

Gastroparesis associated with gastroesophageal reflux disease and corresponding reflux symptoms may be corrected by radiofrequency ablation of the cardia and esophagogastric junction

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Abstract

Background Reflux is a common medical condition with symptoms ordinarily controlled using drug/medical therapy. However, 20% of patients experience unmanageable symptoms despite twice-daily (BID) proton pump inhibitor (PPI) therapy. Growing clinical evidence shows that delayed gastric emptying (gastroparesis) may be a factor associated with severe reflux, dyspepsia, or both. Gastroparesis, concomitant in 25% of patients with gastroesophageal reflux disease (GERD), has been shown to improve after Nissen fundoplication. Radiofrequency treatment for GERD potentially corrects GERD-associated gastroparesis and resultant PPI BID reflux failures.

Methods From July 2000 until July 2004, 227 patients undergoing Stretta for GERD were screened for gastric anomalies. Patients with gastroparesis, documented on a standardized nuclear gastric emptying scans, and patients with heartburn and regurgitation uncontrolled by PPI BID medications underwent radiofrequency ablation of the cardia and esophagogastric junction via the Stretta procedure. The patients had esophagogastroduodenoscopy and/or pH studies, manometry, solid-phase gastric emptying, and

electrogastrography and completed standardized heartburn and health-related quality-of-life surveys before treatment, then 6 months afterward. Patients with pyloric obstruction and those taking motility agents were excluded from the study. Gastric emptying scans were repeated 6 months after Stretta. The nuclear radiologist was blinded to the study design.

Results At baseline, 31 patients were classified as abnormal. At 6 months after the procedure, emptying scores had improved significantly, with the percentage of solid food emptied at 90 min improved from 41% to 66% ($p < 0.0001$) and at 120 minutes from 55% to 84%. Significant improvements were seen at all intervals. Overall, 23 patients (74%) experienced normalization of gastric emptying, and 4 patients were improved but remained abnormal. Four patients showed no improvement on their gastric emptying scans, with one patient electing to undergo a Nissen procedure. All the patients had a 1-year symptom follow-up assessment, which showed significant improvements in GERD health-related quality of life, dyspepsia, and heartburn scores.

Conclusions Radiofrequency treatment has been demonstrated to correct gastroparesis. Patients' symptoms improved significantly. The mechanism of action is unknown but may be related to reduction in transient lower esophageal sphincter relaxations (TLESRs), increased esophagogastric junction barrier, decreased esophageal venting, alteration of the gastric pacemaker function in the region of radiofrequency therapy administration, removal of medications for symptoms, or a combination of all these.

Dr. Noar is responsible for the study design and development, the analysis and interpretation of the study data, drafting and critical revision of the manuscript for important intellectual content and final manuscript approval.

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The management of gastrointestinal symptoms related to dyspepsia and gastroesophageal reflux disease (GERD)

constitutes a major use of medical resources, involving 20% to 40% of the adult population [1]. Empirical use of proton pump inhibitors (PPIs) is an accepted first-line treatment for both sets of patients without alarm features [2, 26]. However, these are lifelong drugs, and it is common for a large percentage of these patients to fail after acid suppression therapy, with as many as 20% of GERD patients demonstrating breakthrough heartburn and regurgitation [3, 4]. Studies within these populations have been completed for further classification of failures and potential pathologic contributory factors, including gastric abnormalities [5–8].

Clinical studies within a GERD population show that patients who have undergone surgical fundoplication demonstrate a correction in their gastroparetic responses along with symptom improvement [9]. Management of GERD using a minimally invasive endoluminal method to deliver low-level radiofrequency energy to the gastroesophageal junction (Stretta procedure) was introduced in 2000. Multiple studies have documented the safety, short-term efficacy, and pathophysiologic changes after the Stretta procedure in GERD patients either partially responsive or refractory to medications [10–13].

Recent publications have demonstrated the long-term durability of the Stretta procedure and its ability to eliminate the nascent requirement for ongoing drug management [14, 15]. This study reports on the use of the Stretta procedure for patients with persistent GERD symptoms (despite the use of twice-daily [BID] PPIs) who have clinically documented gastroparesis.

