ORIGINAL SCIENTIFIC ARTICLE

Clinical Outcomes and Predictors of Favorable Result after Laparoscopic Magnetic Sphincter Augmentation: Single-Institution Experience with More than 500 Patients

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BACKGROUND: Magnetic sphincter augmentation (MSA) is a promising surgical treatment for patients with GERD. The aim of this study was to evaluate the outcomes of MSA in a large cohort of patients with GERD and to determine the factors predicting a favorable outcome.

METHODS: This was a retrospective review of prospectively collected data of 553 patients who underwent MSA at our institution in a 5-year period. Preoperative clinical, endoscopic, manometric, and pH data were used in a univariate analysis. This was followed by a regression multivariable analysis to determine the factors predicting a favorable outcome. Favorable outcome was defined as freedom from proton pump inhibitors and ≥50% improvement in Gastroesophageal Reflux Disease-Health-Related Quality of Life (GERD-HRQL) total score.

RESULTS: At a mean (SD) follow-up of 10.3 (10.6) months after MSA, 92.7% of the patients were free of proton pump inhibitor use and 84% reported at least 50% improvement in their GERD-HRQL total score. The GERD-HRQL total score was improved from a mean (SD) baseline value of 33.8 (18.7) to 7.2 (9.0) ($p < 0.001$) and 76.1% of the patients had normalization of their esophageal acid exposure. Independent predictors of a favorable outcome after MSA included age younger than 45 years (odds ratio [OR] 4.2; 95% CI, 1.1 to 15.2; $p = 0.0305$), male sex (OR 2.5; 95% CI, 1.1 to 5.7; $p = 0.0301$), GERD-HRQL total score >15 (OR 7.5; 95% CI, 3.3 to 16.8; $p < 0.0001$), and abnormal DeMeester score (OR, 2.6; 95% CI, 1.1 to 5.7; $p = 0.0225$).

CONCLUSIONS: In this largest single-institution series, we demonstrate that MSA implantation is associated with very good clinical and objective outcomes. Age younger than 45 years, male sex, GERD-HRQL total score >15, and abnormal DeMeester score are the 4 preoperative factors predicting a favorable outcome and can be used in patient counseling and MSA use. (J Am Coll Surg 2020;■:1−11. © 2020 The Authors. Published by Elsevier Inc. on behalf of the American College of Surgeons. This is an open access article under the CC BY-NC-ND license [http://creativecommons.org/licenses/by-nc-nd/4.0/].)

The era of minimally invasive surgical treatment of GERD began in the early 1990s with laparoscopic Nissen fundoplication (LNF).[1] This procedure still represents the surgical standard of care for patients with medically refractory GERD. It is a safe, effective, and durable treatment if performed in specialized and high-volume centers.[2,3] But wide variability in outcomes and fear of long-term side effects, such as inability to belch and vomit, has limited the widespread adaptation of this procedure as a primary therapy.[4] These factors have impacted referral patterns and <1% of eligible patients pursue this surgical treatment.[5] Therefore, there has been a drive to

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Abbreviations and Acronyms

GEJ	= gastroesophageal junction
GERD-HRQL	= Gastroesophageal Reflux Disease-Health-Related Quality of Life
HH	= hiatal hernia
LES	= lower esophageal sphincter
LNF	= laparoscopic Nissen fundoplication
MSA	= magnetic sphincter augmentation
PPI	= proton pump inhibitor
RSI	= Reflux Symptom Index

design a less invasive surgical option that is applicable and acceptable to patients with early progressive disease.

Magnetic sphincter augmentation (MSA) was developed as an alternative surgical procedure that limits technical variability and results in consistent clinical outcomes.[6-8] This procedure has the potential to overcome the limitations of fundoplication, has been broadly adopted by the surgical community, and is currently offered in more than 300 centers in the US. The LINX device (Ethicon, Johnson & Johnson) applies magnetic force to augment the barrier function of an incompetent lower esophageal sphincter (LES). It is a simple laparoscopic procedure that does not alter gastric anatomy and can be easily reversed if needed.

Several studies have reported comparable efficacy, potentially longer durability, and less-burdensome side effects for MSA compared with LNF.[9,10] Currently, there is a large body of literature outlining the clinical outcomes of the Nissen procedure and the patient population where it is most likely to be successful.[11,12] However, to date, there has been no large single-institution data set outlining the clinical outcomes of patients who underwent MSA when used in a "real-world" application across the spectrum of disease severity. In addition, there is a paucity of data on identifying preoperative factors that predict successful outcomes after MSA.[13] Such data can be used to guide and refine patient selection and improve preoperative patient counseling for the purpose of maximizing successful outcomes.

This study was designed to evaluate the outcomes of MSA in a large cohort of patients with GERD who underwent this procedure in a single institution, and to determine the factors predicting favorable outcomes.

METHODS

Study population

This was a retrospective review of prospectively collected data of 553 patients who underwent MSA at Allegheny Health Network hospitals (Pittsburgh, PA) between June 2013 and September 2018. Approval was obtained from the Allegheny Health Network IRB (IRB 2018-161) before the start of the study.

Patients with GERD or laryngopharyngeal reflux symptoms despite being prescribed maximal antisecretory therapy who were 18 years or older were included in this study. Objective evidence of reflux disease was based on increased esophageal acid exposure on pH monitoring or a positive impedance-pH result based on criteria described previously.[14-16] Patients with a history of esophageal or gastric surgical procedure; significant esophageal dysmotility; gross anatomic abnormality, such as esophageal stricture; or a known allergy to titanium were not included in this study.

