A 71-Year-Old Woman Contemplating a Screening Colonoscopy

William C. Taylor, MD, Discussant

Dr Burns: Ms G is a 71-year-old woman with a past medical history of osteoporosis, mitral valve prolapse, mild rheumatoid arthritis, and hypothyroidism. She has Medicare. Ms G is trying to decide whether to undergo a colonoscopy to screen for colon cancer.

Ms G is currently feeling well and has no active medical issues. Ms G’s physician has encouraged her to have a colonoscopy, but she remains reluctant to proceed for 3 reasons. First, she has had adverse reactions to anesthetic agents in the past and is concerned about a potential reaction to the agents that would be used for a colonoscopy. Second, she is concerned about needing transportation home after receiving a sedative because her husband has driving restrictions. Third, she is unsure about the importance of colonoscopy given her negative family history of colon cancer. In addition, she expressed a concern about the size of colonoscopes designed for adults. Of note, she has completed home-based fecal occult blood testing (FOBT) on a yearly to every-other-year basis, and test results have always been negative. She has never undergone flexible sigmoidoscopy.

She has been screened for breast and cervical cancer. She has had bone densitometry and was found to have osteoporosis for which she currently takes alendronate as well as calcium and vitamin D. Ms G also has had cholesterol screening performed on a yearly basis.

She is currently taking alendronate (70 mg weekly), calcium, vitamin D, and levethoxynine (75 µg daily) and reports vomiting as an adverse reaction to diazepam. She has undergone allergy testing, which revealed an allergy to ephedrine and all members of the “caine” family except carbocaine.

She is married. She does not smoke and drinks red wine with dinner. She remains physically active around the home and in her garden and practices piano on a daily basis. Travel is restricted by her husband’s limited driving ability.

Ms G: Her View

I’ve had a lot of pressure from my doctor to have a colonoscopy, but I’m reluctant to have one for several reasons. First of all, you have to have some sort of a relaxant and I’m afraid to take one of those tranquilizer type things because I just react badly to that stuff. I talked to my doctor and she thought it might be possible to do it without sedation especially if they used pediatric equipment. Second, I could never have it done here. My husband is truly handicapped and cannot drive other than right around the house, so he could not drive me here and I’d have to have somebody else bring me down. The third thing is that my father is 1 of 9 children, my mother 1 of 5 and nobody has ever had colon cancer on either side of the family that we know. So those are my reasons. However, this summer it really hit me because my doctor said she thinks I should go ahead and have one because my health is so good, that I should, barring trucks hitting me, etc, last a long time, and that I should have the colonoscopy just in case there’s something lurking there. And I had never thought about it that way and I thought that was valid.

Dr L, Ms G’s Primary Care Physician: Her View

I have known Ms G for a number of years. She is a generally healthy older woman who has many good years ahead of her. Given this, I have encouraged her to have a colonoscopy as part of routine screening for colon cancer. In the community in which I practice, colonoscopy is the current practice standard for colon cancer screening both among primary care physicians and gastroenterologists. I do think that serial fecal occult blood cards are a reasonable alternative if the pragmatics of her life preclude colonoscopy. I am aware that she lives far away and that her husband is chroni-
cally ill, making transportation a significant impediment. I think that she has readily participated in other cancer screening such as mammography, as she can do this on her own and is not dependent on others.

AT THE CROSSROADS: QUESTIONS FOR DR TAYLOR

Summarize the epidemiology and pathophysiology of colorectal cancer. What is the evidence supporting screening for colorectal cancer? What are the effectiveness, accuracy, and adverse effects of screening tests for colon cancer? What is the evidence for screening patients older than 65 years? What do you recommend for Ms G? What does the future hold?

