

# ADVANCES IN GERD

Current Developments in the Management of Acid-Related GI Disorders

Section Editor: Joel E. Richter, MD

## Endoscopic Treatments for Gastroesophageal Reflux Disease



Blair A. Jobe, MD  
Professor of Surgery  
University of Pittsburgh School of Medicine  
Pittsburgh, Pennsylvania

**G&H** What are the challenges associated with treating gastroesophageal reflux disease via an endoscopic approach?

**BAJ** Endoscopic treatment of gastroesophageal reflux disease requires working from within the lumen of the esophagus and/or stomach to manipulate tissue into a position that will resist the reflux of fluid from within the stomach into the esophagus. Delivering endoscopic therapy for the definitive treatment of gastroesophageal reflux disease is very challenging, as it requires creating a durable repair from inside the body without freeing up any of the external attachments, as is done with surgery. For example, with laparoscopic fundoplication, the phrenoesophageal ligament is circumferentially dissected, the short gastric and posterior gastric vessels are divided, and the esophagus is dissected, such that the esophagogastric junction is returned into the abdominal cavity. These components of the procedure are essential for delivering a repair that is free of tension and, thus, more likely to be durable.

**G&H** Is first-line therapy still the ultimate goal for endoscopic treatments for gastroesophageal reflux disease, or has their role shifted toward second-line therapy or combination therapy with proton pump inhibitors?

**BAJ** There is a therapeutic gap between proton pump inhibitors and surgery (ie, laparoscopic Nissen fundoplication) consisting of individuals on proton pump inhibitor therapy who are still experiencing volume reflux or regurgita-

tion. Creating an anatomic barrier to prevent regurgitation in these patients could help bridge this therapeutic gap. First-line therapy is definitely a consideration in patients who have classic gastroesophageal reflux disease symptoms and respond to proton pump inhibitors. However, the existing endoscopic antireflux procedures are unable to address hiatal hernia, which is very common in gastroesophageal reflux disease patients; therefore, utilization of endoscopic treatment as a first-line therapy would be limited. It will be necessary to further develop endoscopic procedures that have extremely low side-effect profiles and complication rates. There is currently no panacea.

**G&H** Who is the optimal candidate for endoscopic reflux therapy?

**BAJ** It is necessary to determine whether there is a viable endoscopic treatment for gastroesophageal reflux disease in the first place. There is a lack of level 1 data demonstrating that endoscopic therapy is superior to, or even equivalent to, proton pump inhibitor therapy. It is well known that endoscopic antireflux procedures are associated with a significant placebo effect. Where there are level 1 data, the follow-up period is too short to demonstrate meaningful value.

For the 2 currently available endoscopic therapies, the optimal patient would have documented gastroesophageal reflux disease with pH testing and symptom correlation, a dependence on proton pump inhibitor therapy, and no hiatal hernia. Patients who are medically treated are most successful with any type of surgical or

endoscopic intervention; in other words, patients who are dependent on medicine do well with surgery, and their reflux should be confirmed via pH testing.

**G&H** What endoscopic treatments are currently available for treatment of gastroesophageal reflux disease?

**BAJ** Efforts have been made to develop devices that enable the endoscopist to reconstruct or augment the gastroesophageal barrier. The devices use 1 of 3 approaches: radiofrequency ablation, injection therapy (abandoned), or suturing. The first-generation devices have been unable to replicate the improvement in objective measures of gastroesophageal reflux disease and symptoms achieved by laparoscopic fundoplication.

Of the 3 techniques listed, suture plication is most similar to the reconstruction achieved by surgical fundoplication. The fundamental aspect of valve reconstruction inherent in all forms of antireflux surgery (endoscopic and laparoscopic) is the envelopment of the distal esophagus by the proximal stomach. This approach results in the re-creation of the acute angle of His. When viewed with a retroflexed endoscope, there is an intragastric valve present. As intragastric and abdominal pressure increase, the valve (with enveloped esophagus) is compressed, thereby resisting reflux into the esophagus.

Radiofrequency ablation applies energy to the esophagogastric junction, and this approach results in improvements in symptoms and objective measures of gastroesophageal reflux disease. The mechanism by which radiofrequency ablation works is poorly understood.

**G&H** Have any studies examined the efficacy and durability of these endoscopic procedures?

**BAJ** As mentioned above, our largest challenge has been the lack of studies demonstrating effectiveness and durability of endoscopic modalities in gastroesophageal reflux disease patients. The ideal study design to evaluate these modalities would be a randomized, sham-controlled, crossover trial comparing the modalities to proton pump inhibitors; such a trial would demonstrate control of acid exposure to the distal esophagus and show an improvement in both quality of life and the ability to discontinue antisecretory medication, such as proton pump inhibitors. This type of high-quality data will be required in the future in order for payers to embrace the technology and ensure its survivability on a large scale.

