

Endoluminal Full-Thickness Plication and Radiofrequency Treatments for GERD

An Outcomes Comparison

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Hypothesis: Endoluminal therapies have emerged as adjuncts for the treatment of gastroesophageal reflux disease (GERD) in select patients.

Objective: To compare the effectiveness of endoscopic full-thickness plication and endoscopic radiofrequency treatments for patients with GERD.

Patients: A total of 126 patients who underwent either endoscopic full-thickness plication (FTP) of the gastric cardia or endoscopic radiofrequency (RF) treatment of the esophagogastric junction during a 4-year period were included (68 underwent RF and 58 underwent FTP).

Interventions: Follow-up data was obtained for 51% of patients (mean follow-up, 6 months).

Main Outcome Measures: Comparison of medication use, symptom scores, and pH values at baseline and follow-up.

Results: In the RF group, patients with moderate to severe heartburn decreased from 55% to 22% ($P < .01$), and

proton pump inhibitor (PPI) use decreased from 84% to 50% ($P = .01$). Decreases were also seen for dysphagia, voice symptoms, and cough. Percentage of time the pH was less than 4 was unchanged. In the FTP group, patients with moderate to severe heartburn decreased from 53% to 43% ($P = .3$), and PPI use decreased from 95% to 43% ($P = .01$). Percentage of time the pH was less than 4 decreased from 10.0% to 6.1% ($P = .05$). Decreases were also seen for regurgitation, voice symptoms, and dysphagia. There was no change in scores for chest pain or asthma in either group.

Conclusions: For patients with GERD, RF and FTP both resulted in a decrease in both PPI use and in scores for voice symptoms and dysphagia. In addition, RF resulted in decreased heartburn and cough, while FTP resulted in the most dramatic reduction in regurgitation. Our experience indicates that both procedures are effective, providing symptomatic relief and reduction in PPI use. For patients whose chief complaint is regurgitation, FTP may be the preferred procedure.

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GASTROESOPHAGEAL REFLUX disease (GERD) is a chronic condition characterized by a high (>80%) tendency toward relapse when medical treatment is discontinued. The current first-line treatment is medical therapy with proton pump

See Invited Critique at end of article

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inhibitors (PPI), H₂-receptor antagonists, or combination therapy. Continued treatment has proven effective for symptom relief, healing esophagitis, and preventing the esophageal and extraesophageal complications of GERD. However, medical therapy does not restore lower esophageal sphincter (LES) function, and long-term drug intake raises issues of compliance and cost.¹

Beginning in the early 1990s with the introduction of laparoscopic techniques, surgical therapy gained acceptance as a treatment for GERD.² This treatment is offered to patients whose symptoms are inadequately controlled by acid suppression, who are unable or unwilling to take the optimum treatment schedule, or who develop persistent or recurrent esophageal and extraesophageal complications.¹ Surgical therapy in experienced centers offers excellent results, but carries a complication rate of 5% and a mortality rate of 0.2%.³

Recently, endoluminal therapies have arisen as an alternative to conventional anti-reflux therapy—both medical and surgical. These therapies have been offered to patients who are averse to the long-term sequela of prolonged acid suppression therapy, who are partial responders



Figure 1. Before the procedure. The gastroesophageal junction in a symptomatic gastroesophageal reflux disease patient with a small hiatal hernia.

