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Title: A DOUBLE-BLIND SHAM-CONTROLLED STUDY OF THE INFLUENCE OF RADIOFREQUENCY DELIVERY (THE STRETTA[®] PROCEDURE) ON SYMPTOMS, ACID EXPOSURE AND DISTENSIBILITY OF THE GASTRO-ESOPHAGEAL JUNCTION IN GASTRO-ESOPHAGEAL REFLUX DISEASE

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Keywords: Gastro-esophageal reflux disease, gastro-esophageal distensibility, pH monitoring, radiofrequency energy delivery, sham controlled randomised study, Stretta[®] procedure

Corresponding Author: Dr. Jan Tack, MD

Corresponding Author's Institution: University of Leuven

First Author: Joris Arts, M.D., Ph.D.

Order of Authors: Joris Arts, M.D., Ph.D.; Raf Bisschops, M.D., Ph.D.; Kathleen Blondeau, Ph.D.; Ricard Farré, Ph.D.; Rita Vos, Ir.; Lieselot Holvoet; Philip Caenepeel, M.D., Ph.D.; Toni Lerut, M.D., Ph.D.; Jan Tack, MD

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Abstract: Background: Several studies have reported symptom relief in gastro-esophageal reflux disease (GERD) patients treated with radiofrequency delivery (Stretta procedure) at the gastro-esophageal junction (GEJ), but the mechanism underlying this improvement is unclear. Objective: To test the hypothesis that Stretta alters GEJ resistance. Design: We conducted a double-blind randomized cross-over study of Stretta and sham treatment. Patients: Consecutive GERD patients. Setting: Tertiary care center. Interventions: Patients underwent two upper gastrointestinal endoscopies with 3 months interval, during which active or sham Stretta treatment was performed in a randomized double-blind fashion. Symptom assessment, endoscopy, manometry, 24 h esophageal pH monitoring and a distensibility test of the GEJ were done before the start of the study and after 3 months. Main outcome measure: Barostat distensibility test of the GEJ before and after administration of sildenafil. Results: 22 GERD patients (17 females mean age 47±12) participated in the study; 11 in each group. Initial sham treatment did not affect any of the parameters studied. Three months after initial Stretta procedure, no changes were observed in esophageal acid exposure and LES pressure. In contrast, symptom score was significantly improved and GEJ compliance significantly decreased. Administration of sildenafil, an esophageal smooth muscle relaxant, normalized GEJ compliance again to pre-Stretta level, arguing against GEJ fibrosis as underlying mechanism. Limitations: Reflux evaluation did not include impedance monitoring. Conclusions: In this sham-controlled study, Stretta improve GERD symptoms and decreased GEJ compliance. Decreased GEJ compliance, which reflects altered LES neuromuscular function, may contribute to symptomatic benefit by decreasing refluxate volume.

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J. Arts, R. Bisschops, K. Blondeau, R. Farré, R. Vos, L. Holvoet, P.
Caenepeel, A. Lerut,* J. Tack

Department of Gastroenterology, University Hospital Gasthuisberg, University
of Leuven, Belgium

* Department of Thoracic Surgery, University Hospital Gasthuisberg,
University of Leuven, Belgium

Correspondence: Jan Tack, M.D., Ph.D.

Center for Gastroenterological research

K.U. Leuven,

49 Herestraat,

3000 Leuven,

Belgium.

Phone +32 16 344218

Fax +32 16 345939

Take- Home message :

- In a double-blind randomized sham-controlled cross-over study, the Stretta procedure was superior to a sham procedure in providing GERD symptom relief.
- This improvement was not accompanied by improvement of esophageal manometry or esophageal acid exposure on pH monitoring.
- The Stretta procedure was associated with increased resistance at the gastro-esophageal junction, and this may contribute to symptom improvement through decreased reflux volume.
- This increased resistance at the gastro-esophageal junction was not due to fibrosis, as it was reversible by sildenafil administration.

Acronyms :

GEJ	gastro-esophageal junction
GERD:	gastro-esophageal reflux disease
LES:	lower esophageal sphincter
PPI:	proton pump inhibitor
RF:	radiofrequency energy
TLESR:	transient lower esophageal sphincter relaxation

Author contributions :

J. Arts: study concept, patient selection, endoscopic procedures, evaluation procedures, patient follow-up, data analysis, article text

R. Bisschops: patient selection, endoscopic procedures, article text

K. Blondeau: evaluation procedures, article text

R. Farré: evaluation procedures, article text

R. Vos: evaluation procedures, data collection

L. Holvoet: data collection, patient follow-up

P. Caenepeel: patient selection, endoscopic procedures, patient follow-up

A. Lerut: study concept, patient selection

J. Tack: study concept, patient selection, endoscopic procedures, evaluation procedures, data collection, patient follow-up, data analysis, funding, article text

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Lerut,* J. Tack

Department of Gastroenterology, University Hospital Gasthuisberg, University of
Leuven, Belgium

* Department of Thoracic Surgery, University Hospital Gasthuisberg, University of
Leuven, Belgium

Correspondence: Jan Tack, M.D., Ph.D.

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49 Herestraat,

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Belgium.