Disease-related quality of life measures

All patients were asked to complete validated questionnaires preoperatively and at 6 and 12 months postoperatively. The validated questionnaires included Gastroesophageal Reflux Disease-Health-Related Quality of Life (GERD-HRQL) and Reflux Symptom Index (RSI). The GERD-HRQL consists of 16 questions that specifically address GERD symptoms.[17] Each question has a score ranging from 0 to 5, and the best possible aggregate score is 0 (asymptomatic) and the worst score is 80 (very severe symptoms). A total score $\geq$15 is considered abnormal. The RSI was used to assess atypical GERD symptoms.[18] The RSI consists of 9 questions, and each question has a potential score ranging from 0 to 5. A total score $>$13 is considered abnormal. Postoperative values were then compared with the preoperative values for each questionnaire and the rate of symptomatic improvement was calculated.

Preoperative assessment

All patients underwent a comprehensive clinical evaluation with a focus on their foregut symptoms and acid suppression medication use. They completed the Gastroesophageal Reflux Disease-Health-Related Quality of Life (GERD-HRQL) and RSI questionnaires. The routine preoperative objective assessment included the following tests:

1. Videoesophagram: This imaging study was done to evaluate gross pharyngeal and esophageal motility, further delineate the anatomy, assess for any potential mass or mucosal lesions, diverticulum, and evaluate hiatal hernia (HH), esophageal stricture, or scarring presence.
2. Esophagogastroduodenoscopy with biopsy: Used to assess the presence of esophagitis, Barrett's esophagus, and the presence and size of an HH. HH size was

recorded in centimeters based on the distance from the gastroesophageal junction (GEJ) to the crural impression.

3. High-resolution impedance manometry: High-resolution manometry technology (4.2-mm diameter; Medtronic) was used for this test. It was equipped with 36 pressure transducers, 1 cm apart, to assess the esophageal body peristalsis (organization and pressure), as well as upper and lower esophageal sphincter pressures, position, and length as described previously.[19]
4. Esophageal pH or impedance-pH monitoring: The pH tests were performed selectively using either Bravo pH monitoring (Medtronic) or multichannel intraluminal impedance pH monitoring (Sandhill Scientific Inc).[14-16] Proton pump inhibitors (PPIs) were discontinued for 10 days before pH testing. Abnormal distal esophageal acid exposure was defined as a DeMeester score >14.7. Impedance-pH testing was used in patients with predominant symptoms of laryngopharyngeal reflux with or without typical reflux symptoms using criteria described previously.[16]

Postoperative and outcomes assessment

Subjective postoperative outcomes were evaluated at routine visits at 2 weeks, 6 weeks, 6 months, and then yearly after operation. Patients were assessed for resolution of their reflux symptoms, use of antisecretory medications, and procedure-related complications. Length of hospital stay, need for readmission within 90 days after operation, and need for postoperative dilation and device removal were also recorded.

A 50% improvement in the GERD-HRQL total score compared with baseline on antisecretory therapy was considered clinically significant. Favorable outcomes were defined as freedom from PPIs and ≥50% improvement in GERD-HRQL total score. Persistent dysphagia was defined as a postoperative dysphagia score >3 on GERD-HRQL "difficulty swallowing" item at 3 months or later after MSA.

At 1 year after MSA, patients were approached for objective foregut evaluation using the same tests used in the preoperative evaluation. A total of 435 patients completed standardized quality of life questionnaires after operation and 251 patients had objective foregut testing at their 1-year follow-up visit or earlier if the patient presented with symptoms that required objective evaluation.

Recurrence of HH was determined based on follow-up upper endoscopy at 1-year follow-up or if the patient presented with suggestive symptoms before that time.[20] A recurrence was considered present if the GEJ was found to be proximal to the crural impressions on either anterograde or retroflexion endoscopic view.

Device and surgical procedure

The LINX device (Ethicon, Johnson & Johnson) is a series of titanium beads with magnetic cores hermetically sealed inside. The beads form a flexible and expandable ring with a "Roman arch" configuration as a result of interlinked, independent, titanium wires. Each individual bead can move independently of the adjacent one, creating a dynamic implant that mimics the physiological movement of the esophagus without limiting the range of motion. The LINX is manufactured in different sizes, ranging from 13 to 17 beads, and has the capacity to double its diameter when all beads are separated.

The implant procedure is performed laparoscopically and consists of complete posterior mediastinal esophageal mobilization with restoration of intra-abdominal esophageal length (≥3 cm) and interrupted posterior crural closure (without pledgets or mesh). The device placement is at the level of the GEJ with the posterior vagus nerve trunk located on the outside of the magnetic ring. A "minimal dissection" technique was used in patients with little to no HH during the beginning of our procedure employment. This approach did not include mediastinal esophageal dissection, the phrenoesophageal ligament was left intact, and there was no crural closure. Instead, a small window was created within the retroesophageal space, and the device was placed around the GEJ (Fig. 1). We used a sizing procedure that assesses esophageal circumference and is performed before selection of the device size. Earlier in our practice, we selected the size of the LINX device by increasing 2 beads from the point of release of the sizing device; we then changed our sizing protocol by increasing it to 3 beads from the point of release. This approach is used for all patients receiving the device regardless of whether there is a preoperative diagnosis of HH. Many patients have transverse widening of the hiatal opening with minimal axial displacement, and this approach focuses on restoring the crural contribution of the antireflux barrier during MSA placement. An intraoperative esophagogastroscopy is performed during the operation to assist in identifying the anatomic GEJ and to assess device position.

