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Magnetic sphincter augmentation and fundoplication for GERD in clinical practice: one-year results of a multicenter, prospective observational study

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Abstract
Background The techniques available for antireflux surgery have expanded with the introduction of the magnetic sphincter augmentation device (MSAD) for gastroesophageal reflux disease (GERD).
Methods A prospective, multicenter registry evaluated MSAD and laparoscopic fundoplication (LF) in clinical practice (ClinicalTrials.gov identifier: NCT01624506). Data collection included baseline characteristics, reflux symptoms, proton-pump inhibitor (PPI) use, side effects, and complications. Post-surgical evaluations were collected at one year.
Results At report, 249 patients (202 MSAD patients and 47 LF patients) had completed one-year follow-up. The LF group was older and had a greater frequency of large hiatal hernias and Barrett's esophagus than the MSAD group ($P < 0.001$). The median GERD-health related quality of life score improved from 20.0 to 3.0 after MSAD and 23.0 to 3.5 after LF. Moderate or severe regurgitation improved from 58.2 to 3.1 % after MSAD and 60.0 to 13.0 % after LF ($P = 0.014$). Discontinuation of PPIs was achieved by 81.8 % of patients after MSAD and 63.0 % after LF ($P = 0.009$). Excessive gas and abdominal bloating were reported by 10.0 % of patients after MSAD and 31.9 % following LF ($P \leq 0.001$). Following MSAD, 91.3 % of patients were able to vomit if needed, compared with 44.4 % of those undergoing LF ($P < 0.001$). Reoperation rate was 4.0 % following MSAD and 6.4 % following LF.
Conclusion Antireflux surgery should be individualized to the characteristics of each patient, taking into consideration anatomy and propensity and tolerance of side effects. Both MSAD and LF showed significant improvements in reflux control, with similar safety and reoperation rates. In the treatment continuum of antireflux surgery, MSAD should be considered as a first-line surgical option in appropriately selected patients without Barrett's esophagus or a large hiatal hernia in order to avoid unnecessary dissection and preserve the patient's native gastric anatomy. MSAD is an important treatment option and will expand the surgeon's role in treating GERD.

Keywords Antireflux surgery · GERD · LINX · Fundoplication · Regurgitation · Proton-pump inhibitors

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The mainstay medical treatment for gastroesophageal reflux disease (GERD), proton-pump inhibitors (PPIs), works by suppressing the production of gastric acid in the stomach to increase the pH level of the refluxed gastric juice [1]. This treatment is quite effective at controlling symptoms of heartburn and healing esophagitis but has material limitations because non-acid reflux is not

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controlled. Non-acid reflux is significant as it has been shown to play a role in the pathogenesis of Barrett's esophagus [2–4]. Further, chronic use of PPIs is associated with risks and side effects that can be serious and result in injury [5, 6]. Antireflux surgery corrects the incompetent lower esophageal sphincter (LES) to reduce reflux versus alter the pH of the reflux.

Laparoscopic fundoplication (LF) provides mechanical protection from reflux by reconstructing a structurally defective LES using a patient's own gastric fundus to restore the barrier function at the gastroesophageal junction [7]. LF has been shown to be an effective and durable therapy for GERD and an alternative to PPI use [8, 9]. It is an underutilized treatment considering the high prevalence of GERD and that 30–40 % of patients have reflux symptoms while taking PPIs [10, 11]. The LF procedure is technically complex, and outcomes are highly dependent upon a surgeon's experience and judgment. The invasiveness and permanency of wrapping a portion of the stomach around the lower esophagus, and side effects, such as dysphagia, gas bloat, and inability to belch or vomit, have limited its use primarily to advanced GERD.

The magnetic sphincter augmentation device (MSAD, [LINX® Reflux Management System Torax Medical; Shoreview, MN]) was developed as an alternative surgery to fundoplication for augmenting the LES in treating GERD [12]. The MSAD replaces the reconstruction of the gastric fundus with an implantable device consisting of a ring of connected magnetic beads. The attractive forces between the magnetic beads have been calibrated to provide sufficient mechanical augmentation to keep a weak LES closed to reflux, yet open when needed, such as when swallowing a food bolus or with increased gastric pressure from belching or vomiting. Previous reports of the MSAD have shown it to be safe and effective [13–16]. The device is implanted using a minimal dissection technique, with minor disruption to the anatomy at the gastroesophageal junction.