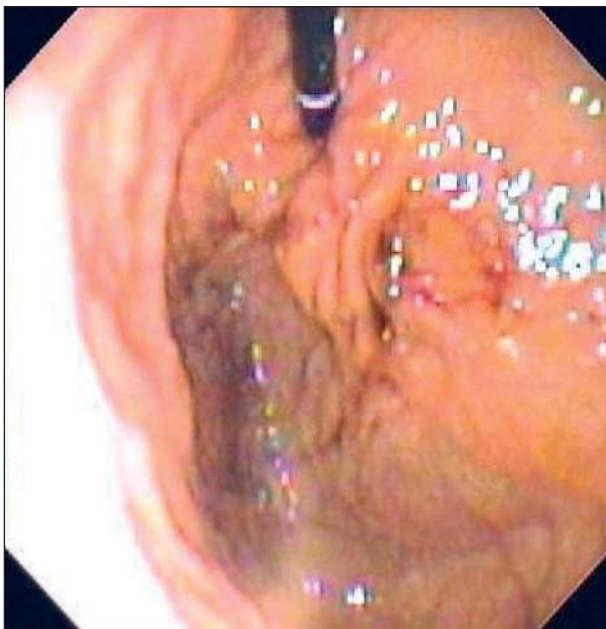


Figure 2. After the procedure. The gastroesophageal junction in the same patient after single plication. A valvular appearance is seen.

to medical treatment and are seeking an alternative to surgery, or who have failed an earlier fundoplication. Two options for endoluminal therapy are full-thickness plication (FTP) and radiofrequency (RF) treatment. Full-thickness plication involves endoscopically tightening the cardioesophageal junction (within 1 to 2 cm of the gastroesophageal [GE] junction) with pre-tied pledgeted polypropylene sutures (**Figures 1, 2, and 3**). Radiofrequency treatment delivers radiofrequency energy to the muscularis layers of the distal esophagus and gastric cardia. This thermal energy is purported to alter LES tone

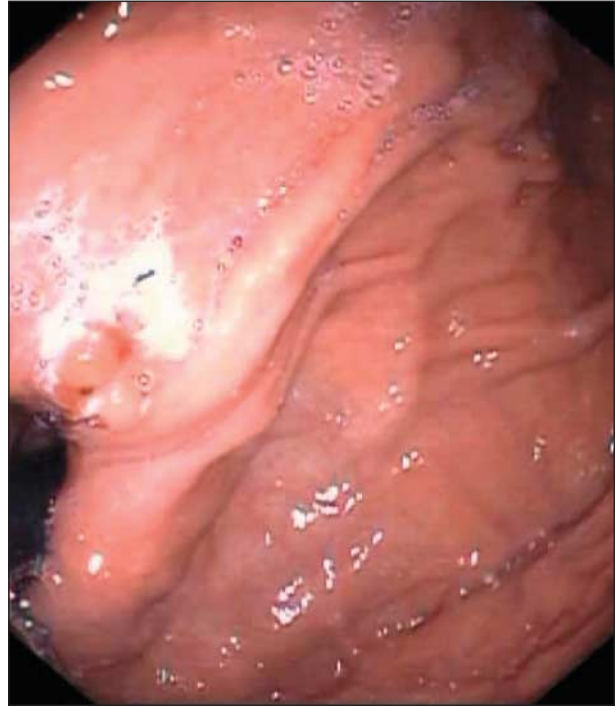


Figure 3. Nine-month follow-up. In another patient, the plication and pledget are noted to be intact at 9-month follow-up.

by inducing collagen deposition. Both of these therapies have had modest success in decreasing symptoms and medication use.^{2,4-6} The aim of this study is to compare the outcomes of endoluminal FTP and RF treatment.

METHODS

After receiving approval from the institutional review board of Emory University, prospective data were collected for all patients undergoing RF or FTP treatment for GERD. From January 2002 to March 2006, 126 patients received treatment; 68 patients underwent RF and 58 underwent FTP. Inclusion criteria were identical between both groups. Symptomatic GERD patients were chosen for endoluminal therapy based on the following indications: obesity, borderline manometric or impedance study (eg, low to normal peristalsis, amplitudes, or bolus transit), inability to tolerate general anesthesia, or desire to avoid surgery. Contraindications to both procedures included large paraesophageal hernia, esophagitis, and stricture. For the first 2 years of the study period, only RF was available; for the period in which both technologies were available, the choice of endoluminal procedure was made based on patient preference, the surgeon's judgment, and anatomic favorability.

Demographic data were collected on all patients. Patients were asked before and after the procedure about their use of antisecretory medications. Patients were also asked to fill out a reflux questionnaire before and after the procedure to assess GERD-type symptoms. Symptoms assessed were heartburn, chest pain, regurgitation, difficulty swallowing, hoarseness or voice problems, cough, and asthma. Patients were asked to grade these symptoms as none, mild, moderate, or severe. A subset of patients underwent preoperative and postoperative pH probe studies. Statistical comparison was performed using a paired *t* test for nominal values and a Wilcoxon test for nonparametric values.