Statistical analysis

Values for continuous variables are expressed as either mean (SD) or median with interquartile range when appropriate. Values for categorical variables are presented as frequency and percentage. Statistical analysis was performed by means of nonparametric tests, including Wilcoxon signed rank test, McNemar's test, Kruskal-Wallis

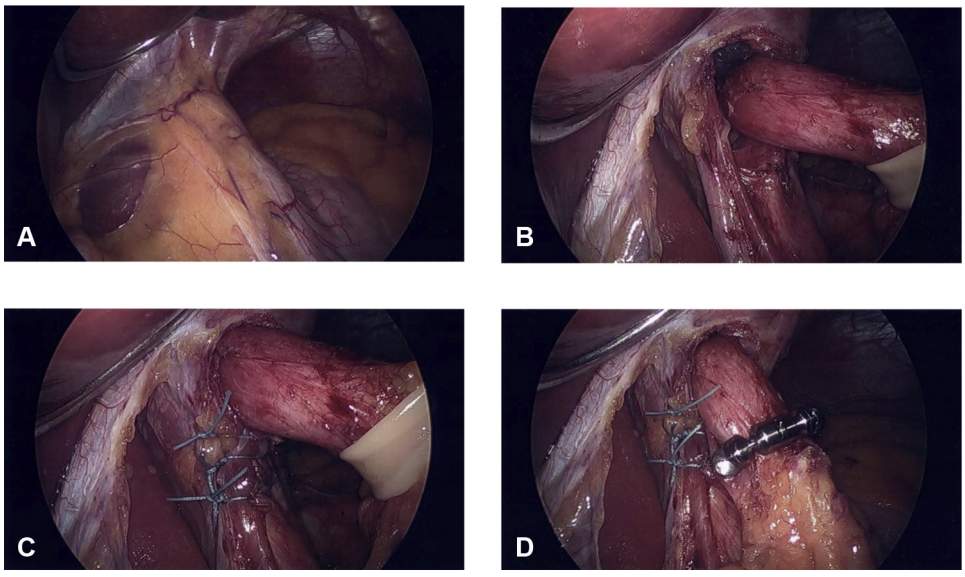

Figure 1. Steps of hernia repair and magnetic sphincter augmentation.

test, Fisher's exact test, and mixed-model *F*-test when appropriate.

Univariate analysis of the preoperative clinical, endoscopic, manometric, and pH data that could support favorable outcomes was performed. The factors with $p < 0.1$ were included in a logistic regression model to produce the independent predictors for postoperative GERD symptom improvement. A p value < 0.05 was considered to be statistically significant. All statistical analyses were performed using SAS software (version 9.4, SAS Institute).

RESULTS

A total of 553 patients underwent laparoscopic MSA during the study period. Baseline demographic and clinical data are shown in Table 1. At a mean (SD) follow-up of 10.3 (10.6) months, 86.7% of the patients were satisfied with the outcomes of operation and 92.7% were free of PPI use.

The mean (SD) GERD-HRQL total score was improved from baseline value of 33.8 (18.7) to 7.2 (9.0) ($p < 0.001$) and RSI total score was improved from 22.2 (10.9) to 8.7 (8.8) ($p < 0.001$). The comparison of the pertinent components of these 2 quality measures is shown in Table 2. Eighty-four percent of the patients were found to have significant clinical improvement, defined by at least 50% improvement in their GERD-HRQL total score.

Manometry performed at 1-year follow-up visit after MSA in a subgroup of 109 patients showed improvement in all 3 resting characteristics of the LES. Comparison of the LES resting characteristics and composite pH score are shown in Table 3. Objective and subjective outcomes across the groups stratified by LINX size are shown in Table 4.

Predictors of favorable outcome

Eighty percent of the patients were considered to have a favorable outcome, defined as both freedom from PPI use and ≥50% improvement in GERD-HRQL total score. The results of univariate analysis of the baseline demographic, clinical, and physiologic parameters with

Table 1. Baseline Demographic and Clinical Characteristics

Characteristic	Data
Age, y, mean (SD)	54.7 (13.9)
Sex, n (%)	
Male	211 (38.2)
Female	342 (61.8)
BMI, kg/m^2, mean (SD)	29.0 (4.6)
DeMeester score, mean (SD)	33.9 (29.4)
Esophagitis, %	
Yes	46.1
No	53.9
Size of the LINX used, beads, median (IQR)	14 (14–15)
Size and type of hernia, n (%)	
None	66 (11.9)
Small (≤3 cm)	373 (67.5)
Large (≥3 cm)	82 (14.8)
Paraesophageal hernia	32 (5.8)

IQR, interquartile range.

Table 2. Comparison of Pertinent Components of Gastroesophageal Reflux Disease-Health-Related Quality of Life and Reflux Symptom Index Before and after Operation

Measurement	Before operation	After operation	p Value
GERD-HRQL scoring, mean (SD)			
Heartburn score	14.7 (8.7)	3.1 (5.8)	<0.001
Regurgitation score	12.7 (9.0)	2.6 (5.0)	<0.001
Total score	33.8 (18.7)	7.2 (9.0)	<0.001
Reflux Symptom Index scoring			
Difficulty swallowing score, mean (SD)	1.7 (1.6)	1.0 (1.3)	<0.001
Difficulty swallowing score ≥3, %	33.7	15.8	<0.001
Total score, mean (SD)	22.2 (10.9)	8.7 (8.7)	<0.001

GERD-HRQL, Gastroesophageal Reflux Disease-Health-Related Quality of Life.

potential contribution to favorable outcomes are shown in Table 5.

Factors found to be relevant in this univariate analysis were used in a multivariable logistic model to determine predictors of favorable outcome after MSA. Age younger than 45 years, male sex, GERD-HRQL total score >15, and an abnormal DeMeester score were found to be the 4 independent predictors of favorableoutcome after MSA (Table 6). Figure 2 shows the probability of favorable outcome across the groups stratified by the number of predictors.

