Longer Term Clinical Outcomes after Radiofrequency Therapy for refractory Gastroesophageal Reflux Disease (GERD)

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Stretta for GERD refractory to PPI therapy has received very limited evaluation. Aim: To evaluate long-term efficacy of Stretta procedure used for management of refractory GERD. Methods: Thirty-two patients with refractory GERD to at least double doses PPI Underwent Stretta therapy. Mean follow-up time was 2.5 years. RESULTS: Stretta procedure was successfully completed in all patients with no serious complications. At baseline, HRQL while off medications was 26.3, compared with 17.1 at the end of the follow-up (p < 0.05). Mean HRQL on medications at baseline was 24.3, compared with 14.24 at the end of the follow-up (p < 0.05). At baseline all patients were taking at least double dose PPI daily. At the end of follow-up, two patients (6.25%) had discontinued their PPI’s, and an additional 18 patients (56%) had reduced PPI doses by ≥50%. HRQL normalized while on medications in nine patients (28%). Conclusions: In this difficult patient population with refractory GERD symptoms, Stretta procedure was a feasible, safe and partially effective in decreasing symptoms and PPI use.

INTRODUCTION

Gastroesophageal reflux disease (GERD) is extremely common and encompasses a diverse spectrum of clinical presentations. It has a substantial impact on patient quality of life and use of health care resources (1). GERD results from failure of the lower esophageal sphincter (LES) and cardia to prevent return of gastric contents into the esophagus. The pathophysiology of GERD is multifactorial and includes the occurrence of inappropriate, non-swallow related LES relaxations, and low resting pressure of the LES. This episodically exposes the esophageal body to gastric acid and enzymes (2). Reflux usually manifests as heartburn and regurgitation, and predisposes to the development of esophagitis, Barrett’s metaplasia, and esophageal adenocarcinoma (3).

Current therapy for GERD begins with lifestyle changes and medical treatment, which prove to be adequate or effective in more than 95% of patients. Such therapy must usually be maintained long term as the recurrence rate of symptoms is as high as 90% after cessation of medication. In addition, long term drug therapy is associated with issues of cost, compliance, and long term safety (4).

Patients who do not tolerate or respond adequately to medication or who wish to avoid life-long drug therapy may be considered surgical candidates. Such surgery necessitates general anesthesia, has a mortality of approximately 0.2%, and can be associated with...
additional morbidity, including dysphagia, gas-bloat syndrome, and postprandial fullness (5).

Recently, minimally invasive endoscopic procedures were used in attempt to improve the anti-reflux barrier function: 1) Delivery of radiofrequency (RF) energy to the LES and cardia (Stretta, Curon Medical, Inc., Sunnyvale, CA); 2) Creation of gastroplications (Bard EndoCinch suturing system, C.R. Bard, Inc. New Jersey; NDO endoscopic full thickness plicator, NDO Surgical, Inc., Mansfield, MA; Esophyx, EndoGastric Solutions Inc., Redmond, WA); and 3) Injection of filler materials into the cardia.

Multiple other techniques such as the His-Wiz infrasphincteric plicator, use of artificial magnetic esophageal sphincter, or implantation of on-demand microstimulator in LES to increase LESP are under study. These endoluminal techniques may provide an alternative to long-term maintenance therapy with proton pump inhibitors (PPI) or surgery. There have been a number of trials evaluating these new procedures mostly focusing on technical feasibility and initial efficacy. Limited data for RF efficacy are available beyond one year, despite FDA approval of the device in the year 2000.

To date, it is estimated that approximately 10,000 Stretta treatments have been done. It has been our observation that Stretta was used for medical responsive and medically refractory patients. Stretta for refractory GERD is an alternative for patients who may be considered at high operative risk, or who may prefer a lesser invasive option. Outcomes from treatments for such patients (especially longer term follow-up studies) are infrequently published. Since GERD is a chronic disease, longer term outcomes are vital in determining ultimate efficacy of any therapy. Outcomes from both medically responsive and medically refractory patients are of interest. These outcomes from medically refractory patients are the basis for this report.