Materials and methods

Since August 2000, we have clinically treated a total of 243 patients with the Stretta procedure in our practice. All these patients had experienced significant GERD with persistent symptoms of heartburn and regurgitation despite the use of PPI drugs taken twice a day (escalated medical therapy). All the patients had their diagnosis of GERD confirmed by erosive esophagitis found at upper endoscopy (Los Angeles Grade A or higher) or by abnormal acid contact time detected at ambulatory esophageal pH testing. Gastric emptying scans were performed for 227 patients (93.4%) using standardized nuclear emptying scans [16] to document gastroparesis.

Patients with documented gastroparesis, heartburn, and regurgitation uncontrolled by PPI BID medications underwent radiofrequency ablation of the cardia and esophagogastric junction via the Stretta procedure. Patients with pyloric obstruction and those taking motility agents were excluded from the study as well as patients with stenosis, stricture, ulceration of the pyloric valve, pregnancy, poor surgical risk (American Society of Anesthesiology [ASA] > 3), achalasia, previous non-Nissen esophageal or

gastric surgery, collagen vascular disease, or severe uncontrolled medical illness.

Gastric emptying scans were repeated 6 months after Stretta, with all results reviewed and interpreted by a nuclear radiologist blinded to the study. The follow-up evaluation at 6 months also included symptom assessment using the GERD Health-Related Quality-Of-Life (HRQL) questionnaire [17] and a validated questionnaire assessing specific GERD and dyspepsia symptoms. This was followed by questions about heartburn severity using a scale of 0 to 5, with higher scores indicating more severe symptoms, and questions about patient satisfaction (quality of life) using a scale of 0 to 5, with higher scores indicating better satisfaction/quality of life [18]. Assessment of medication usage was performed at baseline, then after 6 months with the assistance of patient diaries and direct questioning at the time of gastric emptying studies to assess the use of all GERD medications such as PPIs, H₂ blockers, antacids, and prokinetic agents. All the patients had a follow-up office visit at 1 year, with assessment of symptoms and medication requirements.

The Stretta procedure was performed by a single practitioner (M.N.), as described earlier [15], with treatments of the gastric cardia and lower esophageal sphincter (LES) muscle. Treatment at these sites causes inflammation, subsequent collagen deposition, and muscular thickening, whereas efferent/afferent vagal nerve ablation causes a decrease in total LES relaxations and thus a decrease in esophageal acid exposure, as well as a known increase in gastric yield pressure [19].

After completion of the procedure and catheter removal, a diagnostic endoscopy procedure was repeated to verify that there were no complications such as bleeding or perforation and to document the appropriate site of treatment. All pre-Stretta medication was continued 6 to 8 weeks after the procedure to maintain baseline values and allow time for complete healing.

Statistical analysis

The data were analyzed using SAS software (SAS Institute, Inc., Cary, NC, USA). The ranked discrete data from the scan results and questionnaires (before and after Stretta) were compared using Student's *t*-test. Patient responses were tabulated in blinded fashion to avoid bias of the results. Analysis of variance (ANOVA) was performed on responder and nonresponder subsets to demonstrate outcome differences between the groups.

Results

Delayed gastric emptying (gastroparesis) was clinically documented for 31 of patients (12.7%), who underwent the

subsequent Stretta procedure (Table 1). At the 6-month follow-up evaluation, the mean gastric emptying had improved significantly at each time interval (Table 2). The percentage of solid food emptied at 90 min had improved from 41% before Stretta to 66% ($p < 0.0001$). At 120 min, the percentage emptied had improved from 55% to 84% ($p < 0.0001$). No patient was noted to have retained food at the time of esophagogastroduodenoscopy after an overnight fast. In addition, the degree of abnormality before treatment did not correlate with the degree of improvement after the Stretta procedure (Fig. 1).

Table 1 Study population baseline characteristics

Characteristics	<i>n</i>
No. of patients (<i>n</i>)	31
Gender (<i>n</i>)	
Male: <i>n</i> (%)	25 (82)
Female: <i>n</i> (%)	6 (18)
Age (years)	
Mean	50 ± 13
Range	19–77
Weight (kg)	
Mean	75 ± 10
Range	52–100
PPI BID: <i>n</i> (%)	31 (100)
PPI BID + H2RA: <i>n</i> (%)	12 (39)

PPI, proton pump inhibitor; BID, twice daily

Table 2 Gastric emptying scan results demonstrate significant improvement at every interval

	30 Pre	30 Post	60 Pre	60 Post	90 Pre	90 Post	120 Pre	120 Post
Value	16.2	25.6	39.1	48.8	41.1	65.7	55.3	84.1
SD		18.2		28.5		29.5		22.4
<i>p</i> Value		<0.01		<0.03		<0.0001		<0.0001