Hospital stay, need for readmission, and complication

Five hundred and fourteen of the patients (93%) were discharged home on the day of operation. A total of 39 patients required at least 1 overnight stay, with a mean of 1.5 (1.0) nights. Table 7 shows the reasons for overnight stay after MSA.

Twenty-three of the patients (4.2%) were readmitted within 30 days from operation and another 8 (1.4%) were readmitted within 90 days from operation. One patient was readmitted 3 times; this patient also had implantation of a gastric stimulator at the time of MSA. This patient required 2 admissions for persistent nausea and vomiting and 1 admission for hematoma at the site of gastric stimulator within the anterior abdominal wall. Two patients required 2 readmissions and the remaining patients were readmitted only once after MSA.

There were only 2 major complications (0.4%). These consisted of CO_2 retention requiring reintubation (n = 1) and mediastinal abscess requiring drainage and IV antibiotic (n = 1). Minor complications were observed in 49 of the patients (8.9%) and included poor postoperative pain control (n = 4), significant nausea during immediate postoperative period (n = 5), hypoxia requiring supplemental oxygenation (n = 7), lethargy (n = 3), abdominal pain requiring additional evaluation (n = 5), bothersome nausea or vomiting requiring emergency department visit (n = 11), dysphagia requiring hospital admission (n = 7), abdominal wall hematoma at gastric pacer insertion site (n = 1), deep vein thrombosis (n = 1), urinary retention (n = 1), cardiac arrhythmia (n = 1), dyspnea requiring additional workup (n = 2), and aspiration pneumonia (n = 1). There was 1 death from causes unrelated to placement of the LINX device.

Postoperative dysphagia and need for endoscopic dilation

A total of 99 patients (17.9%) required 1, and 70 (12.7%) required more than 1, dilation for bothersome dysphagia or chest pain. The indication for dilation was dysphagia in 129 (23.3%), chest pain in 14 (2.5%), and both dysphagia and chest pain in 26 (4.7%).

Table 3. Comparison of Lower Esophageal Sphincter Resting Characteristics and Composite pH Score Before and after Magnetic Sphincter Augmentation

Measurement	Before	After	p Value
Lower esophageal sphincter resting characteristic			
Resting pressure, mmHg	23.1 (14.3)	27.7 (14.1)	0.009
Overall length, cm	2.9 (0.8)	3.2 (0.9)	0.003
Intra-abdominal length, cm	1.0 (1.0)	1.7 (1.2)	<0.001
Composite pH score	32.9 (31.9)	12.3 (25.9)	<0.001

Data are presented as mean (SD).

Table 4. Objective and Subjective Outcomes Across Groups Stratified by LINX Size

Post measure	Device size: Small (sizes 13 and 14) (n = 327)	Medium (size 15) (n = 138)	Large (sizes 16 and 17) (n = 85)	p Value
GERD-HRQL total score, mean (SD)	9.0 (11.1)	6.0 (7.7)	5.7 (8.3)	0.0034
Favorable surgical outcome, %	77.4	85.3	80.0	0.3521
Persistent dysphagia, %	20.2	12.3	11.9	0.0991
DeMeester score, mean (SD)	7.2 (10.2)	18.8 (33.2)	21.0 (42.8)	<0.0001
Normalization of DeMeester score, %	82.4	69.1	65.7	0.0349

GERD-HRQL, Gastroesophageal Reflux Disease-Health-Related Quality of Life.

Device removal

Thirty-seven patients (6.7%) required removal of their device. Of these, 20 removals (3.6%) were due to significant dysphagia or chest pain. Pseudoachalsia not responding to dilation was observed in 1 of these patients and another patient requested explantation 2 days after device implantation due to acute dysphagia (Table 8).

Other reasons for removal included possible titanium allergy (n = 1), mediastinal abscess (n = 1), recurrence of hernia and migration of the device (n = 3), unexplained leukocytosis (n = 1), worsening typical reflux symptoms (n = 4), and worsening atypical reflux symptoms (n = 3). Device was removed within 90 days from operation in 7 patients.

Two patients required removal due to need for subsequent operations: esophagectomy for esophageal cancer (n = 1) and gastrectomy for gastroparesis (n = 1). In 2 patients, the device was found to be discontinuous and required explantation, neither of these 2 patients was symptomatic and disconnection was found on the imaging obtained for other reasons.

DISCUSSION

For an operation to be of value, it must attack the underlying derangement with an acceptable degree of success and should be easily reproducible. The operation also needs to be offered to those who would benefit the most from it. In this study, we report intermediate outcomes after MSA in a large series of patients with GERD after undergoing operations in a single institution. We found that MSA implantation is associated with

Table 5. Baseline Potential Predictors for a Favorable Outcome* Adopting Univariate Logistic Model

