

# Stretta procedure versus proton pump inhibitors for the treatment of nonerosive reflux disease

## A 6-month follow-up

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### Abstract

To compare the Stretta procedure with proton pump inhibitors for the treatment of nonerosive reflux disease (NERD).

From July 2018 to April 2019, patients diagnosed with NERD and referred for treatment were enrolled. They were treated with either Stretta procedure or proton pump inhibitor (PPI) medication and followed-up for 6 months. The symptom control, quality of life, lower esophageal sphincter (LES) pressure, 24-hour pH parameters, PPI usage and satisfaction rate were evaluated. The complications were assessed. The outcomes of the 2 groups were analyzed and compared.

Twenty-eight patients in the Stretta group and 21 patients in the PPI group completed the 6-month follow-up. No severe adverse events occurred in both groups. Both interventions were effective in improvement of symptom and quality of life. The symptom score improvement was significantly superior in the Stretta group compared to the PPI group ( $6.3 \pm 3.4$  vs  $8.5 \pm 4.1$ ,  $P = .03$ ). LES pressure increased significantly in the Stretta group compared to the PPI group ( $14.2 \pm 4.4$  mm Hg vs  $10.0 \pm 4.0$  mm Hg,  $P < .01$ ). Although both interventions improved 24-hour pH parameters, including number of acid episodes ( $P = .27$ ), acid exposure time ( $P = .39$ ), and DeMeester score ( $P = .28$ ), no difference was found between the 2 groups. Complete PPI cessation rate (82% vs 52%,  $P = .03$ ) as well as satisfaction rate (89% vs 57%,  $P = .02$ ) was much higher in Stretta group than those in the PPI group.

The Stretta procedure was safe and effective in the short term for the management of NERD. The Stretta procedure resulted in higher LES pressure and achieved better improvement of symptom control and PPI cessation than did PPI in the short term.

**Abbreviations:** AET = acid exposure time, GERD = gastroesophageal reflux disease, LES = lower esophageal sphincter, NERD = nonerosive reflux disease, PPI = proton pump inhibitor, RDQ = reflux disease questionnaire, RE = reflux esophagitis, RF = radiofrequency, SAE = serious adverse event, SCJ = squam-columnar junction, SMB = safety monitoring board.

**Keywords:** nonerosive reflux disease, proton pump inhibitor, radiofrequency therapy, Stretta

### 1. Introduction

Gastroesophageal reflux disease (GERD) is defined as a condition in which gastric contents reflux into the esophagus, causing troublesome esophageal or extraesophageal symptoms as defined by the Montreal definition.<sup>[1]</sup> GERD is typically divided into 3

subtypes: reflux esophagitis (RE), nonerosive reflux disease (NERD) and Barrett esophagus. NERD has been defined as the presence of acid reflux-related symptoms with no esophageal mucosal injury.<sup>[2]</sup> NERD is estimated to affect approximately 50% to 70% of the GERD patients in Western countries<sup>[3,4]</sup> and 60% to 90% in China.<sup>[5]</sup> Furthermore, NERD patients have been reported to be less responsive to traditional proton pump inhibitor (PPI) treatment.<sup>[6]</sup> It has been reported that the symptomatic response rate to once-daily PPIs in patients with NERD is only 37%.<sup>[7,8]</sup> A partial response can occur since PPI treatment does not address an incompetent sphincter or prevent reflux. Consequently, some NERD patients seek alternative treatment if their quality of life is compromised.<sup>[9]</sup>

Radiofrequency (RF) energy application to the lower esophageal sphincter (LES) (Stretta procedure) could be an option for refractory NERD patients who are not willing to take PPIs or undergo surgery (fundoplication). Previous studies have reported that the Stretta procedure could improve both subjective and objective outcomes for patients with GERD.<sup>[10]</sup> However, data for the responsiveness of NERD patients to the Stretta procedure are scant and certainly insufficient for comparing the procedure with the traditional effective medical and/or surgical treatments. We hypothesized that NERD patients could be more appropriate candidates than other GERD patients for the Stretta procedure since hiatus hernia is less common with NERD patients,<sup>[11]</sup> and the lack of mucosal erosion indicates a lower possibility of complications. This study aimed to explore the clinical outcome

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of the Stretta procedure by comparing it to classical PPI treatment for the management of NERD.