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Keywords: Gastro-esophageal reflux disease, gastro-esophageal distensibility, pH
monitoring, radiofrequency energy delivery, sham controlled randomised study,
Stretta® procedure

ABSTRACT

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2 Background: Several studies have reported symptom relief in gastro-
3 esophageal reflux disease (GERD) patients treated with radiofrequency
4 delivery (Stretta procedure) at the gastro-esophageal junction (GEJ), but the
5 mechanism underlying this improvement is unclear. Objective: To test the hypothesis
6 that Stretta alters GEJ resistance. Design: We conducted a double-blind randomized
7 cross-over study of Stretta and sham treatment. Patients: Consecutive GERD
8 patients. Setting: Tertiary care center. Interventions: Patients underwent two upper
9 gastrointestinal endoscopies with 3 months interval, during which active or sham
10 Stretta treatment was performed in a randomized double-blind fashion. Symptom
11 assessment, endoscopy, manometry, 24 h esophageal pH monitoring and a
12 distensibility test of the GEJ were done before the start of the study and after 3
13 months. Main outcome measure: Barostat distensibility test of the GEJ before and
14 after administration of sildenafil. Results: 22 GERD patients (17 females mean age
15 47 ± 12) participated in the study; 11 in each group. Initial sham treatment did not
16 affect any of the parameters studied. Three months after initial Stretta procedure, no
17 changes were observed in esophageal acid exposure and LES pressure. In contrast,
18 symptom score was significantly improved and GEJ compliance significantly
19 decreased. Administration of sildenafil, an esophageal smooth muscle relaxant,
20 normalized GEJ compliance again to pre-Stretta level, arguing against GEJ fibrosis
21 as underlying mechanism. Limitations: Reflux evaluation did not include impedance
22 monitoring. Conclusions: In this sham-controlled study, Stretta improved GERD
23 symptoms and decreased GEJ compliance. Decreased GEJ compliance, which
24 reflects altered LES neuromuscular function, may contribute to symptomatic benefit
25 by decreasing refluxate volume.
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INTRODUCTION

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4 Gastro-esophageal reflux disease(GERD) is a common disorder with major impact on
5 the quality of life and potential complications(1-3). Proton pump inhibitors(PPIs) are
6 the cornerstone of GERD treatment, with Up to 90% of patients become
7 asymptomatic on proton pump inhibitor(PPI) therapy(4). A challenging problem
8 remains the treatment of established GERD patients with unsatisfactory PPI
9 response(5). Laparoscopic fundoplication is often proposed as an alternative, but this
10 is not without morbidity and long-term efficacy has been questioned(6-10).

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24 A number of endoscopic procedures, aimed at improving lower esophageal
25 sphincter(LES) barrier function, have emerged over the last decade. In a porcine
26 model, the application of radiofrequency energy increased LES pressure and gastric
27 yield pressure(11). Several studies, including two sham-controlled studies, have
28 demonstrated that radiofrequency delivery at the gastro-esophageal junction(GEJ),
29 also called the Stretta® procedure, induces symptom relief and decreases PPI
30 intake(12-16). Proposed underlying mechanisms include increased LES pressure,
31 decreased transient LES relaxations(tLESR's), and decreased esophageal
32 sensitivity, but none of these readily explains the symptomatic benefit(12-24).

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48 Recent studies have implicated GEJ distensibility as a pathophysiological factor in
49 GERD(25-29). Increased GEJ compliance is associated with lower LES opening
50 pressure and permits wider opening diameters, facilitating reflux. Several studies
51 have indicated an important role for refluxate volume in symptom generation. Multi-
52 level pH studies and multi-channel intraluminal impedance(MII) studies have shown

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that proximally extending reflux events are more likely to be associated with heartburn(30-32). Hence, we hypothesized that Stretta® might decrease GEJ distensibility, hereby limiting the volume and the symptomatic impact of reflux events. We performed a double-blind sham controlled randomized cross-over study to evaluate the influence of Stretta® on symptoms, esophageal acid exposure and GEJ distensibility in GERD.

MATERIALS AND METHODS

Patients

GERD patients with complete or partial response to high dose PPI were recruited for the study. All patients had a long-standing history of established GERD with typical symptoms and pathological pH monitoring(>4% of time pH<4). The protocol was approved by the Ethical Committee of the University Hospital Leuven, and all patients signed informed consent. Exclusion criteria were age <18 years, a large hiatal hernia(>3 cm) and Barrett's esophagus or a history of high grade erosive esophagitis(33,34).

Symptom scores

A previously described reflux score was obtained off therapy(23). The severity of 14 different typical and atypical reflux symptoms(heartburn, acid regurgitation, food regurgitation, chest pain, nausea, vomiting, choking, dysphagia, odynophagia, throat ache, hoarseness, coughing, dyspnoea, wheezing) was scored from 0 to 3(0 = absent; 3 = interfering with daily activity). A cumulative reflux score was obtained by adding all numbers(24).

Ambulatory pH monitoring and esophageal manometry

Ambulatory esophageal pH monitoring and esophageal manometry were performed as previously reported(24).

GEJ distensibility

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5 To evaluate the effect of Stretta® on GEJ distensibility, a barostat assembly was
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7 used(25-29). The barostat bag(5.5 * 20 cm, cylindrical shape) was placed across the
8
9 GEJ under fluoroscopic control. To increase delineation of the balloon, a small
10
11 amount of barium contrast was swallowed by the patient before the start of the
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13 balloon distention protocol(28). The balloon was progressively insufflated by 2 mm
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15 Hg pressure increments at 2-minute intervals. Throughout the procedure, intra-
16
17 balloon volume was monitored and an x-ray image was obtained at each distending
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19 level until the patient reported discomfort, or a maximum pressure of 30 mmHg.
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26 Basal distensibility is likely to be composed of anatomical factors(GEJ anatomy),
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28 tissue characteristics(smooth muscle and collagen) and neural factors(LES tone). As
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30 Stretta® may alter both tissue characteristics(fibrosis) and neural factors(nerve
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32 ablation), we evaluated distensibility after elimination of smooth muscular tone. A 50-
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34 mg tablet of sildenafil dissolved in water was infused in the stomach through the tip of
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36 the barostat catheter. Sildenafil relaxes smooth muscle by blocking type 5-
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38 phosphodiesterase, transiently eliminating distal esophageal contractions and LES
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40 pressure(35). Twenty minutes later, the distention sequence was repeated.
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49 The main outcome variable of the distensibility measurement is the intra-balloon
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51 volume. For validation, we studied the correlation between the intra-balloon volume
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53 determined from the barostat measurement, and GEJ diameter, determined from the
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55 contrast-enhanced x-ray images of the balloon straddling the GEJ in 7 healthy
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volunteers. In addition, we studied the influence of sildenafil on intra-balloon volumes and diameters at the GEJ.

