ADVANCES IN ENDOSCOPY

Current Developments in Diagnostic and Therapeutic Endoscopy

Section Editor: Todd H. Baron, MD

Update on the Use of Transoral Incisionless Fundoplication for the Treatment of Gastroesophageal Reflux Disease

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G&H What options are available for patients with chronic or treatment-refractory gastroesophageal reflux disease?

PB This is a complicated question. Medicine is known to work quite well for the treatment of gastroesophageal reflux disease (GERD), so the first question that needs to be asked is whether the patient is truly refractory to the medication despite taking it as prescribed or whether a change in dose, timing, or even the specific medication itself can offer a benefit. The second question that needs to be asked before considering endoscopic therapy is whether the patient is a candidate for an endoscopic approach or whether a surgical approach is more appropriate.

This second question is, in fact, the more important one and depends on whether the patient has a significant hiatal hernia. Endoscopy is used to determine the presence of a hiatal hernia, but the condition can be easy to miss and may be underestimated, even in expert hands. There are several reasons that a hiatal hernia may be missed, but the primary one is that not enough time is spent looking at the valve and the hiatus in the retroflexed position. By taking the time to examine the valve and, indirectly, the crural diameter, whether the patient has a small or large crural defect can be understood. If only a minor crural defect is suspected, the option of an endoscopic approach should be discussed with the patient. If a significant crural defect is present and is larger than 2 cm, then surgery should be recommended; however, another increasingly popular option is a combined laparoscopic-endoscopic approach.

G&H How does transoral incisionless fundoplication compare with other fundoplication techniques for the treatment of GERD, and how has it evolved?

PB Transoral incisionless fundoplication (TIF) is a procedure based on the EsophyX platform (EndoGastric Solutions). Most practitioners are now using the EsophyX Z+ device, which is the most recent iteration of EsophyX, to perform TIF. This version is safer and more efficient than earlier versions. It can reduce the procedure time by almost half because fasteners can be deployed two at a time. In addition, a standard gastroscope can be used to perform the procedure, whereas, in the past, a small-caliber scope was required.

The procedure itself also has evolved along with the device. The procedure originally began with endoluminal fundoplication and developed into TIF 1.0, which was essentially a cardiogastric plication. Then, it graduated to TIF 2.0, which created a 270-degree omega valve by deploying at least 20 trans-serosal fasteners. TIF 2.0 not only creates a larger rotational wrap, but it creates a greater length of valve below the diaphragm. One of the main

principles of antireflux surgery is the creation of a valve that is at least 2 to 4 cm, and TIF 2.0 accomplishes this.

Overall, TIF has been a very safe and successful procedure. This was demonstrated in the initial registry started a decade ago, and a good deal of experience has been gained since then. Serious adverse events have been few, with global data demonstrating a serious adverse event rate of no more than half a percent. Furthermore, as mentioned, the procedure is not long, taking no more than 40 minutes for most experienced practitioners.

G&H How is TIF performed?

PB The procedure is performed under general anesthesia with an upper endoscope and the EsophyX overtube. Essentially, the overtube is the working platform for the entire procedure and is fitted over the endoscope, which allows visualization of the fastener deployment.

TIF can be considered to be one of the most well-templated antireflux procedures. There are minor variations between experienced users, as most follow a predetermined protocol. In general, the formation of the valve is started along the posterior aspect. Six to 8 fasteners are deployed at this site to create a rotational and lengthening effect. The same is done along the anterior aspect. This creates an omega shape or a cuff that is approximately 270 degrees. Along the greater curvature aspect, 8 or more fasteners are deployed to build and stabilize that length of the valve. Ultimately, a valve is created that not only looks as if it has been rotated into itself, much like a Toupet or a Nissen is rotated into itself, but it has a length of approximately 2 to 4 cm that is very stable. Any surgeon who has worked in this area after a TIF can attest to the durability of the trans-serosal fasteners; in fact, the main reason for lack of durability is a failure to accurately identify a hiatal hernia.

G&H What features make a patient a good candidate for TIF?

PB Patient selection is the key to clinical success. It is best to select patients who have already shown a symptomatic response to proton pump inhibitor (PPI) therapy and have typical GERD symptoms, although a significant amount of data exists on the ability of TIF to help patients with atypical or extraesophageal symptoms or patients whose condition is not responding to PPI therapy. However, the ideal candidate is a PPI responder, is motivated, has a reasonable body mass index (ie, is not morbidly obese), and has typical reflux symptoms.

G&H Are there any particular adverse events or complications that are of concern?

