

ADVANCES IN GERD

Current Developments in the Management of Acid-Related GI Disorders

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Screening and Surveillance of Barrett's Esophagus

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G&H What are the standard practice guidelines for the screening and surveillance of Barrett's esophagus?

SJP There are no universally accepted guidelines for screening and surveillance of Barrett's esophagus, although several medical societies have suggested guidelines. In the United States, the best known guidelines are probably those from the American College of Gastroenterology (ACG). Approximately 3 years ago, the ACG updated their recommendations, suggesting that surveillance be done every 3 years, instead of every 2 years as was previously recommended. However, this change was not based on any firm evidence.

In fact, the usefulness of screening and surveillance for Barrett's esophagus is questionable. Neither has been shown to have any benefit in terms of prolonging life and/or preventing deaths from cancer of the esophagus. There is indirect evidence that these practices can be beneficial, but there has been no proof in the form of a randomized controlled trial. Therefore, when speaking about guidelines, it is important to note that these are general recommendations and opinions. There has not been a study showing benefit or harm from these practices. That being said, most gastroenterologists will recommend regular endoscopic surveillance for anyone presenting with Barrett's esophagus. Screening for Barrett's esophagus is a more difficult issue.

G&H Could you clarify the difference between screening and surveillance?

SJP When speaking about Barrett's esophagus, screening refers to the use of endoscopy to screen large populations

for this condition. For example, individuals with symptoms of gastroesophageal reflux disease (GERD) would be screened for Barrett's esophagus. By contrast, surveillance refers to the use of endoscopy in order to identify early neoplasia in patients with Barrett's esophagus. Most gastroenterologists practice some form of surveillance for patients with Barrett's esophagus.

G&H Why is screening a more difficult issue?

SJP There are approximately 60 million adults with chronic GERD symptoms. Considering this statistic, the difficulty becomes obvious: should all of these individuals be screened for Barrett's esophagus? Would that approach be cost effective? Would it be desirable? These questions are not easy to answer.

G&H What are the prevailing guidelines regarding screening?

SJP Again, the prevailing guidelines are based on opinion, not solid data. The ACG currently recommends that patients with chronic GERD symptoms, who are those most likely to develop Barrett's esophagus, should be screened. However, this statement is fairly general and does not provide much information. How is "chronic" defined—does it refer to symptoms ongoing for decades, years, or months? This recommendation does not include any guidelines pertaining to age or ethnicity. The majority of individuals with Barrett's esophagus, and in particular esophageal adenocarcinoma, are white men. Should populations that are not composed of predominantly white men be screened? This issue is very contentious. Considering that adenocarcinoma of the esophagus appears to be an extremely rare disease among Asian women, the minor risk associated with endoscopy screening is probably not worth the potential benefit in this population. However, there are no specific guidelines right now about which populations should be screened; the only recommendation pertains to individuals experiencing chronic GERD symptoms.

G&H Could you describe the indirect evidence regarding the benefit of screening and surveillance?

SJP The indirect evidence comes from observational studies of patients who have undergone screening and surveillance for Barrett's esophagus that have shown a benefit with these procedures. The problem posed by observational studies is that they are subject to many biases and therefore are not definitive. There are studies showing that cancer was discovered earlier among patients who were in surveillance programs for Barrett's esophagus compared to those who were not undergoing surveillance. Cancer detected at an earlier stage is probably more treatable, but the study does not answer the question of whether surveillance is effective.

Computer modeling studies have also been done and have suggested that screening and surveillance are beneficial provided that certain baseline assumptions are met. The problem with this approach is that the findings are not definitive either because they vary based on baseline assumptions. Further, many of those assumptions are questionable and not based on hard data, therefore making any subsequent findings equally questionable. However, having acknowledged the inherent challenges with observational studies and computer models, the bulk of evidence from these 2 approaches shows that surveillance is most likely beneficial.

G&H Could screening and/or surveillance cause harm?

SJP Endoscopy is generally safe, but the procedure is not risk-free, and there are occasional severe complications. In addition, it is possible that the information derived from the procedure can lead to harm. For example, if a precancerous dysplasia is identified, an invasive procedure to remove the dysplasia carries its own risk, particularly in elderly patients, who comprise the majority of patients in surveillance programs.

G&H What technologies for screening and surveillance are currently being developed?

