with a strong family history of colon cancer or an inherited predisposition to colon cancer, and those who have never undergone screening.

The following cases illustrate how current evidence-based guidelines can be applied to several different patients.

Case 2: 'Three benign polyps'
A 51-year-old woman with no personal or family history of colorectal neoplasia calls her primary care physician after undergoing her first colonoscopy. The patient noted that she had had "three benign polyps removed." She would like to know when her next colonoscopy should be.

The primary care physician obtains the patient's colonoscopy report, which reveals that three polyps measuring 5 mm, 4 mm, and 4 mm were removed from the patient's descending colon. The pathology report reveals that two of these polyps were tubular adenomas, and one of the 4-mm polyps was hyperplastic.

Case 3: A large tubulovillous polyp
A 46-year-old African American man with no personal or family history of colorectal neoplasia

underwent his first colonoscopy 1 year ago. He had had a 1.5-cm pedunculated polyp removed in toto from his ascending colon. The pathologist characterized the polyp as "tubulovillous."

Not all polyps are precancerous

The histopathology report helps the clinician determine the appropriate post-polypectomy surveillance interval (TABLE 2). Polyps are classified on the basis of their histologic features; the most common types of polyps are adenomas and hyperplastic polyps.

Adenomas are precursors to colorectal cancer, progressing via the widely recognized adenoma-carcinoma sequence.[29] It is not unusual that both of our patients would have adenomatous polyps, since the prevalence of these polyps increases with age.[30] Adenomas are detected in 11% of average-risk people ages 50 to 54, increasing to 33% to 50% in people 65 to 75 years old.[31,32]

Small, left-sided hyperplastic polyps, on the other hand, are considered nonneoplastic and do not require follow-up unless a patient meets the criteria for hyperplastic polyposis (TABLE 2). While current guidelines do not take into account hyperplastic polyps when determining postpolypectomy surveillance, the clinical significance and possible neoplastic potential of large and right-sided hyperplastic polyps is an area of active research.

Often, hyperplastic polyps are erroneously spoken of as "benign" when in fact they are not precancerous and are clinically insignificant. In fact, Boolchand et al[27] found that 61% of primary care physicians would bring a patient with a single 6-mm hyperplastic polyp back for surveillance colonoscopy in 5 years or sooner. Current consensus guidelines do not recommend surveillance colonoscopy for the majority of patients with hyperplastic polyps. These individuals are not at an increased risk of colorectal cancer and should go back to average-risk screening recommendations, ie, colonoscopy in 10 years, the same interval as for the average-risk individual.[33]

Adenomas:
How many? How big? What features?

If adenomas are discovered, three key questions affect how soon the patient should undergo colonoscopy again (TABLE 2):
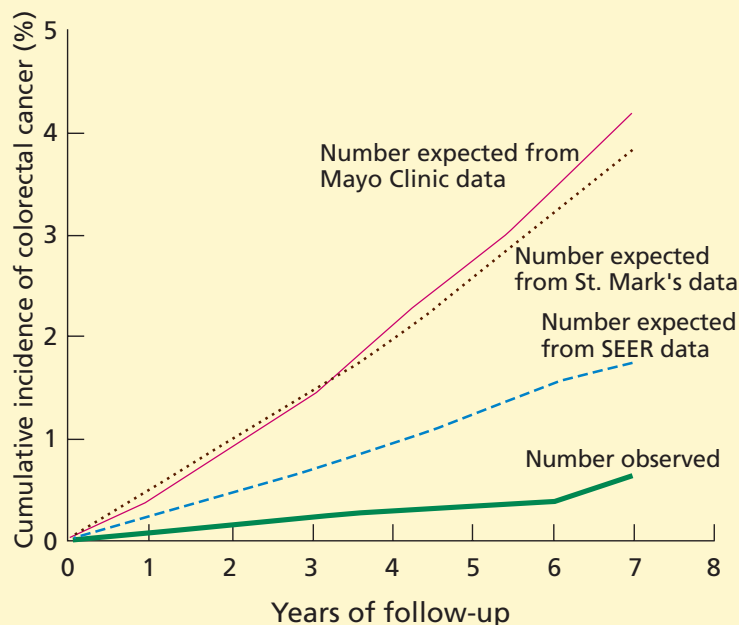

Colonoscopic polypectomy prevents colorectal cancer

FIGURE 1. Observed cumulative incidence of colorectal cancer in the National Polyp Study[6] compared with the expected incidence based on three reference groups.[7–9]

How many? Van Stolk et al[34] analyzed colonoscopy results from 479 participants in the Polyp Prevention Study and found at 3 years' follow-up that the strongest predictor of adenoma recurrence was the number of adenomas detected. On multivariate analysis, the finding of three or more adenomas during the baseline colonoscopy was an independent risk factor for having two or more adenomas on the subsequent colonoscopy. Only 3.3% of patients with one or two adenomas at baseline subsequently developed any clinically worrisome adenoma, compared with 6% of those with three or more adenomas.