Pre, pre-Stretta; Post, post-Stretta; SD, standard deviation

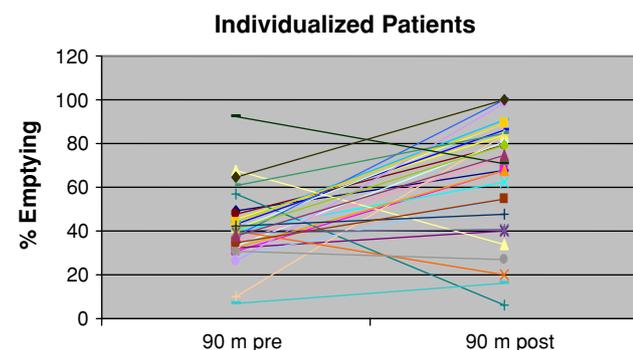


Fig. 1 Individualized pre- and posttreatment gastric emptying scan results

PPI, proton pump inhibitor; BID, twice daily. Of the 31 patients, 23 (74.2%) were responders, defined as those whose gastric emptying scans returned to a defined normal level. Eight patients were nonresponders, defined as patients whose gastric emptying scan did not normalize. Four patients (12.9%) experienced insignificant improvement, and four patients (12.9%) demonstrated no improvement. One nonresponder underwent a Nissen procedure due to lack of symptom improvement.

Minor complications occurred after the procedure including four cases of dyspepsia (12.9%) and one case of minor gastric bleeding (3.2%). These complications resolved without sequelae. No serious complications were noted after the procedure or at the 6-month follow-up evaluation.

No significant differences in patient satisfaction or quality of life were seen compared with the group's baseline assessment, whether medication was received or not. Both the responder and nonresponder groups demonstrated significant improvements in GERD HRQL (Table 3). Responders improved from 18.74 (on medications) to 8.04 at 6 months and to 5.35 at 12 months ($p = 0.0000021$). Nonresponders improved from 25.13 to 14.00 at 6 months and to 11.75 at 12 months ($p = 0.024$). Heartburn scores also improved for responders from 2.43 to 1.0 at 6 months ($p = 0.0001$) and for nonresponders from 3.0 to 1.75 ($p = 0.05$) (Table 3).

Analysis of variance demonstrated a significant difference between responders and nonresponders in both HRQL and heartburn scores ($p < 0.03$). Assessment for the dyspepsia component of the HRQL (gas and bloating) shows that scores improved significantly in the responder group (receiving medication) from 2.22 ± 1.47 at baseline to 0.96 ± 1.46 at 12 months ($p = 0.0027$). The dyspepsia score was not significantly improved in the nonresponder group: 3.25 ± 1.67 at baseline to 2.63 ± 1.51 at 12 months ($p = 0.216$).

Medication requirements

Medication usage decreased significantly ($p < 0.005$) in the responder group, with 22 of 24 patients (91.6%) moving from PPI BID to no medications or to antacids/H2RA as needed. The remaining two responders decreased their medications from PPI BID to H2RA/PPI daily. Of the eight nonresponders, four (50%) moved from PPI BID to antacid/H2RA as needed, two (25%) moved from PPI BID to PPI daily, and two (25%) showed no improvement.

Discussion

Gastroesophageal reflux disease is a common disorder that impairs patients' quality of life significantly. It is

Table 3 Comparison of mean symptom response \pm standard deviation in gastric emptying scan (GES) responders and nonresponders from baseline on medications (meds) to the 12-month follow-up assessment

	Baseline off meds	Baseline on meds	6 Months	12 Months	<i>p</i> Value
GES normalized					
HRQL	25.91 \pm 8.34	18.74 \pm 10.06	8.04 \pm 8.79	5.35 \pm 5.86	0.000021
Heartburn	3.87 \pm 1.01	2.43 \pm 1.53	1.75 \pm 1.67	0.7 \pm 0.88	<0.0001
Dyspepsia Symptoms	2.61 \pm 1.47	2.22 \pm 1.41	1.52 \pm 1.62	0.96 \pm 1.46	<0.0027
GES abnormal					
HRQL	36.75 \pm 7.59	25.13 \pm 12.26	14.00 \pm 11.41	11.75 \pm 8.88	0.024
Heartburn	4.5 \pm 0.76	3.0 \pm 1.69	1.75 \pm 1.67	1.13 \pm 1.13	0.05
Dyspepsia Symptoms	4.13 \pm 0.83	3.25 \pm 1.67	1.88 \pm 1.64	2.63 \pm 1.51	0.2168

