Colorectal Cancer Screening: Confusion Reigns

Peter Lance
Arizona Cancer Center, Tucson, Arizona

In 2008, it is estimated that 148,810 new cases of colorectal cancer (CRC) will be diagnosed in the United States and that 49,960 people will die from the disease (1); lung cancer is the only cancer that kills more people each year in developed countries than CRC. According to almost universal consensus based largely on indirect evidence from a decade or more ago, effective implementation of screening would substantially reduce CRC morbidity and mortality (Table 1).

The population is divided into people at average (~75%) and increased (~25%) risk for CRC. People at average risk for CRC are the topic of the current discussion. The lengthening list of screening test options for average-risk subjects includes guaiac-based fecal occult blood testing (gFOBT), fecal immunochemical testing (FIT), stool DNA, double-contrast barium enema (DCBE), flexible sigmoidoscopy (OC), and computed tomographic colonography (CTC), which is colloquially referred to as virtual colonoscopy. The lengthening list of options has just been further complicated by suggested new joint guidelines from the American Cancer Society, the U.S. Multi-Society Task Force on Colorectal Cancer, and the American College of Radiology (Table 2; ref. 2).

The U.S. Preventive Services Task Force assigns its strongest grade A category of recommendation "that clinicians screen men and women 50 years of age or older for colorectal cancer" (1) (accessed 7/13/2008). The U.S. Preventive Services Task Force approves the use of FOBT, FSIG, OC, and DCBE but not CTC or stool DNA. Until the latest American Cancer Society revisions, the American Cancer Society and U.S. Preventive Services Task Force guidelines were broadly similar (3). What is the current status of CRC screening in this setting of multiple alternative tests and changing recommendations?

In the general population of the United States, FOBT use is in decline and OC is supplanted by the least, that this technology has been recommended by any commercial stool DNA test detected 46% of advanced CRAs with a diameter of ≥10 mm compared with 17% with a sensitive gFOBT (11). There are no published studies comparing the sensitivity and specificity of stool DNA and FIT for asymptomatic CRC in a screening setting. Given the evolving nature of the technology and the lack of widespread evaluation of stool DNA testing in a population setting, not to mention the current lack of availability of any commercial stool DNA test, it is surprising, to say the least, that this technology has been recommended by the American Cancer Society and other professional
organizations for CRC screening in the general population.

What are the relative merits of invasive (FSIG, OC, and DCBE) and noninvasive (CTC) methods of colorectal structural evaluation for CRC screening compared with stool-based technologies? Many would argue that DCBE is obsolete as a screening tool. It is rarely used for this purpose in clinical practice and the test is rapidly disappearing from radiology practice. In contrast to the United Kingdom and other countries, screening FSIG is rapidly disappearing from the practice scene in the United States. The relative merits of OC and CTC as screening tools are coming into clearer focus. In a recent comparison, the prevalence of advanced neoplasia in patients undergoing primary CRC screening by CTC or OC was 3.2% and 3.4%, respectively (12). Although there is now broad agreement that primary screening OC and CTC have equivalent sensitivity and specificity for detecting advanced neoplasms with a diameter of ≥10 mm, several other controversies concerning the relative merits of OC and CTC are unresolved.

Some argue that inferior sensitivity for lesions with a diameter of <10 mm is a drawback to CTC. Others have drawn attention to the prevalence of nonpolypoid (“flat”) CRAs, which might be more easily missed at CTC than OC (13), and reported a greater association for nonpolypoid than polypoid CRAs with carcinoma (14). What is beyond dispute is that CTC is greatly superior to gFOBT and FIT as a screening test for advanced neoplasms with a diameter of ≥10 mm, several other controversies concerning the relative merits of OC and CTC are unresolved.

Dissemination of guidelines for CRC screening is intended to increase the number of at-risk people who undergo screening. The purposes of screening are to identify and treat patients with premalignant CRAs and to maximize the proportion of patients whose CRC is diagnosed and treated at the localized stage while prognosis is excellent. In the recently issued revised CRC screening guidelines, the complexity of recommendations, which were already less than emphatic, is increased without good evidence that their implementation will increase screening uptake or the yield of screen-detected early stage disease. There is sufficient evidence

Table 1. Indirect evidence that screening is likely to reduce CRC mortality

<table>
<thead>
<tr>
<th>Disease stage</th>
<th>Most screen-detected CRCs are localized. Five-year survival following resection of localized CRC 90% (17)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adenomatous polyps</td>
<td>Most CRCs develop from benign adenomatous polyps (syn. colorectal adenomas, CRA). Expected CRC mortality is substantially reduced in patients who have undergone polypectomy (ablation of CRAs; ref. 18)</td>
</tr>
<tr>
<td>FOBT (RCT)</td>
<td>Annual gFOBT reduced cumulative incidence ratio of CRC to 0.80 compared with control (19)</td>
</tr>
<tr>
<td>Rigid sigmoidoscopy (case-control study)</td>
<td>Odds ratio of death from cancer of the rectum or distal colon was 0.3 in patients who had undergone screening rigid sigmoidoscopy compared with controls (20)</td>
</tr>
</tbody>
</table>

Table 2. Colorectal cancer screening options

| Tests that detect adenomatous polyps and cancer | FSIG every 5 y, or Colonoscopy every 10 y, or DCBE every 5 y, or CTC every 5 y |
| Tests that primarily detect cancer | Annual guaiac-based FOBT with high test sensitivity for cancer, or Annual FIT with high test sensitivity for cancer, or Stool DNA test with high sensitivity for cancer, interval uncertain |
to propose dispensing with several screening technologies, specifically gFOBT, stool DNA detection (until the technology is greatly improved), and DCBE. There is a pressing need for careful studies of alternative, simpler protocols, such as the OC or CTC or FIT strategies proposed above. The goal of these studies would be to optimize the costs and detection rates of CRC screening.

Disclosure of Potential Conflicts of Interest
No potential conflicts of interest were disclosed.

References
Colorectal Cancer Screening: Confusion Reigns

Peter Lance

Cancer Epidemiol Biomarkers Prev 2008;17:2205-2207.

Updated version
Access the most recent version of this article at:
http://cebp.aacrjournals.org/content/17/9/2205

Cited articles
This article cites 16 articles, 2 of which you can access for free at:
http://cebp.aacrjournals.org/content/17/9/2205.full.html#ref-list-1

Citing articles
This article has been cited by 1 HighWire-hosted articles. Access the articles at:
/content/17/9/2205.full.html#related-urls

E-mail alerts
Sign up to receive free email-alerts related to this article or journal.

Reprints and Subscriptions
To order reprints of this article or to subscribe to the journal, contact the AACR Publications Department at pubs@aacr.org.

Permissions
To request permission to re-use all or part of this article, contact the AACR Publications Department at permissions@aacr.org.