Screening for Colorectal Cancer: 
Is There Progress for Early Detection?

Starting in 1995, evidence-based guidelines recommended that all average-risk, asymptomatic men and women 50 years of age be screened for colorectal cancer. Five different strategies, each with unique advantages and limitations, are considered acceptable options for screening. The two main objectives of screening are to detect early, curable cancers and to prevent cancer by detecting and resecting advanced, premalignant adenomatous polyps. Public policy initiatives and multipronged educational programs promote compliance with these screening recommendations. Evidence that these efforts are increasing early detection of colorectal neoplasia in the U.S. include positive trends in measured compliance with screening, the favorable stage of most screen-detected cancers, survival from cancer, and in both overall colorectal cancer incidence and mortality. Current efforts to better define and reduce barriers to colorectal cancer screening should help insure that these improvements in colorectal cancer control will accelerate during the rest of this decade.

INTRODUCTION

The past decade experienced a great deal of debate about whether asymptomatic people should be screened for colorectal cancer. Fortunately, this debate largely is over and evidence-based guidelines now strongly recommend population-based screening for this major malignancy (1–3). Scientific and public discussion has shifted to the question of which of several screening strategies should be “preferred” and to practical considerations of how to implement screening in different medical delivery systems. The past decade also has seen dramatic changes in public policy regarding colorectal cancer screening, and a number of large multipronged educational programs promoting compliance with screening recommendations have been carried out or currently are ongoing. Although national surveys still indicate that colorectal cancer screening rates remain relatively low compared with screening for other major malignancies, we are beginning to see favorable upward trends in the level of public awareness about this disease and in rates of screening. Coincidently, after decades of gradual rises, we now are detecting downward trends in both overall colorectal cancer incidence (continued on page 50)
and mortality in the U.S. Attention is being directed at identifying and reducing barriers to screening for colorectal cancer neoplasia that hopefully will result in even more dramatic improvements in early detection and outcome from this major cancer killer during the rest of this decade. This paper reviews the current guideline recommendations for colorectal cancer screening, briefly discusses the advantages and limitations of each screening option, and assesses current progress for early detection of this major malignancy.

OBJECTIVES OF COLORECTAL CANCER SCREENING

There are two main objectives of colorectal cancer screening. The first is to detect cancers before they have metastasized from the bowel to lymph nodes or beyond. Large case series show that the surgical cure rate for such Dukes A and B cancers (Stage I and II) exceeds 85% (4). Since nearly all of these early cancers do not cause symptoms, they must be detected by screening.

The second important objective of screening is cancer prevention. Studies indicate that almost all colorectal cancers originate in benign adenomatous polyps (adenomas) that develop and grow very slowly in the colon over many years before they turn malignant (5). Detection and removal of premalignant adenomas therefore prevents cancer, and this has become a goal of screening that quantitatively perhaps is even more important than finding early cancers. Studies, such as the National Polyp Study and the Minnesota Fecal Occult Blood Screening Trial demonstrated that when screening leads to resection of advanced adenomas, not only is cancer death prevented, but the incidence of colorectal cancer with its attendant morbidity and treatment costs is substantially reduced (6,4).

THE ADVANCED ADENOMA AS THE PRIMARY TARGET OF SCREENING

Autopsy and colonoscopy series show that the prevalence of small (1 cm) tubular adenomas in people over age 50 in Western countries exceeds 30%. These common small adenomas, however, have a very low malignant potential. Longitudinal studies show that most remain static or actually regress with time, whereas only a few develop the additional acquired genetic changes that make them grow, develop advanced histologic features, and turn eventually to cancer. As defined by the National Polyp Study, advanced adenomas are those that are >1 cm in size or contain villous tissue or high-grade dysplasia. These advanced adenomas are much less common than small tubular adenomas, but they are much more likely to progress to cancer if not detected by screening. A large body of recent scientific data indicates that clinicians should shift their efforts away from just detecting and removing large numbers of small tubular adenomas, toward strategies that reliably detect advanced adenomas. Long-term post-polypectomy studies demonstrate the validity of this concept. Reports from the Mayo Clinic and from St. Mark’s Hospital, London, show that patients who have had resection of only one or two small tubular adenomas have no measurable increased risk of developing metachronous colorectal cancer. In contrast, those with large (1 cm) or multiple (3) adenomas, or adenomas with villous changes or high-grade dysplasia, have a risk of subsequent cancer that is increased 3–6-fold. Thus, the two main objectives of colorectal cancer screening are to 1) detect cancers before they metastasize and surgical cure is very likely, or 2) to detect and resect advanced adenomas thereby preventing cancer. The choice of a screening option should be guided by how well it accomplishes these two objectives.