## 2. Materials and methods

Patients with GERD, seeking care in the Department of Digestive Disease in Suining Central Hospital, Sichuan, China, were recruited consecutively between July 2018 and April 2019. The inclusion criteria were as follows:

- (1) NERD diagnosed by acid exposure time (AET) >6% or DeMeester score  $\geq 14.7$  with symptom correlations  $\geq 50\%$ <sup>[12]</sup>;
- (2) endoscopically evidenced absence of esophagitis or Barrett esophagus<sup>[12]</sup>;
- (3) responsiveness to PPIs defined as a  $\geq 50\%$  reflux symptom control after 2 weeks of standard PPI treatment<sup>[13]</sup>;
- (4) lower than normal LES pressure detected by high-resolution esophageal manometry;
- (5) no hiatal hernia or small (<2 cm) hiatal hernia;
- (6) a chronic history of persistent typical symptoms of heartburn and/or regurgitation despite daily use of PPIs; and
- (7) age between 18 and 70 years.

The exclusion criteria were as follows:

- (1) under 18 or over 70 years of age;
- (2) pregnant;
- (3) achalasia or other primary esophageal motility disorders;
- (4) no response to PPI treatment, which was defined as <50% reflux symptom control after 2 weeks of standard PPI treatment<sup>[13]</sup>;
- (5) sliding hiatal hernia >2 cm;
- (6) collagen vascular disease or other autoimmune disease;
- (7) previous esophagogastric surgery;
- (8) coagulation disorders or contradictions for surgery; or
- (9) severe uncontrolled medical illness.

All patients were symptomatically stable and generally medically fit for antacid or endoscopic antireflux procedures. Patients were allocated into the PPI treatment group or Stretta procedure group according to their own preferences and physical conditions based on the following assumptions: PPI medication focused on reducing acid which may require a long treatment time, even life-long medication but does not cause other damage or complications to the upper gastrointestinal tract. The Stretta procedure is a minimally invasive procedure that aims to create a 1-way antireflux barrier, with a greater possibility of injury and potential complications but a lower recurrence rate.

## 3. Interventions

### 3.1. PPI group

The patients assigned to the medical treatment group received the same PPI dose they received previously to control their symptoms. Their symptoms were assessed at baseline. If a patient's symptoms had been well controlled in the past month, the PPI regimen was decreased by 1 step, and the effect was reassessed 1 month later. If a patient's symptoms were poorly controlled in the past month, the PPI regimen was increased by 1 step. This approach provided a standardized treatment algorithm, consistent with good clinical practice. Patients were carefully instructed on the importance of adherence to the

treatment regimen. Patients were free to use over-the-counter antacids. The use of all drugs was recorded carefully.

### 3.2. Stretta group

Patients were allocated to the Stretta procedure group. The Stretta procedure was performed using the Stretta system (Curon Medical Inc., Sunnyvale, CA) by 1 skilled endoscopist in an operation room. The endoscopist had experience with more than 50 Stretta cases. The Stretta procedure catheter uses a balloon basket assembly to deploy 4 nitinol needle electrodes into the muscular layer of the esophageal wall. RF energy delivered by the needle electrodes causes a thermal reaction in the LES with controlled temperature elevation to 85°C, while continuous mucosal irrigation with chilled water prevents the development of stricture or ulceration. Deploying the needle electrodes at 5 mm levels above and below the squam-columnar junction (SCJ) produced 56 thermal lesions. Briefly, the procedure was performed under general anesthesia with endotracheal intubation by the anesthesiologist in the operating room. After endotracheal intubation, patients were placed in the left lateral position. A diagnostic upper endoscopy was performed carefully to inspect the esophagus and the cardia before the procedure. The exact distance from the incisor to the SCJ was carefully determined by the diagnostic endoscopy before the insertion of the Stretta catheter. Then, the endoscope was withdrawn, and the Stretta catheter was introduced orally using a guide wire. The Stretta catheter was passed over the guidewire and introduced into the esophagus, where it is positioned 1 cm above the SCJ. After appropriate inflation of the balloon, the electrode needles were deployed, and RF energy was delivered for 1 minute. Then, the needles were withdrawn, the balloon was deflated and the catheter was rotated 45°. The treatment elements were deployed 1 to 2 mm into the LES muscle, where energy is delivered in a series of thermal treatments at 4 levels in 2 positions (distal esophagus, which covers an area 1 cm above and 0.5 cm below the SCJ) and at 2 levels in 3 positions (gastric cardia, which is determined by 22 mL balloon inflation and 25 mL balloon inflation, respectively). Constant monitoring and feedback of temperature and impedance ensured that each treatment element was maintained safely within the target tissues. The mucosa was cooled by continuous mucosal irrigation with chilled water during the treatment. After completion of the procedure and catheter removal, the 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. Patients were kept in the hospital overnight and were generally discharged the next day on omeprazole 40 mg for 14 days to help mucosal healing. For the first 2 weeks, patients were asked to consume a liquid and/or soft food diet. A regular diet was reinstated 2 weeks following the procedure.