In this report, we explore the clinical experience and insights gained from a large multicenter registry that enrolled patients treated with either MSAD or LF in the clinical practice setting to better understand and define the role of MSAD and LF for GERD.

Methods

Study design

Data were obtained from a multicenter, prospective, observational study of antireflux surgical patients (ClinicalTrials.gov identifier: NCT01624506). The study collected data on both the MSAD and LF in clinical practice at 22 medical centers, in four countries (Austria, Germany, Italy, and the United Kingdom). The study allowed enrollment of all patients who were candidates for a surgical antireflux procedure, including patients with advanced GERD defined as meeting one or more of the following conditions: large hiatal hernia (>3 cm diameter of the esophageal hiatus), Barrett's esophagus, motility disorder, and Grade C or D esophagitis by Los Angeles (LA) classification. Patients without advanced GERD characteristics were considered to have moderate GERD (abnormal esophageal pH, reflux symptoms despite medication). The study was conducted under a common protocol and approved by each center's Ethics Committee. Informed consent was obtained before enrolling patients into the study. Data collection included baseline characteristics and pre- and post-surgical symptoms, use of PPIs, side effects, and complications. Post-surgical evaluations were collected at one year.

Study population

As of July 2013, 249 patients had completed the one-year follow-up and were included in this report. Any patient undergoing either the MSAD or LF antireflux surgical procedure was eligible for enrollment in the study. All patients had a diagnosis of GERD confirmed by abnormal esophageal acid exposure on a prolonged pH or pH-impedance study. Further, all patients had chronic reflux symptoms despite the use of medical therapy with PPIs. Patients were excluded if they had known conditions that would make it unlikely for them to complete a 3-year follow-up.

Pre-surgical evaluation

Patients completed the pre-surgical work-up per standard of care at the participating medical center. Data collected from the medical records included the following: patient demographics, body mass index (BMI), esophagitis grade (LA Classification), esophageal acid exposure as total percent (%) time pH <4, hiatal hernia size, Barrett's esophagus, distal esophageal contraction amplitude <35 mmHg on wet swallow or <70 % peristaltic sequence, anatomical esophageal abnormalities, history of prior gastroesophageal surgery, allergies to titanium, stainless steel, nickel or ferrous materials, number of years with GERD, and number of years with PPI use. Additionally, a study-related questionnaire was administered to all patients prior to surgery, and these responses served as a comparator to responses obtained one year after surgery to evaluate symptom improvement. The pre-surgical questionnaire included a question regarding the patient's motivation for having antireflux surgery and the primary reason for selecting either MSAD or LF.

Surgical procedure through discharge

The type of antireflux procedure performed (MSAD or LF [Nissen and Toupet]) was provisionally agreed upon by the surgeon in close consultation with the patient, in which the risks and benefits of both procedures were explained in detail. The final choice of procedure was made by the surgeon at the time of laparoscopy, taking into account a variety of factors, including the presence of a large hiatal hernia. Post-operative care was directed by the surgeon based on the patient's clinical condition and practices of the institution. Data collected for the surgical procedure included procedure time and complications. Additionally, length of hospital of stay, the ability to eat solids food at discharge, and post-operative complications through discharge were tracked.

Evaluation of clinical effectives

Study-related questionnaires were administered to all patients prior to and one year after surgery. The questionnaires included the GERD-Health Related Quality of Life (GERD-HRQL), an abbreviated Foregut Symptom Questionnaire (FSQ), and a question about reflux interfering with sleep. The GERD-HRQL is a validated, disease-specific questionnaire composed of ten questions relating to severity of symptoms such as heartburn, dysphagia, odynophagia, bloating, and effect of medications [17]. The total GERD-HRQL score represents a summation of each of the ten items, with a score of 0–5 (most severe). The best possible score is a zero (i.e., asymptomatic in each item), and the worst possible score is 50 (incapacitated in each item). The abbreviated FSQ evaluated severity of regurgitation, extra-esophageal symptoms, ability to belch, and ability to vomit. Use of PPIs was tracked before and after surgery as well as healthcare utilization related to procedural complaints or complications. Additionally, patients were asked about their willingness to undergo surgery again and to rate their post-surgical GERD status as improved, unchanged, or worse since having antireflux surgery.