RISK STRATIFICATION FOR COLORECTAL CANCER

Most people are at average risk for colorectal cancer because they have reached the age when the prevalence of cancer and advanced adenomas is sufficient to justify screening. Based on age-incidence curves for colorectal neoplasia, guidelines recommend that screening of the asymptomatic, average-risk population (both men and women) begin at age 50. Direct screening colonoscopy of people age 40–49 years confirms the very low prevalence of advanced neoplasia in average-risk people under age 50. Patients with a personal or family history of colorectal neoplasia and those with longstanding ulcerative colitis or Crohn’s colitis may have an above-average risk of colorectal cancer that often begins at an earlier age. These high-risk patients may benefit from more intensive evaluation or screening. Recommend-
tions for these high-risk groups are clearly outlined in the GI Consortium Guideline and won’t be discussed further here (2). In order to determine whether a patient is average- or above-average risk, a careful family and personal history should be taken before initiating any of the screening options.

GUIDELINE OPTIONS FOR SCREENING

Unlike screening for other major malignancies (i.e., breast, cervix, and prostate) where a single screening test usually is recommended, the colorectal cancer screening guidelines present a menu of five different options, any one of which is considered satisfactory. These options are listed in Table 1. The guidelines emphasize that each of these five options has advantages and limitations that might be presented to the patient. Then, in a “shared decision process” the patient could be given an opportunity to help choose their own way to be screened.

ADVANTAGES AND LIMITATIONS OF THE FIVE SCREENING OPTIONS

The FOBT is the only screening method that has been shown to be efficacious in large, randomized, controlled trials. The Minnesota FOBT Trial reported a reduction in colorectal cancer mortality of 33.4% and 21%, respectively, for annual and biennial FOBT screening followed by colonoscopy for those with a positive screening test (7). Participants who complied with all recommended screening tests during this study experienced a 45% colorectal cancer mortality reduction as the result of annual screening. This is an important number because it is the benefit patients can expect if they comply perfectly with recommended annual FOBT screening. Long-term follow-up in the Minnesota Trial also demonstrated a significant reduction in colorectal cancer incidence in those screened annually, presumably the result of resection of advanced adenomatous polyps. FOBT screening has a number of proven practical advantages. A program of annual screening using a reasonably sensitive test (i.e., HemoccultSensa guaiac cards [Beckman-Coulter, Palo Alto, CA] or one of the newer immunochemical FOBTs) followed by colonoscopy when a test is positive, detects most colorectal cancers and many advanced adenomas. FOBT screening has a low up-front cost, reduces both colorectal cancer mortality and incidence, and is feasible, widely available, and generally acceptable to patients. Disadvantages of FOBT screening include low sensitivity for polyps, especially smaller ones, and a relatively high false-positivity rate for advanced neoplasia. In addition, to be effective, frequent screening is required.

Flexible sigmoidoscopy screening also has a number of advantages. It detects most colorectal cancers and advanced adenomas. An analysis from the VA Multicenter Colonoscopy Screening Study indicated that a single screening flexible sigmoidoscopy would detect 70%–80% of all advanced colorectal neoplasia provided that those that are found to have a left-sided neoplasm undergo subsequent colonoscopy (8). When performed by well-trained, experienced examiners, flexible sigmoidoscopy is accurate, safe, and well-tolerated. The examination is relatively inexpensive and can be performed quickly following a simple bowel preparation. Screening sigmoidoscopy has been shown in cohort and case-control studies to reduce mortality from colorectal cancer within its reach by 60% to 80%. These studies also suggest that the protective effect of a single examination may last for 5–9 years, so infrequent screening is possible.

The combination of annual FOBT screening plus flexible sigmoidoscopy every five years is an especially effective approach to screening because it largely corrects many of the limitations of doing either method of screening alone. The FOBT misses many polyps and has been shown to be relatively insensitive for cancers located in the distal colon and rectum. When repeated annually, however, it will detect most colorectal cancers before they become incurable. Flexible sigmoidoscopy

Table 1

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<tr>
<th>Colorectal Cancer Screening Guidelines: Acceptable Screening Options for Asymptomatic, Average-risk Men and Women</th>
<th>50 Years of Age</th>
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<tr>
<td>1. Annual screening with fecal occult blood tests (FOBT)</td>
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<tr>
<td>2. Flexible sigmoidoscopy screening every five years</td>
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<tr>
<td>3. The combination of annual FOBTs and flexible sigmoidoscopy every five years</td>
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<tr>
<td>4. Double-contrast barium enema every five years</td>
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<td>5. Direct colonoscopy screening every ten years</td>
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(continued on page 54)
is highly accurate in the left colon where most cancers and polyps develop, but will miss up to 30% of proximal advanced neoplasia in patients who do not also have a synchronous distal neoplasm.