PB Every procedure has some serious adverse events. As mentioned, this procedure has an exceptional safety profile. In very rare instances, pain may occur afterward, and perforations can occur. The physician's expertise is key. Many of the potential complications can be minimized if the physician has a good understanding of the extraluminal structures, specifically the diaphragm.

The manufacturer of the EsophyX platform has done a good job of training physicians, and professional societies have done well raising awareness and providing training to physicians who want it. These efforts have contributed to EsophyX's good safety profile.

G&H What is the long-term efficacy of TIF?

PB With every antireflux therapy, the physician needs to consider endpoints regarding short-, mid-, and long-term efficacy. Data suggest that TIF has good long-term outcomes. However, no endoscopic or surgical treatment can be expected to be perfectly durable over a 10-year period. The area involved is prone to high wear and tear.

Among the several major trials involving this procedure, the TEMPO trial is very important. This was a multicenter US trial of TIF 2.0 vs PPI therapy with the primary outcomes of elimination of regurgitation or extraesophageal symptoms. At 6 months, 97% of patients who received TIF 2.0 had improvement in regurgitation and 90% stopped PPI use. Interestingly, half of the patients also had significant improvement in extraesophageal manifestations of GERD.

The TEMPO trial looked at outcomes at 3 and 5 years. Improvement in regurgitation was stable at year 5. At year 1, 88% of patients had improvement in regurgitation. At year 5, the rate was 86%. At baseline, all of the patients were on PPIs. At year 1, PPI use was approximately 17% and increased to approximately 34% at year 5. These numbers are not that different from those seen with laparoscopic hernia repairs and fundoplication. The other major finding was that symptom scores stayed low, so patient satisfaction was strong at year 5.

Another major trial is RESPECT. It included 129 patients who were randomized to either EsophyX TIF 2.0 or a sham endoscopy with maximum PPI therapy. In the intention-to-treat analysis at 6 months, 67% of the patients randomized to TIF were off PPIs compared with 47% of patients who received the sham procedure. Seventy-six percent of the sham group elected to cross over to undergo TIF at 12 months. Seventy-two percent of treated patients achieved control of regurgitation and were PPI-free.

These studies focused on good patient selection, and their results were better than those from the original TIF registry that was initiated in 2011. In that trial, 66%

of patients reported an improvement in GERD scores. Seventy percent reported improvement in their regurgitation, and daily PPI use decreased from 91% to 25%. Unfortunately, there was a lack of long-term endoscopic follow-up and pH data.

In the longest-running cohort in this area to date, Testoni and colleagues are following approximately 50 patients who continue to have good outcomes regarding regurgitation and PPI use up to 10 years. This team has shown that response stabilizes at 2 years and remains relatively unchanged from there on. The primary real-world objective should be for patients to feel well and not be dependent on PPIs.

G&H What other applications may emerge for this technology in the future?

PB TIF cannot achieve repair of the crural diaphragm, which is one of the most important aspects of antireflux surgery; however, it does have utility in combination with surgery. Some practitioners of TIF are partnering with surgeons whereby hernia repairs are followed by TIF in the operating room. Unlike traditional fundoplications that can affect fundic accommodation and create a gas-bloat syndrome, depending on how the fundus is treated and how it is wrapped, TIF is very rarely associated with dysphagia and virtually never causes a gas-bloat syndrome. TIF does not produce a stricture or a valve that the esophagus cannot overcome. It creates a remarkably reproducible antireflux barrier from patient to patient. If the hiatal hernia repair fixes 90% of the problem, a TIF then creates a flap valve, reconstituting the angle of His. This is a very good hybrid procedure and has been associated with good patient satisfaction.

The other major application for TIF is peroral endoscopic myotomy (POEM). Following POEM, patients typically have a problem with GERD. The main issue is achalasia, which creates a situation in which patients have difficulty clearing the esophagus of reflux material. After the valve is cut, reflux can be expected to occur in approximately 40% or more of these patients. In fact, one of the most important questions to grapple with now is how to control reflux after POEM. TIF may be the solution for patients with significant GERD symptoms following POEM.

TIF can be performed after POEM as well as during the same session as POEM. Because these patients have poor esophageal motility and do not have significant crural defects—which manifest as a hiatal hernia—TIF may be the perfect solution for providing an antireflux barrier.

Research on these expanded applications for TIF is now in the form of case series and retrospective data, but better data will likely emerge in the coming years.

Disclosures

Dr Benias has served as a consultant for Boston Scientific, FujiFilm, and Apollo Endosurgery.

Suggested Reading

Testoni PA, Vailati C, Testoni S, Corsetti M. Transoral incisionless fundoplication (TIF 2.0) with EsophyX for gastroesophageal reflux disease: long-term results and findings affecting outcome. *Surg Endosc.* 2012;26(5):1425-1435.

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