Perhaps the most important and understudied aspect of these devices has been in regard to repair durability. This finding is telling, and I believe it reflects the complex nature of the esophagogastric junction and the multiple

forces (both intraluminal and extraluminal) that impact repair integrity over time.

In terms of specific studies, there is currently a randomized trial evaluating endoluminal fundoplication versus proton pump inhibitors. The results of this ongoing study are eagerly awaited and will hopefully be available within the next 2 years.

**G&H** Have these studies consisted of all types of gastroesophageal reflux disease patients or just select patient subgroups?

**BAJ** These studies have examined only highly selected patient subgroups, such as those who fit the following criteria: no hiatal hernia, little or no esophageal mucosal injury, proton pump inhibitor responsiveness, and typical reflux symptoms. Large hiatal hernias require a laparoscopic trans-abdominal therapeutic approach to reduce the hernia and to repair and reinforce the diaphragmatic hiatus.

**G&H** What side effects and complications have been associated with endoscopic procedures for treatment of gastroesophageal reflux disease?

**BAJ** Some of the endoscopic procedures no longer being performed led to severe complications such as enteric fistulae, as well as hemorrhage, pneumonia, mediastinitis, empyema, esophageal perforation, and, in extremely rare cases, death. These complications have led to wariness on the part of payers, and as a result, the bar has been raised: These procedures must have extremely low side-effect profiles and complication rates, and, most importantly, they must demonstrate effectiveness.

**G&H** Since there is a lack of data supporting the use of these endoscopic treatments for gastroesophageal reflux disease, what do you recommend for treating reflux patients?

**BAJ** Currently, proton pump inhibitors and laparoscopic antireflux surgery are the 2 main treatment options for patients with gastroesophageal reflux disease. Although some doctors may view laparoscopic antireflux surgery as the therapy of last resort, our patients who currently undergo this procedure are in the hospital for 23 hours, have extremely limited pain, and are back to work within 2–3 weeks if they have a desk job. These patients are on a soft diet for 3–6 weeks and have a lifting restriction of less than 25 pounds for 6 weeks. (These same restrictions apply for endoscopic fundoplication. In my experience, all patients who undergo endoscopic fundoplication stay in the hospital for a minimum of 23 hours and have pain that requires narcotic analgesia.) As mentioned above, there is no panacea.

**G&H** Does it appear that endoscopic procedures will offer a benefit in terms of cost-effectiveness for treating gastroesophageal reflux disease?

**BAJ** In theory, yes, but in reality, this question cannot be answered until the effectiveness and durability of these procedures are proven and we know whether insurance companies will reimburse them. Answering this question will require a long-term and methodic commitment by start-up companies to generate level 1 data.

**G&H** Are these procedures difficult to perform?

**BAJ** This answer depends on the procedure. Radiofrequency ablation is relatively easy to perform, as it involves point-and-click technology. However, anatomic reconstruction of the valve, whether surgical or endoscopic, can be quite technically difficult to perform. The endoscopic instrument used to perform endoluminal fundoplication has many working parts and is relatively user-unfriendly. This may be the reason why there is a wide variation in procedural outcomes; doctors may be concerned that they will be left behind by a wave of new technology and may be performing these highly complicated procedures before they are ready to do so.

It is important to remember that surgical principles are being applied to endoscopic therapies and that we should adhere to the principles that have withstood the test of time in order to produce successful outcomes; this relates to providing a repair that is free of tension, which is a tall order. It is difficult to balance creativity and technological innovation with these aforementioned surgical principles.

**G&H** Are there any promising endoscopic procedures or devices currently under investigation for treatment of gastroesophageal reflux disease?

**BAJ** Several new devices are currently under investigation, but, as previously mentioned, there is hesitancy on

the part of both venture capitalists and payers due to the failures experienced during the first wave of endoscopic therapies. However, we would not be able to move forward without the spirit of innovation and immense creativity delivered during this initial experience.

**G&H** What are the next steps in research in this area?

**BAJ** The next steps are to take the existing methods of creating an anatomic barrier and to improve their user interface and deployment capabilities of tissue fixation via a complication-free approach; in other words, we need to make procedures easier and more user-friendly for providers while improving the effectiveness of the modalities.

**Suggested Reading**

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