Screening double-contrast barium enema (DCBE) is included in the menu of guideline options, however it is not used much for screening in the U.S. and has never been directly studied for this purpose. Furthermore, DCBE has been shown to be relatively insensitive for detecting advanced neoplasia. A large retrospective study by Rex and co-workers in 20 centers in Indiana showed that about 15% of colorectal cancers are missed by barium enema examination (9). The National Polyp Study performed back-to-back DCBE and colonoscopy on 580 patients undergoing post-polypectomy surveillance and found that the sensitivity for detecting large adenomas (>1 cm) was only 48% (10). When DCBE is used for screening, the guidelines recommend a screening interval of five years.

Although practically unheard of 5–10 years ago, direct colonoscopy screening has become the overwhelming preference of gastroenterologists and many others in the U.S. This option is somewhat of a perturbation of the classic World Health Organization definition of a screening test. Instead of performing a simple, acceptable, inexpensive and indirect test to identify those who might benefit from a definitive evaluation, we are substituting a highly complex, expensive and somewhat invasive, definitive diagnostic and therapeutic method. Direct screening colonoscopy, however, is now being increasingly championed by many physician and patient groups because it detects almost all cancers and advanced adenomas, and it allows for resection of almost all polypos during a single examination with a single bowel preparation. Although there are no prospective, randomized trials showing the efficacy of colonoscopy screening, it clearly is the most reliable way of accomplishing both of the major objectives of screening—cancer prevention through resection of advanced adenomas and reduced mortality through the detection of early cancers. Because of colonoscopy’s great accuracy and the long natural history of the adenoma-carcinoma sequence, infrequent screening every ten years is recommended by the guidelines. A number of recent reports including that of the VA Multicenter Colonoscopy Screening Study have demonstrated that, when performed by well-trained experienced colonoscopists, colonoscopy screening is feasible, acceptable, and very safe (11). Compelling indirect evidence suggests that this approach is very effective at reducing both the incidence and mortality of colorectal cancer. For example, colonoscopy and polypectomy in the National Polyp Study reduced colorectal cancer incidence by up to 90%; a number of case-control studies of both flexible sigmoidoscopy and colonoscopy suggest efficacy; and the large FOBT trials effected their reduction of cancer incidence and mortality mostly by doing colonoscopy on those with a positive screen. Limitations of screening colonoscopy that still need to be addressed include issues of risk, cost, patient acceptability and capacity. Conscious sedation with its attendant risk, cost, and inconvenience usually is required for screening colonoscopy. A recent study also emphasized that there is an appreciable indirect cost to doing screening colonoscopy. A screening examination requires the better part of two days to complete the bowel purging preparation, the examination, and recovery. When time lost from work for the patient and his accompanying “responsible adult,” plus transportation costs and other attendant expenses are considered, the indirect cost of a screening colonoscopy averaged over $600 per case. While screening colonoscopy has been shown to be safe when performed by experienced physicians, there still are concerns about both the accuracy and risk of this option when it is carried out in increasing numbers by less experienced examiners. Lastly, the great demand for screening colonoscopy shows signs of overwhelming the capacity to perform these examinations. Many centers currently are experiencing long waiting times to have a screening colonoscopy, and this threatens to diminish the attractiveness or practicality of this option.

**HISTORY OF THE SCIENCE SUPPORTING COLORECTAL CANCER SCREENING**

It is important for those who are assessing progress in colorectal cancer screening to keep in perspective the history of the science that supports the recommendations of the screening guidelines (Table 2). One of the reasons screening rates for colorectal cancer appear to be disappointingly low today is because the studies that show that screening is effective did not begin to report their findings and conclusions until relatively recently. Case-
control studies suggesting efficacy of both FOBT and flexible sigmoidoscopy screening were first reported in 1992. A year later, the Minnesota randomized controlled trial of FOBT screening reported a significant reduction in colorectal cancer mortality as the result of annual screening (4). Also in 1993, the National Polyp Study reported that removing adenomatous polyps from a large cohort of patients reduced colorectal cancer incidence by up to 90% (6). In December 1995, based on these new data, the U.S. Preventive Services Task Force reversed its previous neutral position, and for the first time strongly recommended screening of all average-risk, asymptomatic Americans (men and women) over age 50 (1). Then, in rapid succession in 1997, the comprehensive GI Consortium guideline and the guideline of the American Cancer Society were published and promulgated (2,3). Since then, an additional large number of studies of FOBT, flexible sigmoidoscopy, and direct colonoscopy screening have been reported from around the world that substantially confirm the efficacy and value of screening, and better define how screening with each option should be carried out.

