

Magnetic Sphincter Augmentation with the LINX Device for Gastroesophageal Reflux Disease after U.S. Food and Drug Administration Approval

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Magnetic sphincter augmentation (MSA) of the gastroesophageal junction with the LINX Reflux Management System is an alternative to fundoplication for gastroesophageal reflux disease (GERD) that was approved by the U.S. Food and Drug Administration (FDA) in March 2012. This is a prospective observational study of all patients who underwent placement of the LINX at two institutions from April 2012 to December 2013 to evaluate our clinical experience with the LINX device after FDA approval. There were no intraoperative complications and only four mild postoperative morbidities: three urinary retentions and one readmission for dehydration. The mean operative time was 60 minutes (range, 31 to 159 minutes) and mean length of stay was 11 hours (range, 5 to 35 hours). GERD health-related quality-of-life scores were available for 83 per cent of patients with a median follow-up of five months (range, 3 to 14 months) and a median score of four (range, 0 to 26). A total of 76.9 per cent of patients were no longer taking proton pump inhibitors. The most common postoperative complaint was dysphagia, which resolved in 79.1 per cent of patients with a median time to resolution of eight weeks. There were eight patients with persistent dysphagia that required balloon dilation with improvement in symptoms. MSA with LINX is a safe and effective alternative to fundoplication for treatment of GERD. The most common postoperative complaint is mild to moderate dysphagia, which usually resolves within 12 weeks.

GASTROESOPHAGEAL REFLUX DISEASE (GERD) affects approximately 10 to 20 per cent of the Western world, defined by at least weekly heartburn and/or acid regurgitation.¹ Although many patients have resolution of their symptoms with medical therapy, 10 to 40 per cent have either incomplete or no response to standard dose proton pump inhibitors (PPIs).^{2, 3} The gold standard for treating patients with incomplete response to medical therapy is the laparoscopic Nissen fundoplication (LNF). Before development of the LINX Reflux Management System (RMS) (Torax Medical), fundoplication was the only widely adopted treatment option available to reinforce and strengthen the defective lower esophageal sphincter (LES). Fundoplication has been shown to significantly reduce not only reflux symptoms,

but actual reflux episodes with 80 to 90 per cent of patients off PPIs at five years.^{4, 5} However, fundoplication is associated with gas-bloat syndrome (up to 85%), dysphagia (10 to 50%), diarrhea (18 to 33%), and recurrent heartburn (10 to 62%) with a reoperation rate of up to 15 per cent.⁶ As a result of the technical difficulty and the undesirable side effects, LNF is used in one per cent of patients with GERD.⁷⁻⁹ Given that 10 to 40 per cent of patients with GERD will fail medical therapy, this leaves a significant number of patients with inadequate control of their GERD.⁷⁻⁹

Laparoscopic magnetic sphincter augmentation (MSA) of the gastroesophageal junction (GEJ) with the LINX RMS is an alternative to fundoplication for GERD that was approved by the U.S. Food and Drug Administration (FDA) in March of 2012. The LINX device consists of a series of independently linked titanium beads, each of which has a magnetic core. When placed around the lower esophageal sphincter, the LINX device helps to prevent stomach contents from flowing back into the esophagus by augmenting LES function. However, it does not prevent movement of food or liquids down the esophagus into the stomach and allows for normal belching and vomiting. When a patient

Presented at the 25th Annual Scientific Meeting of the Southern California Chapter of the American College of Surgeons, January 17-19, 2014, in Santa Barbara, California.

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swallows, the pressure in the esophagus increases and the magnetic beads move apart on the titanium wires. As the beads move apart, the magnetic force decreases. This separation of the beads allows the LES to open so food or liquids can pass normally into the stomach. After the pressure wave passes into the stomach, the magnetic beads reapproximate to close the LES.¹⁰ Torax Medical conducted a feasibility trial before FDA approval that followed 44 patients implanted with the LINX device for two years.¹¹ They were able to achieve normalization of pH values in 90 per cent of patients at two years with 86 per cent off PPIs without any major complications and only one device explant for persistent dysphagia.¹¹ We report our independent experience with the LINX device after FDA approval.

