# Sustained improvement in symptoms of GERD and antisecretory drug use: 4-year follow-up of the Stretta procedure

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**Background:** Approximately 20% of patients with GERD do not respond to medical therapy. The Stretta radiofrequency antireflux procedure represents an alternative to failed drug therapy for GERD.

**Objective:** The aim of this study was to assess symptom and medication changes after the Stretta procedure during a 4-year follow-up period.

**Design:** Prospective case series on intent-to-treat basis.

**Setting:** Community practice.

**Patients:** Patients with GERD with persistent symptoms despite twice-daily proton pump inhibitor (PPI) medications.

**Interventions:** The Stretta procedure was performed in drug-refractory patients with GERD diagnosed by the presence of endoscopically evidenced esophagitis or abnormal esophageal pH testing. Symptom assessment was performed with a validated health-related quality-of-life questionnaire (with and without medication) at baseline and 6, 12, 24, 36, and 48 months after treatment. Complications of the procedure and medication usage were analyzed.

**Main Outcome Measurements:** Significant changes in symptom scores, GERD quality-of-life parameters, and medication usage on the basis of clinical outcomes.

**Results:** We report on a series of 109 consecutive patients treated with the Stretta procedure who have reached 4-year follow-up. Complete long-term follow-up assessment was available in matched data for 109 patients at 12 months, 108 patients at 24 months, 102 patients at 36 months, and 96 patients at 48 months. A second procedure was performed in 13 patients. Heartburn scores decreased from 3.6 to 1.18 ($P < .001$), total heartburn score (GERD health-related quality-of-life questionnaire) decreased from 27.8 to 7.1 ($P < .001$), and patient satisfaction improved from 1.4 to 3.8 ($P < .001$) (see Table 2). Medication usage decreased significantly from 100% of patients on twice-daily PPI therapy at baseline to 75% of patients showing elimination of medications or only as-needed use of antacids/over-the-counter PPIs at 48 months ($P < 0.005$). There were no serious complications of the procedure.

**Limitations:** This is an uncontrolled, nonrandomized case series in consecutive patients that does not include long-term pH or motility studies.

**Conclusions:** This study in drug-refractory patients with GERD found the Stretta procedure to be a safe, effective, and durable treatment that produced significant improvements in heartburn and quality of life and decreased medication usage during a 4-year period of follow-up. (Gastrointest Endosc 2007;65:367-72.)

GERD is a common condition associated with severe health-related quality-of-life impairment comparable to patients afflicted with diabetes mellitus, congestive heart failure, or arthritis.[1] Although GERD is known to be a chronic disease requiring life-long treatment, many patients have inadequate symptom control with medication, usually proton pump inhibitors (PPIs).[2,3] About 20% of patients will have breakthrough heartburn and regurgitation causing detrimental effects on quality of life. Moreover, long-term use of these medications may provide a significant and life-long economic expense. GERD treatment using a minimally invasive endoluminal method to deliver low-level radiofrequency energy to the gastroesophageal junction (Stretta procedure) was introduced in 2000. Multiple


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studies have documented the safety and short-term efficacy of the Stretta procedure in patients with GERD who are either partially responsive or refractory to medications, but its longer-term efficacy (beyond 27 months) and effect on patient symptoms and medication requirements have not been established.[4-10] This study reports our experience using the Stretta procedure in patients with persistent GERD symptoms (despite use of twice-daily PPIs) who have been followed up for 4 years.

**Capsule Summary**

**What is already known on this topic**

- Approximately 20% of patients with GERD have inadequate symptom control with medication, and long-term use of proton pump inhibitors is expensive.
- Radiofrequency energy delivery to the gastroesophageal sphincter (Stretta procedure) is a safe and effective endoscopic therapy for GERD, but its long-term effectiveness is not known

**What this study adds to our knowledge**

- In a series of 109 consecutive drug-refractory GERD patients treated with the Stretta endoscopic antireflux procedure and followed up for 48 months, heartburn scores decreased, patient satisfaction improved, and medication use decreased.

