

# ADVANCES IN GERD

Current Developments in the Management of Acid-Related GI Disorders

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## Management of Nondysplastic Barrett Esophagus with Ablation Therapy

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### G&H How have patients with nondysplastic Barrett esophagus traditionally been managed?

**RS** Management of nondysplastic Barrett esophagus has consisted of interval endoscopy with systematic biopsies (4 quadrants every 2 cm). Although this procedure has been routinely practiced for many years, analyses have shown that it is not cost-effective. There has also been a problem with the method of biopsies. Biopsies can be time-consuming, particularly when segments of Barrett esophagus are 5 cm or longer. Studies have shown that the longer a segment of Barrett esophagus is, the fewer biopsies an endoscopist takes every 2 cm. For example, a 10-cm Barrett esophagus would probably require 6 levels of 4-quadrant biopsies, for a total of 24 biopsies. However, it is unlikely that the average practitioner would take so many biopsies, as they would require an extra 15–20 minutes. In addition, each level of specimens must be placed in a separate bottle after being obtained, so more than 1 assistant is needed during the procedure—an additional person is necessary to manage all of the biopsies. More biopsies also translate into higher costs from the pathologist.

### G&H Why has ablation therapy been historically used for dysplastic—but not nondysplastic—Barrett esophagus?

**RS** Ablation therapy has become the standard for treating dysplastic Barrett esophagus due to positive results

from the AIM dysplasia trial. The results of this very high-quality, randomized, sham-controlled trial of low-grade dysplasia and high-grade dysplasia were published in *The New England Journal of Medicine*. In Europe, there was an equivalent-quality, randomized trial of radiofrequency ablation versus endoscopic resection of the entire Barrett esophagus. This study demonstrated that radiofrequency ablation was technically easier to use and had fewer complications than endoscopic resection. Circumferential resection of the Barrett esophagus was associated with a high frequency of strictures. These 2 high-quality, randomized trials demonstrated the efficacy of radiofrequency ablation; the quality of this evidence is as good as the quality of the evidence that a pharmaceutical agent needs for obtaining approval from the US Food and Drug Administration.

### G&H Is ablation therapy currently being performed in nondysplastic Barrett esophagus patients on a regular basis?

**RS** Yes, ablation is now commonly being performed in patients with nondysplastic Barrett esophagus. In fact, because nondysplastic Barrett esophagus is the most common form of Barrett esophagus (95%), ablation is being performed more often in nondysplastic than dysplastic Barrett esophagus patients. There are estimated to be as many as 3 million individuals with Barrett esophagus in the United States. Approximately 1.5% have high-grade dysplasia and early cancer, and approximately 5% have

low-grade dysplasia. No more than 10% of all individuals with Barrett esophagus would meet the criteria for the dysplasia trials.

**G&H** What have studies shown thus far regarding the use of ablation therapy for treating nondysplastic Barrett esophagus?

**RS** The results thus far have been very favorable. Fleischer and associates have conducted the largest trial in this area; this trial—which was similar to an open-label trial in that all patients were treated with ablation—had a 5-year follow-up and reported a very high success rate (97%) for eradicating all of a patient's Barrett esophagus (biopsy-documented).

Ablation therapy has been shown to eradicate the entire segment of Barrett esophagus in multiple trials. The endpoint of therapy is the eradication of all intestinal metaplasia and the entire Barrett esophagus segment; the same endpoint is used whether Barrett esophagus is nondysplastic or dysplastic and has to be documented with a systematic biopsy protocol.

Long-term durability has been shown for new squamous epithelium post–radiofrequency ablation. In addition to the Fleischer trial, the randomized, sham-controlled trial has been extended to a 2–3 year follow-up (in press). Recurrence of Barrett esophagus can occur if a patient stops proton pump inhibitor therapy.

**G&H** What side effects and complications have been reported in these studies?

**RS** Ablation is very safe; in fact, there has never been a modality for treating these patients that has such a low side-effect profile. The most common side effects are local (chest pain, dysphagia) and transient, typically lasting only a few days. The most significant side effect is a stricture following therapy, which can usually be managed with only 1 or 2 dilations. Perforation occurs only when the ablation protocol is not followed. The need for hospitalization is uncommon—1%. Radiofrequency ablation is not associated with a risk of mortality.

**G&H** How many ablation sessions are usually needed in these patients?

**RS** The number of sessions depends on the length of the Barrett esophagus. A segment that is less than 3 cm long usually takes 1 or 2 sessions. The focal probe (HALO 90, Barrx Medical) is only 2 cm long and 1 cm wide, and it fits on the end of a standard endoscope. The endoscopist moves the probe around the circumference of the Barrett

esophagus and then pulls it up toward the mouth to treat the more proximal part of the segment. The recommendation from the manufacturer of the probe is to treat no more than 6 cm at a time. Treating 6 cm would probably take at least 2–3 sessions, whereas treating 10 cm would probably take 4–6 sessions.