Variable	Parameter (SE)	Odds ratio (95% CI)	p Value
Age (< 45 y)	1.41 (0.54)	4.12 (1.43–11.85)	0.0088
Sex, male	0.59 (0.32)	1.80 (0.96–3.37)	0.0663
Typical primary symptom	1.18 (0.31)	3.27 (1.80–5.95)	0.0001
BMI (≥30 kg/m^2)	0.039 (0.29)	1.04 (0.59–1.83)	0.8943
Presence of esophagitis	0.49 (0.29)	1.63 (0.92–2.88)	0.0923
Presence of grade C or D esophagitis	0.97 (0.62)	2.64 (0.78–8.99)	0.1193
Presence of hiatal hernia	−0.26 (0.51)	0.77 (0.28–2.11)	0.6126
Presence of large or paraesophageal hernia	0.15 (0.34)	1.16 (0.60–2.26)	0.6557
GERD-HRQL total score (≥15)	1.84 (0.34)	6.28 (3.24–12.17)	<0.0001
Short LES overall length (<2.7 cm)	−0.002 (0.29)	0.99 (0.56–1.77)	0.9952
Short LES abdominal length (<1.7 cm)	−0.30 (0.32)	0.74 (0.39–1.41)	0.3625
Hypotensive LES pressure (mmHg)	0.20 (0.33)	1.22 (0.64–2.33)	0.5554
Manometrically defective LES	0.21 (0.37)	1.24 (0.60–2.55)	0.5664
>20% incomplete bolus clearance	0.38 (0.36)	1.46 (0.73–2.93)	0.2873
Low distal wave amplitude (<43 mmHg)	0.24 (0.79)	1.28 (0.27–6.01)	0.7583
Low distal contractile integral (<500 mmHg/s/cm)	0.46 (0.64)	1.58 (0.45–5.55)	0.4773
Elevated distal contractile integral (>5,000 mmHg/s/cm)	−0.62 (0.56)	0.54 (0.18–1.62)	0.2715
>80% peristalsis waves	0.15 (0.37)	1.16 (0.57–2.39)	0.6827
Abnormal DeMeester score (>14.7)	0.75 (0.34)	2.12 (1.09–4.12)	0.0264

*Favorable surgical outcome is defined as >50% GERD-HRQL total score improvement and freedom from proton pump inhibitor.
GERD-HRQL, Gastroesophageal Reflux Disease-Health-Related Quality of Life; LES, lower esophageal sphincter.

Table 6. Independent Predictors of Favorable Outcome after Magnetic Sphincter Augmentation Using Multivariable Logistic Model

Variable	Parameter (SE)	Odds ratio (95% CI)	p Value
Age (< 45 years)	1.43 (0.66)	4.17 (1.14−15.23)	0.0305
Sex (male)	0.91 (0.42)	2.49 (1.09−5.66)	0.0301
GERD-HRQL total score (>15)	2.01 (0.41)	7.47 (3.32−16.81))	<0.0001
Abnormal DeMeester Score (>14.7)	0.93 (0.41)	2.55 (1.14−5.68)	0.0225

GERD-HRQL, Gastroesophageal Reflux Disease-Health-Related Quality of Life.

excellent clinical and objective outcomes, comparable with results reported by other centers. We also found that age younger than 45 years, male sex, GERD-HRQL total score ≥15, and abnormal DeMeester score are the 4 preoperative factors predicting favorable outcomes. Presence of all 4 of these predictors was associated with 95% favorable result and the success rate decreased as the number of predictors decreased (Fig. 2).

During the past 5 decades, there has been an increasing interest in the pathophysiology of GERD and its surgical management.[21] The basic derangement in GERD is a transient or permanent loss of LES competency. Recognition of the high failure rates after solely an anatomic HH repair led to the development of different procedures designed to re-establish the competency of the GEJ. The ability of LINX to restore the antireflux barrier is unique among these procedures. MSA enables restoration of the antireflux barrier without extensive anatomic disruption or reconstruction. In addition, it functions as a 2-way valve that preserves the ability for eructation and therefore functions as a more physiologic barrier.

Our study found that MSA can correct the LES manometric abnormalities and indicates that the operation is able to restore normal physiology to a mechanically defective LES (Table 3). The concept of sphincter augmentation was developed to prevent transient sphincter relaxation due to effacement and LES shortening secondary to gastric distention.[22,23] Our findings support this principal. Although we observed an increase in the overall length of the LES after MSA, this was the result of an increase in the sphincter length exposed to the intra-abdominal pressure, as the thoracic length of the LES remained unchanged after MSA. The characteristics of a mechanically defective LES were defined in previous studies relating esophageal manometry to increased distal esophageal acid exposure. In our study, restoring the manometric competency of the LES resulted in a significantly lower distal esophageal acid exposure and normalization of the composite pH score in 76% of the patients.

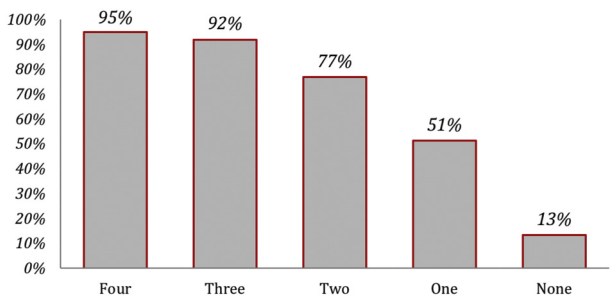

Figure 2. The probability of a favorable outcome across the groups stratified by the number of predictors.

The predictability of success after any antireflux procedure relates directly to the degree of certainty that gastroesophageal reflux is the underlying cause of the patient's symptoms. Esophageal pH monitoring has the highest sensitivity and specificity of the available tests to establish this causality. This explains our finding of an abnormal composite pH score as an independent predictor of favorable outcomes after MSA. This is in contrast to indicators of the severity of disease, such as esophagitis, a defective LES, and large HH, which were not predictive of outcomes in our study. This emphasizes that the outcomes of MSA are more dependent on establishing the presence of disease rather than on its severity. In fact, patients who have these risk factors of disease severity should be given the option of operation early in the course of their disease, before development of other long-term consequences of GERD.

