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Radiofrequency energy delivery to the lower esophageal sphincter improves gastroesophageal reflux patient-reported outcomes in failed laparoscopic Nissen fundoplication cohort

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Abstract
Background Patients with uncontrollable gastroesophageal reflux disease (GERD) often undergo laparoscopic Nissen fundoplication (LNF); however, long-term there are often recurring symptoms and need for continuous medication use. Refractory LNF patients may receive radiofrequency energy delivery to the lower esophageal sphincter (Stretta) to ameliorate symptoms and medication requirements. The aim was to assess and compare long-term patient-reported outcomes of Stretta in refractory patients with and without previous LNF.
Methods We prospectively assessed and compared patient-reported outcomes in 18 refractory LNF patients and 81 standard refractory GERD patients that all underwent Stretta during 10-year follow-up. Patient-reported outcomes measured were GERD-HRQL (health-related quality of life), patient satisfaction scores, and daily medication requirements.
Results The refractory LNF subset demonstrated median improvements in GERD-HRQL, satisfaction, and medication use at all follow-up time points ≥6 months to 10 years, which was significant from a baseline of both on- and off-medications ($p < 0.05$). Specifically at 10 years, median GERD-HRQL decreased from 36 to 7 ($p < 0.001$), satisfaction increased from 1 to 4 ($p < 0.001$), and medication score decreased from 7 to 6 ($p = 0.040$). Nine patients decreased medication use by half at 10 years. No significant differences existed between refractory LNF and standard refractory GERD subsets at any follow-up time point ≥6 months to 10 years ($p > 0.05$) after Stretta. At 10 years, no significant differences were noted between refractory LNF and standard Stretta subsets regarding medication use ($p = 0.088$), patient satisfaction ($p = 0.573$), and GERD-HRQL ($p = 0.075$). Stretta procedures were completed without difficulty or significant intraoperative or long-term adverse events.
Conclusion Within a small cohort of refractory LNF patients, Stretta resulted in sustained improvement over 10 years with equivalent outcomes to non-LNF standard Stretta patients. Refractory LNF patients are a subpopulation that may be safely, effectively, and robustly aided by Stretta with fewer complications compared to redo of Nissen or chronic medication use.

Keywords Radiofrequency energy · Stretta · Antireflux surgery · Laparoscopic Nissen fundoplication · GERD

Gastroesophageal reflux disease (GERD) treatment typically includes a wide range of management strategies beginning with lifestyle modifications then escalating to pharmacologic, endoscopic, and surgical intervention. For medically refractory patients, many choose to undergo what has been considered the "gold standard" in reflux correction, laparoscopic Nissen fundoplication (LNF).

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Successful intermediate follow-up of LNF has been established demonstrating dramatic improvements in esophageal pH, symptoms, medication usage, and patient satisfaction [1]. In the largest 10-year study following 250 laparoscopic fundoplication patients, 21 % of patients required regular antireflux medication and 17 % needed reoperation [2]. Until recently, typical treatment options for refractory laparoscopic Nissen fundoplication (LNF) included chronic medication use with its attendant costs and risks of long-term use and the option to undergo repeat LNF or Roux-en-Y (RNY). LNF reoperation is more difficult than the original procedure, more likely to fail, and associated with greater postoperative morbidities [3]. Follow-up of open Nissen and LNF after 10 years showed that 22.4 and 26.6 % were back on antireflux medications, respectively [4]. In a sample of 13,000 LNF patients, 5- and 10-year LNF reoperation rates have been reported as 5.2 and 6.9 %, respectively [5].

Radiofrequency energy delivery to the lower esophageal sphincter (Stretta) offers a minimally invasive alternative treatment modality to repeat LNF or chronic lifetime medication dependence.