HRQL, health-related quality of life

associated with pathophysiologic alterations such as transient LES relaxations and the presence of a hiatal hernia. Although antisecretory medications such as PPIs are considered the standard empirical GERD treatment, they do not address any underlying pathophysiologic derangements, including pH normalization associated with GERD [4]. It is not surprising, therefore, that at least 20% of patients do not experience adequate symptom control despite escalated drug therapy [3, 4].

On nuclear scans for a subset of patients with GERD, we documented conditions of delayed gastric emptying that may be contributors to the nonresponding symptoms [14]. Pallotta et al. [20] documented the relationship of persistent gastrointestinal symptoms and delayed gastric emptying in dyspeptic patients. Cahan et al. [21] showed that PPI therapy may be a causative factor in depressing digestive output.

The results of the Stretta treatment in the current study demonstrate statistically significant improvement in gastroparesis, HRQL, heartburn, and dyspepsia at follow-up evaluation compared with baseline values, with 74.2% of gastroparetic responders to therapy. There was a difference in symptom response in responders compared with nonresponders after the procedure. It should be noted that although the authors did not control for potential variation in the gastric emptying scan study, it was thought that this did not contribute to a profound effect on the results because the patients served as their own controls. All the patients undergoing the Stretta procedure were refractory to medical therapy although they were receiving a minimum of PPI BID therapy.

The Stretta 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 of 118 patients treated with Stretta, in which clinical responders (asymptomatic on daily PPI) were found to have significant improvements and normalization in both proximal and distal esophageal acid exposure [11].

The current study confirmed that the symptom improvement after Stretta was related to a decrease in esophageal acid exposure time and not desensitization to esophageal acid. Richards et al. [22] compared the results of the Stretta procedure for 65 patients with results after laparoscopic antireflux surgery for 75 patients. Significantly improved results were observed from quality-of-life questionnaires and GERD symptom scores in both groups 6 months after these treatments, with both patient groups highly satisfied with their respective procedures. Discontinuation of PPI medication was noted in 97% of the fundoplication patients and 47% of the Stretta patients at 6 months.

Torquati et al. [23] presented 27 months of follow-up evaluation for 36 Stretta patients. In his follow-up evaluation, 56% of the patients had discontinued use of all antisecretory drugs. For the 20 patients identified as responders, the pH decreased significantly.

In a randomized sham study, Corley et al. [24] demonstrated the Stretta procedure as having a significantly better effect on patients' symptoms than the sham procedure. However, it was noted that in the very short-term follow-up evaluation presented, there was no significant difference in the collected pH measurements or residual medication usage.

Longer-term studies recently published [14, 15] show the durability of the Stretta procedure, with its ability to eliminate or significantly reduce patients' need for ongoing PPI managements. The current study adds significantly to the available literature regarding the outcomes of the Stretta procedure for patients dissatisfied with escalated medical therapy. The results for this group of patients documents that radiofrequency therapy applied to the gastric cardia and muscle of the LES can normalize gastroparesis for patients with delayed gastric emptying while correspondingly eliminating symptoms and the need for ongoing medications. The mechanism of action is uncertain but may be related to a reduction in TLESRs, an increase in the esophagogastric junction barrier, decreased esophageal

venting, alteration of the gastric pacemaker function in the region of radiofrequency therapy administration, or removal of medications from patient regimens. Recent work by Randall [25] using electrogastragrams with gastroparesis patients (dyspeptic) shows electrical abnormalities in all patients that may be applicable for the GERD patient included in this study and that also may provide a potential basis for additional study.

In summary, the large majority of patients in this study had statistically significant improvement and correction of gastroparesis. There were corresponding improvements in patients' symptoms, with a demonstrated difference between responder and nonresponder groups. The need for PPI therapy was eliminated for almost all gastric emptying scan responders. The symptom improvements were maintained for at least 12 months. The safety record and sustained efficacy indicate that the Stretta procedure is a viable, minimally invasive, endoluminal procedure for the management of GERD patients considering alternatives to failed drug therapy and those with coexistent GERD-associated gastroparesis [10–15].

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