

Updates in colorectal cancer screening

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Abstract

Recent advances in the field of colorectal cancer screening have led to updated guidelines from several national societies. Although various strategies have been illustrated to reduce mortality from colorectal cancer, screening tests differ in their ability to detect neoplasia. While this is an issue for all lesions, it is a particular problem for non-polypoid or 'flat' colonic neoplasia, which has been recognized to be prevalent in Western countries. Guidelines also recommend the age at which screening is initiated and discontinued; however, emerging data suggest these thresholds may lead to missed lesions. Finally, evidence points to disparities in the availability and utilization of colorectal cancer screening tests, which may be successfully addressed through interventions that educate both patients and their providers. The focus of future efforts includes increasing adherence to recommended screening strategies.

Introduction and context

The availability of new colorectal cancer screening (CRCS) modalities, including computed tomography (CT) colonography, fecal DNA testing and capsule colonoscopy, has rejuvenated interest in this topic, culminating in the publication of two updated guidelines for CRCS this year. Despite the availability of similar data for review, these societal guidelines arrived at different conclusions regarding recommended strategies. In March 2008 the American Cancer Society, the US Multi-Society Task Force on Colorectal Cancer (including the major US national gastroenterology societies) and the American College of Radiology jointly published their guidelines [1]. These guidelines offer a menu of options that include flexible sigmoidoscopy every 5 years, colonoscopy every 10 years, double-contrast barium enema every 5 years, computed tomographic colonography (virtual colonoscopy) every 5 years, annual 'sensitive' fecal occult blood testing (FOBT) using highly sensitive guaiac or fecal immunochemical testing, or stool DNA testing. However, it was strongly recommended CRCS be conducted with strategies that detect adenomatous polyps in addition to early cancer. This recommendation includes CT colonography, which

has not been shown to reduce colorectal cancer incidence or mortality.

Subsequently, the US Preventive Services Task Force (USPSTF) published their recommendations for CRCS, in which the decisions to include strategies were based on evidence of reductions in mortality from colorectal cancer [2]. Based on these criteria, they approved screening with FOBT, flexible sigmoidoscopy or colonoscopy. FOBT has high-quality evidence to support reductions in colorectal cancer mortality from multiple randomized controlled clinical trials [3–5]. Colonoscopy and flexible sigmoidoscopy have been demonstrated to achieve mortality benefit through retrospective case-control and prospective cohort studies with historical controls [6–9]. CT colonography, barium enema and fecal DNA testing were not recommended, based on the lack of data to determine whether they improve clinical outcomes. It also remains to be seen whether the results achieved in the context of clinical trials can be replicated in the community practice setting, where variation in procedure performance may impact the goals of cancer mortality reduction.

The differences in recommendations appear to be based on whether existing evidence supports reduction in colorectal cancer mortality (USPSTF) or whether comparison of newer methods with colonoscopy to detect colonic lesions is sufficient to include a recommendation (Multi-Society Task Force). With the backdrop of these conflicting guidelines, substantial issues were raised in the past year through publications that addressed factors that impact the outcomes achievable through competing CRCS strategies.

Recent advances

Flat adenomas

One of the advances in CRCS was the finding that 'flat polyps' were prevalent among United States residents. These lesions were previously believed to be limited to people in Asian countries. A study by Soetikno *et al.* [10] revealed that flat, otherwise known as non-polypoid, colorectal neoplasia was present in 9% of the screening population, and up to 15% of patients with a prior history of colonic neoplasia. While the prevalence of *in situ* or invasive cancer was less than 1%, they were more likely to occur in non-polypoid compared to traditional polypoid lesions. Moreover, an astounding 33% of 'depressed' non-polypoid lesions were malignant. The clinical implications of these findings are that certain screening modalities such as CT or magnetic resonance colonography (virtual colonoscopy) are less likely to identify flat lesions, which may limit their applicability for CRCS.

The clinical relevance of small lesions with regards to their risk of progression to malignancy was further addressed by Lieberman *et al.* [11] through analysis of almost 14,000 patients who had undergone screening colonoscopy. The outcome of interest was the prevalence of 'advanced histology', defined as an adenoma with villous or serrated histology, high-grade dysplasia or an invasive cancer. While the proportion of polyps >10 mm harboring advanced histology was 30.6%, 6.6% of polyps within the 6–9 mm range and 1.7% of polyps 1–5 mm in diameter also possessed advanced histology.

These findings impact indirect imaging methods such as virtual colonoscopy, since even among experienced radiologists CT colonography has a sensitivity of 88% for 6 mm lesions [12]. Using current recommendations, patients with lesions <10 mm in diameter diagnosed by CT colonography would not necessarily undergo immediate polypectomy. It has been suggested that they instead be followed by surveillance colonography. Additionally, it has been advised that lesions <5 mm in diameter diagnosed by CT not be reported [13]. Although the proportion of small lesions having

advanced histology is small, the prevalence of small lesions is high. However, the importance and clinical implications of not removing these lesions with respect to the ability of virtual colonoscopy to reduce colorectal cancer mortality is unknown.