Stretta (Mederi Therapeutics, Norwalk, CT) physiologically aids in restoration of anatomical abnormalities present in reflux patients. Low-power/low-temperature radiofrequency stimulation results in muscle fiber bundle proliferation and increased muscle cell volume within each bundle, subsequent sphincter lengthening, thickening, and increased physiological barrier function, all of which contribute to a mechanical decrease in refluxate volume into the esophagus and thereby limiting of receptor activation and the disease process [6–8]. Short- and long-term follow-up studies extending to a decade have demonstrated results to be immediate and durable over time, consistently demonstrating significant improvements in quality of life and medication requirements [9–12]. In a 10-year study of patients receiving Stretta, 72 % of this patient cohort demonstrated normalization of GERD symptoms and 64 % decreased medication use by at least half at 10 years with 41 % eliminating medication use completely [12]. An exploratory investigation of eight refractory LNF patients who underwent Stretta showed performing the procedure on this subset was feasible, safe, and effective in significantly reducing GERD symptom severity one-year post-procedure [13]. To date, there have been no long-term studies investigating the effect of previous LNF on Stretta outcomes. Since the physiological basis for Stretta improvement is universal, it would be expected that patients with refractory reflux following laparoscopic Nissen fundoplication who then underwent Stretta (RLNF + S) would demonstrate similar or greater improvements to that of a refractory reflux patient who only had Stretta (RR + S). A safe, effective, and long-term means of aiding reflux symptoms in refractory LNF patients merit a clinical consideration as a viable alternative treatment to LNF reoperation. The aim of this study was to prospectively assess and compare long-term patient-reported outcomes of the Stretta procedure in refractory patients with and without previous LNF.

Methods

Study design and end points

The study was designed as a 10-year, open-label, prospective comparative cohort analysis of two subsets of GERD patients (RLNF + S vs. RR + S) with inadequate symptom control despite minimum twice-daily PPI therapy who underwent the Stretta procedure. Primary end point was to demonstrate improved patient-reported outcomes (GERD-HRQL, satisfaction, and medication use) in patients with RLNF + S before and throughout 10 years after Stretta. Secondary end points were to compare patient-reported outcomes between RLNF + S and RR + S patient subsets after Stretta throughout 10 years of follow-up, to allow for investigation and determination of long-term efficacy of Stretta contingent upon history of previous LNF intervention.

Patients

From August 2000–June 2002, 149 patients underwent Stretta and were followed prospectively for 10 years. Eligible patients had daily recurring symptoms of heartburn and regurgitation despite twice-daily PPI use. GERD was confirmed by upper endoscopy revealing erosive esophagitis (Los Angeles grade A or higher). If no erosive esophagitis was present, GERD was confirmed by abnormal esophageal acid exposure with ambulatory esophageal pH testing. Patients with erosive esophagitis were maintained on medical therapy until healed before undergoing the Stretta procedure. Eligible RLNF + S patients had endoscopically appearing intact full wrap LNF as well as the aforementioned criteria. Most patients had normal esophagogastric anatomy. A small subset of patients demonstrated large (>3 cm) hiatal hernia [5]. Patients with short-segment Barrett's were included. Exclusion criteria were stenosis, stricture, or ulceration of the pylorus, pregnancy, poor surgical risk (ASA grade > III), achalasia, previous non-Nissen esophageal or gastric surgery, scleroderma-type collagen vascular disease, or severe uncontrolled medical illness.

This study was approved by the human subject study review board at the Heartburn and Reflux Study Center.

Study procedures

Prior to undergoing Stretta (on- and off-medication), patients completed the Velanovich reflux severity symptom assessment (GERD-HRQL questionnaire), a reliable and practical health-related quality-of-life scale for GERD [14]. This validated questionnaire assesses current satisfaction and overall heartburn severity, specifically evaluating: (1) heartburn lying down, standing, and post-meals, (2) effect on diet, (3) sleep impairment, (4) difficulty swallowing, (5) painful swallowing, (6) bloating/gassy feelings, and (7) impact of medication need on daily activities. Responses are ranked 0–5; higher scores indicate more severe symptoms. Patient satisfaction is rated 0–5, with higher scores indicating greater satisfaction. Medication usage was assessed via standardized GERD medication scoring, capturing type, dose, and frequency of use, scale 0–20, with lower scores indicative of as needed or no medication use. At 0.5, 1, 2, 3, 4, and 10 years after the Stretta procedure, an attempt was made to contact all patients in the 149-patient cohort. Unless patients were determined to be deceased or unwilling to participate, GERD-HRQL questionnaire, overall patient satisfaction, and GERD medication assessment were obtained off-medication. Various modes of communication, primarily in-office interviews as well as when necessary, via telephone interview, direct mail, and email were utilized.