We also suggested that lifestyle modifications (elevating the head during bedtime, avoiding fatty foods or eating close to bedtime, eating more frequent smaller meals, and reducing cigarette, alcohol, and caffeine consumption) should be adopted for all patients.

### 3.3. Outcome assessments

The primary outcome measure of this study was the frequency and severity of symptoms and quality of life, which was evaluated by 2 standard questionnaires:

- (1) the reflux disease questionnaire (RDQ).<sup>[14]</sup> The RDQ is a 12-item self-administered questionnaire designed to assess symptom frequency and severity in 3 dimensions corresponding to heartburn, regurgitation, and dyspepsia symptoms. Responses are scored on a 6-point scale, with higher scores indicating more severe or frequent symptoms. A validated Chinese-language version of the RDQ was used in this study.<sup>[15]</sup>
- (2) The SF-36 Health Survey, which is the most commonly used generic health-related quality of life test. The original answers obtained for the questions on the SF-36 questionnaire were recoded and scored using the original 0 to 100 scoring algorithms and then averaged using their respective scales and forms as per the instructions. Three summarized measures were calculated as follows: the total average SF-36 survey score, the physical health component, and the mental health component.<sup>[16]</sup>

Changes in RDQ scores and SF-36 scores (from baseline to 6 months after the corresponding treatment) were then compared between the 2 groups.

The second outcome measure was LES pressure and 24-hour pH monitoring results, including acid reflux episodes, AETs, and DeMeester scores.

The third outcome measure was PPI usage and satisfaction status after the corresponding treatment. These were collected through a questionnaire survey consisting of

- (1) Are you dependent on PPIs? The answers were categorized as completely, on-demand and daily;
- (2) Are you satisfied with the treatment? The answers were categorized as yes or no.

The questionnaires were prepared in simplified Chinese and administered to the subjects before the Stretta procedure and 6 months after the Stretta procedure, respectively.

### 3.4. Adverse events and safety

All adverse events were scrutinized by a safety monitoring board (SMB). The SMB consisted of a gastrointestinal physician and a gastroenterologist not involved with the performance of the study. The SMB used clearly specified criteria to determine the seriousness of the adverse event and its relationship to the medical or Stretta procedure. A serious adverse event (SAE) was predefined as any event resulting in any of the following outcomes: death, a life-threatening event that requires inpatient hospitalization or prolongation of existing hospitalization or persistent disability/incapacity.<sup>[17]</sup> All SAEs were reported immediately to the investigators, and appropriate therapy or the continued participation of the patient was discussed. Any SAEs were reported to the institutional research ethics committees and the patient's referring physician.

### 3.5. Statistical methods

All analyses were performed using SPSS software (version 17.0; SPSS, Chicago, IL). Data with normal distributions are expressed as the mean  $\pm$  standard deviation, whereas data with skewed distributions are expressed as median values (interquartile ranges). Normality was assessed by the Kolmogorov–Smirnov test. Data were analyzed by the independent/paired-sample Student *t* test or nonparametric tests based on the normality of data distribution. Independent-sample *t* test and Mann–Whitney

*U* test were performed for independent samples in the Stretta and PPI groups, the paired-sample *t* test and the Wilcoxon test for within-group paired samples. Differences were considered significant when  $P < .05$ .

## 4. Results

### 4.1. Patient characteristics

Of the 618 patients screened, 63 were eligible for the study. However, 8 patients refused to take part in the study immediately after they were screened. A total of 55 consecutive patients were enrolled prospectively and assigned to the study over 6 months. Of these, 32 patients were treated using the Stretta procedure, while the other 23 patients were treated with a standard dose of PPIs once daily. Of the 55 patients, 6 patients dropped out and could not be contacted at 6 months after the corresponding treatment (4 patients in the Stretta group and 2 patients in the PPI group). For the 6-month assessment, 49 patients were ultimately available (28 patients in the Stretta group, 21 patients in the PPI group) (Fig. 1). The baseline characteristics of the 2 groups are presented in Table 1.