FTP TECHNIQUE

In the endoscopy suite, patients were placed in the left lateral recumbent position. A 5-mm endoscope was passed into the stomach. A Savary spring-tipped metal guidewire (Wilson-Cook Medical, Inc, Salem, North Carolina) was passed through the endoscope and left in place. The endoscope was then removed and a 45F full-thickness plication device (Plicator; NDO Surgical, Mansfield, Massachusetts) was threaded over the guidewire and introduced into the stomach. The slim endoscope was then advanced within the plicator device under direct visualization, resulting in a "mother-daughter" system. The instrument was retroflexed to provide a view of the GE junction. A single plication stitch with pledgets was placed at the anterior cardia, approximately 1 cm below the squamocolumnar junction, creating a tissue valve at the LES. The endoscope and plicator device were then straightened out and removed under direct visualization. The endoscope was reintroduced and the GE junction examined.

RF TECHNIQUE

The procedure was performed using the technique described by Triadafilopoulos and Utley.⁷ Standard upper endoscopy was performed and the distance to the squamocolumnar junction was measured. A guidewire was placed through the scope into the stomach. The RF catheter, consisting of a flexible balloon-basket assembly with 4 electrode needle sheaths (Stretta System; Curon Medical, Sunnyvale, California), was introduced over the guidewire.

The balloon was inflated proximal to the squamocolumnar junction, the electrode needles were employed, and each treatment was delivered for more than 90 seconds. The needles were then withdrawn, the balloon was deflated, the scope was rotated 45°, and the procedure was repeated. These steps were serially repeated every 0.5 cm such that an area covering 2 cm above and 1.5 cm below the squamocolumnar junction received treatment. Subsequently, 6 sets of treatment were provided in the cardia region, resulting in a total of 22 sets of needle deployments. After the last treatment, the balloon was deflated and the catheter removed. Endoscopy was repeated to assess all treatment regions and to recognize any potential complications. The stomach was then deflated and the endoscope removed.

POSTPROCEDURE INSTRUCTIONS

After both procedures, patients were placed on a liquid diet for 7 days and instructed to continue their anti-reflux medication for 7 days. Patients were instructed to follow up after 1 month, and then annually.

RESULTS

Follow-up data (symptom score survey and/or pH study) were obtained for 51% of the patients, with a mean follow-up of 6 months. Data are expressed as mean (SD) unless otherwise specified. There was no significant difference in sex, age, or body mass index between the 2 groups (**Table 1**). In the RF group, 14.7% of patients had a history of previous fundoplication, compared with 9.1% in the FTP group.

In the RF group, PPI use was reduced from 84% to 50% ($P=.01$; **Figure 4**), and patients with moderate to severe heartburn decreased from 55% to 22%

Table 1. Demographic Data

| | RF | FTP | P Value |
|----------------|---------------------------------|-------------------------------|---------|
| Age, y | 48.8 ± 16.8 | 41.75 ± 15.2 | .09 |
| M/F ratio | 1:1.7 | 1:4.75 | .08 |
| BMI | 27.8 ± 7.7 | 32.9 ± 9.6 | .05 |
| Mean follow-up | 5.1 mo (range, 13 d to 37.4 mo) | 8.1 mo (range, 20 d to 29 mo) | |
| Follow-up, % | 60 | 40 | |

Abbreviations: RF, radiofrequency; FTP, full-thickness plication; BMI, body mass index (calculated as weight in kilograms divided by the square of the height in meters).