The Stretta procedure was performed by a single practitioner, as an outpatient at the Heartburn and Reflux Study Center in Baltimore, Maryland. All received conscious sedation with a combination of midazolam and fentanyl. Using standard technique [15], a diagnostic upper endoscopy was performed to locate the gastroesophageal junction as well as possible hiatal hernia. Upon endoscope removal, a wire-guided flexible RF delivery catheter (a balloon-basket assembly with four treatment elements positioned radially around balloon) is passed transorally and then positioned within the gastroesophageal junction. After appropriate balloon inflation (<2.5 ψ), the treatment elements are deployed 3–4 mm into the lower esophageal sphincter muscle, where energy is delivered in a series of thermal treatments at four levels in two positions (distal esophagus) and at two levels in three positions (gastric cardia). The monitoring of temperature and impedance at each treatment element ensured safe and precise RF delivery to only the muscularis propria. As radiofrequency energy is applied during the procedure, chilled water is irrigated from the catheter to the esophageal mucosa to prevent damage. After completion of the procedure and catheter removal, the endoscopy 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 medications are maintained for 6–8 weeks after the procedure to maintain baseline and allow time for complete procedural effect, and prevent potential complications.

Statistical methods

End point patient-reported outcome data (GERD-HRQL, satisfaction, and medication scores) were summarized at each time point using medians and interquartile ranges for respective RLNF + S and RR + S subsets using only patients that completed a full 10-year follow-up. Primary analyses were preformed using Wilcoxon signed rank and Mann–Whitney *U* testing where appropriate. A subanalysis comparing patients lost to follow-up at 10 years to both RLNF + S and RR + S subsets was conducted at baseline (off- and on-medication) as well as at 0.5, 1, 2, 3, and 4 years by performing a Kruskal–Wallis *H* test in effort to reduce the potential of type I statistical error. Baseline characteristics were analyzed utilizing Chi-squared or Student's unpaired *t* test for comparison of categorical or continuous variables, respectively. A p value below 0.05 was regarded as statistically significant. Statistical analysis was performed using SPSS 24.0 (SPSS, Chicago, IL, USA).

Results

Patient characteristics

There were 149 patients who underwent Stretta which reached the 10-year follow-up evaluation cutoff. Of these, 50 did not complete 10-year follow-up questionnaires or phone surveys, (36 could not be contacted, 11 were deceased of natural causes or non-gastrointestinal-related disease, and 3 declined). A total of 99 remaining patients, who completed all time points up to 10 years, represent the respondent cohort. One patient in the RLNF + S group reported medication score, however, did not complete GERD-HRQL and satisfaction at 10 years. Patients were then divided into two subpopulations according to history of previous LNF: RLNF + S ($n = 18$) and RR + S ($n = 81$). Study population baseline characteristics are reported in Table 1. Baseline characteristics comparing RLNF + S, RR + S, and patients lost to follow-up at 10 years including: age, sex, weight, medication use, lower esophageal sphincter pressure, and hiatal hernia prevalence demonstrated no significant differences ($p > 0.05$) with the exception of gastric emptying time at 90 and 120 min ($p < 0.05$). Despite this difference, the average gastric empting results were normal in all subgroups.