**EVIDENCE THAT SCREENING LEADS TO EARLY DETECTION**

In addition to the direct and indirect evidence that colorectal cancer screening reduces mortality from the disease discussed above, what evidence shows that screening results in earlier detection of colorectal neoplasia? To date, only the major FOBT trials have compared the stage of screen-detected cancers with those diagnosed by usual clinical means (i.e., usually in response to signs and symptoms of cancer) in randomized control groups. Table 3 shows cancer stage data for the five large randomized controlled studies (12). Cancers detected in the screened groups were, on average, nearly twice as likely to still be localized to the bowel at the time of surgery (Dukes A or B) than were cancers diagnosed in the control groups. In addition, as discussed above, extended follow-up in the Minnesota FOBT Trial demonstrated a significant reduction in colorectal cancer incidence in the groups screened annually and biennially compared with the control group (13). The only plausible explanation for this difference in subsequent colorectal cancer incidence in the Minnesota Trial is that screening resulted in the diagnosis and resection of premalignant adenomas before they otherwise would have turned cancerous. Additional direct evidence that screening reduces the subsequent incidence of colorectal cancer comes from a small randomized controlled trial of sigmoidoscopy conducted in Norway (14). Screening sigmoidoscopy with follow-up colonoscopy for all patients with polyps compared to no screening demonstrated an 80% reduction in colorectal cancer incidence in the screened patients.

**CHANGES IN PUBLIC POLICY**

Based on the large volume of high quality scientific evidence supporting screening, U.S. public policy recently has shifted strongly in support of screening. Because screening for colorectal cancer was shown to be highly cost-effective relative to other established medical interventions, the U.S. Congress provided for the first time

<table>
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<th>Table 2</th>
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<td>1992</td>
<td>Case-control studies of FOBT and flexible sigmoidoscopy</td>
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<tr>
<td>1993</td>
<td>Minnesota FOBT Trial, annual screening reduces cancer mortality</td>
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<td>1993</td>
<td>National Polyp Study, polypectomy reduces cancer incidence</td>
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<td>1995</td>
<td>U.S. Preventive Services Task Force endorses screening</td>
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<td>1997</td>
<td>GI Consortium Guideline</td>
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<td>American Cancer Society Guideline</td>
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<td>1997–2003</td>
<td>Confirmatory studies of FOBT, sigmoidoscopy, and direct colonoscopy screening</td>
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<th>Table 3</th>
<th>Stage of Cancers in Controlled Trials of FOBT Screening</th>
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<td>Dukes A &amp; B Cancers (%)</td>
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<td>Screened Group</td>
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<td>U.S.—Minnesota</td>
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<td>U.S.—New York</td>
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<td>Sweden</td>
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<td>U.K.</td>
<td>90</td>
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<td>Denmark</td>
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reimbursement for screening for Medicare patients in January 1998. Many large insurance payers and managed care organizations also now are implementing screening programs for their non-Medicare patients over age 50 years. As of July 2001, Medicare reimbursement also is provided for direct colonoscopy screening of average-risk people. Large national educational programs that promote awareness about the disease and encourage compliance with the screening guidelines, directed at both primary care providers and the public, have been carried out by the American Digestive Health Foundation (a past joint effort of the American Society for Gastrointestinal Endoscopy and the American Gastroenterological Association), the American College of Gastroenterology, the Centers for Disease Control and Prevention (CDC), the American Cancer Society (ACS), the Cancer Research and Prevention Foundation, the Agency for Healthcare Research and Quality, The American Academy of Family Physicians, the Colon Cancer Alliance, the Stop Colon/Rectal Cancer Foundation, Katie Couric’s Colorectal Cancer Foundation, and many other highly dedicated national, regional and local groups. A National Colorectal Cancer Roundtable has been convened under the sponsorship of the ACS and the CDC to help coordinate many of these efforts. An additional boost to these efforts occurred in 2000 when the U.S. Congress and the President of the United States declared that March of each year would be “National Colorectal Cancer Awareness Month.” Lastly, as the result of a three-year study and intensive lobbying by the CDC, the National Committee for Quality Assurance (NCQA) approved a measure of colorectal cancer screening for inclusion in the Health Plan Employer Data and Information Set (HEDIS) beginning this year. HEDIS is a set of standardized performance measures that permits comparison of managed care organizations. Once a given measure is included in HEDIS, managed care organizations generally make special efforts to see that the intervention is carried out by providers in their plans.

