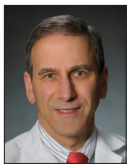
ADVANCES IN GERD

Current Developments in the Management of Acid-Related GI Disorders

Section Editor: Joel E. Richter, MD

Updated Guidelines for Diagnosing and Managing Barrett Esophagus



Gary W. Falk, MD, MS
Professor of Medicine
Division of Gastroenterology
University of Pennsylvania Perelman School of Medicine
Philadelphia, Pennsylvania

G&H Why were the guidelines for Barrett esophagus updated?

GF The last iteration of the guidelines for diagnosing and managing Barrett esophagus was published in 2008. There have been significant changes in the field during that 8-year gap, especially with respect to endoscopic therapies and screening recommendations. Given the time interval and developments in the field, the time was right to publish updated and more comprehensive guidelines.

G&H How were the new guidelines developed?

GF The guidelines were developed by Drs Nicholas J. Shaheen, Prasad G. Iyer, Lauren Gerson, and myself under the auspices of the American College of Gastroenterology and the Practice Parameters Committee. We conducted a systematic review of the literature by searching for certain keywords in MEDLINE from 1980 to the time the guidelines were written. We then used the GRADE (Grading of Recommendations Assessment, Development, and Evaluation) criteria to evaluate the level of evidence, which ranged from high (additional research was unlikely to change the estimate of effect) to very low (any estimate of effect is very uncertain). The strength of the recommendation was graded as strong (the benefits outweigh the risks) or conditional (the tradeoff is uncertain).

G&H What were the most significant changes and additions in terms of diagnosing Barrett esophagus?

GF There are 3 significant changes in terms of establishing the diagnosis of Barrett esophagus. The first change deals with columnar lining. The 2008 guidelines state that changes of any length that could be recognized as columnar-type mucosa and confirmed to have intestinal metaplasia (the cell type that is associated with the diagnosis) were felt to be Barrett esophagus. The new guidelines suggest at least a 1-cm threshold of columnar lining above the gastroesophageal junction in order to diagnose the condition due to considerable interobserver variability in segments less than 1 cm.

In patients with suspected Barrett esophagus, 8 biopsies, at minimum, need to be obtained in order to maximize the yield of finding intestinal metaplasia on a biopsy specimen.

The second change is that normal Z lines as well as Z lines with less than 1 cm of variability should not be biopsied in individuals who are undergoing endoscopy.

The third change states that endoscopists should utilize the Prague classification to describe what is seen in the Barrett segment.

G&H What changes were made regarding screening recommendations?

GF The 2008 guidelines state that screening for Barrett esophagus should focus on older, white men with longstanding heartburn. It is now recommended that screening be performed in men with chronic symptoms (≥5 years) of gastroesophageal reflux disease who have at least 2 additional risk factors. Those risk factors include

age greater than 50 years, white race, presence of central obesity, current or past history of smoking, or a confirmed family history of Barrett esophagus.

A key difference with the new guidelines is that screening is no longer indicated in women with chronic symptoms of gastroesophageal reflux disease because of the very low risk of adenocarcinoma in this patient population. However, the guidelines do state that screening can be considered in women who present with multiple risk factors (the number is undefined) similar to those required for screening in men. Additionally, screening is not recommended for the general population (ie, patients without reflux symptoms).

An important note to mention is that if erosive esophagitis (Los Angeles Classification B, C, or D) is seen at the time of baseline endoscopy, a repeat endoscopy performed within 8 to 12 weeks is recommended to ensure that there is no underlying Barrett esophagus.

G&H How do surveillance recommendations differ between nondysplastic and low- or high-grade dysplastic Barrett esophagus?

GF The current surveillance recommendation for nondysplastic Barrett esophagus is to perform adequate biopsies at the initial endoscopy and follow up with surveillance at an interval of 3 to 5 years. This differs from what was published in 2008, which recommended 2 endoscopies with biopsy within 1 year, followed up with surveillance every 3 years.

A recommendation that was emphasized in the 2008 guidelines that remains important is that dysplasia of any grade merits a confirmatory look by a second pathologist who has extensive experience in interpretation of Barrett-associated neoplasia before any other decision is made in terms of treatment or surveillance. Patients with biopsy indefinite for dysplasia should undergo a repeat endoscopy 3 to 6 months following optimization of acid suppression. If indefinite for dysplasia is confirmed at a second endoscopy, those individuals should be surveyed at intervals of 12 months until 2 readings in a row are negative for dysplasia.

An area of major change is for patients with low-grade dysplasia. A repeat endoscopy after optimization of acid suppression may result in downgrading and should be performed in conjunction with a review of the initial biopsies by a second pathologist with expertise in Barrett esophagus. For patients with confirmed low-grade dysplasia, the guidelines now recommend consideration of endoscopic ablative therapy (which was not an option in 2008), with endoscopic surveillance at 1-year intervals as an alternative.

High-grade dysplasia should also first be confirmed by a second pathologist with appropriate expertise. Any mucosal abnormality in these patients should be addressed with endoscopic mucosal resection, and if high-grade dysplasia is confirmed, endoscopic intervention is warranted unless they have life-limiting comorbidities.