Dr Taylor: Ms G is a vigorous 71-year-old woman who has preferred not to undergo colonoscopy to screen for colorectal cancer despite her physician’s advice to do so. She has not previously undergone colonoscopy or sigmoidoscopy, but has participated every 1 to 2 years in home-based fecal occult blood testing (FOBT). She has no symptoms of colorectal cancer and no past history of colorectal cancer or inflammatory bowel disease. She has no family history of familial adenomatous polyposis or of cancers that would suggest a hereditary nonpolyposis cancer syndrome.1,2 Ms G is reluctant to undergo colonoscopy due to concerns about an adverse reaction to an anesthetic agent and the size of instruments for adults, as well as difficulty arranging transportation. In addition, she believes the absence of colorectal cancer in her family and normal FOBT results may make colonoscopy unnecessary for her.

Epidemiology of Colon Cancer

Worldwide approximately 1 million new cases of colorectal cancer are diagnosed every year, with about a half million deaths.3 In the United States, the corresponding annual numbers are almost 140 000 new cases and almost 60 000 deaths.4 This makes colorectal cancer the second leading cause of cancer deaths in the United States. Based only on Ms G’s characteristics as a 71-year-old woman living in the United States, the likelihood that she will be diagnosed with colorectal cancer is approximately 0.2% in the next year and approximately 2.6% in the next 10 years.5

Incidence of colon cancer varies geographically: persons in industrialized societies develop colon cancer at higher rates than do persons in developing countries.3 The role of diet and other environmental factors in the development of colorectal cancer has not been fully elucidated.6,7 Genetics plays a role in the epidemiology of colorectal cancer, with estimates that heritable factors are involved in approximately 35% of all cases.7 This genetic component of risk is responsible for the prominence of family history in current recommendations for screening, with starting age and type of screening based on a determination of how many family members of which relationship developed colon cancer or adenomatous polyps at what age.8 For Ms G, however, because she is older than 65 years, family history provides virtually no useful information in predicting colorectal cancer risk.9

Pathophysiology of Colon Cancer

It is currently believed that a series of genetic alterations is necessary for colon cancer to occur, producing the sequence of transformation of normal mucosa to adenomatous polyp and then to carcinoma.10,11 Some of these alterations can be inherited, and some arise as somatic mutations. Persons with familial adenomatosis and genetic colon cancer syndromes inherit some of these mutations. Persons who develop colon cancer without inherited syndromes probably acquire the same changes in their DNA as random somatic events, usually over many years, thereby explaining the increase in incidence of colon cancer at older ages.12

Evidence Supporting Screening for Colon Cancer

Three well-designed and properly conducted randomized trials of FOBT have shown a relative reduction in deaths caused by colorectal cancer of 16% to 33% over 8 to 13 years, with similar reductions achieved among women and men.13-15 All of these trials included women and men aged 45 to 75 years, and 1 trial included participants as young as 40 years and as old as 80 years.13 All 3 trials excluded persons at increased risk of colon cancer based on various factors such as personal history of inflammatory bowel disease, adenomatous polyps, or colon cancer; or a family history consistent with familial adenomatous polyposis or of hereditary nonpolyposis cancer. Therefore, these studies included persons like Ms G, and their results can reasonably be applied in estimating the benefit Ms G might derive from screening.

No trials have measured whether barium enema, flexible sigmoidoscopy, colonoscopy, or newer screening modalities such as computed tomographic (CT) colonography or fecal DNA analysis improve survival or decrease colon cancer mortality; instead, models have been developed to estimate the benefits and risks of these procedures.16,17 Models have generally calculated favorable cost-effectiveness of home-based FOBT every year, flexible sigmoidoscopy every 5 years, and colonoscopy every 10 years, with results roughly equivalent for all 3 of these screening modalities.16,17 In most analyses, screening compared with no screening resulted in a cost-effectiveness ratio of less than $30 000 per year of life saved.17 Based on the evidence from randomized trials that showed annual home-based FOBT reduced the number of colon cancer deaths, and from the favorable cost-effectiveness models, most expert groups have concluded that screening for colorectal cancer should be offered to average-risk adults starting at age 50 years, that any of these 3 screening modalities is acceptable, and that choice of screening modality should be individualized based on available resources and patient preferences.8,18