## METHODS

### Patients

Since August 2000 in our practice we have clinically treated a total of 243 patients with the Stretta procedure, 109 of whom we have followed up and have now reached 4-year follow-up. All patients had significant GERD with persistent symptoms of heartburn and regurgitation despite the use of PPI drugs taken twice a day (escalated medical therapy). All patients had the diagnosis of GERD confirmed by finding erosive esophagitis at upper endoscopy (Los Angeles grade A or higher) or abnormal acid contact time detected at ambulatory esophageal pH testing. Patients with erosive esophagitis were maintained on medical therapy until all erosions had healed. Esophageal motility was performed in all patients to exclude those patients with achalasia. Patients with metaplasia were treated and followed up according to standard Barrett's protocol with EGD and 4-quadrant biopsy at each follow-up. Gastric emptying scans (GES) were performed on all patients and 31 of 109 demonstrated abnormal emptying. Patients with stenosis, stricture, or ulceration of the pyloric valve were excluded. Other exclusion criteria were pregnancy, poor surgical risk (American Surgical Association grade $>$III), achalasia, previous non-Nissen esophageal or gastric surgery, collagen vascular disease, or severe uncontrolled medical illness.

### Procedures

Before undergoing the Stretta procedure, patients (both on and off prescription medications) underwent symptom assessment with the GERD health-related quality-of-life questionnaire (rated 0-50 with scores less than 10 considered normal).[11] GERD symptom assessment is known to be the most appropriate measure of treatment success because it relates to patients and their treating physicians.[12] This is a validated questionnaire assessing specific GERD symptoms, followed by questions about heartburn severity on a scale of 0 to 5, with higher scores indicating more severe symptoms, and with questions about patient satisfaction (quality of life) on a scale of 0 to 5, with higher scores indicating better satisfaction/quality of life.[13] Assessment of medication usage was performed at baseline and 6, 12, 24, 36, and 48 months with the assistance of patient diaries and detailed questions addressing the use of all GERD medications such as PPIs, histamine-2 blockers, antacids, and prokinetic agents.

The Stretta procedure was performed by a single practitioner (M. N.), with the patient under conscious sedation with midazolam or fentanyl. The Stretta system uses a radiofrequency generator and a flexible delivery catheter with a balloon-basket device with 4 treatment elements stationed around the balloon. Diagnostic upper endoscopy is used to locate the gastroesophageal junction. The endoscope is then removed and the Stretta catheter is placed in this location. After appropriate balloon inflation, the treatment elements are deployed 1 to 2 mm into the lower esophageal sphincter muscle, where energy is delivered in a series of thermal treatments at 4 levels in 2 positions (distal esophagus) and at 2 levels in 3 positions (gastric cardia).[14] Constant monitoring and feedback of temperature and impedance ensures that each treatment element is maintained safely within target tissues. Production and healing of these lesions causes inflammation, subsequent collagen deposition, and muscular thickening, whereas efferent/afferent vagal nerve ablation causes a decrease in total lower esophageal sphincter relaxations and thus a decrease in esophageal acid exposure.[5-7,15] As radiofrequency energy is applied during the procedure, chilled water is irrigated from the catheter down the esophageal mucosa to prevent ulceration or stricture. After completion of the procedure and catheter removal, the diagnostic endoscopy procedure is repeated to verify that there have been no complications such as bleeding or perforation and to document the appropriate site of treatment. All pre-Stretta medication is maintained for 6 to 8 weeks after the procedure to maintain baseline and allow time for complete healing.

### Statistical methods

The ranked discrete data from the questionnaires (before and after the Stretta procedure was performed)

were compared with the Student *t* test (SAS Software, Cary, NC). Patient responses were tabulated in blinded fashion to avoid bias of the results. Although there was multiple testing of outcome data arising from individual patients, correction by the Bonferroni method would not have removed significance from any findings, so *P* values are presented uncorrected for multiple testing.

## RESULTS

The Stretta procedure was performed on 109 consecutive patients (Table 1) who have reached their 48-month follow-up. All patient data have been matched to baseline.