Table 1 Study population baseline characteristics

	Respondent cohort	RLNF + S	RR + S	Lost to follow-up	*p* value
Number of patients	99	18	81	50	–
Male	57 (58)	8 (44)	32 (40)	20 (40)	0.988
Female	42 (42)	10 (56)	49 (60)	30 (60)	–
Mean age (SD)	50 (13.5)	51 (11.5)	49.5 (14)	49.9 (16)	0.897
Age range	19–77	28–75	19–77	16–81	–
Mean weight (SD)	78.5 (19)	76 (10)	79 (20.5)	80 (18)	0.810
Weight range	43–155	63.5–91.5	43–155	46–122	–
Mean BMI (SD)	28 (6.5)	27 (3.5)	28.5 (7)	29.8	0.530
BMI range	18.8–47.6	21–35	18.8–47.6	18.7–41	–
BID PPI	99 (100)	18 (100)	81 (100)	50 (100)	–
BID PPI + H_2RAs	46 (46)	8 (44)	38 (47)	18 (36)	0.476
Mean LESP	21.6	21.2	21.6	16.8	0.117
GES mean % emptied 90 min	57.2	62.5	56.1	67.9	0.020
GES mean % emptied 120 min	70.4	77.7	68.9	81.6	0.017
Hiatal hernia prevalence	19 (19)	1 (5.5)	18 (22)	7 (14)	0.177

Data are presented as *N* (%) unless otherwise indicated

SD standard deviation, *BMI* body mass index, *PPI* proton pump inhibitor, *H_2RAs* histamine type 2 receptor antagonist, *LES* lower esophageal sphincter, *GES solid-phase nuclear* gastric emptying scan, *RLNF + S* refractory laparoscopic Nissen fundoplication who then underwent Stretta, *RR + S* refractory reflux who only had Stretta, *Lost to follow-up* at 10 years

* $p < 0.05$ is statistically significant

Procedural information

Mean procedure time was 25 min with no immediate adverse events occurring in either patient subset. A total of 149 Stretta devices were used without failure or malfunction. Patients were discharged within 60 min on a diet restricting nuts, chips, or pretzels for 24 h. Prior medication continued without dosing change. Minor transient side effects lasting under 2 weeks were experienced by 50 % of RLNF + S patients and 56 % of RR + S patients. The most common symptoms were chest pain (44 %) and dysphagia (11 %) in the RLNF + S group and chest pain (46 %) and abdominal pain (9 %) in the RR + S subset. There were two episodes of minor proximal gastric bleeding in one patient diagnosed by gastroscopy from the RLNF + S subset within 30 days after Stretta. The bleeding was self-limited, required no intervention or transfusion, and resolved with the reinstitution of PPIs. No additional short-term adverse events occurred, and throughout the 10-year study period no long-term adverse events developed in either subset. Of the 99 patients in the respondent cohort, 12 were unsatisfied with initial results and requested a second antireflux procedure. No patient with RLNF + S requested a second Stretta or LNF reoperation. Within the RR + S subset, one patient underwent a LNF and 11 a second Stretta procedure.

Efficacy and end points

Both RR + S and RLNF + S subsets demonstrated significant improvement both off- and on-medications at all follow-up time points ≥6 months to 10 years after Stretta ($p < 0.05$). In the 18 RLNF subsets, significant improvements were noted to 10-year post-procedure: Median GERD-HRQL score for RLNF + S improved from 36 (baseline off-medication) to 7 at 10 years ($p < 0.001$, Fig. 1A). Median satisfaction score for RLNF + S improved from 1 (baseline off-medication) to 4 at 10 years ($p < 0.001$, Fig. 1C). Median medication score for RLNF + S decreased from 7 (baseline on-medication) to 6 at 10 years ($p = 0.040$, Fig. 1E). The greatest decrease in medication score in the RLNF + S subset was a score of 4 demonstrated at 0.5, 1, and 4 years ($p = 0.002$, <0.001, 0.002, Fig. 1E). Utilizing a baseline of "on-medications" also demonstrated significant median improvement in GERD-HRQL and satisfaction at 10 years ($p < 0.001$). These improvements occurred in all medication use subsets, including those that decreased from baseline BID PPI therapy to off-medication ($n = 2$), or QD PPI ($n = 9$), as well as those that remained on BID PPI ($n = 6$). Six patients remained on twice-daily PPI with mean GERD-HRQL improving from 37.83 to 15.67 and satisfaction from 1 to 3.67. Nine patients (50 %) still required once-daily PPI with mean GERD-HRQL decreasing from 29.78