Stretta and sham procedure

The Stretta® procedure was performed as an outpatient procedure after sedation with pethidine and midazolam, as previously reported(24). The sham procedure was performed exactly like the Stretta® procedure, with the same amount of sedation, but needles were not deployed and the catheter was not connected to the RF generator.

Randomization

Patients were randomized in a double-blind fashion into two groups: the first group had the Stretta® procedure first and a sham procedure three months later. The second group followed the opposite sequence. At follow-up after the first procedure, the patient was evaluated by one of the investigators and a study nurse who were unaware of the randomization sequence.

Study Design

Prior to randomization, each patient underwent upper endoscopy, esophageal manometry, and pH monitoring after at least one week PPI interruption. GERD symptom scores and QOL assessment on and off PPI were obtained, and GEJ distensibility was assessed. During a four week treatment period prior to the endoluminal treatment, the patient registered his or her PPI need. Boxes of

1 PPI(esomeprazole 20 mg, Nexiam®, AstraZeneca Belgium) were provided and the
2 number of pills taken was verified by counting residual pills at each subsequent visit.
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7 Three weeks after endoluminal treatment, patients were asked to stop PPI therapy
8 and they were allowed to restart PPI therapy in case of recurrent symptoms and
9 continue until the next endoscopic procedure, or to try and interrupt treatment again
10 at 3 months after the last endoscopic procedure.
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19 Three months after the first procedure, patients were re-evaluated by repeat
20 endoscopy, pH monitoring off PPI, symptom score off-PPI and assessment of GEJ
21 distensibility. After the second procedure(in a cross-over design) patients were again
22 instructed to try and interrupt treatment after 3 weeks. A follow-up visit with
23 endoscopic evaluation, manometry and pH monitoring was scheduled 3 months later.
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31 **Data analysis.**

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34 The primary outcome variable was the change in GEJ compliance. Compliance was
35 calculated as the slope of the linear regression of the pressure-volume relationship.
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39 Secondary outcome variables were change in symptom scores, esophageal acid
40 exposure, esophageal motility characteristics and resting LES pressure.
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50 **Statistical analyses**

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56 Data are shown as mean±SEM or as median(interquartile range). Differences were
57 analyzed by two-tailed Student's t-test, by Mann-Whitney U test, by Chi-square
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testing and by two-sided ANOVA. P values <0.05 were considered significant. The study had 85% power to detect a 35% change in compliance.

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RESULTS

Patients

Twenty-two GERD patients (17 females, age 46.5 ± 2.4 years, body weight 75.1 ± 3.4 kg; history of reflux symptoms of on average 5.1 ± 0.8 years) participated; 11 received Stretta first and 11 sham first. All patients had pathological pH monitoring off-therapy. In Belgium, endoscopy with grading of esophagitis according to the modified classification of Savary and Miller was the basis for PPI reimbursement at the time of the study. The historical index endoscopy before the start of proton pump inhibitor therapy showed no esophagitis in 6 patients, grade 1 esophagitis in 10 and grade 2 esophagitis in 4. One patient had grade 3 and one a grade 4 esophagitis. All patients had a long-standing history of PPI treatment.

Radiofrequency energy delivery procedure

One patient underwent the procedure under general anesthesia; the others were pre-treated with a mean of 6.4 ± 1.9 mg midazolam and 69.0 ± 23.6 mg pethidine. All radiofrequency or sham procedures were performed on PPI therapy. Erosive esophagitis was detected during the initial Stretta® procedure in 5 patients (2 grade 1 and 3 grade 2) and during the sham procedure in 3 patients (all grade 1). The mean procedure time was 36.0 ± 8.5 min. The Stretta® procedure was incomplete in 3 patients (2 in the first group and 1 in the second group) for technical reasons (difficulty with needle deployment). In these patients RF could be delivered at only half of the treating points. Transient retrosternal pain, not necessitating analgesics, up to five

1 days after the procedure was reported by several patients. Throat ache was also
2 reported by three patients after the active treatment and in 2 patients after the sham
3 procedure.
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7 8 9 **Symptom scores and medication use**

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14 Symptom scores were obtained in all patients before and after 3 months. After initial
15 Stretta® procedure, the symptom score improved significantly(14.7 ± 1.5 vs. 8.3 ± 1.9 ,
16 $p < 0.005$), and was not significantly further altered after the second(sham)
17 procedure(7.8 ± 2.1). In contrast, symptoms did not improve significantly after initial
18 sham treatment(16.1 ± 2.5 vs. 15.6 ± 2.2 , NS), but was significantly decreased by the
19 subsequent(active) treatment(7.2 ± 1.6 , $p < 0.05$)(Fig.2).
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31 **Follow-up endoscopy**

