AGS Meeting: TIF shows therapeutic and economic value for GERD

By Amanda Pedersen

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An incisionless procedural therapy for gastroesophageal reflux disease (GERD) was shown to be a viable alternative to proton pump inhibitors (PPIs) to control chronic symptoms of GERD both from a therapeutic and an economic perspective. This week at the **American College of Gastroenterology** (Bethesda, Md.) meeting in Honolulu, researchers presented data from two studies supporting the transoral incisionless fundoplication (TIF) procedure, developed byEndogastric Solutions (EGS; Redmond, Wash.).

"The TIF procedure is showing potential not only as a desirable GERD treatment, but as a cost-effective solution for patients," said Lauren Gerson, a gastroenterologist at **California Pacific Medical Center** (San Francisco) and the lead author of a two-year study that demonstrated improved cost and health care utilization benefits of TIF.

In Gerson's study, she and her colleagues analyzed the Optum health care database to determine overall resource utilization, which includes costs for hospitalizations, outpatient visits and pharmacy fills for proton pump inhibitor (PPI) therapy to control chronic symptoms of GERD. The researchers compared medical therapy costs to traditional surgical therapy and to the TIF procedure. Of the 13,293 total patients included in the analysis, 10,486 patients were on high-dose PPI therapy, 2,734 underwent Nissen fundoplication (traditional surgical therapy), and 73 patients had the TIF procedure. At two years post-TIF procedure, median costs were comparable to post-Nissen (TIF - $7,397, Nissen - $8,412) and health care utilization and total health care costs decreased compared to those associated with PPIs (TIF - $7,397, PPIs - $9,697).

Despite the impressive overall size of the database, Gerson told *Medical Device Daily* there is no actual (current procedural terminology) CPT code for TIF yet, which limited the number of TIF patients included in the database. "Obviously it would be good to have a longer follow-up period and once we get a code we can identify more patients," she said.

RESPECT data

One-year data from the Randomized Esophyx vs. Sham/Placebo Controlled Trial (RESPECT) were also presented at ACG this week. According to EGS, RESPECT is the first-ever randomized, blinded, sham- and placebo-controlled study of the TIF procedure. In RESPECT, 87 patients were randomly assigned to the group that underwent the TIF procedure then received an ongoing treatment of placebo medication. After more than 12 months, 72 percent reported elimination of troublesome regurgitation per Montreal consensus criteria.

The study also found that the mean DeMeester Score decreased from 33.6 to 23.9 at 6 months and to 24.7 at 12 months post-TIF. Eight participating U.S. academic and community centers screened 696 patients of which 129 were enrolled into the RESPECT study with 87 patients in the TIF/placebo group and 42 patients in the Sham/PPI group.

Gerson said sham arms are important in GERD studies because GERD patients have traditionally always had a high response rate, about 30 percent to 40 percent, to placebo in any kind of trial, medical or surgical. She said the reason for that is not completely understood but it may be that the disease fluctuates in some patients.

"Some people may have GERD and it's problematic for a couple weeks and then goes away," she said. "It's definitely a recurrent chronic disease but most patients have ups and downs and periods of time when they're not symptomatic at all, so that's one explanation, but traditionally there's always been a very high response rate to placebo."

That's why it's important that studies like RESPECT have a sham arm to evaluate improvement compared to a sham treatment, Gerson said. Both groups of RESPECT patients, and their caregivers, were blinded to therapy during follow-up which occurred at two, 12 and 26 weeks. At the six-month follow-up, all patients were un-blinded and the sham control patients were given the opportunity to have a TIF procedure. Of those patients, 76 percent elected to crossover and receive a TIF procedure after un-blinding.

The investigators of the RESPECT study concluded that the TIF procedure is an effective option for GERD patients and that it improves the quality of life for select chronic GERD patients. That's important, Gerson said, because for a lot of GERD patients, quality of life issues are the real problem. "Can they eat normally? Are they having sleeping issues? Can they function normally? That's what you want to see," she said. "This study showed quality of life (improvements) was maintained for about a year after TIF."

"Based on the improvements seen in these patients, we believe the TIF procedure is filling a treatment gap for patients who do not respond to PPI medications and want a less invasive procedure," said Skip Baldino, president/CEO of EGS.

The technology

The FDA cleared the original Esophyx device for marketing in 2007. EGS launched a third-generation Esophyx device, called the Esophyx Z, earlier this year. The technology is used to reconstruct the gastroesophageal valve and restore its function as a barrier, preventing stomach acids refluxing back into the esophagus. The device is inserted through the patient's mouth with direct visual guidance from an endoscope. The latest generation enabled physicians to use a wider selection of endoscopes, including low profile and larger high-definition models, to treat the underlying anatomical cause of GERD.

Traditionally, for patients failing medical therapy, physicians had the option of surgery, which Gerson said is an operation that performs "very well" and most patients are off medication for up to 10 years after surgery. The problem is that although their regurgitation is gone, surgical patients often have trouble with gas and bloating and sometimes difficulty swallowing, which makes many patients reluctant to have surgery.

"The nice thing about TIF is it's all endoscopic, no actual incisions are made," Gerson said. "Right now it's being done in the OR and most patients do stay overnight. I think the hope would be to simplify it further so it could be done in the endoscopy suite."

So far, the data shows TIF to be as effective as surgery but without the side effects, she said. One limitation of TIF is that patients with a large hernia (3 centimeters or more) can't have a TIF procedure unless they first have surgery to reduce their hernia, Gerson said.

Future studies need to focus on how long the device lasts and for how many years patients benefit from the TIF procedure, she said.

Other data

In addition to the studies presented at ACG, findings were recently published by *Alimentary Pharmacology and Therapeutics* from a separate double-blind, sham-controlled, multi-center European study of 121 patients, which also supported the TIF procedure as a viable alternative to PPI therapy to control chronic GERD symptoms.

Baldino said the data aligns with RESPECT data and that the study, led by Lars Lundell of **Karolinska University, Huddinge Hospital** (Stockholm), met the rigorous scientific requirements of a sham controlled trial.

In Lundell's study, patients were required to refrain from PPI consumption for at least 10 days prior to the TIF procedure. Of the randomized patients treated with the procedure, 59 percent were determined to be in remission after six months compared to 9 percent in the sham treatment arm.

The study also reported TIF procedure patients had improved acid reflux time (measurements of esophageal acid exposure) from 8.89 to 3.73 compared to the sham-controlled group which had no changes in acid reflux time.

Lundell concluded that TIF offers chronic GERD patients, being on long-term PPI therapy, an effective alternative. "In fact, we can also conclude that the level of scientific proof of its efficacy and therapeutic gain surpasses anything that is available outside the area of traditional laparoscopic anti-reflux therapy," he said. //

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