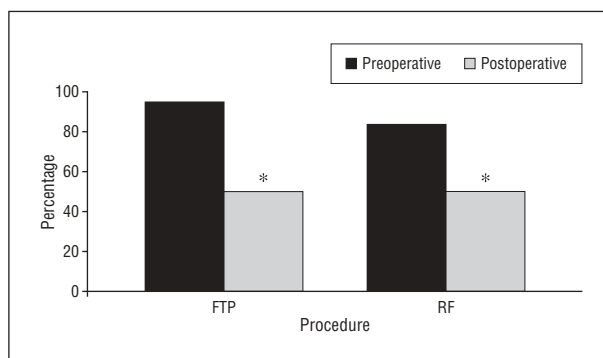


Figure 4. Proton pump inhibitor use. Percentage of patients reporting any use of a proton pump inhibitor before and after endoluminal gastroesophageal reflux disease therapy. FTP indicates full-thickness plication; RF, radiofrequency. * $P<.05$.

($P<.01$; **Figure 5**). Percentage of time the pH was less than 4 was statistically unchanged from 10.8% to 9.1% ($P>.9$; **Figure 6**). Decreases in moderate to severe scores were also seen for dysphagia (17.4% to 14.6%, $P=.04$), voice symptoms (29.8% to 14.6%, $P=.04$), and cough (32.6% to 12.2%, $P=.01$). There was no significant change in symptom scores for chest pain or asthma in the RF group (Figure 5). Three patients (4.4%) underwent laparoscopic Nissen fundoplication for refractory symptoms an average of 11.4 months after RF. Mean follow-up for the RF group was 5.1 months (range, 13 days to 37.4 months), with 10.3% of patients undergoing a 48-hour pH study.

In the FTP group, PPI use was reduced from 95% to 43% ($P=.01$; Figure 4), and moderate to severe heartburn decreased from 53% to 43% ($P=.3$; **Figure 7**). Percentage of time the pH was less than 4 decreased from 10.0% to 6.1% ($P=.05$; Figure 6). Decreases in moderate to severe scores were also seen for regurgitation (62.5% to 18.8%, $P=.02$), voice symptoms (35.7% to 18.8%, $P=.01$), and dysphagia (28.6% to 0%, $P=.01$). Like the RF group, there was no significant change in symptom scores for chest pain or asthma in the FTP group (Figure 7). Three FTP patients (5%) underwent laparoscopic Nissen fundoplication for refractory symptoms an average of 11.4 months after the endoluminal procedure. Mean follow-up for the FTP group was 8.1 months (range, 20 days to 29 months), with 14% of patients undergoing a 48-hour pH study.