G&H How do the new guidelines address endoscopic and surgical therapies?

GF One of the major changes in the literature has been in the area of endoscopic therapies for Barrett esophagus, both in terms of when and how to apply these therapies and how to follow up with patients. As part of the approach to endoscopic therapy, an endoscopist should carefully examine the Barrett segment, paying particular attention to mucosal abnormalities. The best results for endoscopic therapy occur if mucosal abnormalities are removed with endoscopic mucosal resection prior to applying any broader ablative technologies. If the mucosa is flat, the guidelines recommend applying radiofrequency ablation therapy. This recommendation is appropriate for low-grade dysplasia as well as high-grade dysplasia and intramucosal cancer; ablative therapy should not be routinely applied to patients with nondysplastic Barrett esophagus.

Surgical therapies are no longer felt to be the preferred initial approach for high-grade dysplasia or intramucosal cancer because of the morbidities associated with the procedures. However, surgery can be considered as part of a multidisciplinary approach if a patient has intramucosal cancer with poor prognostic findings (eg, poor differentiation, lymphovascular invasion, evidence of an incomplete endoscopic mucosal resection) or if the patient is found to have submucosal cancer.

G&H What do the new guidelines recommend regarding proton pump inhibitor use?

GF The recommendation regarding proton pump inhibitors is that patients should receive once-daily proton pump inhibitor therapy, and the routine use of twice-daily dosing should be avoided unless necessitated by poor symptom control. Previously, there was no consensus regarding treatment if symptoms were absent. There is now evidence of a chemopreventive effect in which proton pump inhibitors decrease the risk of progression to neoplastic Barrett esophagus, as compared to either no acid suppression or H2 blockers; therefore, proton pump inhibitor therapy should now be considered in Barrett esophagus patients even in the absence of reflux symptoms.

G&H How will the use of biomarkers, advanced imaging technologies, and new screening modalities affect these guidelines?

GF Biomarkers and advanced imaging technologies continue to be an area of tremendous research interest.

Biomarkers of increased risk have not yet reached the level at which they can be employed in routine clinical practice, which was the belief 8 years ago as well. It remains to be seen if biomarkers will be ready for clinical practice in the next update of the guidelines.

The guidelines now recommend routine use of high-definition white-light endoscopy as part of surveillance; beyond electronic chromoendoscopy, other advanced imaging techniques are not yet recommended at this time.

The issue of screening is another area of research advances. While these new guidelines discuss the use of endoscopy, other approaches are being developed that are not yet ready for clinical use, but will likely be included in the next set of guidelines.

G&H Are there any other important areas for future research?

GF Yes. The areas for future research remain similar to what have been studied over the past several years, including developing better methods of risk-profiling individuals with Barrett esophagus. Radiofrequency ablation is recommended for low-grade dysplasia; however, not all individuals with low-grade dysplasia are at risk for developing high-grade dysplasia or cancer. Risk factors for progression for low-grade dysplasia need to be better studied.

Another area of research is how best to follow up individuals after ablative therapy. The guidelines clearly state that patients will continue to need follow-up care after completed ablation, but how they should be followed up is based primarily on expert opinion. We need better data to guide us in our follow-up protocols and biopsies.

I look forward to advances in alternative treatment options to radiofrequency ablation and endoscopic mucosal resection, and expect continuing advances in endoscopic submucosal dissection and cryoablation. Different approaches to screening in terms of targeted screening and population health, as well as the economics of these approaches, will continue to evolve. I would also like to see more research focused on biomarkers and alternative imaging platforms.

G&H Do you think there will be any challenges to the adoption of these new guidelines?

GF Absolutely. Multiple studies show that guidelines in general are not routinely followed and face challenges in terms of uptake by the practicing community. The exact reason for this remains unclear.

It is important to emphasize that although many of the recommendations in the new guidelines are based on weak evidence or expert opinion, my colleagues and I have tried to provide a pragmatic framework for the care of patients with Barrett esophagus, focusing on what the American College of Gastroenterology endorses as best practices in 2016 and keeping in mind the practicing physician.

Dr Falk has no relevant conflicts of interest to disclose.

Suggested Reading

Bennett C, Moayyedi P, Corley DA, et al; BOB CAT Consortium. BOB CAT: a large-scale review and Delphi consensus for management of Barrett esophagus with no dysplasia, indefinite for, or low-grade dysplasia. *Am J Gastroenterol*. 2015;110(5):662-682; quiz 683.

Rubenstein JH, Lieberman D, Fennerty B, Gellad ZF. Measuring the quality of Barrett esophagus management with measures that are high quality. *Gastroenterology*. 2015;149(6):1298-1301.

Shaheen NJ, Falk GW, Iyer PG, Gerson LB; American College of Gastroenterology. ACG clinical guideline: diagnosis and management of Barrett esophagus. *Am J Gastroenterol*. 2016;111(1):30-50; quiz 51.

Sharma P, Katzka DA, Gupta N, et al. Quality indicators for the management of Barrett esophagus, dysplasia, and esophageal adenocarcinoma: international consensus recommendations from the American Gastroenterological Association Symposium. *Gastroenterology*. 2015;149(6):1599-1606.