There is a 3-cm radiofrequency balloon device (HALO 360, Barrx Medical) that can be used for longer-segment Barrett esophagus. This is a more complex technique that is often not available in the ambulatory endoscopy setting. A small scope is placed in the esophagus along with the balloon to ensure proper placement. Treatment of the distal esophagus is difficult because this section of the esophagus is commonly tortuous, even in young patients. The esophagogastric junction represents a special challenge to the endoscopist because of the wider aperture. One of the reasons for the introduction of the focal device was to treat areas that the balloon missed.

**G&H** Is surveillance needed after ablation therapy?

**RS** The need for surveillance after ablation therapy has not yet been defined. In the most recent American College of Gastroenterology guidelines for the management of Barrett esophagus, the authors proposed that 3 consecutive endoscopic surveillances lacking Barrett esophagus might be sufficient. However, this issue has not been addressed in adequate numbers of patients with long enough follow-up.

Barrx Medical is compiling a nationwide registry, with the goal of having 3,000–4,000 patient-years of follow-up with the power to document the decreased development of cancer. The results of this registry will help to answer the question of the need for ongoing surveillance after ablation.

**G&H** Do you foresee ablation therapy becoming a first-line treatment option for nondysplastic Barrett esophagus patients?

**RS** I do not think that we are there yet. Ablation is currently only a first-line treatment in nondysplastic Barrett esophagus patients with a family history of esophageal adenocarcinoma. More data are necessary to define other nondysplastic Barrett esophagus patients who are candidates for ablation.

The previously mentioned, published, randomized trials have been performed in centers with a major interest in Barrett esophagus. Publications from other practice centers have shown that an endoscopist with an interest in Barrett esophagus and experience in the

technique can be just as successful in ablation therapy as endoscopists from a major center. The learning curve for ablation therapy in nondysplastic Barrett esophagus has not yet been defined, but it is reasonable to expect a gastroenterologist to treat at least 50–100 patients every year to embark on this procedure. This procedure requires skill in correctly recognizing Barrett esophagus, experience in contemporary endoscopy, and a working relationship with pathology colleagues who can adequately read biopsy specimens.

Some of the concern about treating nondysplastic Barrett esophagus patients may result from an irrational opposition to ablation therapy in general. Every endoscopist has to make their own decision about what procedure they are going to perform. Ablation therapy requires significant endoscopic expertise. Especially in the context of high-grade dysplasia or early cancer when nodular areas are recognized, an endoscopic resection is necessary prior to performing radiofrequency ablation. Endoscopic resections are not generally performed by most practicing gastroenterologists in the United States. Excellent contemporary radiology and endoscopic ultrasound are also necessary techniques for evaluating patients with early cancer.

### G&H Should ablation therapy be avoided in certain patients with nondysplastic Barrett esophagus?

**RS** Ablation therapy is not recommended in patients who have extremely long segments of Barrett esophagus that would require many procedures. Likewise, the procedure would be difficult in patients who have technical problems, such as pseudodiverticula in the esophagus, as diverticula usually cannot be entered with the focal radiofrequency ablation device. Ablation should also be avoided in high-risk patients, such as those with cardiopulmonary disease or whose anticoagulation therapy cannot be stopped.

### G&H Does the presence of gastroesophageal reflux disease affect management of Barrett esophagus?

**RS** The presence of gastroesophageal reflux disease (GERD) usually does not impact patient management, although patients with GERD and Barrett esophagus may find it more difficult to control their symptoms. Patients with “GERD-plus disease” have symptoms that are not eliminated with proton pump inhibitor therapy. They may have altered esophageal perception and may require additional therapeutic options.

### G&H Do proton pump inhibitors play a role in ablation therapy of nondysplastic Barrett esophagus patients?

**RS** Absolutely. In fact, ablation therapy is a combination therapy with a proton pump inhibitor administered at a BID dose. This therapy maximizes the opportunity for restoration of squamous epithelium in patients undergoing ablation therapy. There is a suggestion that proton pump inhibitor therapy alone may in fact reduce dysplasia progression.

### G&H Has cost-effectiveness analysis been conducted in this patient population?

**RS** Ablation therapy has been shown to be more cost-effective than surveillance. There have been at least 2 studies conducted on this issue, a study by Hur and colleagues and a study by Inadomi and associates. If no surveillance is needed after ablation, the procedure is very cost-effective.

### G&H Are there any ongoing or upcoming studies in this patient population that you are anticipating?

**RS** A large trial of nondysplastic Barrett esophagus patients is currently underway in the United Kingdom; this trial has 4 arms: aspirin versus no aspirin and low-dose versus high-dose proton pump inhibitor therapy. (There is no placebo arm.) The trial will demonstrate the impact of the proton pump inhibitor alone as well as the impact of the aspirin and the proton pump inhibitor together. If this study shows that aspirin and proton pump inhibitors can prevent the progression of dysplasia, they could comprise a more cost-effective treatment modality than ablation therapy. However, this study will take a number of years, as the investigators are currently recruiting more study participants.

### Suggested Reading

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