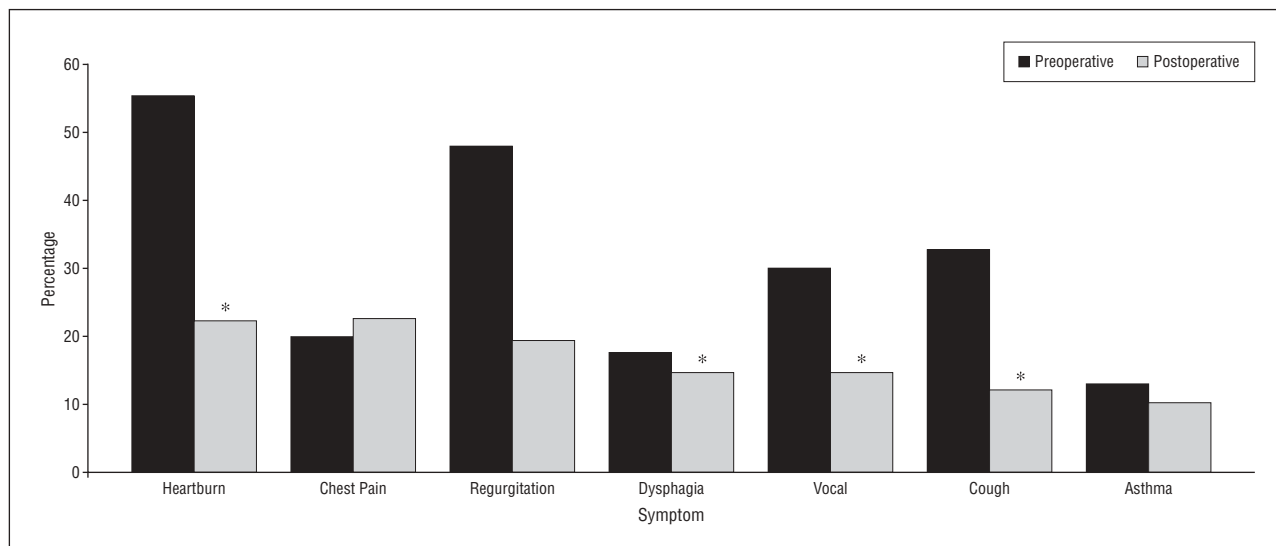


Figure 5. Stretta symptom scores. Percentage of patients reporting either moderate or severe score for aerodigestive symptoms before and after radiofrequency therapy. * $P < .05$.

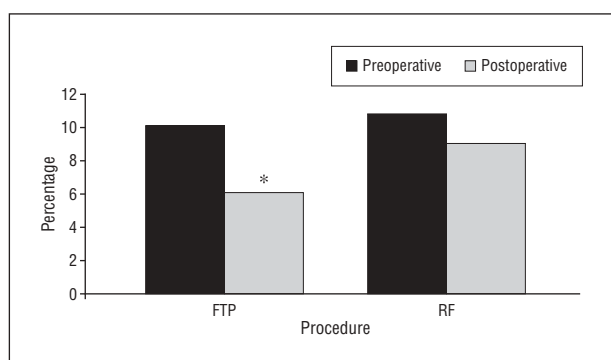


Figure 6. Mean percentage of time pH was less than 4 during a 48-hour pH study before and after endoluminal therapy for gastroesophageal reflux disease. FTP indicates full-thickness plication; RF, radiofrequency. * $P = .05$.

COMMENT

Although medical therapy continues to be the first-line treatment for GERD, many patients require more aggressive intervention owing to symptom progression, relapse, and/or an unwillingness to undergo prolonged pharmacologic therapy. Endoscopic treatment of GERD is an acceptable option for patients who are poor surgical candidates yet still require intensive treatment to adequately manage their GERD.

The data presented in this study add to the growing body of literature supporting the use of endoscopic treatment of GERD in carefully selected patients. To our knowledge, it is the first study that compares outcomes from 2 different endoluminal treatment modalities in similar patient populations. Although the Stretta RF product is currently not in production, this technique is still used by some centers in the United States and internationally, and it is possible that some other form of RF treatment will become available in the future.

In the present study, both procedures were effective, but there were marked differences in the specific parameters affected by each procedure. Both procedures re-

sulted in a reduction in PPI use and relief of some symptoms. However, FTP resulted in a greater decrease in pH scores than RF, while RF resulted in a greater decrease in heartburn symptom scores than FTP. These findings are consistent with the differing mechanisms of action in the 2 procedures. Although RF is believed to increase LES pressure and decrease transient LES relaxations,⁷ FTP creates a more effective mechanical barrier, resulting in a greater decrease in the objective pH score. This may also explain the dramatic reduction in regurgitation in the FTP group; although FTP seems more effective for patients with regurgitation, this symptom was not used as a selection criterion for FTP during the study period.

Although patients usually experienced an improvement in or elimination of heartburn symptoms after FTP at our institution, a subset of patients have experienced refractory symptoms, frequently from larger hiatal defects or a very loose cardia diameter. To address this issue, we have modified our technique to include 2 plications along a slightly diagonal vector. We believe that this technique more adequately recreates the normal anti-reflux valve by reestablishing the angle of His. Anecdotally, results from this technique have been superior to single plication, but further study is needed to definitively demonstrate this.

Several studies have been published showing that endoscopic therapy is both feasible and effective in managing symptoms in patients with GERD (**Table 2**). A recent study by Pleskow and colleagues¹⁰ found a decrease in symptom scores and PPI use in 29 patients at 1 year that was sustained at 3 years after FTP. Rothstein and colleagues⁴ randomized patients to either FTP or a sham procedure, and found greater decreases in PPI use, symptoms, and acid exposure in the treatment group. An early study by Chuttani et al² in 2003 showed decreased symptom scores at the 6-month follow-up in 6 patients who underwent FTP. These results were sustained after 1 year, and most patients were no longer receiving PPI at that time.