### 4.2. Safety

The Stretta procedure was successful in all patients. No severe adverse events occurred during the procedure or the 6-month follow-up period. Mild adverse events occurred in 4 patients (12.5%, 4/32) after the procedure. Two patients (6.2%) complained of sore throat in the first 24 hours after the Stretta procedure. One patient (3.1%) suffered from mild fever, and 1 patient (3.1%) complained of severe bloating and vomiting 11 days after the procedure. Gastroparesis was documented after a computed tomography scan. All of these adverse events were mild and alleviated with medication. Only the patient with gastroparesis was re-hospitalized, and their symptoms were alleviated after 2 days of fasting and water deprivation with parenteral nutrition. No adverse events occurred in the PPI group.

## 5. Efficacy

### 5.1. Subjective assessments

At the 6-month follow-up, compared with baseline values, both interventions were effective in reducing total symptom scores, as evaluated by the RDQ. The scores ranged from  $17.3 \pm 5.0$  to  $6.3 \pm 3.4$  in the Stretta group and from  $16.8 \pm 4.7$  to  $8.5 \pm 4.1$  in the PPI group ( $P < .01$ ). Comparing the Stretta group to the PPI group, no difference was found between the baseline symptom scores ( $17.3 \pm 5.0$  vs  $16.8 \pm 4.7$ ,  $P = .69$ ). However, the symptom score was significantly lower in the Stretta group than in the PPI group at the 6-month follow-up ( $6.3 \pm 3.4$  vs  $8.5 \pm 4.1$ ,  $P = 0.03$ ) (Table 2).

Regarding the quality of life assessment, both interventions were effective in improving the total quality of life scores evaluated by SF-36 scores at the 6-month follow-up compared to the baseline values ( $P < .01$ ). No difference was found between the 2 groups in the baseline SF-36 scores ( $P = .96$ ). Although the total SF-36 scores were higher in the Stretta group than in the PPI group ( $607.2 \pm 135.1$  vs  $586.8 \pm 152.0$ ) at the 6-month follow-up, no statistical significance was found when comparing the 2 groups ( $P = .62$ ) (Table 2).

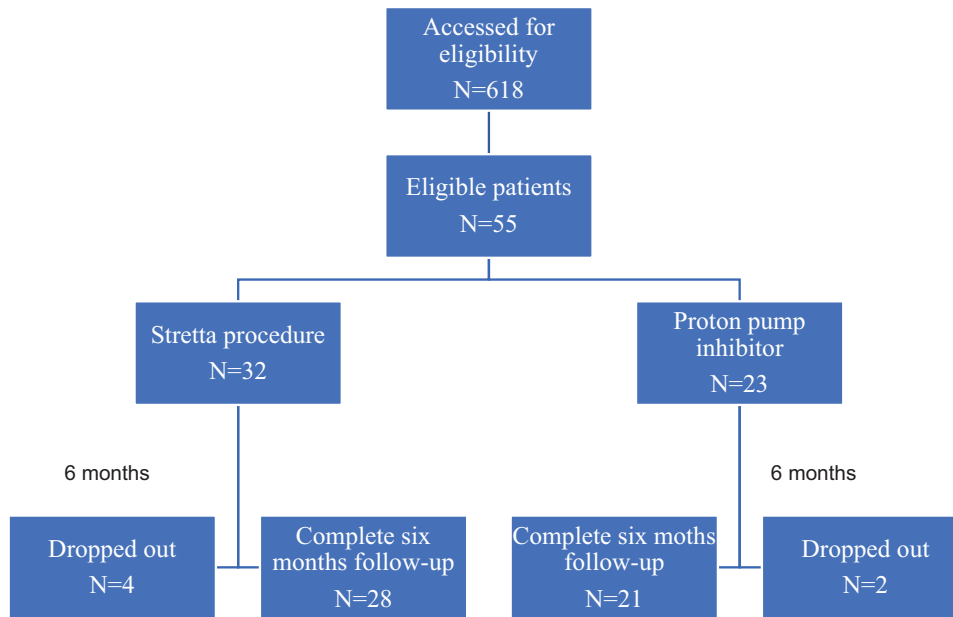


Figure 1. Flow chart on patients selected for the study.