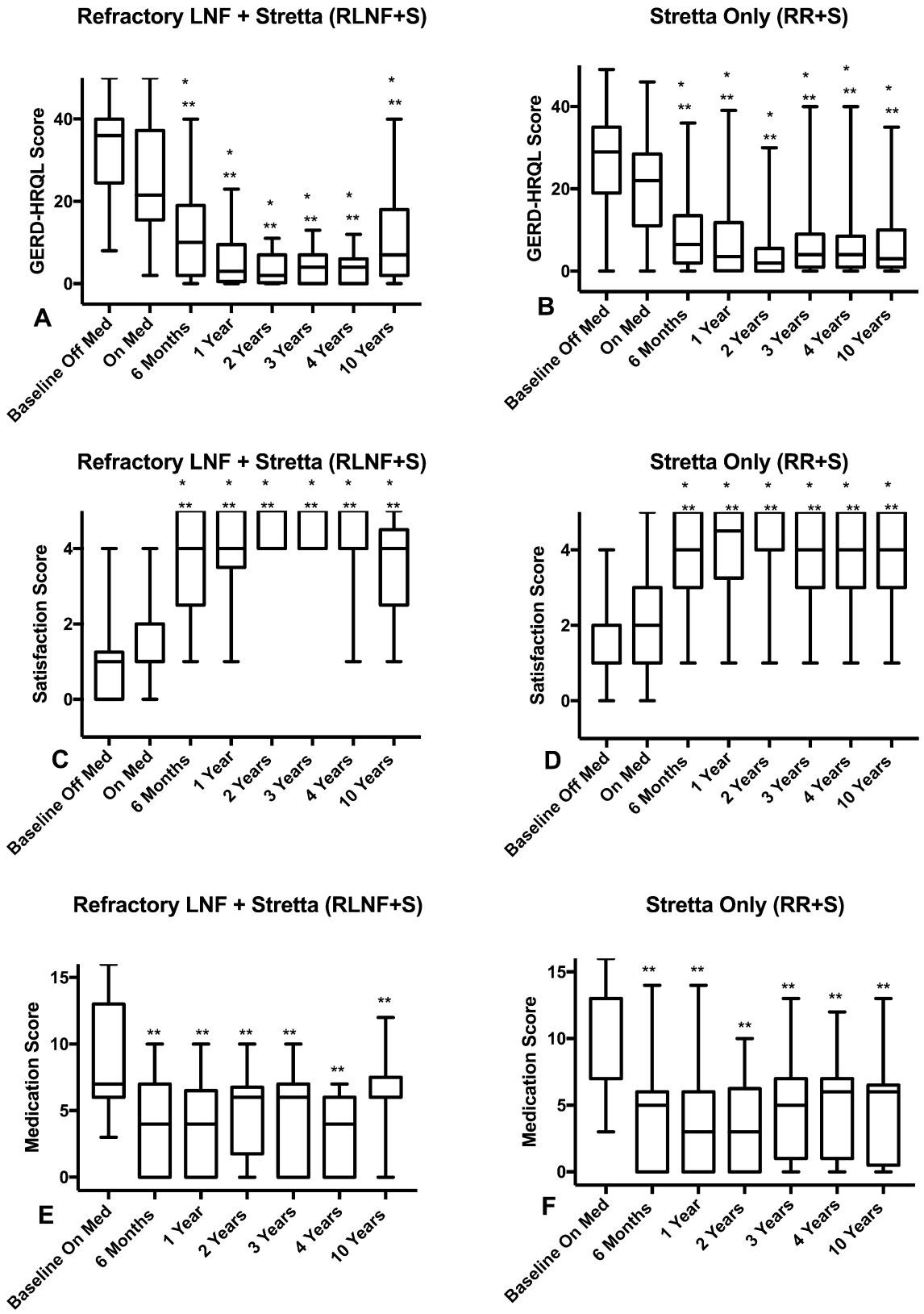

Fig. 1 Median (*horizontal line inside box*), interquartile range (*box*), maximum and minimum values (*vertical line*), for GERD-HRQL, satisfaction, and medication score in those with refractory laparoscopic Nissen fundoplication with subsequent Stretta [RLNF + S] (**A**, **C**, **E**) and patients with standard refractory reflux who only received Stretta [RR + S] (**B**, **D**, **F**). $*p < 0.016$ compared with baseline off-medication. $**p < 0.041$ compared with baseline on-medication. $p < 0.05$ is statistically significant