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36 At follow-up endoscopy, 3 and 6 months after the initial Stretta® procedure and sham
37 procedure, no significant changes occurred in the number of patients with an erosive
38 esophagitis or in the severity grade of the esophagitis(Table 1).
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46 **24- hour pH monitoring**

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51 Esophageal pH monitoring off PPI was pathological with a pathological exposure to
52 intra-esophageal pH below 4 in all patients(11.3% (6.3 ; 13.7)). Sham treatment as well
53 as active Stretta® treatment did not significantly alter esophageal acid exposure after
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59 3 or 6 months(Fig.3).
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Medication use

At three months there were no differences in PPI use between active or sham treatment. Initial Stretta® procedure followed by sham was not associated with a significant decrease in monthly PPI use (baseline 32.0 ± 4.8 tablets to 3 and 6 months respectively 33.3 ± 2.9 and 32.5 ± 7.0 pills/month, NS). Similarly, initial sham procedure followed by Stretta® did not alter monthly PPI use (baseline 32.1 ± 3.5 tablets to 3 and 6 months respectively 24.0 ± 3.0 and 24.1 ± 5.7 pills/month).

Esophageal motility and GEJ distensibility

LES resting pressure at baseline, 3 months and 6 months did not change after initial Stretta® followed by sham procedure (11.9 ± 1.2 to 13.3 ± 1.9 and 13.7 ± 2.2 mmHg, resp, NS). Similarly, initial sham followed by Stretta® procedure did not affect LES resting pressure (baseline, 3 months and 6 months 15.6 ± 2.1 to 16.3 ± 2.0 and 15.2 ± 3.5 mmHg respectively, NS). Esophageal contractile amplitude and peristaltic nature of the contractions was also not affected (data not shown).

Validation studies of GEJ distensibility in healthy volunteers, showed GEJ compliance, calculated as the slope of the linear pressure-volume relationship, of 9.5 ± 4.7 ml/mm Hg (Fig.4A). Evaluable X-ray images were obtained in 5 volunteers; the distribution of barium around the balloon was inadequate in the 2 remaining subjects (Fig.4B). A significant correlation was found between the intra-balloon

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volume and GEJ diameter as determined on X-ray images($R^2=0.41$, $p<0.0001$). Linear interpolation showed a slope of 0.8 ± 0.1 cm/100 ml for the relationship between the intra-balloon-volume and GEJ diameter. After sildenafil, the slope of the pressure-volume relationship was shifted to larger volumes(Fig.4), and compliance of the GEJ was increased to 17.5 ± 7.5 ml/ mm Hg($p<0.05$). The correlation between the intra-balloon volume and GEJ diameter was preserved after sildenafil administration($R^2=0.45$, $p<0.0001$). The slope of the relationship between the intra-balloon-volume and GEJ diameter was increased to 1.4 ± 0.3 cm/100 ml(NS compared to baseline).

Distensibility data were available for 11 Stretta®-treated and 8 sham-treated patients. Missing data were due to balloon leak($n=1$), patients intolerance($n=1$) and incorrect balloon position($n=1$). GEJ compliance was not significantly altered after sham procedure(14.0 ± 5.3 vs. 13.3 ± 4.30 ml/mmHg, NS), but Stretta® was associated with a significant decrease of the compliance(17.8 ± 3.6 vs. 7.4 ± 3.4 ml/mm Hg, $p<0.05$)(Fig.5A,B). After sildenafil GEJ compliance after Stretta® was normalized to pre-Stretta® level(14.9 ± 3.8 ml/mmHg, NS)(Fig.5B). No significant correlation was found between changes in GEJ compliance and changes in esophageal acid exposure($R^2=0.04$, NS) or symptom severity scores($R^2=0.12$, NS).

Quality of life

The quality of life scores at baseline for the different subdomains did not differ between both groups(Table 2). Three months after the Stretta® procedure, the quality of life score for bodily pain was significantly improved compared to pre-

1 treatment score(49.5±9.5 vs. 24±4.3, p<0.05). Sham treatment did not significantly
2 affect any of the quality of life parameters. However, 3 months after cross-over active
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4 treatment, significant improvement occurred for bodily pain(69.2±7.8 vs. 31.9±4.4
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6 months after sham, p<0.03).
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DISCUSSION