5.2. Objective assessments

Regarding the LES pressure, as expected, there was a significant LES pressure increase in the Stretta group (from  $9.7 \pm 4.3$  mm Hg to  $14.2 \pm 4.4$  mm Hg,  $P < .001$ ), but there was no statistically significant change in the PPI group (from  $10.1 \pm 4.1$  mm Hg to  $10.0 \pm 4.0$  mm Hg,  $P = .89$ ) at the 6-month follow-up. Comparing the 2 groups, no difference was found between the 2 groups at baseline ( $9.7 \pm 4.3$  mm Hg vs  $10.1 \pm 4.1$  mm Hg,  $P = .76$ ), while the LES pressure was much higher in the Stretta group than in the PPI group at the 6-month follow-up ( $14.2 \pm 4.4$  mm Hg vs  $10.1 \pm 4.1$  mm Hg,  $P = .002$ ) (Table 3).

Regarding the 24-hour pH monitoring, at the 6-month follow-up, there was a statistically significant improvement in the number of acid reflux episodes, percentage of acid reflux into the esophagus and DeMeester scores based on 24-hour pH monitoring in both groups ( $P < .001$ ) (Table 3).

Comparing the PPI group with the Stretta group at baseline, no statistical significance was found regarding the number of acid reflux episodes (mean 60 vs mean 66,  $P = .38$ ), AETs (mean 8.0 vs mean 8.5,  $P = .13$ ), and DeMeester scores (mean 26.0 vs mean 31.7,  $P = .35$ ). At the 6-month follow-up, fewer acid reflux episodes (mean 23 vs mean 38,  $P = .27$ ), lower AETs (mean 4.2 vs mean 4.7,  $P = .39$ ), and DeMeester scores (mean 11.5 vs mean 15.0,  $P = .28$ ) were found in the PPI group than in the Stretta

group. However, there was no statistical significance ( $P > .05$ ) (Table 3).

5.3. PPI usage and patient satisfaction

All patients were taking PPIs at baseline.

At the 6-month follow-up, complete PPI cessation was achieved in 23 (82%) patients in the Stretta group and 11 (52%) patients in the PPI group. Two (7%) patients in the Stretta group and 6 (29%) patients in the PPI group were taking nondaily, on-demand PPIs. Another 3 (11%) patients in the Stretta group and 4 (19%) patients in the PPI group continued to take daily PPIs. The PPI cessation rate was significantly higher (82% vs 52%,  $P = .03$ ) in the Stretta group than in the PPI group (Table 4).

The satisfaction rate was significantly higher in the Stretta group than in the PPI group ( $P < .05$ ). Specifically, 25 out of the total 28 patients (89%) in the Stretta group responded with “yes,” while 12 out of the total 21 patients (57%) in the PPI group responded with “yes” in patients’ satisfaction surveys.

6. Discussion

As a large proportion of the patients with GERD, patients with NERD have been reported to be less responsive to PPI treatment,<sup>[6]</sup> leading to the development of various minimally invasive endoluminal therapies, such as the Stretta procedure, to give an alternative approach for the management of NERD. For the first time, we compared the Stretta procedure to PPI medication for the management of patients with NERD by using a short-term follow-up. We standardized the procedure and the endoscopist’s experience, optimized the medical therapy, and included only patients with NERD who responded to PPI therapy to evaluate the clinical outcome of the Stretta procedure.

Three major findings of this study were as follows:

- (1) When performed by an experienced endoscopist, the Stretta procedure is safe for the management of NERD;

Parameters	Stretta group	PPI group	P-value
Age, yr	45.4 ± 9.6	50.0 ± 8.5	.09
Male, n (%)	16 (57%)	13 (61%)	.74
BMI, kg/m <sup>2</sup>	22.1 ± 2.9	22.8 ± 3.4	.47
History of GERD, yr	4.4 ± 3.4	3.9 ± 2.4	.35
PPI treatment (%)	100%	100%	–

Differences were considered significant when  $P < .05$ . BMI = body mass index, GERD = gastroesophageal reflux disease, PPI = proton pump inhibitor.

**Table 2**  
The RDQ score and SF-36 score before and 6 mo after the corresponding treatments.

Score	Stretta group		PPI group		P-value
	Baseline	6-mo	Baseline	6-mo	
RDQ score	17.3 ± 5.0	6.3 ± 3.4	16.8 ± 4.7	8.5 ± 4.1	$P_1 < .001$ $P_2 = .69$ $P_3 = .03$
SF-36 score	546.1 ± 140.7	607.2 ± 135.1	543.7 ± 159.8	586.8 ± 152.0	$P_1 < .001$ $P_2 = .96$ $P_3 = .62$

Differences were considered significant when  $P < .05$ .