Methods

Study Population

At a single Midwestern medical center, patients with refractory GERD symptoms (HRQL did not normalize on at least double dose PPI, with on PPIs HRQL ≥15) were offered Stretta therapy as a minimally invasive alternative.

Inclusion Criteria

- Heartburn and/or regurgitation symptoms clinically judged to be due to GERD
- Patients taking daily double dose PPI
- Esophagogastroduodenoscopy (EGD) showing low grade esophagitis (Los Angeles grade A-B)

Exclusion Criteria

- Patients with large sliding hiatal hernia
- Pregnant female patients
- Poor surgical candidates
- Patients with severe active esophagitis (grade C or D LA classification)
- Patients with collagen vascular diseases or autoimmune diseases
- Patients with severe dysphagia
- Esophageal or gastric surgery or other GERD endoscopic treatments done before or after the procedure
- Patients with coagulation disorder
- Patients with atypical GERD symptoms (cough, asthma and hoarseness)

Beginning May 2000, all patients with refractory GERD were evaluated by the participating physician. Those patients were offered Stretta therapy as a minimally invasive alternative. Need for medical therapy and/or RF treatment was based on clinical symptoms of heartburn and regurgitation, and endoscopic findings. Manometry and pH probe studies were done in some patients for further evaluation. Patients with a follow-up period longer than 12 months were qualified for the study. Standardized symptoms scoring were prospectively collected for baseline, point of maximal benefit, and current symptoms. The tallied parameters were the GERD HRQL (Velanovich scale) and medication doses. Medication doses were tallied from outpatient records both before and at the end of the follow-up. Patients still requiring anti-secretory medications after Stretta were asked to discontinue their use one week before the off medications questionnaire. Subjects reported the time interval from the Stretta procedure to the onset of GERD symptom relief or partial relief as immediately, within three months, from three-to-six months, six-to-twelve months, or no

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improvement. Subjects were instructed to answer all follow-up questions while off drugs to maintain standardization. Subjects graded their GERD severity at base line (separately on and off medications) and at a follow-up (off medications) when the patient felt his best, and at the end of the survey (separately on and off medications). Patients who had other endoscopic GERD treatment (two patients had polymer injection and one patient had double Stretta treatments) or surgical fundoplication (three patients) after the procedure were excluded. Baseline and follow-up medication used for GERD symptoms (type, dose and frequency) were recorded. The study was approved by the Institutional Review Board. All patients provided written informed consent prior to the procedure.

**RADIOFREQUENCY ENERGY DELIVERY TECHNIQUE**

During a sedated EGD (using propofol), the operator measured the distance to the gastroesophageal junction (the squamocolumnar junction). A guidewire with a flexible tip is passed through the channel of the endoscope and left in the gastric antrum while removing the endoscope. The radiofrequency delivery catheter was passed orally with a guidewire assistance. The catheter consisted of a flexible balloon-basket assembly with four electrode needle sheaths (the RF therapy system; Curon Medical, Sunnyvale, CA). The investigator then inflated the balloon 1 cm proximal to the squamocolumnar junction, deployed the electrode needles (22 gauge; 5.5 mm length), and delivered radiofrequency energy for 90 seconds. The needles were then withdrawn, the balloon was deflated, the catheter was rotated 45°, and the procedure was repeated. This process was serially repeated every 0.5 cm, between 1 cm proximal and 0.5 cm distal to the squamocolumnar junction (eight lesions at each level). An additional six lesion sets were also made at the gastric cardia by inflating the balloon with 22 mL and 25 mL of air, respectively, and withdrawing the catheter until the balloon engaged in the cardia (12 lesions at each level). An additional six lesion sets were also made at the gastric cardia by inflating the balloon with 22 mL and 25 mL of air, respectively, and withdrawing the catheter until the balloon engaged in the cardia (12 lesions at each level). Thus totals of 14 lesion sets, or 56 RFe lesions, were created in each patient. All patients, except one, were discharged in the same day. Simple analgesics (acetaminophen/codeine) were administrated, as needed for pain. Patients were instructed to eat a soft diet for three days, to continue their usual acid suppressive therapy for three weeks, and then to stop GERD related medications if possible.