to 9.89 and satisfaction from 1 to 3.67. Similarly within the 81 RR + S subset that only received Stretta, significant improvements were also seen at 10-year post-procedure: Median GERD-HRQL score for RR + S improved from 29 (baseline off-medication) to 3 at 10 years ($p = 0.001$, Fig. 1B). Median satisfaction score for RR + S improved from 1 (baseline off-medication) to 4 at 10 years ($p = 0.001$, Fig. 1D). Median medication score for RR + S improved from 7 (baseline on-medication) to 6 at 10 years ($p = 0.001$, Fig. 1F).

Secondary end points demonstrated that RLNF + S and RR + S groups trended together consistently throughout 10 years (Table 2) with no significant differences in GERD-HRQL, satisfaction, and medication use at all follow-up ≥6 months to 10 years after Stretta ($p > 0.05$). Specifically at 10 years, no significant differences were noted between the subsets regarding medication use ($p = 0.088$), patient satisfaction ($p = 0.573$), and GERD-HRQL ($p = 0.075$).

The subanalysis comparing the 50 subjects lost to follow-up at 10 years, to both RLNF + S and RR + S subsets at baseline (off- and on-medication) as well as at 0.5, 1, 2, 3, and 4 years, found there were no significant differences in GERD-HRQL, satisfaction scores, and medication scores at any time point ($p > 0.05$) except at 6 months for GERD-HRQL ($p = 0.024$) and satisfaction ($p = 0.018$). Additionally, this group of subjects lost to follow-up demonstrated significant improvements from baseline (off- and on-medication) to 0.5, 1, 2, 3, and 4 years for GERD-HRQL, satisfaction, and medication scores ($p < 0.05$).

One patient in the RLNF + S group had prior Barrett's esophagus defined as positive metaplasia on four quadrant biopsies at baseline; however, metaplasia was not observed at 10-year follow-up endoscopy.

Discussion

The Stretta procedure resulted in safe, significant, and sustained improvement of patient-reported outcomes in RLNF + S patients throughout a decade of follow-up with only slight variation noted between RLNF + S and RR + S subsets. In a small cohort of patients with RLNF + S, the Stretta procedure consistently resulted in significantly improved patient-reported outcomes from baseline throughout 10 years including: GERD-HRQL, satisfaction, and medication requirements. RLNF + S and RR + S subsets demonstrated no significant differences between subsets regarding GERD-HRQL, patient satisfaction, and medication requirements throughout follow-up

Table 2 Comparison of medians from baseline throughout 10 years for both subgroups

	Subgroup	GERD-HRQL score			Satisfaction score			Medication score		
		(*n*)	Median (IQR)	*p* value	(*n*)	Median (IQR)	*p* value	(*n*)	Median (IQR)	*p* value
Off-medication	RLNF + S	18	36 (24.5–40)	0.062	18	1 (0–1.25)	0.028*	N.A.	N.A.	
	RR + S	81	29 (19–35)		81	1 (1–2)				
On-medication	RLNF + S	18	21.5 (15.5–37.25)	0.194	18	1 (1–2)	0.063	18	7 (6–13)	0.696
	RR + S	81	22 (11–28.5)		81	2 (1–3)		81	7 (7–13)	
6 months	RLNF + S	17	10 (2–19)	0.336	17	4 (2.5–5)	0.632	17	4 (0–7)	0.745
	RR + S	80	6.5 (2–13.5)		80	4 (3–5)		80	5 (0–6)	
1 year	RLNF + S	17	3 (0.5–9.5)	0.93	17	4 (3.5–5)	0.575	17	4 (0–6.5)	0.761
	RR + S	80	3.5 (0–11.75)		80	4.5 (3.25–5)		80	3 (0–6)	
2 years	RLNF + S	12	2 (0.25–7)	0.891	12	5 (4–5)	0.579	12	6 (1.75–6.75)	0.201
	RR + S	65	2 (0–5.5)		65	5 (4–5)		66	3 (0–6.25)	
3 years	RLNF + S	11	4 (0–7)	0.391	11	4 (4–5)	0.223	11	6 (0–7)	0.838
	RR + S	59	4 (1–9)		59	4 (3–5)		59	5 (1–7)	
4 years	RLNF + S	11	4 (0–6)	0.496	11	4 (4–5)	0.442	11	4 (0–6)	0.271
	RR + S	58	4 (1–8.5)		58	4 (3–5)		58	6 (1–7)	
10 years	RLNF + S	17	7 (2–18)	0.075	17	4 (2.5–4.5)	0.573	18	6 (6–7.25)	0.088
	RR + S	81	3 (1–10)		81	4 (3–5)		81	6 (0.5–6.5)	