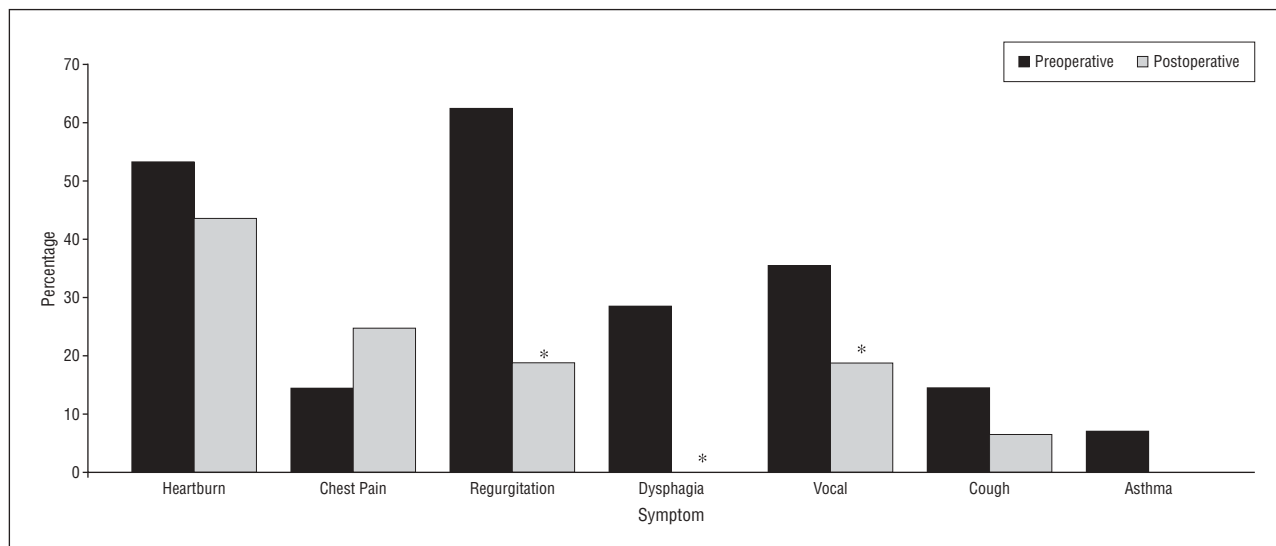


Figure 7. Plicator symptom scores. Percentage of patients reporting either moderate or severe score for aerodigestive symptoms before and after full-thickness plication therapy. * $P < .05$.

Table 2. Summary of Plicator Data

| Source | Study Summary |
|------------------------------|--|
| Chuttani, 2003 ² | First pilot trial; 7 patients enrolled, 6 procedures performed. Safety demonstrated. |
| Pleskow, 2004 ⁸ | Multicenter trial; 6-mo follow-up, single plication, 64 patients, 74% off medication; 67% GERD-HRQL improvement, reduced acid exposure, 30% patients normalized pH; 1 gastric perforation. Mean procedure time <20 min. |
| Pleskow, 2005 ⁹ | 12-mo Follow-up from 2004; 57 of 64 patients followed; 70% less PPI use; 80% reduced acid exposure, 30% pH normalized. |
| Rothstein, 2006 ⁴ | Sham-controlled RCT; 78 treated, 81 sham. Treatment group had improved GERD-HRQL, reduced acid exposure, and reduced PPI use. |
| Pleskow, 2007 ¹⁰ | 3-y Follow-up of 2004 report; 29 patients followed up; 57% off PPI; GERD-HRQL same as 12-mo. |
| Jeansonne, current study | Compared RF (n = 68) cohort with single-Plicator cohort (n = 58). Both had significant reduction in PPI ($P = .01$). Plicator had most reduction in regurgitation and acid exposure ($P < .05$). pH not normalized. Three patients in each group crossed over to Nissen. |

Abbreviations: GERD-HRQL, gastroesophageal reflux disease health-related quality of life; PPI, proton pump inhibitor; RCT, randomized clinical trial; RF, radiofrequency.