We also found that male sex and younger age are the other 2 predictors of favorable outcomes after MSA. Similarly, Oelschlager and colleagues[24] identified male sex and younger age as important predictors of symptom resolution after fundoplication.[24] O'Boyle and colleagues[25] also reported that male sex is a predictor of better clinical outcomes after Nissen fundoplication. Studies on fundoplication have shown that women are more likely to report poorer outcomes than men, and this likely contributes to a higher rate of subsequent revisional procedures in women. Studies have shown that woman who are seeking antireflux operations are, on average, older than men, more likely to have an HH, and report higher levels of heartburn and dysphagia symptoms before operation. Despite this, they are less likely to have ulcerative

Table 7. Reasons for Overnight Stay After Magnetic Sphincter Augmentation

Reason	Data, n
Poor postoperative pain control	4
CO_2 retention and need for reintubation	1
Significant postoperative nausea	5
Need for supplemental oxygen	7
Lethargy	3
Cardiac arrhythmia	1
Advanced age and comorbidity	9
Patient request and social reason	9

Table 8. Reasons for Device Removal

Reason	Data
Removal indicated by a clinical reason	37
Troublesome dysphagia or chest pain not responding to dilation, n (%)	20 (3.6)
Recurrence of hernia and migration of the device, n	3
Recurrence of hernia and mediastinal abscess, n	1
Worsening typical reflux symptoms, n	4
Worsening atypical reflux symptoms, n	3
Possible titanium allergy, n	1
Unexplained leukocytosis, n	1
Need for subsequent operation, n	2
Esophagectomy for esophageal adenocarcinoma	1
Gastrectomy for severe gastroparesis	1
Removal indicated by device malfunction	2
Disconnected device	2

esophagitis and have lower levels of esophageal acid exposure at their preoperative testing. It is possible that women interpret their symptoms as being more severe, and differences in symptom perception could explain both the preoperative and postoperative differences seen in women after antireflux operations. This explanation is supported by the following 2 observations that woman with gastroesophageal reflux have higher symptom scores than men for equivalent endoscopic grades of esophagitis,[26] and they have a lower threshold for pain induced by balloon distension of the esophagus.[27]

The finding of younger age as a predictor of outcomes highlights the importance of early intervention in management of progressive GERD. This will optimize the surgical outcomes and can also prevent progression to inflammatory and metaplastic complication of the disease. Risk of Barrett's esophagus is shown to rise linearly with increasing frequency, severity, and duration of GERD symptoms.[28] Patients who develop GERD symptoms at an earlier age are at highest risk for esophageal adenocarcinoma.[28] Early intervention will augment a near-normal LES that has not yet been significantly deteriorated from reflux-induced inflammatory injury and provide additional support during transient failure. Currently, referral for operation for patients with early and medically dependent disease is resisted. This stems mainly from the lack of confidence of referring physicians in the outcomes and durability of a fundoplication and concern about the side effects of this operation. Because MSA has been demonstrated to overcome these shortcomings, it appears that the gastroenterology community is more receptive to early referral of patients for surgical intervention.

Studies focused on Nissen fundoplication have reported that patients with typical reflux symptoms, for example heartburn, regurgitation, and dysphagia, are more likely to report favorable outcomes compared with those that presented with atypical symptoms, like cough, hoarseness, wheezing, and chest pain. Because there are fewer mechanisms for their generation, typical symptoms are more likely to be secondary to increased esophageal acid exposure than are atypical symptoms that might also be caused by non-GERD-related diseases of the head and neck and lungs. In this study, presentation with typical reflux symptoms was associated with favorable outcomes at the univariate level, but it was not associated with outcomes within the multivariate logistic regression model.

In the analysis of risk factors for favorable outcomes, presence of a defective LES did not emerge as a predictor of outcomes. This finding might call into question the importance of LES resting pressure, length, and position in preoperative decision making when considering MSA. This observation is consistent with the findings of Campos and colleagues.[12] They also found that a defective LES is not a predictor of outcomes after Nissen fundoplication. Their explanation was that the LES can be either structurally defective or structurally normal but functionally defective. There is no measure of the latter, because it requires identification of the effect of a gastric challenge on LES competence, a test not yet developed for clinical use.[23] Interestingly, MSA is designed to primarily address the functionally defective LES by stopping effacement during gastric challenge.

MSA provides the surgeon and patient with a relatively rapid, reproducible, and less-invasive tool to effectively treat GERD and improve the patients' quality of life.[29] Ninety-three percent of patients in this cohort were discharged home on the day of the operation. The 30- and 90-day readmission rates were very low (4.2% and 1.4%, respectively) and the rate of major complication was also extremely low (0.4%). This safe procedure results in significant improvement in quality of life measures,

assessed by 2 current validated questionnaires: GERD-HRQL for typical reflux symptoms and RSI for atypical symptoms (Fig. 3).

The overall rate of device explantation was 6.6% (n = 37), and of these, 20 (3.6%) were to address persistent dysphagia or chest pain. Our removal rate is consistent with those reported in the literature. This rate is significantly lower than other implants placed around GEJ. Lap band removal rate is around 10% and Angelchik around 20%.[30,31] In addition, reversibility is one of the advantages of the LINX, and removal is technically straightforward, resulting in a return to baseline or even an improvement over pre-MSA symptoms.

We acknowledge that a limitation of our study is short duration of follow-up. In this study, we report the intermediate outcomes of MSA in a large cohort of patients in a single institution and determine the preoperative factors that predict favorable outcomes after operation. We continue the follow-up of these patients and plan to report outcomes at 3 and 5 years.

The rate of favorable surgical outcomes was slightly higher in patients when a medium-sized device was used,[15] but the difference was not statistically significant. Patients with a smaller-sized device had a higher rate of normalization of distal esophageal acid exposure, but this came at the cost of a higher rate of postoperative dysphagia (Table 4).

