ADVANCES IN ENDOSCOPY

Current Developments in Diagnostic and Therapeutic Endoscopy

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Screening Tests for Colon Cancer

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G&H Which screening tests are currently recommended for colon cancer, and how often should they be performed?

DR Several tests are recommended in all colon cancer screening guidelines, particularly colonoscopy and fecal occult blood testing. Within the United States, colonoscopy is the most commonly utilized test and should be performed every 10 years in average-risk persons (Figure 1). Fecal occult blood testing, which should be performed annually as a fecal immunochemical test (FIT) rather than a guaiac-based test, is growing in importance.

Screening tests that are included in at least some guidelines but are not utilized frequently include flexible sigmoidoscopy, fecal DNA testing, computed tomography colonography (CTC) or virtual colonoscopy, and double-contrast barium enema (DCBE). Flexible sigmoidoscopy is appropriate either every 5 or 10 years, and the US Preventive Services Task Force has recently suggested that flexible sigmoidoscopy can be used in combination with fecal blood testing. Fecal DNA testing and CTC, neither of which is projected to be in the revised US Preventive Services Task Force recommendations, should be performed at 3- and 5-year intervals, respectively. There are no observational data to support the 3-year interval for fecal DNA testing; however, most experts recommend it as the optimal balance between the high cost of the test and its performance. DCBE frequency should be every 5 years, although this test is rarely used and will likely be removed from all guidelines after the next round of revisions.

G&H What are the reasons for removing DCBE from the guidelines?

DR DCBE has no advantages compared with CTC except cost. The sensitivity of DCBE for polyps at least 1 cm in size is only 50%, and patients have much less discomfort with CTC compared to DCBE.

G&H Is the use of flexible sigmoidoscopy and CTC decreasing?

DR Flexible sigmoidoscopy use is decreasing. Reimbursement is so poor for this procedure that doctors prefer not to perform it, contributing to decreased use. Flexible sigmoidoscopy is much less effective than colonoscopy in preventing right-sided cancer. Further, patients who have undergone flexible sigmoidoscopy are more likely than patients who have undergone colonoscopy to say that they will not be screened again because of an unpleasant experience. CTC has never had significant use for screening outside of a few select centers. CTC has been around for 22 years now with very limited impact.

G&H What are the advantages and disadvantages associated with stool or blood tests compared with structural examinations?

DR Stool and blood tests are less expensive, are less invasive, and have lower risk compared to colonoscopy. Fecal blood testing selects a population of patients for colonoscopy who are enriched for polyps, including advanced polyps. However, both stool and blood tests are less sensitive than colonoscopy for both cancer and polyps—although the combination of FIT and the fecal DNA test does have a greater than 90% sensitivity for cancer (Figure 2). There is currently no commercially available blood screening test for colorectal cancer with good enough performance

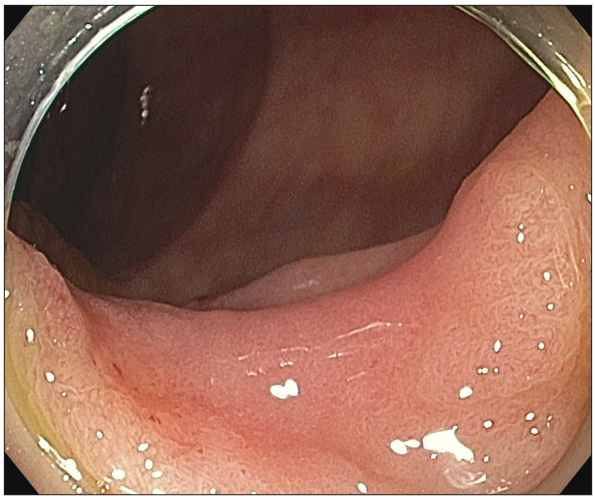

Figure 1. A flat conventional adenoma with central depression. Flat and depressed lesions are skewed in distribution toward the proximal colon, and colonoscopy is the most effective test for their detection.

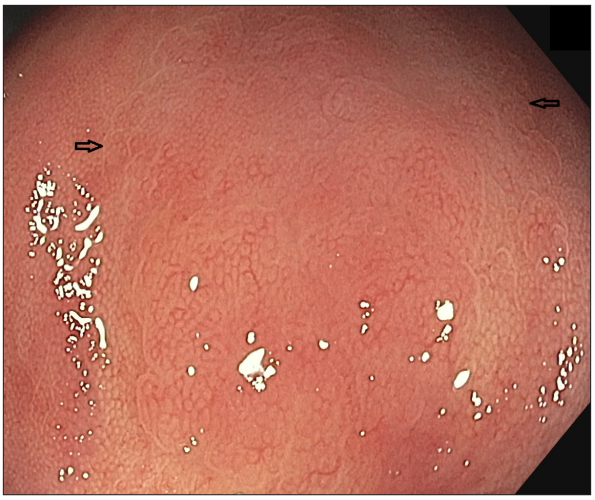

Figure 2. A flat sessile serrated polyp. The edges are subtle and indiscrete (black arrows). This is the one class of precancerous lesions for which fecal DNA testing is far superior to the fecal immunochemical test for blood. However, colonoscopy is the most effective detection test for serrated class lesions.

to endorse its use. Lower sensitivity generally requires the tests to be repeated more often than colonoscopy. Colonoscopy is the only screening test that can be performed at intervals of 10 years when test results are negative.

G&H What are the most common risks associated with colonoscopy?