Statistical analysis

Data received from clinical sites were entered into a centralized database (Clindex, Fortress Medical Systems). Central monitoring practices were used to generate and resolve queries. Post-surgical data were compared with data collected prior to surgery. Mean and standard deviation (SD) were used to describe continuous variables such as patient demographic data and baseline characteristics. Categorical demographic and baseline variables were summarized via frequency distributions. Clinical effectiveness was evaluated by comparing pre- and post-surgical responses on the patient reported questionnaire. Categorical variables were summarized as frequency counts, percentages and quantitative variables as means and/or medians. The study was not powered to evaluate a study hypothesis. A two-tailed paired Student's t test or the Wilcoxon signed-rank test was used to compare values before and after surgery. Differences were considered to be significant at the 0.05 level.

Results

Pre-surgical demographics and characteristics

The number of patients reaching the one-year follow-up consisted of 202 MSAD and 47 LF patients. The pre-surgical demographics and characteristics are summarized in Table 1.

Age, large hiatal hernia, and Barrett's esophagus differed significantly between MSAD and LF. Pre-surgical hiatal hernias >3 cm were 1.6 % in the MSAD group compared to 45.7 % in the LF group ($P < 0.001$). More patients in the LF group had Barrett's esophagus (19.1 % vs. 1.0 %, $P < 0.001$). Ninety-four percent of patients in the MSAD group met the definition of moderate GERD (without significant anatomical abnormalities, motility disorders, or Barrett's esophagus) compared to 38.3 % in the LF group. However, severity symptoms at baseline were similar between the patients who had MSAD versus LF. The mean GERD-HRQL score for MSAD was 20 and for LF it was 23. Moderate/severe regurgitation was reported by 58 and 60 % of patients having MSAD and LF, respectively.

Motivations for antireflux surgery

The primary reasons for patients seeking antireflux surgery are listed in Table 2. The majority of patients reported either symptoms were severe enough to interfere with daily activities or their symptoms were getting worse despite taking medications. The primary reason for selecting a particular procedure differed between the two groups. In the MSAD group, 48.3 % of the patients selected the procedure because it appeared to be less invasive; whereas in the LF group, the most frequent response provided was that the surgeon influenced my choice in 63.6 % of patients.

Surgical procedure through discharge

No significant differences were noted in the rate of intra-operative or procedure-related complications during the hospitalization ($P = 1.00$ for both). For intra-operative complications, an injury to the pleura was noted in both

Table 1 Baseline characteristics by antireflux surgery

Measure	MSAD $N = 202$	LF $N = 47$	P value
Age, years[a]	46.6 ± 13.9	52.8 ± 12.8	0.007
Gender, % of patients			0.866
Male	61.7 %	60.0 %	
Female	38.3 %	40.0 %	
BMI[a] (kg/m^2)	25.7 ± 3.8	26.1 ± 5.3	0.611
Years with GERD[a]	8.7 ± 7.8	7.3 ± 4.4	0.086
Years of PPI Use[a]	6.3 ± 5.4	5.1 ± 4.0	0.098
Esophagitis, % of patients			0.212
None	57.5 %	46.8 %	
Grade A	32.1 %	23.4 %	
Grade B	9.3 %	21.3 %	
Grade C	0.5 %	6.4 %	
Grade D	0.5 %	2.1 %	
Barrett's Esophagus, % of patients	1.0 %	19.1 %	<0.001
Hiatal Hernia Size, % of patients			<0.001
None	14.1 %	10.9 %	
1–3 cm	84.4 %	43.5 %	
>3cm	1.6 %	45.7 %	
Total % Time pH >4[a]	10.7 ± 9.5	12.6 ± 16.0	0.509
Moderate GERD, % of patients[b]	93.6	38.3	
Severe GERD, % of patients[c]	6.4	61.7	

[a] Mean ± SD

[b] Moderate GERD defined as hiatal hernia (≤3 cm), no Barrett's esophagus, no motility disorder, and esophagitis no greater than Grade B by LA Classification

[c] Severe GERD defined as one or more of the following hiatal hernia >3 cm, Barrett's esophagus, motility disorder and/or esophagitis Grade C or D by LA Classification

groups and the MSAD group also reported minor bleeding in two patients (<300 mL) with no clinical consequences. Procedure-related complications for MSAD included post-operative dysphagia and one case of pneumothorax. In the LF group, one patient underwent a laparoscopic surgical revision for herniation of the fundic wrap prior to discharge. The difference in the number of patients eating solid food at discharge can be accounted for by the standard post-op care practices established for the two procedures. Most MSAD patients are encouraged to eat a normal diet at discharge; whereas, LF patients are typically prescribed a restricted diet.