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5 In the present study, we evaluated the effect of radiofrequency energy delivery at the
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7 GEJ(the Stretta® procedure) in a single-center, randomized double-blind cross over
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9 trial. Stretta® significantly improved GERD symptoms and decreased GEJ
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11 compliance. Sildenafil, an esophageal smooth muscle relaxant, normalized GEJ
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13 compliance again to pre-Stretta® level, arguing against GEJ fibrosis as an underlying
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15 mechanism.
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19 Several studies assessed Stretta® in GERD (11-16,18). In uncontrolled multi- or
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21 single-centre studies, improved GERD symptoms and reduced PPI need were
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23 reported, despite small or absent reductions in esophageal acid
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25 exposure(12,13,15,16,18). In a randomized sham-controlled study, Stretta® provided
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27 significant improvement of symptoms and quality of life(14), but esophageal acid
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29 exposure and PPI use did not differ between active and sham. In another multi-center
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31 randomized controlled study, Stretta® was superior to sham in allowing patients to
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33 decrease or stop PPI therapy(16).
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42 In the present sham-controlled study, we found symptomatic benefit of Stretta® over
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44 sham treatment. Unlike previous studies, we already evaluated and confirmed this
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46 symptomatic benefit 3 months after the active or sham procedure. The 3-month term
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48 was used to enhance patient compliance in a sham-controlled study design, by
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50 diminishing the time to active treatment, and was also based on previous
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52 observations of rapid onset of symptom relief(24). However, similar to previous
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54 randomized studies, this was not associated with a significant difference in PPI
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2 use(14). Using the SF-36 we observed significant improvement in the quality of life,
3 domain of bodily pain after active treatment, either initially or after cross-over.
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7 Animal studies reported that radiofrequency energy delivery at the LES increased
8 GEJ resistance and gastric yield pressure(11). In the present study, we evaluated the
9 effect of Stretta® on esophageal manometry, acid exposure and GEJ distensibility.
10 Like previous studies, we observed no significant improvement of pH monitoring or
11 resting LES pressure(12,24). However, we observed a significant decrease in GEJ
12 distensibility after Stretta®. We assessed GEJ distensibility using a barostat(25-29)
13 and we validated this approach by concomitant fluoroscopic controls and by its
14 responsiveness to sildenafil. Given the collagen-depositing effect of RF energy, the
15 decrease in GEJ distensibility after Stretta® could reflect fibrosis, which is probably
16 undesirable. However, sildenafil, an esophageal smooth muscle relaxant, normalized
17 GEJ compliance back to pre-Stretta® level. This rules out GEJ fibrosis as an
18 underlying mechanism, and points towards changes in neuromuscular control of the
19 LES. The nature of these changes remains to be elucidated in future studies.
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42 Symptom improvement observed after Stretta® cannot be explained by pH or
43 manometry data, or by a placebo effect in this double-blind study. Reduction of
44 esophageal sensitivity, as previously reported by our group could be involved, but we
45 found that improvement of acid exposure was an factor underlying reduced
46 esophageal sensitivity, making this a less likely explanation(24). Decreased GEJ
47 compliance, reflecting altered LES neuromuscular function, may improve symptoms
48 by decreasing refluxate volume(25,27,29,36). Reflux events are more likely to be
49 perceived when the proximal extent is higher and when volume and acid clearance
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1 are delayed(30-32). Reduced GEJ distensibility, resulting in a lower open diameter
2 for the same distending pressure, may be associated with a lower refluxate volume
3 and lower probability of symptom generation. Unfortunately, at the time of the study,
4 MII-pH which provides information on proximal extent of reflux, was not routinely
5 used in our unit. Distal esophageal acid exposure, evaluated by pH monitoring, would
6 not necessarily reflect changes in refluxate volume. Further studies matching
7 analysis of GEJ distensibility to proximal esophageal reflux exposure before and after
8 therapeutic interventions seems warranted based on our observations.
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TABLES

Table 1: evolution of erosive esophagitis before and after initial treatment

		Grade 1	Grade 2
Stretta / Sham	Baseline	2	3
	3 months	3	1
	6 months	1	1
Sham / Stretta	Baseline	3	0
	3 months	3	1
	6 months	2	1

Table 2. SF-36 scores before and after treatment; * p<0.05 compared to pre-treatment control value. ** p<0.005 compared to pre-treatment control.

	Physical functioning	Role physical	Role emotional	Bodily pain	Social Functioning	Mental Health	Vitality	General Health
Control for Stretta	56.7±13.4	44.4±13.7	51.9±19.3	24.0±4.3	52.8±5.4	64.9±6.8	50.0±3.9	43.6±5.6
3 months after Stretta	73.8±9.3	43.8±17.5	62.5±18.3	49.5±9.5*	78.1±8.8	65.5±8.1	52.5±6.8	61.6±7.1
6 months after Stretta	65.6±12.0	62.5±14.9	62.5±16.0	52.3±13.6	75.0±7.8	60.0±9.8	42.1±7.6	55.0±8.5
Control for Sham	57.5±6.4	29.2±12.6	66.7±13.0	25.6±5.9	42.7±7.6	60.8±4.5	53.8±5.2	31.4±8.2
3 months after Sham	76.1±5.6	33.3±14.4	85.2±8.1	31.9±4.4	55.6±10.8	70.7±6.2	53.5±6.5	42.7±8.1
3 months after cross-over to STretta	80.5±6.0**	66.7±14.9*	90.0±7.1	69.2±7.8**	73.8±7.6\$*	72.4±5.5*	54.5±5.3	61.0±9.6*

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FIG.LEGENDS

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5 **Fig.1:** Overview of the randomised sham-controlled study protocol.
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9 **Fig.2.** Influence of radiofrequency energy delivery or sham on reflux symptom scores
10 before and 3 months after the procedure. * $p < 0.05$ compared to pre-treatment
11 scores.
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18 **Fig.3.** Influence of radiofrequency energy delivery or Sham intervention on acid
19 exposure before and 3 months after the intervention. * $p < 0.05$ compared to pre-
20 treatment scores.
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28 **Fig.3.** Influence of radiofrequency energy delivery or Sham intervention on basal
29 pressure of the lower esophageal sphincter before and 3 months after the
30 intervention. * $p < 0.05$ compared to pre-treatment scores.
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38 **Fig.4.** A. Pressure-volume relationships at the GEJ in healthy controls before and
39 after administration of sildenafil in 7 healthy controls. B. Representative still frames
40 from videofluoroscopic evaluation of balloon diameter at the GEJ.
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48 **Fig.5.** A. Pressure-volume relationships at the GEJ in patients before and after
49 administration of sildenafil, at baseline and 3 months after sham treatment. B.
50 Pressure-volume relationships at the GEJ in patients before and after administration
51 of sildenafil, at baseline and 3 months after Stretta® treatment.
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Figure 1