**STATISTICS**

Analysis of the data was performed using the SPSS (Version 9, Chicago, Illinois) software. Results are expressed as mean (range) or number (proportion) of patients. Comparison between pre- and post-Stretta data were performed using paired $t$ test. $p$ values of $<0.05$ were considered statistically significant.

**RESULTS**

Thirty-two patients underwent single Stretta procedure for the treatment of their refractory GERD symptoms. All procedures were performed on an outpatient basis. Mean follow-up time was 2.5 years (range, one-to-five). Mean age was 59.2 years (range, 18–80).

**Feasibility**

The Stretta procedure was successfully completed in all patients. Patients were sedated by intravenous administration of propofol. Fourteen lesion sets (four lesions per set) with a total goal 56 lesions were created. RF current was delivered for 90 seconds per lesion.

**Safety/Tolerability**

No serious complications were reported. There were no post-procedure perforations, bleeding episodes requiring transfusion, or deaths. Minor complications were temporary post-procedural retrosternal discomfort requiring oral analgesics, mild fever and transient nausea/vomiting. The only apparent persistent adverse event was prolonged gastroparesis observed in one patient. Initial endoscopy was done in this patient and showed no retained food. After the procedure, the patient experienced excessive fullness when eating and abdominal bloating. Follow-up endoscopy was done and showed retained food in the stomach. Patient was followed-up for two years with no improvement in his delayed gastric emptying symptoms, despite prokinetic medications. Radionucleotide emptying time was not measured.
Efficacy

The onset of maximum GERD symptom relief was reported as immediately after the procedure by two patients (6.25% of patients), first three months by 12 patients (37.5%), three-to-six months by ten patients (31.25%), six-to-twelve months by two patients (6.25%), and no improvement by six patients (18.75%), (Figure 1). At baseline, HRQL while off medications was 26.3 (range, 18–42), compared with 17.1 (range, 0–42) (p < 0.05) (Figure 2).

The mean HRQL on medications at baseline was 24.3 (range, 15–36), compared with 14.24 (range, 0–34) at the end of the follow-up (p < 0.05) (Figure 3). All our results are summarized in Figure (4).

At baseline all patients were taking at least double dose PPI daily. At the end of follow-up assessment, two patients (6.25%) had completely discontinued their PPI medications, and an additional 18 patients (56%) had reduced their PPI doses by ≥50%. The HRQL normalized in nine patients (28%).

DISCUSSION

Medical therapy is a mainstay of GERD treatment. PPIs are safe and well tolerated, but their cost and the necessity for lifelong use may contribute to difficulties with long-term compliance (6). Despite the widespread use of these medications, a proportion of patients remains incompletely satisfied, even with a dose-escalated regimen, and may seek additional GERD therapy. In addition, many patients with complicated GERD (Barrett’s metaplasia or esophageal stricture) or atypical GERD (patients with noncardiac chest pain or extraesophageal GERD symptoms) require much higher than standard medication doses,
and they are often even more difficult to treat satisfactorily with anti-secretory drugs.

Anti-reflux surgery has a well-established record of effectively controlling GERD and normalizing esophageal acid exposure in up to 90% of cases. Laparoscopic antireflux surgery has produced results similar to those of the open approach; however, safety and effectiveness outcomes vary among surgeons. Among even the most expert surgeons, the small yet present risks for dysphagia, bloating, diarrhea, and rarely mortality, and the need for general anesthesia, remain issues that may dissuade some patients from undergoing antireflux operations (7).