Clinical effectiveness

A summary of clinical effectiveness data is provided in Table 3. At the one-year follow-up, both groups showed

Table 2 Patient reported motivations for antireflux surgery

	% of patients	
	MSAD	LF
Primary reason for antireflux surgery		
Symptoms severe enough to interfere with daily activities	43.2	37.8
Symptoms are getting worse despite taking medications	27.6	26.7
Acid reflux medication causes significant side effects	9.7	4.4
Developed other atypical symptoms	8.1	6.7
Symptoms disrupt my sleep or affect my sleep quality	7.6	13.3
Symptoms limit my ability to work or be productive at work	3.8	11.1
Primary reason for selected procedure		
Appears to be less invasive	48.3	12.1
Surgeon influenced my choice	19.7	63.6
Reversible	16.9	0.0
Appears to have fewer side effects	10.1	0.0
Procedure is established with extensive clinical experience	5.1	18.2
Procedure does not involve an implanted device	0.0	6.1

improvement in total GERD-HRQL score. Antireflux surgery had a positive impact on sleep, with decreased reports of heartburn waking from sleep, or reflux interfering with sleep. A majority of patients reported moderate or severe regurgitation prior to surgery, and following surgery, fewer patients for both the MSAD (3.1 %) and LF (13.0 %) ($P = 0.014$) reported moderate or severe regurgitation. The resolution of extra-esophageal symptoms was comparable in both groups ($P = 0.555$). Discontinuation of any PPI use at one-year follow-up was significantly greater for the MSAD patients compared to the LF patients, with 81.8 % reporting no PPI use after MSAD compared to 63.0 % after LF ($P = 0.009$). Nearly all patients reported a willingness to have antireflux surgery again, with 91.8 % of MSAD patients and 86.7 % or LF patients reporting an improvement in their GERD.

Side effects

The side effects evaluated one year after antireflux surgery included bloating, dysphagia, and inability to belch or vomit and are presented in Table 4. The percentage of patients reporting bothersome bloating or gassy feelings occurring at least daily at one-year follow-up was 10.0 % after MSAD and 31.9 % after LF ($P < 0.001$). The percentage of patients reporting bothersome dysphagia was comparable between MSAD and LF ($P = 0.373$). A

Table 3 Clinical effectiveness at one year after antireflux surgery

Measure[a]	MSAD		LF		*P* value
	Baseline	1 Year	Baseline	1 Year	
GERD-HRQL score (median)	20.0	3.0	23.0	3.5	0.177
Heartburn waking from sleep	30.8	3.5	40.0	8.5	0.229
Reflux interfering with sleep	62.1	11.9	72.7	17.4	0.334
Sleep with bed elevated or in reclining chair	48.2	6.7	46.6	8.7	0.517
Moderate or severe regurgitation	58.2	3.1	60.0	13.0	0.014
Extra-esophageal symptoms	63.9	22.3	53.3	17.4	0.552
Discontinuation of PPIs	NA	81.8	NA	63.0	0.009

[a] Percent of patients unless otherwise noted

Table 4 Side effects 1 year after antireflux surgery

Measure	% of patients		*P* value
	MSAD	LF	
Bloating and gassy feeling[a]	10.0	31.9	<0.001
Difficulty swallowing[a]	7.0	10.6	0.373
Ability to belch	98.4	88.9	0.007
Ability to vomit[b]	91.3	44.4	<0.001

A response of ≥3 indicates the symptoms occurred at least daily and was bothersome

[a] Data are from the GERD-HRQL. It is % of patients reporting a response of ≥3 for the related question

[b] Based on the patients reporting a need to vomit

greater percentage of MSAD patients reported being able to belch than LF patients (98.4 % vs. 88.9 %, $P = 0.007$). Similarly, a larger proportion of patients after MSAD reported being able to vomit (91.3 %) compared with LF (44.4 %, $P < 0.001$).

Healthcare utilization

Healthcare utilization related to procedural complaints or complications was tracked for office visits, emergency department visits, hospital admissions >24 h, and reoperations through the one-year follow-up. The percentage of patients with an unscheduled office visit was comparable, as was the number of patients undergoing an outpatient intervention/testing, such as esophageal dilation, barium esophagram, endoscopy, or manometry. Visits to the emergency room were reported for 3.5 % of MSAD patients and 2.1 % of LF patients. Re-admission to the hospital for >24 h occurred in 5.4 % of MSAD patients and 4.3 % LF. The rate of reoperation was 4.0 % MSAD and 6.4 % LF. Reoperations in the MSAD group were performed for device removal due to dysphagia, pain or persistent GERD, while in the LF group were for persistent GERD and herniation of the fundic wrap.