Dysphagia remains the most prevalent symptom after MSA. Early postoperative dysphagia has been reported in 43% to 83% of patients and resolves in most of these patients.[32,33] But this symptom can persist in some and might require endoscopic dilation or device removal. In this study, 15% of the patients had persistent dysphagia and 30.1% required at least 1 dilation. Earlier in our practice, we selected the size of the LINX device by increasing 2 beads from the point of release of the sizing device; we then changed our sizing protocol by increasing it to 3 beads from the point of release. In a recent publication, our group reported that the change in sizing protocol, in addition to introduction of postoperative diet modification and avoiding early dilation, results in decreases in the dysphagia rate and need for dilation.[34]

Although the clinical benefits of MSA are well established, the cost associated with the device has been perceived as a drawback by payers and this has slowed the widespread dissemination of this technique. A recent study by our group examined the economic impact of introducing MSA for the primary treatment of GERD. Using payer data, we reported that patients with GERD treated with MSA had higher same-day surgical costs compared with LNF, but disease-related cost to the payers more than 12 months postoperation were lower for MSA compared with LNF. In addition, there was a trend toward lower overall medical expenses and costs related to PPI use after MSA compared with LNF.[35] Although MSA was associated with a higher procedural payer cost compared with LNF, the payer costs might be offset due to reductions in the expenses after the operation.

CONCLUSIONS

In the largest single-institution series, we demonstrated that MSA implantation is associated with very good clinical and objective outcomes in GERD patients. Age younger than 45 years, male sex, GERD-HRQL total score ≥15, and abnormal DeMeester score are the 4 preoperative factors predicting favorable outcomes and can be used in preoperative counseling and patient selection.

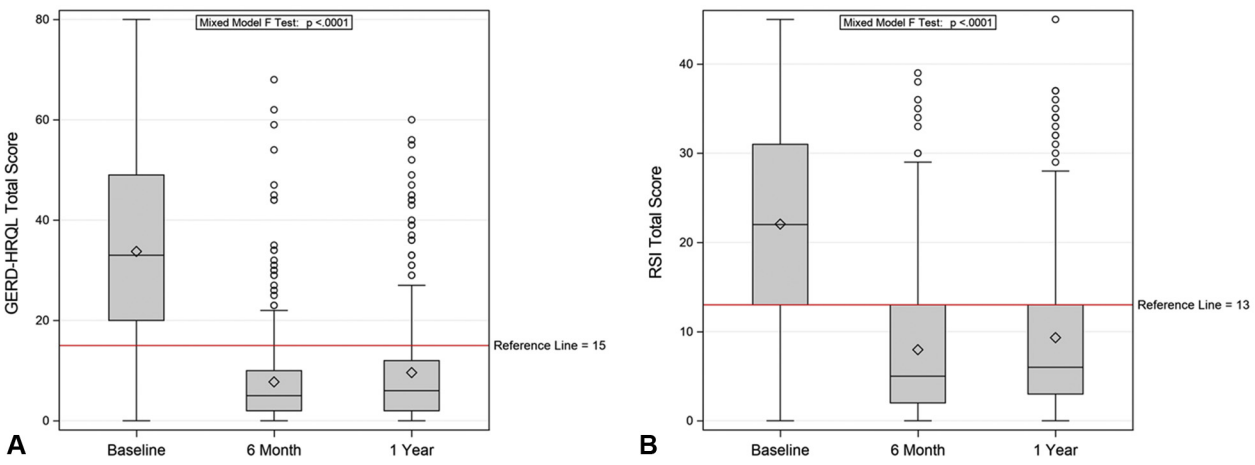

Figure 3. Comparison of quality of life measures, assessed by the current 2 validated questioners, (A) Gastroesophageal Reflux Disease-Health-Related Quality of Life (GERD-HRQL) for typical reflux symptoms and (B) Reflux Symptom Index (RSI) for atypical symptoms.