$P_1$  = baseline versus 6-mo,  $P_2$  = baseline versus baseline,  $P_3$  = 6-mo versus 6-mo, PPI = proton pump inhibitor, RDQ = reflux disease questionnaire.

**Table 3**  
The LES pressure and pH-metry before and 6 mo after the corresponding treatments.

Parameters	Stretta group		PPI group		P-value
	Baseline	6-mo	Baseline	6-mo	
LES pressure	9.7 ± 4.3	14.2 ± 4.4	10.1 ± 4.1	10.0 ± 4.0	$P_1 < .001$ $P_2 = .76$ $P_3 < .001$
Number of acid episodes	60 (30–99)	38 (0–80)	66 (32–90)	23 (2–73)	$P_1 < .001$ $P_2 = .38$ $P_3 = .27$
AET (%)	8.0 (4.5–20.2)	4.7 (0–13.2)	8.5 (5–16.7)	4.2 (0.4–8.6)	$P_1 < .001$ $P_2 = .13$ $P_3 = .39$
DeMeester score	26.0 (14.9–110.5)	15.0 (0.2–50.3)	31.7 (17.8–67.8)	11.5 (0.9–25)	$P_1 < .001$ $P_2 = .35$ $P_3 = .28$

Differences were considered significant when  $P < .05$ .

AET = acid exposure time, LES = lower esophageal sphincter,  $P_1$  = baseline versus 6-mo,  $P_2$  = baseline versus baseline,  $P_3$  = 6-mo versus 6-mo, PPI = proton pump inhibitor.

- (2) compared with optimized PPI treatment, the Stretta procedure can improve LES pressure and is associated with better symptom control, a higher PPI cessation rate and a higher satisfaction rate ( $P < .05$ ); and
- (3) the Stretta procedure did indeed decrease the esophageal acid exposure at the 6-month follow-up. However, the Stretta procedure was not superior to PPI treatment in this regard.

Regarding our first finding, the Stretta procedure turned out to be safe and tolerable. Four mild complications were documented. Among these complications, only 1 patient complained of severe bloating and vomiting 11 days after the procedure and was re-hospitalized, which is in accordance with previous studies. Liang et al. reported only mild abdominal distention in 12 (8.7%) out of 152 patients after the Stretta procedure.<sup>[18]</sup> However, other studies reported bleeding or ulcerative esophagitis post-Stretta, which required rehospitalization.<sup>[19,20]</sup> After careful analysis, we

found that all of these studies included patients with RE. We speculate that the lesions due to the RF may aggravate the already existing mucosal lesions, leading to bleeding and/or ulcerative esophagitis, and may explain why no bleeding or ulcerative esophagitis occurred in our study since we included only patients with NERD.

As for our second findings, both the Stretta procedure and PPI can obtain good symptom control and improve patients' quality of life. However, the Stretta procedure achieved higher PPI cessation and higher satisfaction rates at the 6-month follow-up. This result is in line with the previous study. Kalapala et al performed a prospective randomized study to compare the clinical results of the Stretta procedure with PPI treatment at a 3-month follow-up. Three months after the Stretta procedure, 80% reported improvement in quality of life compared to 40% in the control group. Significant improvement in GERD symptom scores compared with those of the control group was also observed. Sixty percent of the patients achieved PPI cessation, while no change was observed in the PPI group. The satisfaction rate was much higher in the Stretta group than in the PPI group (80% vs 30%,  $P < .05$ ).<sup>[21]</sup> Liang et al performed another long-term prospective observational study that followed the patients for 5 years after the Stretta procedure.<sup>[18]</sup> A total of 59 (42.8%) patients achieved complete PPI therapy independence, and 104 (75.4%) patients were completely or partially satisfied with the GERD symptom control. Since we included only patients with documented NERD and those responsive to PPIs in our study, compared to the previous study, both the satisfaction rate (89% vs 57%,  $P < .05$ ) and the PPI cessation rate (82% vs 52%,

**Table 4**  
PPI usage and satisfaction rate after the corresponding treatments of the 2 groups.

PPI usage n (%)	Stretta group	PPI group	P-value
PPI cessation	23 (82%)	11 (52%)	.03
On-demand	2 (7%)	6 (24%)	
Daily PPI	3 (11%)	4 (19%)	
Satisfaction rate	25 (89%)	12 (57%)	.02

Differences were considered significant when  $P < .05$ .