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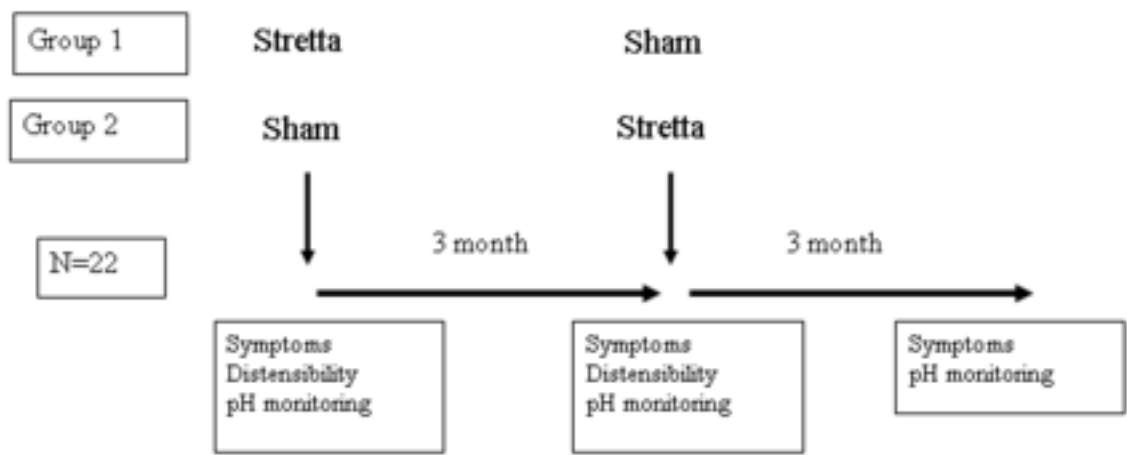


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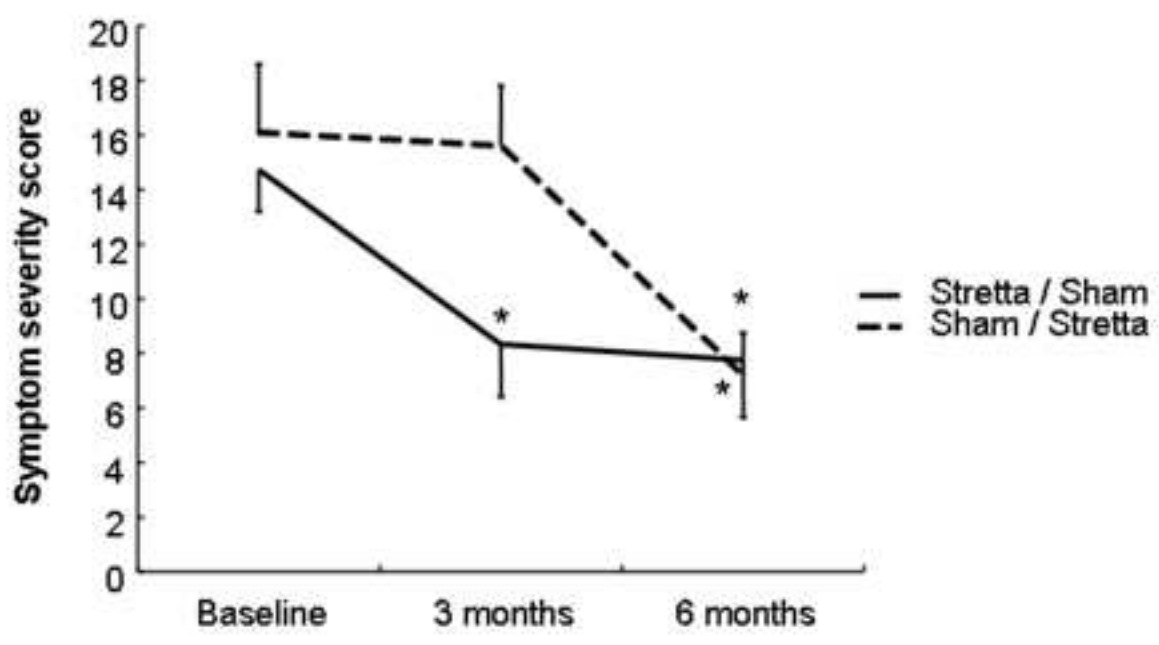


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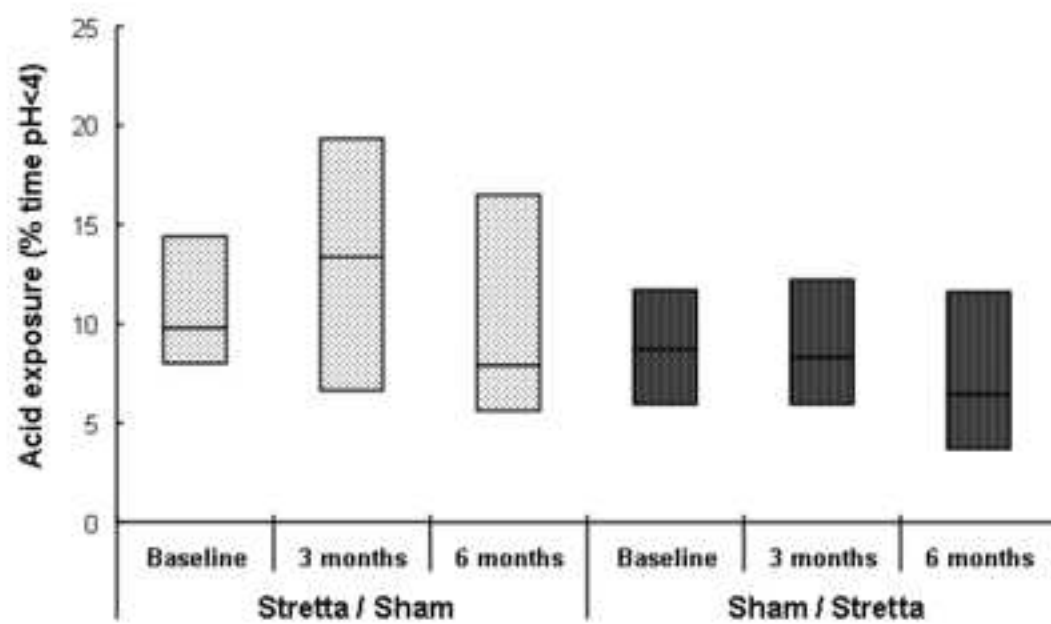