Author Contributions

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REFERENCES

1. Dallemagne B, Weerts JM, Jehaes C, et al. Laparoscopic Nissen fundoplication: preliminary report. Surg Laparosc Endosc 1991;1:138–143.
2. Galmiche JP, Hatlebakk J, Attwood S, et al. Laparoscopic antireflux surgery vs esomeprazole treatment for chronic GERD: the LOTUS randomized clinical trial. JAMA 2011;18[305]:1969–1977.
3. Ayazi S, DeMeester SR, Hagen JA, et al. Clinical significance of esophageal outflow resistance imposed by a Nissen fundoplication. J Am Coll Surg 2019;229:210–216.
4. Richter JE, Dempsey DT. Laparoscopic antireflux surgery: key to success in the community setting. Am J Gastroenterol 2008;103:289–291.
5. Niebisch S1, Fleming FJ, Galey KM, et al. Perioperative risk of laparoscopic fundoplication: safer than previously reported-analysis of the American College of Surgeons National Surgical Quality Improvement Program 2005 to 2009. J Am Coll Surg 2012;215:61–68.
6. Bonavina L, DeMeester TR, Ganz RA. LINX(TM) Reflux Management System: magnetic sphincter augmentation in the treatment of gastroesophageal reflux disease. Expert Rev Gastroenterol Hepatol 2012;6:667–674.
7. Bonavina L, DeMeester T, Fockens P, et al. Laparoscopic sphincter augmentation device eliminates reflux symptoms and normalizes esophageal acid exposure: 1- and 2-year results of a feasibility trial. Ann Surg 2010;252:857–862.
8. Asti E, Aiolfi A, Lazzari V, et al. Magnetic sphincter augmentation for gastroesophageal reflux disease: review of clinical studies. Updates Surg 2018;70:323–330.
9. Reynolds JL, Zehetner J, Wu P, et al. Laparoscopic magnetic sphincter augmentation vs laparoscopic Nissen fundoplication: a matched-pair analysis of 100 patients. J Am Coll Surg 2015;221:123–128.
10. Sheu EG, Nau P, Nath B, et al. A comparative trial of laparoscopic magnetic sphincter augmentation and Nissen fundoplication. Surg Endosc 2015;29:505–509.
11. Warren HF, Brown LM, Mihura M, et al. Factors influencing the outcome of magnetic sphincter augmentation for chronic gastroesophageal reflux disease. Surg Endosc 2018;32:405–412.
12. Campos GM, Peters JH, DeMeester TR, et al. Multivariate analysis of factors predicting outcome after laparoscopic Nissen fundoplication. J Gastrointest Surg 1999;3:292–300.
13. Maret-Ouda J1, Wahlin K1, El-Serag HB, et al. Association between laparoscopic antireflux surgery and recurrence of gastroesophageal reflux. JAMA 2017;12[318]:939–946.
14. Ayazi S, Lipham JC, Portale G, et al. Bravo catheter-free pH monitoring: normal values, concordance, optimal diagnostic thresholds, and accuracy. Clin Gastroenterol Hepatol 2009;7:60–67.
15. Hoppo T, Komatsu Y, Jobe BA. Gastroesophageal reflux disease and patterns of reflux in patients with idiopathic pulmonary fibrosis using hypopharyngeal multichannel intraluminal impedance. Dis Esophagus 2014;27:530–537.
16. Hoppo T, Sanz AF, Nason KS, et al. How much pharyngeal exposure is "normal"? Normative data for laryngopharyngeal reflux events using hypopharyngeal multichannel intraluminal impedance (HMII). J Gastrointest Surg 2012;16:16–24.
17. Velanovich V. The development of the GERD-HRQL symptom severity instrument. Dis Esophagus 2007;20:130–134.
18. Belafsky PC, Postma GN, Koufman JA. Validity and reliability of the reflux symptom index (RSI). J Voice 2002;16:274–277.
19. Ayazi S, Crookes PF. High-resolution esophageal manometry: using technical advances for clinical advantages. J Gastrointest Surg 2010;14[Suppl 1]:S24–S32.
20. Lord RVN, Kaminski A, Oberg S, et al. Absence of gastroesophageal reflux disease in a majority of patients taking acid suppression medications after Nissen fundoplication. J Gastrointest Surg 2002;6:3–9.
21. Worrell SG, Greene CL, DeMeester TR. The state of surgical treatment of gastroesophageal reflux disease after five decades. J Am Coll Surg 2014;219:819–830.
22. Bonavina L, Saino GI, Bona D, et al. Magnetic augmentation of the lower esophageal sphincter: results of a feasibility clinical trial. J Gastrointest Surg 2008;12:2133–2140.
23. Ayazi S, Tamhankar A, DeMeester SR, et al. The impact of gastric distension on the lower esophageal sphincter and its exposure to acid gastric juice. Ann Surg 2010;252:57–62.
24. Oelschlager BK, Quiroga E, Parra JD, et al. Long-term outcomes after laparoscopic antireflux surgery. Am J Gastroenterol 2008;103:280–287.
25. O'Boyle CJ, Watson DI, DeBeaux AC, et al. Preoperative prediction of long-term outcome following laparoscopic fundoplication. ANZ J Surg 2002;72:471–475.
26. Lin M1, Gerson LB, Lascar R, et al. Features of gastroesophageal reflux disease in women. Am J Gastroenterol 2004;99:1442–1447.
27. Nguyen P, Lee SD, Castell DO. Evidence of gender differences in esophageal pain threshold. Am J Gastroenterol 1995;90:901–905.
28. Thrift AP, Kramer JR, Qureshi Z, et al. Age at onset of GERD symptoms predicts risk of Barrett's esophagus. Am J Gastroenterol 2013;108:915–922.
29. Ayazi S, Chowdhury N, Zaidi AH, et al. Magnetic sphincter augmentation (MSA) in patients with hiatal hernia: clinical outcome and patterns of recurrence. Surg Endosc 2019 Jul 8 [Epub ahead of print].
30. Carandina S, Tabbara M, Galiay L, et al. Long-term outcomes of the laparoscopic adjustable gastric banding: weight loss and removal rate. A single center experience on 301 patients with a minimum follow-up of 10 years. Obes Surg 2017;27:889–895.

31. Smith RS, Chang FC, Hayes KA, DeBakker J. Complications of the Angelchik antireflux prosthesis. A community experience. Am J Surg 1985;150:735–738.
32. Zadeh J, Andreoni A, Treitl D, et al. Spotlight on the Linx™ Reflux Management System for the treatment of gastroesophageal refluxdisease: evidence and research. Med Devices (Auckl) 2018;31[11]:291–300.
33. Bielefeldt K. Adverse events after implantation of a magnetic sphincter augmentation device for gastroesophageal reflux. Clin Gastroenterol Hepatol 2016;14:1507–1508.
34. Ayazi S, Zheng P, Zaidi AH, et al. Magnetic sphincter augmentation and postoperative dysphagia: characterization, clinical risk factors, and management. J Gastrointest Surg 2020;24:39–49.
35. Ayazi S, Zaidi AH, Zheng P, et al. Comparison of surgical payer costs and implication on the healthcare expenses between laparoscopic magnetic sphincter augmentation (MSA) and laparoscopic Nissen fundoplication (LNF) in a large healthcare system. Surg Endosc 2019 Aug [Epub ahead of print].