The Stretta procedure is an endoluminal intervention for the treatment of GERD with mechanisms of action that include a reduction of gastoesophageal junction tissue compliance subsequent to heat-induced collagen shrinkage and wound healing (8). Data on short-term outcomes of the Stretta procedure safety and efficacy have been presented and published previously with follow-up as long as one year (9–14). In a sham-controlled trial, Corley, et al (15), randomly assigned 64 GERD patients to Stretta or to a sham procedure. At six months, active treatment significantly and substantially improved patients’ heartburn symptoms and quality of life. More active patients than sham patients were without daily heartburn symptoms [n = 19 (61%) vs. n = 7 (33%)], and more had a >50% improvement in their GERD-related quality of life score [n = 19 (61%) vs. n = 6 (30%)]. Symptom improvements persisted at 12 months after treatment. More recently, two long-term follow-up studies were published and showed sustained efficacy of the Stretta procedure up to four years follow-up (16,17). The efficacy of Stretta procedure for the treatment of refractory GERD symptoms was minimally studied. The primary objective of our study was to evaluate the longer term follow-up (up to five years) of GERD symptoms control and the need for continued anti-secretory drug use in patients with refractory GERD treated with Stretta procedure.

The overall major complication rate of Stretta procedure has improved to less than 0.25%, lower than that reported for surgical antireflux procedures, and none were life-threatening. Unlike operator experience in a laparoscopic antireflux procedure, with a large number of cases required to attain proficiency, operator experience with the Stretta procedure has not been reported to impact on GERD symptom improvement.

To date, there have been very limited reports of medically refractory patients treated with Stretta. Noar, et al (17), reported a series of patients referred for “inadequate symptom control,” despite compliance with medical therapy including PPI at least once daily. Long-term therapeutic benefits of the Stretta procedure were observed. Mattar, et al (18), reported their experience in applying RF (Stretta) to treat recurrent and refractory GERD in post-laparoscopic Roux-en-Y gastric bypass patients. In their series of seven patients, they were able to achieve significant symptomatic improvement and objective decrease in esophageal acid reflux per pH studies in follow-up. McClusky, et al (19), evaluated the use of the Stretta procedure in treating eight patients with recurrent reflux after fundoplication. Subjective symptoms of GERD were significantly reduced in six out of the eight patients. The authors concluded that Stretta procedure may serve an important role as an additional management strategy to help manage recurrent GERD after antireflux surgery.

In our study, despite high levels of baseline pharmaceutical utilization, GERD symptom control and overall satisfaction with pharmacologic therapy of patients were very low, and these patients sought an (continued on page 80)
alternative approach. Although, only two patients (6.25%) stopped their medications at the end of follow-up, the majority of the studied patients showed improvement in their on medications symptoms, and also reduction of their daily PPI doses.

The authors recognize the limitations of this study design. First, a control group is lacking, although a patient serves as their own control (before treatment). Second, pH studies were not done in all cases prior to and after RF treatment.

These data were collected before the Stretta manufacturer (Curon Medical, Inc., Sunnyvale, CA) reported additional major financial problems. Unfavorable billing codes and lack of long-term efficacy data, led to low market penetration. Stretta is reimbursed more like an upper endoscopy, thereby discounting the breadth of expertise and skill necessary not only to perform the procedure but to appropriately evaluate and manage the patient with GERD. Establishing appropriate reimbursement that would recognize the procedure as an antireflux procedure and set reimbursement more in line with other antireflux procedures would be essential. Recent discussions with the manufacturer indicate interest and effort for return to the GERD arena.

Overall we conclude that:

1. Stretta is partially effective in a medically refractory patient group
2. Stretta can be done in the private practice settings
3. Lack of a control group makes conclusions less certain
4. Further studies are required to determine if the effectiveness of this technique can be improved either by increasing the dose of radiofrequency lesions (by doing multiple sessions), or by identifying more diagnostic parameters that better select patients who are likely to benefit from the Stretta procedure.

As manufacturers of endoscopic GERD therapies enter and exit the market place, lessons learned from initial devices should be applied to the next generation devices. Dose response studies are needed for both medically responsive and less responsive patients. Also, combination therapy trials such as plications plus Stretta would be recommended. Several generations of surgical techniques were required before current “best state of art” laparoscopic fundoplication was achieved. Continued trials of various GERD endoscopic therapies are awaited.

References