DR One of the most underappreciated risks of colonoscopy is aspiration pneumonia that can accompany sedation use. Bleeding from polypectomy is the most common complication, although most of it should occur from large polyps; however, other screening tests that detect large polyps will lead to colonoscopy, meaning patients will incur the bleeding risk anyway. Injury to the spleen and perforation during screening colonoscopy are very serious risks, although they are less common. The other very substantial risk is that the unwitting patient might be assigned to a colonoscopist with inadequate detection skills, which may place the patient at excess risk of developing colorectal cancer after colonoscopy.

G&H Is there a role for capsule endoscopy in colon cancer screening?

DR The role for capsule endoscopy is currently very limited. The US Food and Drug Administration originally approved capsule endoscopy for patients with an incomplete colonoscopy. Reimbursement for capsule endoscopy is currently extremely limited. We can expect that capsule endoscopy will be a viable imaging option for a small group of patients who are either concerned about the risks of colonoscopy or who need imaging but are advised against colonoscopy due to their comorbidities.

G&H What is the current status of genetic screening in relation to the risk of colon cancer?

DR There are several defined inherited syndromes that increase the risk for colon cancer. The most important inherited conditions are Lynch syndrome and familial adenomatous polyposis. It is now recommended that all colorectal cancers be tested for features of Lynch syndrome (eg, microsatellite instability testing or immunohistochemistry stains for the protein products of the 4 mismatch repair genes). If Lynch syndrome features are present in the tumor, the patient should be offered genetic testing.

Unfortunately, the genetic basis of the most common colorectal polyp syndrome (ie, serrated polyposis) remains unknown. Clinical criteria are still used to define serrated polyposis.

Patients who have a strong family history of colorectal cancer that does not meet traditional criteria that would suggest a defined inherited syndrome (eg, a relative with colon cancer before age 60 or 2 first-degree relatives with colon cancer at any age) should also be considered for genetic testing. There are a variety of scoring tools available to assess the appropriateness of genetic testing.

G&H How should colon cancer screening be offered to patients?

DR There are several approaches to this important question. Some physicians believe that a single "best" test should be offered to the exclusion of others, and they often feel strongly that that test is FIT. This approach is

often used in large institutional programs and in organized national screening programs outside the United States.

Another approach, which is the basis of several guidelines, is known as multiple-option testing. In this approach, physicians present multiple screening options to patients and discuss the advantages and disadvantages of each with regard to cost, risk, and efficacy. Patients then choose the screening test they feel is best suited to their own preferences.

The approach that is generally used in the United States is a variant of the single best test approach called sequential testing, in which physicians offer what they consider to be the most effective test first, and then if the patient declines, they offer the next best test. In the United States, patients are usually offered colonoscopy first, followed by FIT if colonoscopy is declined. In some trials, sequential testing resulted in both the maximum number of subjects undergoing screening and the maximum number of screenees utilizing the most effective test.

G&H What are the primary barriers to screening?

DR Important barriers are lack of awareness of screening and lack of appreciation of risk. Patients often report that they have never been offered screening and indicate they would have agreed to screening if it had been offered. In the United States, most screening is opportunistic rather than programmatic, which essentially means that screening results from a physician-patient interaction. Therefore, it is important that primary care physicians and specialists make an enthusiastic recommendation to patients. Programmatic screening, in which patients are offered screening systematically (eg, by mail), is often considered a better approach, but is utilized in the United States by just a few large insurance plans.

Beyond that, there are barriers attributable to the attitudes and beliefs of patients and physicians, including denial, being too busy, and fatalism about cancer. Physicians can help dispel these beliefs through education and by improving understanding of risk.

G&H What are the most common errors in screening?

DR The most common error is to not offer screening. Another common error is failing to follow up on a positive screening test, particularly a positive fecal occult blood test. Positive fecal tests should lead to colonoscopy. Primary care physicians often continue fecal blood testing after a negative colonoscopy, which is incorrect for guaiac testing. It is not clear yet whether FIT or the fecal DNA–FIT combination might have a role in the interval after a negative colonoscopy.

Of course, significant errors are possible in the technical performance of colonoscopy, as well as in the selection of screening and surveillance intervals after colonoscopy. A major source of error is the ongoing use of screening colonoscopy at 5-year intervals in certain regions of the country. Some of these errors are based on the reimbursement system, which rewards the performance of colonoscopy at frequent intervals even when performed poorly in each instance. Patients would benefit from movement to a reimbursement system that rewards high-level detection and selection of long intervals between examinations for patients at low risk of cancer.

G&H What are the next steps in research?

DR The next innovations and the eventual disruption of screening colonoscopy are likely to be based on molecular technology. Whether a highly effective blood test based on abnormal DNA is feasible remains unknown. The current commercially available blood test in the United States has poor performance and high cost, and should only be used in informed patients who refuse the other forms of screening.

In the near future, improvement of colonoscopy lies in easier bowel preparation and a reduction in operator dependence. Colonoscopy is already good enough in excellent hands that there is a real possibility that 1 or 2 well-timed negative colonoscopies provide a near guarantee against the development of colorectal cancer. Merging colonoscopy or perhaps CTC with molecular imaging might both reduce operator dependence and provide once-in-a-lifetime protection against colorectal cancer. Research in improving colonoscopy and reducing operator dependence is an important adjunct to research directed toward improvement of noninvasive screening tools.

Dr Rex is a consultant to Olympus Corporation, EndoChoice, and Boston Scientific, and receives research support from Olympus Corporation, Paion, Boston Scientific, EndoChoice, and EndoAid. He is also on the scientific advisory board of Check-Cap.

Suggested Reading

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