Discussion

In this study, we present results at one-year follow-up of a large number of patients undergoing MSAD implantation, together with a smaller group of patients undergoing LF. The average duration of PPI use was between 5 and 6 years, and the majority of patients reported extra-esophageal symptoms, moderate/severe regurgitation, and reflux interfering with sleep. The severity of symptoms was comparable between the MSAD and LF, even though the LF group had what is traditionally considered more advanced GERD, such as the presence of a large hernia or Barrett's esophagus. The clinical experience reported here reflects how the MSAD and LF were used in clinical practice at 22 centers, outside of a controlled, clinical trial.

We found our experience with the MSAD mirrored previous reports. To date, all publications about the MSAD have noted that patient selection should target no or small hernias, normal motility, and patients without Barrett's esophagus [13–15]. Not unexpectedly, we found that the patients undergoing LF in our series typically had large hernias and/or Barrett's esophagus. These differences in anatomy and disease progression suggest a treatment continuum is emerging, and that the treatment should be based on the clinical presentation (symptoms, endoscopy, and function test data) of the patient. Because the LF procedure involves extensive dissection and major anatomical disruption to reconstruct the LES with a fundic wrap, it is more ideally suited for patients with clinically significant hernias or advanced disease where the LES function is mostly lost, such as with Barrett's esophagus [20, 21]. Whereas, implantation of the MSAD is an alternative technique that uses minimal dissection and minor anatomical disruption at the gastroesophageal junction to achieve LES augmentation in patients with relatively normal anatomy, who have not yet progressed to the point of Barrett's esophagus. Our experience with the MSAD builds further upon previous reports that improved symptoms and discontinuation of PPIs can be achieved with a minimal dissection technique in patients with an incomplete response to PPIs.

Because this study was not intended to formally evaluate a hypothesis about the differences between MSAD and LF,

the differences in outcomes between the two groups need to be interpreted with care since LF patients were older and more likely to have a large hiatal hernia and/or Barrett's esophagus. The impact of these differences on outcomes is unclear since both groups had similar symptom severity at baseline. For other differences in outcomes (e.g., the ability to belch or vomit), the observed differences between LF and MSAD patients are likely more attributable to the different mechanism of surgery in each case, and are therefore more likely to be real than not. Moreover, given that the final decision as to which procedure was performed was made by the surgeon at laparoscopy, in practice, a genuinely objective comparison between MSAD and LF would have been difficult to achieve.

A key factor in the decision-making process was the presence of a large (>3 cm) hiatal hernia, in which case a full hiatal dissection and fundoplication may be viewed as the better option. If a patient does not have a clinically significant hiatal hernia, then it may be preferable to avoid this unnecessary dissection of the hiatus and to proceed with MSAD, potentially avoiding risks of herniation in the future. Side effects, additionally, are an important consideration for patients undergoing antireflux surgery. A patient should expect the possibility of bothersome gas bloat symptoms and an inability to normally vomit following LF [22]. If a patient has expressed specific concerns related to these side effects, or has a history of nausea, then these concerns may become amplified with LF. MSAD appears to offer an improved surgical option for these patients as far as side effects are concerned.

This study shows that both MSAD and LF are viable techniques for LES augmentation in patients with chronic GERD. Antireflux surgery should be individualized to the characteristics of each patient, taking into consideration anatomy and propensity and tolerance of side effects. Reserving surgery for only the most advanced cases of GERD, or waiting for progression of the disease, should be reconsidered with the availability of a less invasive surgical option such as the MSAD. Both procedures are safe and effective, and provide resolution of heartburn as well as improved symptoms of regurgitation and extra-esophageal symptoms, which are not effectively addressed by PPIs. Whether the surgical procedure involves the MSAD or LF, the willingness of ≥90 % patients to undergo antireflux surgery again, and 87–92 % reporting improvement in their overall GERD status, shows antireflux surgery is a beneficial treatment for patients who have persistent reflux symptoms despite maximum medical therapy, and particularly for those who have developed symptoms not well-managed by PPIs, such as regurgitation and extra-esophageal symptoms. The published evidence to date for the MSAD has been defined by patients who meet the labeled indication for the device. Before considering expanded use of MSAD to patients with more complicated GERD, such as large hernias or Barrett's esophagus, a prospective randomized trial with LF may be appropriate.

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