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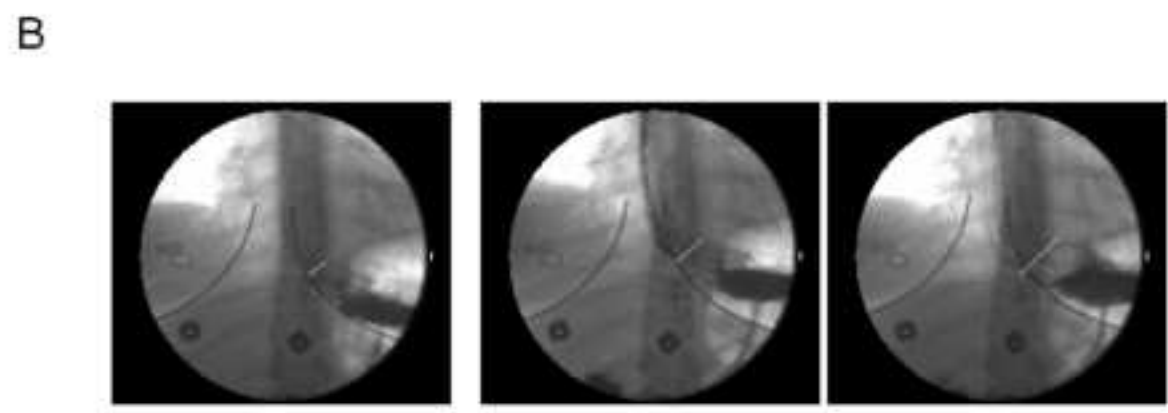
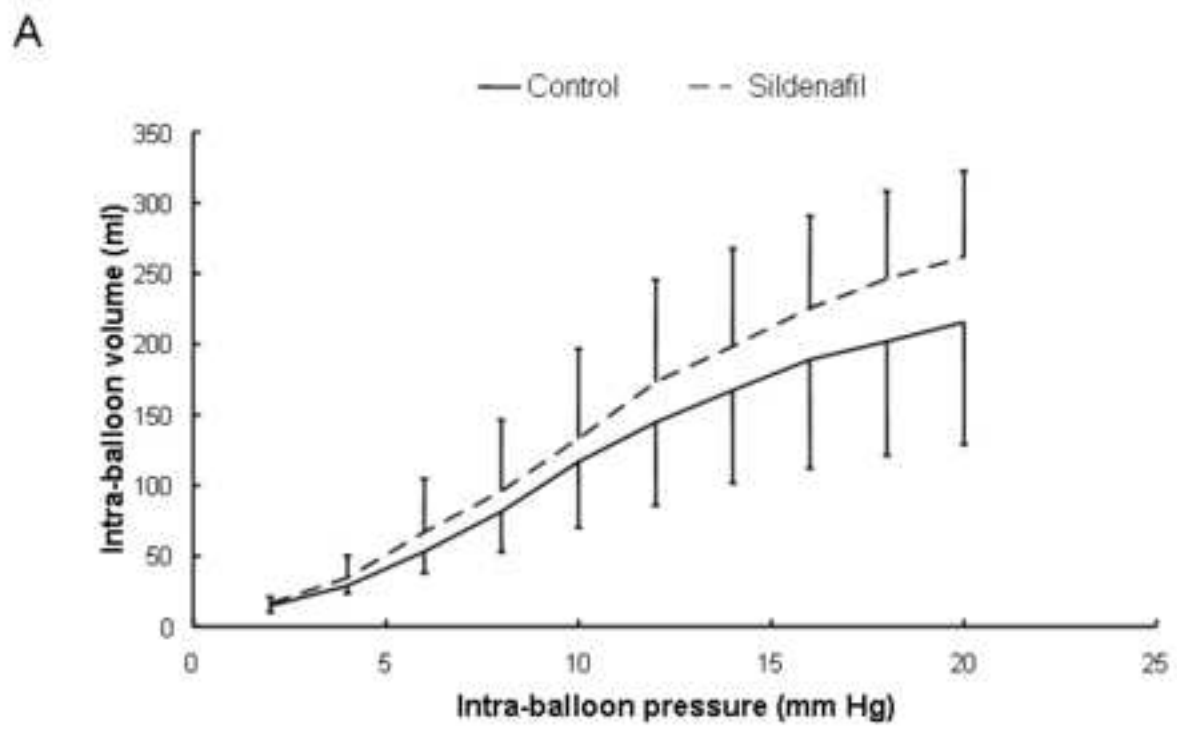


