Quantifying the Potential Benefit of Sigmoidoscopic Rescreening for Colorectal Cancer

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After a person has tested as negative on their first screening test for a given cancer, how soon should a second test be performed? In a perfect world, the answer to this question, at least in terms of efficacy, would be obtained from the results of randomized trials that examine the occurrence of cancer mortality in persons assigned to different rescreening frequencies. However, trials of this type are difficult and not commonly conducted, so it is necessary to look for guidance from studies that seek to estimate the occurrence of clinically important lesions after an initially negative screen (1).

Some relevant data can come from studies that document the incidence of clinically detected disease over time following a negative screening exam. For flexible sigmoidoscopy, such studies have been both cohort (2) and case–control (3–6) in design. The results of randomized trials of screening sigmoidoscopy, in which the incidence of distal colon and rectal cancers is monitored over time among initially screen-negative persons, are relevant as well (7,8). Each of these study designs has the virtue of focusing on an endpoint that generally is clinically relevant but has some potential limitations with respect to informing decisions regarding a screening interval. For example, some tumors are not detectable by screening before their clinical presentation. It is also possible that by the time they are clinically apparent, some malignancies may no longer be amenable to effective treatment; a screening interval determined by the period between a negative screening exam and the clinical diagnosis may be longer than the one that could best achieve a reduction in cancer mortality.

These limitations can be addressed, in part, by studies of the yield on repeat screening among individuals who initially tested negative. In this issue of the Journal, Weissfeld et al (9) report a study of this type that was conducted among participants in the Prostate, Lung, Colorectal, and Ovarian Cancer (PLCO) screening trial. Its results suggest that a second screening flexible sigmoidoscopy performed 3–5 years after a negative initial exam can identify one additional person with colorectal cancer and 17 others with an advanced colorectal adenoma in every 1000 rescreened persons. The very large size of this study, and consequently the large number of cancers (26) and advanced adenomas (503) identified, provide statistically solid estimates for us to incorporate in cost–benefit evaluations of different rescreening strategies. However, some limitations regarding the nature of the PLCO trial must be taken into account when interpreting the data obtained.

1. For rescreening exams that were positive for any abnormality, some 22% were not followed by a diagnostic intervention. To the extent that some persons with advanced adenoma or carcinoma were in this group, the prevalence of these lesions at the time of rescreening would be underestimated.
2. Only about half of the PLCO participants who were initially screened received a second exam. It is possible that the prevalence of abnormalities at rescreening in this group might not entirely represent the frequency among PLCO participants as a whole.
3. Not all persons with an advanced adenoma detected at the time of rescreening had the potential to benefit from this lesion being identified, as a certain percentage of the adenomas would not have progressed to cancer during the lifetime of the person.

The above limitations notwithstanding, the article by Weissfeld et al. (9) provides data that nicely complement those from the PLCO experience with rescreening that were presented earlier (10) and those from cohort and case–control studies of endoscopy. However, the limitations of all studies in this area will need to be explicitly considered when attempting to arrive at policy recommendations regarding rescreening intervals for colorectal cancer.

References

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