**TABLE 1. Study population baseline characteristics**

| Characteristics | No. |
|---|---|
| No. of patients | 109 |
| Sex (%) | |
| Male | 62 (56.8) |
| Female | 47 (43.2) |
| Age (y) | |
| Mean (SD) | 51 (13) |
| Range | 23-75 |
| Weight (kg) | |
| Mean (SD) | 77 (10) |
| Range | 52-100 |
| Barrett's esophagus (%) | 39 (35) |
| Esophagitis (%) | 33 (30.3) |
| PPI twice daily (%) | 109 (100) |
| PPI twice daily + $H_2$ receptor antagonists (%) | 34 (31.2) |

### Complications

Minor complications occurred after the procedure, including 11 cases of dyspepsia (10.1%), 27 chest discomfort (25%), and 2 minor gastric bleeding (1.8%). These complications resolved within 2 weeks, without sequelae. No serious complications were noted after the procedure or in long-term follow-up. All patients had complete follow-up at 12 months, 108 patients at 24 months, 102 patients at 36 months, and 93 patients at 48 months. No significant differences in patient satisfaction or quality of life were seen at baseline assessment on or off medications. Three patients did not complete follow-up questionnaires or phone surveys: 2 were deceased and there was 1 refusal to comply. Thirteen patients were not satisfied with their initial results and went on to request a second procedure: 6 had a Nissen fundoplication and 7 had a second Stretta procedure. The mean time to failure in these 13 patients was 18 months (range 12-24 months). For analysis, all failed patients were treated on an intent-to-treat basis and their last value scores carried forward to 4 years for complete data analysis. At 4 years the results were significantly improved from baseline in all questionnaire parameters.

### Symptoms

Heartburn scores decreased from a mean of 3.67 to 1.18 (SD 1.28, $P < .001$) (Table 2), whereas total heartburn score (GERD health-related quality-of-life questionnaire) decreased from a mean of 27.8 to 7.1 (SD 8.42, $P < .001$) (Table 2).

### Quality of life

Patient satisfaction also improved from a mean of 1.4 to 3.8 (SD 1.09, $P < .001$) (Table 2). There were no significant differences in results among follow-up time periods for any parameter.

### Medication requirements

Medication usage decreased significantly ($P < .005$). At baseline, 100% of patients were receiving twice-daily PPI therapy. At 48-month follow-up, patients were divided into 4 distinct medication use categories: (1) no medications, (2) as-needed antacids/over-the-counter PPI, (3) daily PPI, and (4) twice-daily PPI. At 48 months, 75% of patients showed a significant reduction in PPI use and were in categories 1 or 2 ($P < .005$) (Table 2). A total of 85% of the patients had reduced their medication requirement by half or eliminated it completely. The other patients were in category 3 or 4.

A subgroup analysis was performed between patients with and without erosive esophagitis (Fig. 1) at initial assessment as to their satisfaction outcomes. At baseline, there was a significant difference in patient satisfaction while on medications before the Stretta procedure. At 1-year follow-up there was a significant improvement in satisfaction in both groups with no difference between groups. Durability of patient satisfaction results was maintained throughout the 4 years with no significant statistical differences between groups (Fig. 1).

### Barrett's metaplasia

An annual EGD was performed in the 39 (35%) patients with Barrett's metaplasia. Esophageal biopsy specimens obtained at each follow-up visit through 4 years revealed no cases of dysplasia or adenocarcinoma. Follow-up EGDs were not performed on other patients.

## DISCUSSION

GERD is a common disease that significantly impairs the quality of life of patients, and it is associated with pathophysiologic alterations such as transient lower esophageal