PPI = proton pump inhibitor.

$P < .05$ ) were higher in both groups, especially in the Stretta group, in our study.

As expected, we found that LES pressure was significantly improved in the Stretta group in our study but not in the PPI group. This result is in line with the findings of Kalapala et al, who reported that LES pressure was significantly increased 3 months after the Stretta procedure (7.8 vs 9.22,  $P < .05$ ).<sup>[21]</sup>

However, some studies reported no obvious LES increase after the Stretta procedure. Fass et al performed a meta-analysis recently that included 28 studies that demonstrated that the Stretta procedure is able to reduce esophageal acid exposure but cannot increase LES pressure at a mean follow-up time of 25.4 months.<sup>[10]</sup> We speculate that the different follow-up time of 6 months in our study, as well as our different inclusion criteria, may help to explain this discrepancy. All of these studies were performed in patients with GERD. Our study is the first to include patients with NERD as study subjects. Three reasons can be given for our specific inclusion criteria. First, neither patients with Barrett esophagus nor patients with RE are appropriate candidates for the intervention using the Stretta procedure. According to the mechanism of Stretta, the needle of the catheter should be extended into the LES muscle layer, which means that it is not as helpful for targeting the mucosal epithelium for the treatment of Barrett esophagus. In fact, another mucosal RF ablation therapy for the treatment of Barrett esophagus has been investigated for a long time.<sup>[22]</sup> More importantly, the Stretta procedure can be safely performed under the condition that either the mucosa is intact or the mucosal erosions are healed since the average thickness of the lower esophageal wall is approximately  $3.9 \pm 0.9$  mm,<sup>[23]</sup> and the muscle layer of the lower esophageal wall is only approximately  $1.6 \pm 0.7$  mm,<sup>[24]</sup> which means that deep erosion due to RE could be more likely to result in complications during the procedure. Second, the relationship between RE and hiatus hernia has been well established for a long time. Since hiatus hernia has major pathophysiological effects favoring gastroesophageal reflux and hence contributes to esophageal mucosal injury, it is common to see that RE occurred with hiatus hernia, especially hernia with a sliding size greater than 3 cm.<sup>[11]</sup> It has been reported that 63% of patients with RE have hiatus hernia. However, in patients without RE, the incidence of hiatus hernia was only 8%.<sup>[25]</sup> Considering that the underlying mechanism of the Stretta procedure was through tissue contraction and remodeling, leading to tightening and reduced compliance of the esophageal gastric junction and ablation of nerves that trigger transient LES relaxations,<sup>[26]</sup> it cannot be used to treat hernias. Moreover, the coexisting hiatus hernia may influence the clinical effect of the Stretta procedure and may explain why the PPI cessation rate as well as the symptom control was lower in previous studies than in our study. Thus, we suggest that patients with NERD are more likely to be offered the Stretta procedure as an available option for treatment.

A limitation of this study is that it was a single-center, uncontrolled, nonrandomized study, which made it impossible to control for baseline demographics. Although all of the patients underwent either the Stretta procedure or PPI therapy, the methods of therapy were not randomly chosen. In fact, the small number of enrolled patients and the intention of the patients to undergo the Stretta procedure did not permit us to perform any kind of randomization. However, all of the patients included in the study were well-defined and homogenous. Another limitation

of the study is its small sample size and the loss of participants during follow-up. Only 87.5% of patients completed the 6-month follow-up. However, the results are promising as there are few previous Chinese data that compare the Stretta procedure with PPI treatment for the management of NERD.

In summary, the Stretta procedure is relatively safe and effective in the management of NERD in the short-term follow-up period. It can improve both subjective and objective outcomes compared to PPI treatment in short-term follow-up. However, a multicenter, randomized, controlled trial with more samples and long-term follow-up is required to reach a conclusion regarding the superiority of the Stretta procedure for the management of NERD.

### 6.1. Ethical statement

This study was approved by the Institutional Review Board of the Suining Central Hospital in Suining and conducted in compliance with the ethical principles for medical research involving human subjects stated in the World Medical Association Declaration of Helsinki (version 2013). Informed consent was obtained from all subjects.

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