Median comparisons of GERD-HRQL, satisfaction, and medication between RLNF + S (refractory laparoscopic Nissen fundoplication who then underwent Stretta) and RR + S (refractory reflux who only had Stretta) from various time points through 10 years

IQR interquartile range, *GERD-HRQL* gastroesophageal reflux disease health-related quality of life

* $p < 0.05$ is statistically significant

points over a 10-year period. RLNF + S and RR + S subsets trended together in GERD-HRQL, satisfaction, and medication scores.

Although mostly successful, LNF reoperation rates range widely from 3 to 30 % calling into question the absolute definition of failure and whether objective, subjective, or both parameters delineate successful patient outcomes [16]. To date, seven 10-year LNF follow-up studies appear in the literature [2, 17–22]. At 10 years, daily antisecretory drug therapy usage in these studies ranged from 14 to 40.9 % of patients [20, 21]. The largest cohort, comprising 250 patients, demonstrated that 21 % of patients required regular antireflux medication and 17 % of patients required revision operations within 10 years [2]. Recurrent hiatal hernia, dysphagia, and recurrent reflux were the most common indications for revision [2]. Reported rates of satisfaction in LNF patients were 83–96 % [2, 20]. Approximately 80 % reported they would opt for surgery again [21, 22]. Only one study measuring quality of life utilizing a validated visual analog scale after esophageal surgery found a significant increase in quality of life from baseline to 3 months as well as 10 years after surgery [22].

LNF reoperation is associated with greater postoperative morbidities [5]. Instead of LNF reoperation often a Roux-en-Y gastric bypass is performed with both procedures having high morbidity and mortality [23]. Stretta may offer a critical option to patients who do not wish or do not qualify for additional invasive surgery. Other endoluminal therapies carried out to correct refractory LNF have been shown to be problematic when redo is later considered. EsophyX (EndoGastric Solutions) or transoral incisionless fundoplication has been associated with a high risk of gastric injury during LNF and a relatively high rate of post-fundoplication dysphagia [24, 25]. Similarly, LNF after failed EndoCinch gastroplication (Bard) was associated with troublesome dysphagia [26]. This is converse to LNF after Stretta of which no complications or risks have been reported in pediatric and adult populations [25, 27]. Islam noted, in line with Stretta's mechanism of action, performing LNF after Stretta encountered no difficulty or scar formation, which is consistent with our findings. No surgical complications or postoperative symptoms such as dysphagia were present in the RLNF + S subgroup.

As no medical, endoscopic, or surgical treatment can completely control or reverse reflux, this investigation of 18 RLNF + S patients demonstrates that symptomatic improvements were seen up to 10-year post-Stretta. Without surgical reintervention, safety concerns, postoperative morbidities, or treatment failures, marked improvements were seen in all measured parameters. The one patient with Barrett's esophagus in the RLNF + S group also showed regression of the disease. Previous findings in GERD patients without LNF demonstrate similar regression of Barrett's esophagus with Stretta alone. Despite 50 % of the RLNF + S patients still using daily acid-suppressing agents at 10 years, significant improvements and/or normalization of GERD symptoms and patient satisfaction were noted in these patients, who at baseline were uncontrolled requiring at minimum twice-daily PPI. Alternative to a lifetime of medication use, which is costly and requires discipline to remain compliant, patients may chose to undergo the Stretta procedure or LNF reoperation. Patients choosing LNF reoperation and RLNF + S have shown an approximately similar satisfaction of 82 and 86 %, respectively [13, 28].