Despite the view of experts that home-based FOBT, sigmoidoscopy, and colonoscopy are all acceptable screening modalities, Ms G’s physician, Dr L, recommended colonoscopy because he believed that colonoscopy was the “practice standard” in her community. The physician’s use of the term “practice standard” may indicate a concern about le-
gal liability, since “standard of care” is the criterion by which a physician’s behavior is judged when a physician is accused of malpractice. Despite the stated position of expert groups that FOBT and sigmoidoscopy are acceptable as screening modalities, these expert statements do not constitute a legal standard. An editorial in which colonoscopy as screening modalities, these expert statements do not constitute a legal standard. An editorial in which colonoscopy was recommended and other screening modalities were denigrated may have fostered the view that colonoscopy is the preferred screening method. In a highly publicized case that addressed whether to use prostate-specific antigen to screen for prostate cancer, a court found a physician who did not screen based on lack of evidence to be negligent. Although the case in which a court found less aggressive cancer screening to be negligent concerned screening for prostate cancer, not colon cancer, knowledge of this case may have contributed to Dr L’s belief that more aggressive screening for colon cancer with colonoscopy rather than FOBT or sigmoidoscopy was the “practice standard” for Ms G.

No study has directly measured the effect of screening on colorectal cancer mortality among persons at increased risk of developing colorectal cancer based on longstanding inflammatory bowel disease, a personal history of colon cancer, or a family history of cancer or polyps. Nonrandomized studies of screening provide weak evidence of benefit among persons with familial adenomatous polyposis and among persons with a family history of hereditary nonpolyposis colon cancer (Lynch syndrome). Recommendations for screening in these groups are therefore extrapolated from studies showing increased risk and specificity of about 90% after a single screen and 60% when used over several years. Although the ability of FOBT to reduce colorectal cancer mortality was hypothesized to result from false-positive results causing more patients to undergo colonoscopy, which could then be responsible for the reduction in cancer deaths, more recent analyses have found that FOBT is effective in reducing mortality with the minority of reduction due to chance detection.

Flexible sigmoidoscopy requires less preparation than colonoscopy, requires no anesthesia, and may offer a lower rate of colon perforation than colonoscopy, but does not detect lesions beyond the reach of the sigmoidoscope. Barium enema and CT colonography (“virtual colonoscopy”) require the same preparation as colonoscopy (although studies without cathartic preparation have been reported), with the additional disadvantage that abnormal test results require a follow-up colonoscopy for biopsy of identified lesions. Although some have reported high accuracy of CT colonography, others have not. Perhaps most telling, when patients in one trial underwent both CT colonography and colonoscopy, more preferred colonoscopy.

Screening Patients Older Than 65 Years
Because screening involves risks and costs in the present, with a potential benefit achieved only in the future, risks and benefits must be weighed carefully. Failure to do so artificially inflates the apparent benefit of screening. In older people, this consideration is particularly important and decision making must be individualized. The ethics committee of the American Geriatrics Society has pointed out the uselessness of screening among persons with short life expectancies, while cautioning that chronological age alone is not a sufficient basis for making the decision to withhold screening.

RECOMMENDATIONS FOR MS G
Ms G should understand that yearly home-based FOBT, which she has undergone previously and can continue to undergo on an annual basis, is supported by evidence from...
trials13-15 and by expert opinion.8,17,18 If Ms G’s physician is concerned about legal liability, she should note in the medical record the details of her discussion with Ms G of the benefits and risks of the various screening modalities,19 although the documentation of such a discussion does not guarantee a finding of no negligence if malpractice is alleged,21 adds to the tasks assigned to physicians for prevention,56 and takes time that could instead be spent on improving the health of Ms G or others.57