For patients who underwent RF treatment, a study by Cipoletta et al¹¹ showed significant reduction in GERD symptoms, improved GERD health-related quality of life, and improved general quality of life, but did not show a difference in esophageal acid exposure time at 12 months. This is consistent with the result of the present study, which also did not show a significant decrease in pH scores for RF. However, 1 study did show a decrease in acid exposure and De-meester score in morbidly obese patients who underwent RF after gastric bypass surgery.⁵ In addition, a 2-year follow-up study of RF showed that acid exposure decreased, but only among patients who had ceased PPI use.⁶

The present study contains a number of limitations. The relatively small sample size could result in type II

error, and we believe that a larger pool of patients may change some of the results, most notably the heartburn symptom scores of the FTP patients. This study was not randomized or sham-controlled; the choice of procedure was determined by the patient and physician. In addition, symptom scores are inherently subjective in nature and arguably not as meaningful as objective pH data. Finally, the results must be viewed in light of the short duration of follow-up; whether these procedures are durable in the long-term (>3 years) remains to be determined.

For patients with GERD, RF and FTP both resulted in a decrease in PPI use and symptom scores for voice symptoms and dysphagia. In addition, RF resulted in a decrease in heartburn and cough, while FTP resulted in a more dramatic reduction in regurgitation. Our experience indicates that RF and FTP are both effective, providing symptomatic relief and reduction in PPI use. For patients whose chief complaint is regurgitation, FTP may be the preferred procedure. Further study is needed to determine the long-term effectiveness of endoluminal treatments.

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Author Contributions: The corresponding author had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. *Study concept and design:* Khaitan, Davis, Smith, and Lin. *Acquisition of data:* Nguyen, Jafri, Swafford, Katchooi, Khaitan, Davis, Smith, Sedghi, and Lin. *Analysis and interpretation of data:* Jeansonne, White, Jafri, and Lin. *Drafting of the manuscript:* Jeansonne and Lin. *Critical revision of the manuscript for important intellectual content:* Jeansonne, White, Nguyen, Jafri, Swafford, Katchooi, Khaitan, Davis, Smith, Sedghi, and

Lin. *Statistical analysis*: Jeansonne and White. *Obtained funding*: Lin. *Administrative, technical, and material support*: Jeansonne, Nguyen, Swafford, Katchooi, and Lin. *Study supervision*: Jafri, Khaitan, Davis, Smith, and Lin. **Previous Presentations**: Presented in part at Digestive Disease Week; May 21, 2007; Washington, DC. **Financial Disclosure**: None reported.

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INVITED CRITIQUE

Gastroesophageal reflux disease is one of the most commonly encountered gastrointestinal disorders. Medical therapy for GERD is limited by long-term costs and effectiveness, while antireflux surgery is limited by its inherent morbidity. A durable and effective procedure that focuses on disease control (and not symptom control alone), and that can be accomplished on an outpatient basis without surgery, is needed. For the past 10 years, there has been an intense interest in developing and defining such a procedure. Numerous endoluminal GERD treatments have come and gone during this time. Some devices have been withdrawn from the market owing to safety concerns, and others have fallen out of favor because of a lack of long-term effectiveness. In fact, at the time of this writing, a device for delivering endoscopic radiofrequency treatment for GERD such as the one employed in this trial is not commercially available. Jeansonne and colleagues have nicely demonstrated and compared the short-term symptomatic outcomes of 2 different endoscopic GERD treatment modalities. Both procedures resulted in GERD symp-

tom improvement and demonstrated an excellent safety profile. What this study and others fail to definitively demonstrate is the kind of consistent symptom improvement and durability of therapy related to laparoscopic fundoplication in the hands of an experienced surgeon. In this era of limited health care dollars, especially considering the prevalence of severe GERD in our society, we have a responsibility to ensure that these endoluminal therapies effect durable and consistent results on par with our time-tested treatments. In my opinion, we still have a long way to go before a clear alternative to laparoscopic antireflux surgery emerges for those with medically refractory GERD symptoms.

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