Age to initiate and cease CRCS

Published guidelines recommend initiation of CRCS for patients at average risk for development of cancer at age 50 years. There is an exception from the American College of Gastroenterology guidelines [14] that recommends beginning screening at age 45 years among African-Americans based on epidemiological data [15]. The greater question is whether these age thresholds are valid for any group regardless of racial categorization. Rundle *et al.* [16] analyzed 905 colonoscopies performed for screening on average-risk persons from 40–59 years of age and reported no difference in the proportion diagnosed with colonic adenomas between those 40–49 years of age (14%) and those 50–59 years of age (16%). While there was a trend towards an increase in the proportion of persons with advanced adenomas among those 50–59 years of age (4%) compared to those 40–49 years of age (2%), this difference was not statistically different. Thus, while it is known that the incidence of cancer is lower for persons younger than 50 years of age, it appears that if the goals of screening are to detect and remove adenomas, perhaps initiation of screening at an age earlier than 50 years is reasonable. The economic impact of lowering the age at which to initiate screening, however, is unknown.

An equally contentious issue is the age at which to cease screening. The USPSTF recommends discontinuation of screening of average risk persons after the age of 75 years [2]. The rationale for this recommendation is that while the incidence of, and mortality from, colorectal cancer continue to increase with age, so does the risk of mortality from competing disease. However, these recommendations are not based on solid data; thus, from health quality and economic perspectives, recommendations regarding the age at which to stop screening remain fluid.

Adherence to colorectal cancer screening

Finally, the most important question regarding choice of CRCS strategies may not revolve around which is most effective but rather to which strategy will patients more often adhere? Several studies have been published this past year focusing on issues of adherence to CRCS tests. McAlearney *et al.* [17] conducted face-to-face interviews with 941 women older than 50 years of age who were living in subsidized housing in selected Southern communities. While adherence to CRCS was reported

by half of respondents and did not vary by race, African-American women were half as likely as white women to report having undergone screening by colonoscopy. In conjunction with this disparity was awareness of different tests for CRCS, which was significantly lower among African-Americans than whites. Correspondingly, there was a similar significant difference in lack of insurance coverage between African-Americans and whites. Disparities in the rate of CRCS also exist among non-black minorities, with reduced rates in Asians and Hispanics [18,19]. Furthermore, use of colonoscopy among those persons who are screened is particularly deficient among non-white populations [20]. This evidence points to the need for greater awareness and availability of CRCS focused specifically on populations vulnerable to disparities based on racial or socioeconomic factors.

In order to address these disparities in health care utilization, another group of investigators tested a novel intervention using computer-assisted patient teaching and tailored written recommendations in rural primary care practices to improve communication and discussion about CRCS [21]. In clinics exposed to this intervention, providers and patients discussed CRCS more often, providers more often recommended CRCS, and patients described a higher intention to be screened than in clinics not exposed to the intervention. Thus, it appears that some of the deficits based on socioeconomic factors may be overcome through the use of new technology and techniques for disseminating information among patients and their providers. It should be realized, however, that other significant barriers remain based on access to primary and specialty care, insurance, acculturation and language. Capacity limitations of colonoscopy and the unequal distribution of capacity also impacts access to CRCS. Finally, variation among physicians with regards to the level of recommendation to undergo screening may constitute a target for reducing disparities in CRCS.

Implications for clinical practice

Recently published guidelines differ with regards to recommended strategies to reduce mortality from colorectal cancer. The differences stem from the level of evidence from clinical studies required by the societies for inclusion of screening modalities. The USPSTF recommendations, which are based on more rigorous criteria requiring evidence for improvement in colorectal cancer mortality support FOBT, flexible sigmoidoscopy and colonoscopy as screening tests. The Multi-Society Task Force included CT colonography and fecal DNA testing based on comparative studies using colonoscopy

as the gold standard for detection of colonic lesions. From a clinical perspective, reports of a substantial prevalence of non-polypoid lesions in the US reduce the viability of strategies that do not directly visualize the colonic mucosa. Practically speaking, however, the limit to adoption of CT colonography and fecal DNA testing may be more linked to reimbursement for use of these technologies for CRCS rather than the level of evidence supporting their use.

Regardless of the efficacy of competing strategies to reduce mortality from CRC, the more important issue may be whether patients adhere to any form of CRCS. Recent evidence illustrates significant disparities in the availability and utilization of CRCS tests based on racial/ethnic or socioeconomic factors. Additional studies, however, have demonstrated that specific educational interventions can improve the acceptability of CRCS tests and may ultimately increase overall adherence to CRCS strategies. The key issue to improve the health of populations may not be to determine the most efficacious test, but rather to identify to which CRCS test a particular patient is most likely to adhere.

Abbreviations

CRCS, colorectal cancer screening; FOBT, fecal occult blood testing; USPSTF, US Preventive Services Task Force.

Competing interests

The author declares that he has no competing interests.

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