SELF-REPORTED SURVEYS OF COLORECTAL CANCER SCREENING RATES

Despite all of the new publicity and public support for colorectal cancer screening, published surveys conducted during the late 1990s indicated that less than 30%–40% of the at-risk population was being screened. However, a more recent survey carried out by the CDC suggests that we are beginning to experience an upward trend in screening (15). The CDC analyzed data from the 2001 Behavioral Risk Factor Surveillance System (BRFSS) on the use of FOBT and lower GI endoscopy (flexible sigmoidoscopy or colonoscopy), and compared data from 2001 with those of 1999 and 1997. BRFSS is a state-based random telephone survey of the civilian, U.S., non-institutionalized population. In 2001, all 50 states and the District of Columbia participated. Respondents aged 50 years (the age group for which colorectal cancer screening is recommended) were asked whether they ever had used “a special kit at home to determine whether the stool contains blood” (FOBT), whether they ever had “a tube inserted through the rectum to view the bowel for signs of cancer or other health problems” (sigmoidoscopy/colonoscopy), and when these tests were last performed. For the year 2001, the median state response rate was 51.1%. A total of 87,729 persons aged 50 completed the survey. In 2001, 44.6% of adults aged 50 years had ever had FOBT, and 47.3% had ever had a lower endoscopy. An estimated 23.5% had FOBT within 12 months; 43.4% had lower endoscopy within 10 years, and 53.1% had one or both tests within these time periods. In contrast, the percentage of persons aged 50 years who had received FOBT within 12 months was 19.4% in 1997 and 20.4% in 1999. For lower endoscopy within 5 years, the proportions were 29.9%, 33.3%, and 38.7% for 1997, 1999, and 2001, respectively. Thus, although the report indicates that colorectal cancer test use among U.S. adults remains disappointingly low, we are finally seeing an upward trend that may be the result of recent intensive educational efforts. Still, approximately half of U.S. adults aged 50 years have not received the recommended screening.

TRENDS IN OVERALL COLORECTAL CANCER INCIDENCE AND MORTALITY

According to American Cancer Society statistics, after years of slow but steady increases, the annual age-adjusted incidence of colorectal cancer for both men and women began to slowly decline after about 1985 (continued on page 60)
(16). During the same time period, age-adjusted mortality from the disease decreased in both genders at an even faster rate. Mortality had fallen in 2000 by about 20% compared to that reported in 1985. Colorectal cancer still remains a formidable health risk. In 2003 it is estimated that there were 147,500 new cases diagnosed and over 57,000 deaths—making it the second most common cancer killer in the U.S.

The reasons for the favorable downward trend in incidence and mortality are, of course, multifactorial. Along with dietary changes and more healthy living, other forms of primary prevention, and improved diagnosis and treatment, implementation of screening and more widespread use of colonoscopy that began in the mid to late 1980s undoubtedly play an important role. Early detection appears to be having an important impact on colorectal cancer and survival. The reported five-year survival from colorectal cancer for men and women of all races in the U.S. has improved from 50% (1974 to 1976) to 62% (1992 to 1998) according to the American Cancer Society data. An analysis of colorectal cancer survival over time performed in the Veterans Affairs Hospital System, the largest equal-access healthcare system in the U.S., showed similarly favorable trends (17). Survival in 46,044 patients with colorectal cancer improved over 1986 to 1998 from 39% to 47% for all sites. Most proponents of colorectal cancer screening predict even more dramatic improvements in colon cancer control during the remainder of this decade.

SUMMARY AND RECOMMENDATIONS

Screening for colorectal cancer clearly saves lives and is cost-effective. High-quality scientific studies published over the past decade are the basis for three evidence-based guidelines that urge screening with one of a menu of five screening options, each of which has unique advantages and limitations. Each clinician or health care delivery system should carefully consider the information contained in this review and, based on available resources, choose which of the five options to offer to at-risk patients. At the present time, the two options that appear to be most effective or promising are 1) screening with the combination of annual FOBT and flexible sigmoidoscopy every five years, or 2) direct colonoscopy screening every 10 years. Advocates of screening emphasize, however, that the most effective screening method may be the one that a given patient actually will agree to do. The only unacceptable option is to do no screening. There now is substantial accumulating data that indicate that screening leads to early detection of colorectal neoplasia—either early curable cancer or premalignant advanced adenomatous polyps. We now are beginning to see favorable national trends in the rates of screening, survival from colorectal cancer, and overall colorectal cancer incidence and mortality.

References