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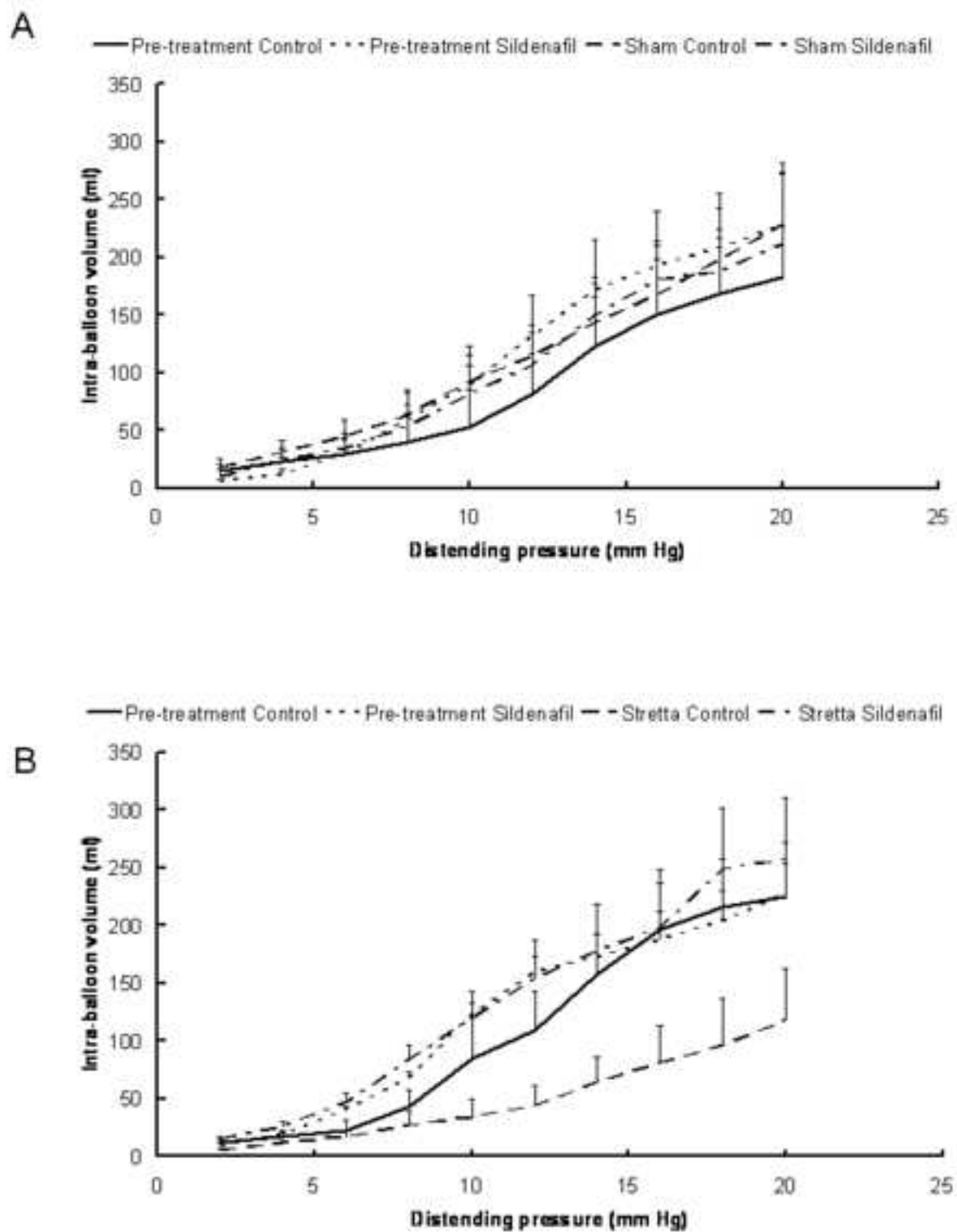


Figure 5

Clinical trial registration :

This clinical trial was approved by the ethics committee of the Leuven University Hospital in 2003.



Journal CME Conflict of Interest: Disclosure and Attestation

Lead Author: Jan Tack

Article: A DOUBLE-BLIND SHAM-CONTROLLED STUDY OF THE INFLUENCE OF RADIOFREQUENCY DELIVERY (THE STRETTA® PROCEDURE) ON SYMPTOMS, ACID EXPOSURE AND DISTENSIBILITY OF THE GASTRO-ESOPHAGEAL JUNCTION IN GASTRO-ESOPHAGEAL REFLUX DISEASE

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Lead Author: Jan Tack

Email Address*: jan.tack@med.kuleuven.be

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Company	Type of Relationship**	Content Area (if applicable)

Author: Joris Arts

Email Address*: joris.arts@pandora.be

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Company	Type of Relationship**	Content Area (if applicable)

Author: Raf Bisschops

Email Address*: raf.bisschops@med.kuleuven.be

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Author: Kathleen Blondeau

Email Address*: Kathleen.blondeau@med.kuleuven.be

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Author: Ricard Farre

Email Address*: Ricard.farre@med.kuleuven.be

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Company	Type of Relationship**	Content Area (if applicable)

Author: Rita Vos

Email Address*: Rita.vos@uz.kuleuven.be

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Company	Type of Relationship**	Content Area (if applicable)

Author: Lieselot Holvoet

Email Address*: lieselot.holvoet@uz.kuleuven.be

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Company	Type of Relationship**	Content Area (if applicable)

Author: Philip Caenepeel

Email Address*: Philip.caenepeel@zol.be

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Company	Type of Relationship**	Content Area (if applicable)

Author: Toni Lerut

Email Address*: toni.lerut@uz.kuleuven.ac.be

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