SJP There are quite a few experimental techniques currently being explored, particularly new imaging modalities. These techniques include narrow band-imaging endoscopy, magnification endoscopy, and confocal microendoscopy, with which tissue can be examined at the microscopic level. None of these techniques have yet been proven to be beneficial and most are not available to the practicing gastroenterologist. At the moment, the best technology available for screening and surveillance is conventional endoscopy.

G&H Could screening and surveillance be studied in a clinical trial setting in order to obtain hard data regarding their efficacy?

SJP The ideal setting in which to study surveillance would be a randomized controlled trial in which patients with Barrett's esophagus would be randomized to either undergo or not undergo surveillance. The patients would be followed for several years and the results would demonstrate whether there is a difference in the outcomes of the 2 groups, where the primary endpoints would be death or morbidity from cancer of the esophagus. This approach would establish the efficacy of surveillance.

However, there are many obstacles to this approach, which is why such a trial has not yet been conducted. First, the rate of cancer development from Barrett's esophagus is low on an absolute scale, with approximately 0.5% of patients per year—1 in 200—developing cancer. In order to measure an event that occurs in every 1 of 200 patients, thousands of patients would need to be enrolled in the study, and they would need to be followed for a long time, probably a decade. Obtaining funding for a study of that size and duration is very difficult. But even if the funding were available, it would be very difficult to enroll patients to a study in which they might not be undergoing endoscopy. If a patient has been informed that he or she has a precancerous condition, it would be very difficult to ask them to agree to not undergo surveillance for cancer development. These challenges are not insurmountable, but were a study to begin today, the results would still not be available for perhaps another 10 years.

G&H Is it possible to obtain hard data without a randomized controlled trial of this kind?

SJP Some clinicians have discussed measuring an intermediate marker such as certain biochemical abnormalities as a more practical approach. The problem with such an approach is that there is no solid evidence on how often these abnormalities lead to cancer. Consequently, the marker is still intermediate and does not provide a definitive answer.

G&H Are there prognostic factors that could narrow down the populations to be screened for Barrett's esophagus?

SJP The prognostic factors appear to be white race, an age of 50 years or more, and chronic heartburn (ongoing for 5 years or more). These groups of patients yield the highest incidence of esophageal cancer stemming from Barrett's esophagus. However, we do not know if the same factors apply among a population of people with Barrett's esophagus. In other words, a retrospective study would

reveal that the majority of patients with esophageal cancer who had Barrett's esophagus as a precursor are older white men. But among a population of people with Barrett's esophagus, would white men be the only individuals to develop cancer, or are white men predisposed to Barrett's esophagus and therefore the major patient subgroup? There are no answers to these questions, which is why developing specific guidelines has proven difficult.

G&H Should a physician want to err on the side of caution when it comes to screening and surveillance?

SJP Yes. I think that by preponderance the data suggest that surveillance is a good practice for Barrett's esophagus in that it might help prevent cancer. Certainly there are no data showing that surveillance results in more deaths than no surveillance. Cost is not a negligible factor, but for a patient with Barrett's esophagus, surveillance does seem to be appropriate.

G&H Is there an issue regarding insurance coverage for surveillance if a definitive benefit has not been identified?

SJP Some insurers will cover surveillance. However, a related issue is that if a patient is diagnosed with Barrett's

esophagus, his or her ability to obtain life insurance may be affected. If life insurance can be obtained, the cost of the premiums will be substantially higher. Most studies suggest that Barrett's esophagus does not shorten life, but the diagnosis can still prove problematic. This potential difficulty is a downside of screening; as we often tell students, don't do a test if you don't want the answer.

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pANCA with antibiotics or probiotics is effective. If the initial postoperative immune response can be blunted, then it may be possible to decrease the incidence or severity of chronic pouchitis.

Studies have suggested that patients with CD who are positive for pANCA do not respond as robustly to treatment with infliximab (Remicade, Centocor) as patients without this marker (Taylor et al. *Gastroenterology*. 2001).

From a research standpoint, clinical associations have been described with the newer antimicrobial antigen markers. The relevance of these findings to the management of patients with IBD is under investigation.

G&H Are there different ways to test for these markers?

EV Yes, different laboratories use different techniques. Dr. William Sandborn, of the Mayo Clinic, conducted a study in which blood samples from a well-characterized cohort of

UC and CD patients were sent to a number of laboratories around the world and found that the results varied widely, with some facilities performing the tests more accurately than others (Sandborn et al. *Inflamm Bowel Dis*. 2001). It is important to be aware of the methods and reliability of the testing done at the selected laboratory.

Suggested Reading

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