**TABLE 2. Comparison of clinical parameters at various follow-up intervals show significant changes in all measures**

| | Baseline | | Follow-up (mo) | | | | |
|---|---|---|---|---|---|---|---|
| **Parameter** | **Off medication** | **On medication** | **12** | **24** | **36** | **48** | ***P* value** |
| GERD health-related quality-of-life questionnaire | 27.8 | 20.5 | 6.8 | 4.6 | 6.7 | 7.1 | .001 |
| Heartburn | 3.6 | 2.6 | 0.9 | 0.7 | 1.06 | 1.18 | .001 |
| Satisfaction | 1.4 | 2.2 | 3.97 | 4.4 | 3.8 | 3.8 | .001 |
| Percent without PPI | 100 | 0 | 82 | 83 | 77 | 75 | .05 |

sphincter relaxations and the presence of a hiatal hernia. Although antisecretory medications such as PPIs are considered the mainstay of GERD treatment, they do not address any of the underlying pathophysiologic derangements, including pH normalization associated with GERD.[16] It is not surprising, therefore, that at least 20% of patients do not have adequate symptom control despite escalated drug therapy.[17] Although antireflux surgery appeals to many patients because it corrects the hiatal hernia and increases lower esophageal sphincter pressure,[18] postsurgical gas-bloat dyspepsia and diarrhea are common and may be severe; up to 50% of patients may require maintenance medical therapy for unresolved symptoms.[19]

The results of the Stretta treatment in this study demonstrate statistically significant improvement in mean GERD symptom scores for heartburn, patient satisfaction, quality of life, and decreased or eliminated need for medication sustained over 4 years of follow-up compared with baseline values. It is noted that we report on symptomatic improvement and that no data regarding pH or motility was included to determine the long-term effect on these parameters. However, because all patients were previous failures of escalated PPI medication, the data showing elimination of continuing PPI management are encouraging and practical in clinical practice. Additionally, in the limited EGD sequences that were obtained in managing Barrett's esophagus, we do show no advancement in metaplasia with no increased risk of dysplasia or cancer observed.

The Stretta endoscopic antireflux procedure was introduced in 2000 for the treatment of patients with GERD who had suboptimal symptom control with medical therapy. Important recent studies include a post hoc analysis in 118 patients treated with the Stretta procedure where clinical responders (asymptomatic on daily PPIs) were found to have significant improvements and normalization in both proximal and distal esophageal acid exposure.[5] This study confirmed that the symptom improvement after the Stretta procedure was related to a decrease in esophageal acid exposure time and not desensitization to esophageal acid. Richards et al[7] compared the results of the Stretta procedure in 65 patients with results after laparoscopic antireflux surgery in 75 patients. Six months after these treatments, there was significant improvement in results from quality-of-life questionnaires and GERD symptom scores in both groups, with both patient groups highly satisfied with their respective procedures. Discontinuation of PPI medication was noted in 97% of fundoplication patients and 47% of Stretta patients at 6 months. Torquati et al[8] presented 27 months of follow-up in 36 patients treated with the Stretta procedure. In their follow-up, 56% of patients discontinued use of all antisecretory drugs. In the 20 patients identified as responders, the pH did decrease significantly.

Longer-term studies show that in patients with limited response to medical therapy the complete improvement from the Stretta procedure, which occurs over 12 months, continues for up to 4 years, as shown in the current study. Another recent report has described results using the Stretta procedure in the treatment of 6 pediatric patients (ages 8-16 years) with refractory GERD. Symptom improvement after the Stretta procedure was noted in 5 of 6 patients and antisecretory drug use was discontinued in 3 of 6 patients.[20] Additionally, other studies that have supported the use of the Stretta procedure include a randomized sham-controlled study, single-center and multicenter prospective trials, and community practice reports.[7,21-23] In the randomized sham study, Corley et al[10] demonstrated the Stretta procedure as having a significantly better effect than the sham procedure on patients' symptoms. However, it is noted that in the very short-term follow-up presented there was no significant difference in the collected pH measurements or residual medication usage.