Ms G and her physician should have accurate information about all screening modalities to help ensure the decision is fully informed. As Ms G has apparently already learned, it is possible to undertake colonoscopy without an anesthetic agent.58 Second, smaller instruments that are currently used make successful colonoscopy without anesthesia more likely. Third, transportation likely can be arranged through consultation with a case manager, a community resource specialist, or a social worker.59

<table>
<thead>
<tr>
<th>Screening Test</th>
<th>Effectiveness</th>
<th>Accuracy</th>
<th>Adverse Effects</th>
<th>Quality of Evidence</th>
<th>Recommendations of Expert Groups</th>
</tr>
</thead>
<tbody>
<tr>
<td>Digital rectal examination</td>
<td>Ineffective27</td>
<td>&lt;10%76</td>
<td>Unknown</td>
<td>Opportunity cost for clinician; cost of unnecessary evaluation of false-positive results</td>
<td>No evidence</td>
</tr>
<tr>
<td>Single sample fecal occult blood test (office)</td>
<td>Ineffective29</td>
<td>5%29</td>
<td>98%29</td>
<td>$1018</td>
<td>High-quality study showed inferiority of office-based fecal occult blood testing in comparison with home-based testing29</td>
</tr>
<tr>
<td>Six sample fecal occult blood test (home)</td>
<td>33% Relative reduction in colon cancer deaths over 13 y; absolute reduction in colon cancer deaths of 2.95/100013</td>
<td>30%-70% for cancer; 19%-29% for advanced neoplasms16</td>
<td>90% for single test; 62% with annual test over 10-13 y18</td>
<td>$3818</td>
<td>Three randomized trials showed reduction in colorectal cancer deaths13-15,16, insufficient power to evaluate effect on total mortality; inconsistency in rehydration of slides</td>
</tr>
<tr>
<td>Sigmoidoscopy</td>
<td>59% Relative reduction in colon cancer deaths within reach of sigmoidoscope26</td>
<td>30%-70%; depends on criteria for positive test30</td>
<td>99%30</td>
<td>Perforation 1/10,00026; may be less sensitive in women31</td>
<td>$27925</td>
</tr>
<tr>
<td>Barium enema</td>
<td>Unknown</td>
<td>48% Overall71; 48% for polyps &gt;10 mm, 35% for 6-9 mm, 41% for &gt;5 mm33</td>
<td>82%-90%33,34</td>
<td>Perforation 1/25,00026; radiation</td>
<td>$29832</td>
</tr>
<tr>
<td>Colonoscopy</td>
<td>57% Relative reduction in colon cancer deaths26</td>
<td>89%-95%30,42 and &gt;90% for adenomas26; probably higher for cancers16</td>
<td>≥90%30</td>
<td>Perforation 1/1000 for screening26; perforation rate, 1/500-1/1000 for polypectomy; mortality, 1/20,000</td>
<td>$101230</td>
</tr>
<tr>
<td>Computed tomographic colonography (“virtual colonoscopy”)</td>
<td>Unknown</td>
<td>48%-85%43</td>
<td>92%-97%43</td>
<td>Radiation; cost of false-positive incidental extracolonic findings43; colonoscopy required when lesions identified</td>
<td>$650-$120043</td>
</tr>
</tbody>
</table>

Abbreviations: ACS, American Cancer Society; AGA, American Gastroenterology Association; IOM, Institute of Medicine; USPSTF, US Preventive Services Task Force.

*Every screening test with sensitivity and specificity less than 100% has the risks and costs associated with false-positive and false-negative test results.

CLINICAL CROSSROADS

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nally, Ms G should be informed that she is beyond the age when family history is predictive of colon cancer risk, so her negative family history should have no bearing on her decision.