The physiological basis for Stretta is that it anatomically corrects lower esophageal sphincter incompetence by means of radiofrequency stimulation and subsequent restoration of natural physiological barrier function, and therefore, patients with RLNF + S would respond similarly to those with RR + S in long-term follow-up. LNF primarily corrects for the extrinsic lower esophageal sphincter defects, while the use of Stretta corrects for intrinsic esophageal sphincter defects only. Therefore, a Stretta procedure performed on patients with LNF can be used to address both components of the lower esophageal sphincter, providing additive results with lower rates of complication [13, 28]. Only two prior short-term, small subset studies have investigated outcomes of Stretta after LNF of which both demonstrated significant decreases in symptoms [13, 27]. In an exploratory investigation of eight patients by McClusky et al. [13], it was determined that the Stretta procedure after refractory LNF is feasible, safe, and effective in reducing symptom severity 1-year post-procedure. Within a pediatric subset of six, with some patients having a previous history of three fundoplications, Islam et al. [27] found that GERD symptoms improved significantly at 6 months with three patients eliminating reflux medications entirely. Our results further confirm the findings in these studies demonstrating significant improvements in the RLNF + S subset at both 6 months, 1 year, and out to 10 years. We noted that at one-year post-Stretta, 66 % of the RLNF + S cohort eliminated PPI requirements entirely in a group of patients that at baseline was on at minimum twice-daily PPI. Islam's pediatric study also demonstrated that a patient with recurrent symptoms successfully underwent a second Stretta with good initial results. Double-dose Stretta therapy, an option for patient's unsatisfied with their first Stretta, produces a more frequent normalization of GERD-HRQL and a reduction in both the use of PPI medications and esophageal acid exposure [29]. In our study, no RLNF + S group patients received a second Stretta or LNF reoperation. Of these 18 patients, high levels of satisfaction and symptomatic improvement without reintervention suggest Stretta's utility as a safer

alternative to LNF reoperation as a means of aiding long-term GERD control.

Limitations of this study include the following: (1) This is a non-randomized, single-center, open-label prospective comparative trial; (2) there is no inclusion of long-term pH and motility data; (3) there is only a subset of 18 patients in the (RLNF + S) subset; (4) 50 patients (which would have all been comprised of the RR + S group) were lost to follow-up and unavailable at 10 years; and (5) the data presented are only 10-year data, and longer-term data may be needed to show continued durability of response. Despite the small subset of data, these 18 patients represent not only the largest cohort, but also a decade long data set, which has never been previously published. In addition, when taking into account subjects lost to follow-up, compared to the RR + S and RLNF + S groups there were no statistical differences noted in the 1-, 2-, 3-, and 4-year follow-up periods, reducing the potential of type I statistical error within the analysis. Although at 10 years, 50 % of RLNF + S remained on reduced doses of regular antireflux medication, there were significant improvements in satisfaction and control of GERD symptoms, which were uncontrolled at baseline.

In summary, the comparative cohort analysis demonstrated long-term safety, efficacy, and durability resulting directly from the effects of the Stretta procedure in refractory LNF patients, which were similar to results in non-operated refractory reflux patients. Given the high complication and low success rates of reoperation in LNF patients, and the growing concerns about the safety of chronic PPI medication for reflux, based upon these data, Stretta should potentially be considered as the primary rescue procedure in patients with refractory reflux after LNF, with chronic medication use as a secondary alternative.

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Compliance with ethical standards

Disclosure Dr. Mark D. Noar has received honoraria for speaking and training for Mederi Therapeutics Inc., and has no other conflicts of interest or financial ties to disclose. Patrick J. Squires and Sulman R. Khan have no conflicts of interest or financial ties to disclose.

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