There are few data available regarding the long-term benefits of the Stretta procedure. The multicenter Stretta registry study of 558 patients reported significant GERD symptom control and procedure satisfaction superior to that achieved with drug therapy. Subgroup analysis found that this superior effect on symptom control and drug use persisted more than 1 year and that most patients were off all antisecretory drugs at follow-up.[24] The median drug requirement improved from PPIs twice daily to antacids as needed ($P < .001$). Patient satisfaction with drug therapy was poor at baseline (23.2%) but significantly improved at follow-up after the Stretta procedure (86.5%, $P < .001$). Yeh and Triadafilopoulos[9] presented a review of the published Stretta clinical reports showing outcomes

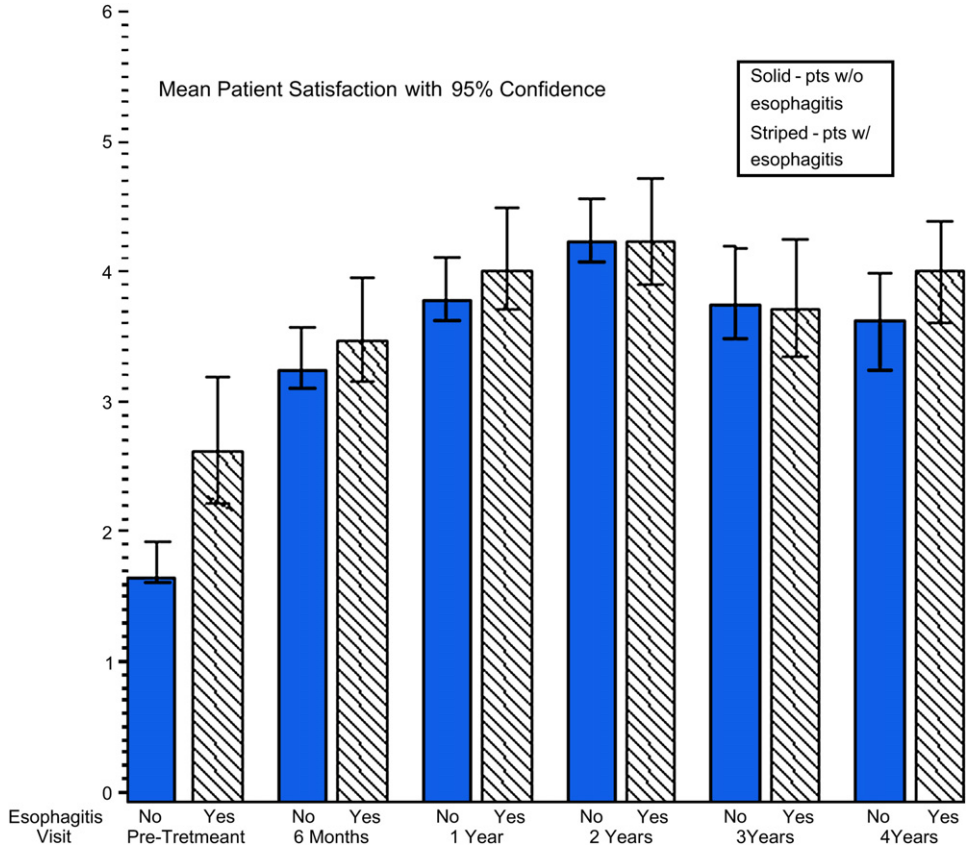


**Figure 1.** Baseline and follow-up subgroup analysis of patient satisfaction of patients with and without initial erosive esophagitis demonstrating significant sustained improvement over the 4-year study follow-up ($P < .001$).

of pH and medication requirements up to 27 months after the procedure. The current study adds significantly to the available literature regarding the number of patients and the long-term efficacy of the Stretta procedure. The results in this large group of patients document important long-term durability of beneficial symptomatic effects and elimination of medication usage effects of the Stretta procedure in patients who have failed escalated PPI therapy.

In summary, the patients in this study had statistically significant improvement and a sustained effect in all parameters for up to 4 years. In these patients, the observed improvement was superior to that achieved with escalated PPI therapy above baseline dosing. The safety record and the sustained efficacy indicate that the Stretta procedure is a viable, minimally invasive endoluminal procedure for the management of patients with GERD considering alternatives to failed drug therapy.[7,25-27]

## DISCLOSURE

*M. D. N. has served in the capacity as a member of the clinical advisory board and has received honoraria for speaking and training for Curon Medical, Inc, and has no other conflicts of interest to disclose. S. L.-E. has no conflicts of interest to disclose.*

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