For Ms G, the risk of developing colon cancer in the next 10 years is approximately 2.6 per 100, and negative annual FOBT produces a risk approximately 30% lower, or about 1.8% over 10 years. The potential magnitude of the benefit of colonoscopy must be put in this context, since the only reason to choose colonoscopy over Ms G's current screening regimen if she resumes annual FOBT would be to produce a further reduction in this rate below 1.8 per 100 over the next 10 years. Put another way, more than 55 women like Ms G would need to undergo colonoscopy to find one who will develop colon cancer in the next 10 years, and many more than 55 women would need to undergo colonoscopy to find one whose outcome could be improved by colonoscopy.

Therefore, I believe the best choice for Ms G would be to resume home-based FOBT annually, with an understanding that an abnormal result would require a colonoscopy. If colonoscopy were necessary, it could be done with a small instrument, likely without anesthesia, with transportation arranged by a social worker, case worker, or community resource specialist.

Future Directions

New screening tests such as analysis of fecal DNA, sophisticated molecular diagnostic tools, and video capsule endoscopy are on the horizon. Methods to finance medical innovations that focus on benefit rather than profit are needed to improve the development of new tests. Before applying new tests, it will be important to weigh the benefits and risks, including ethical issues such as confidentiality of genetic information. In addition, evaluation of new tests should include consideration of the potential impact of the financial interests of those who conduct research. However, as long as screening is applied to those at average risk, any screening will have poor predictive value, since even tests with near-perfect specificity performed on patients with low pretest probability of disease will result in many false-positive results. A sophisticated understanding of the genetic polymorphisms and other factors that influence risk will be necessary to permit much more selective application of screening with higher diagnostic yield. Ultimately, a system of health care that fosters the equitable delivery of medical services to those who should be screened and treated will be necessary to minimize the risk of death and morbidity from colon cancer.

QUESTIONS AND DISCUSSION

QUESTION: From what you said, it sounds like Ms G's chances are 998 out of a 1000 that a colonoscopy, even if it's done with a tiny pediatric scope, will not have any effect on her life.

DR TAYLOR: Unfortunately it's more complicated than that. You correctly calculated that Ms G, a 71-year-old American woman of European descent, will be unlikely to be identified as having colon cancer in the next year. But the purpose of doing a colonoscopy would be not simply to find a cancer she might develop in the next year. The purpose would be to find and remove an adenomatous polyp or a colon cancer at an early stage to produce a better outcome than would occur without screening. The decision to undergo screening involves a difficult judgment weighing the negative consequences of a screening test including slight risk of perforation or other complications with inconvenience and cost now, weighed against potential benefit of a better outcome in the future by detecting and removing or treating early a lesion that might, without treatment, cause a problem in the future. This weighing of risks and costs now and potential benefit in the future must be viewed in the context of the values of this 71-year-old woman.

QUESTION: Can you give us your thoughts about the discrepancy between the sigmoidoscopy and colonoscopy data?

DR TAYLOR: Simply put, colonoscopy looks at more of the colon. Epidemiologically over time it appears that more of the cancers are migrating away from the reach of the sigmoidoscope. For people who have something to find (cancer or adenomas larger than 1 cm), 30% to 70% will have cancer or adenoma detected by sigmoidoscopy. If a cancer or adenoma is identified on sigmoidoscopy, colonoscopy will be recommended and most of those lesions will be found. The disadvantage of sigmoidoscopy is that 30% to 70% of lesions are missed. The advantage is that this test can be done by primary care physicians and by physician assistants, may have a lower rate of complications, is cheaper, and may be acceptable to more patients.

QUESTION: If Ms G had multiple medical problems, how would that have changed the discussion?

DR TAYLOR: That would change things a lot. Screening is about doing something with risks and costs now for a potential benefit in the future. If she has bad coronary disease, if she's dealing with metastatic breast cancer or some other potentially life-threatening disease, it doesn't make any sense to talk to her about colorectal cancer screening, since screening would provide more harm than good. Discussing screening as providing more harm than good makes it clear why screening would not be worthwhile in this situation.
REFERENCES


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