Other studies also found that the number of adenomas predicts the subsequent development of more adenomas, and in particular advanced colorectal neoplasia.[35–38]

TABLE 2

Postpolypectomy surveillance strategies according to risk of recurrent advanced adenoma

COLONOSCOPIC FINDINGS	RECOMMENDATION
Above-average risk	
Small, left-sided hyperplastic polyps in a patient who does not meet criteria for hyperplastic polyposis syndrome[a]	Continue average-risk screening strategy (See text)
1–2 small (< 1 cm) tubular adenomas	Colonoscopy every 5–10 years
High risk	
3–10 adenomas, or any adenoma > 1 cm with villous features or high-grade dysplasia	Colonoscopy every 3 years
> 10 adenomas	Colonoscopy more often than every 3 years, consider genetic counseling for familial syndrome
Hyperplastic polyposis syndrome	Colonoscopy, no clear recommendation on interval, further investigation needed

[a] Diagnostic criteria for hyperplastic polyposis syndrome according to the World Health Organization International Classification:
- At least five histologically diagnosed hyperplastic polyps proximal to the sigmoid colon, of which two are greater than 10 mm in diameter, or
- Any number of hyperplastic polyps occurring proximal to the sigmoid colon in an individual who has a first-degree relative with hyperplastic polyposis, or
- More than 30 hyperplastic polyps distributed throughout the colon.

ADAPTED FROM WINAWER SJ, ZAUBER AG, FLETCHER RH, ET AL. GUIDELINES FOR COLONOSCOPY SURVEILLANCE AFTER POLYPECTOMY: A CONSENSUS UPDATE BY THE US MULTI-SOCIETY TASK FORCE ON COLORECTAL CANCER AND THE AMERICAN CANCER SOCIETY. GASTROENTEROLOGY 2006; 130:1872–1885.

Adenomas are precancerous and warrant surveillance. Small, left-sided hyperplastic polyps are not considered neoplastic and no surveillance is indicated

How big? Noshirwani et al[35] retrospectively analyzed data from their adenoma registry and found that polyps 1 cm or larger were significantly associated with the finding of advanced adenomas 3 years later.

What features? Tubulovillous or villous features in an adenoma have been shown to increase the risk of future advanced adenomas and cancer.[39,40] Similarly, high-grade dysplasia is associated with the subsequent development of advanced adenomas. In the Veterans Affairs Cooperative Study,[41] 10.9% of patients who had a polyp of any size with high-grade dysplasia developed an advanced neoplasm within 5 years, compared with only 0.6% of those with small polyps that did not harbor high-grade dysplasia.

Recognizing advanced adenomas is important when interpreting a patient's colonoscopy results because multiple studies have shown them to predict recurrent advanced neoplasms or colorectal cancer.[35,39–42]

What does this mean for our patients?

If a patient (like our patient in case 2) who is otherwise at average risk is found to have an adenoma or adenomas without advanced features, the postpolypectomy surveillance interval should be dictated by the number of adenomas found. Current guidelines recommend that patients like this one—with one or two small tubular adenomas without features of advanced colorectal neoplasia—have a low risk of recurrent advanced adenomas and should undergo colonoscopy again in 5 to 10 years (**TABLE 2**).[33]

In contrast, in case 3, the polyp (which was completely removed) had two characteristics of advanced neoplasia: size larger than 1 cm and a villous component. This patient should come back in 3 years.

In colonoscopy, quality matters

An important caveat is that current postpolypectomy surveillance recommendations

are based on the assumption that the bowel has been prepared adequately and that the entire colon is examined thoroughly up to the level of the cecum. Therefore, when deciding on the proper surveillance interval, one must take into account certain factors regarding the patient's colonoscopy. Patients who have had an inadequate bowel preparation, incomplete examination, or large lesions removed piecemeal should be recalled at a shorter interval.

A final observation: another possible reason that patients are being sent back for repeat colonoscopy sooner than recommended is the concern for missed polyps. Nonpolypoid adenomas, which include flat and depressed lesions, can be easily missed using conventional endoscopy.[43] A systematic review of six studies involving 465 patients who underwent tandem colonoscopy found a pooled miss rate of 26% for adenomas 1 to 5 mm.[44] One way endoscopists can improve adenoma detection is to perform a slow endoscopic withdrawal over at least 6 minutes.[45] ■

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