Methods

Study Population

After FDA approval of the LINX device in March 2012, 67 patients underwent placement of the LINX device through laparoscopic surgery for GERD between April 2012 and December 2013 at two institutions by four surgeons (57 of 67 by a single surgeon) as part of a registry. Patient selection was guided by manufacturer's labeling and surgeon experience. Patients were considered eligible for the device if they were older than 18 years of age, had reflux symptoms for greater than six months, and had an abnormal pH study. Patients were considered ineligible if they had a hiatal hernia greater than 3 cm on preoperative screening, abnormal esophageal motility on preoperative screening, esophagitis Grade C or D (Los Angeles Classification), Barrett's, gross esophageal structural abnormalities, or allergy to metals. All patients underwent esophageal pH testing off PPIs, esophagogastroduodenoscopy, and video esophagram (VEG) to determine if they met eligibility criteria.

Study Design

A prospective observational study was conducted of consecutive patients evaluated the LINX RMS for GERD. All patients were contacted by telephone or in person by a surgeon at least three months after surgery to answer the GERD health-related quality-of-life (HRQL) questionnaire and questions regarding PPI use, dysphagia, side effects, and complications from the procedure. The study and all evaluations were approved by the University of Southern California Health Sciences Institutional Review Board and verbal consent was obtained from all patients at the time of follow-up.

Procedure

The LINX system is laparoscopically implanted around the esophagus at the area of the LES. It is indicated for use in patients with GERD confirmed by abnormal pH testing who continue to have symptoms despite using maximal medical therapy. All patients underwent laparoscopic placement of the LINX RMS according to the standard protocol. In brief the GEJ was minimally dissected from the right and left crus of the diaphragm to create a space for the device. The hepatic branch of the vagus nerve was preserved in all patients. The laparoscopic sizing device supplied by Torax was placed around the esophagus and adjusted until snug to determine the size of the LINX device. The LINX device was then placed around the esophagus and secured using either a Ti-Knot System (LSI Solutions) or an integrated clasp device depending on the model of the LINX. If the posterior vagus nerve was dissected out and the LINX placed anterior to it, it was recorded. All procedures were performed by four surgeons (J.C.L., N.B., J.Z., N.K.) at two institutions (Keck Medical Center of the University of Southern California or Hoag Hospital Newport Beach). Repair of hiatal hernias with reapproximation of the crura was done at the surgeons' discretion.

Postoperative Care

Patients are advised to eat a regular diet as tolerated after implantation of the LINX device. This is intended to actuate and expand the beads during healing. Patients are also advised to discontinue all PPIs.

Statistical Analysis

Data were reported as frequencies or medians according to variable. Categorical data were compared with the χ^2 test or Fisher's exact test. The reported *P* values are based on a two-sided test. *P* < 0.05 was considered significant.

Results

Sixty-seven patients were implanted with the LINX device over a 19-month period and had a median age of 53 years old (range, 19 to 81 years). A total of 70.1 per cent were male and 29.9 per cent female. Median operative time was 60 minutes (range, 31 to 159 minutes) and median length of stay 11 hours and 8 minutes (range, 4 hours 48 minutes to 34 hours 57 minutes). Fifty-one per cent of patients were discharged within 12 hours of admission. There were no intraoperative complications and only four mild postoperative complications, which included three patients with urinary

retention and one readmission for dehydration secondary to nausea and vomiting on postoperative Day 2. This patient was treated with intravenous fluids and antiemetics and was able to be discharged with 24 hours without further complications.

Sixty-three patients were at least three months postoperative and eligible for follow-up at the time of data analysis. Follow-up information was obtained for 83 per cent with a median follow-up of five months (range, 3 to 14 months). The median GERD-HRQL score at follow-up was 4 (range, 0 to 26) on a scale of 0 to 50 and 76.9 per cent of patients were off PPIs. The most common side effect was dysphagia, which was seen in 82.7 per cent of patients. A total of 5.7 per cent of patients experienced painful esophageal spasm, which was the second most common side effect reported.

All patients had their esophageal motility assessed preoperatively with a VEG and none of the patients had ineffective esophageal motility. Only one patient had dysphagia preoperatively and she had immediate resolution of her symptoms after placement of the LINX device. Of the 43 patients who experienced dysphagia after placement of the LINX, 55.8 per cent described it as mild, characterized by a feeling of food sticking or occasional regurgitation. A total of 44.2 per cent described their dysphagia as severe as characterized by daily regurgitation and the inability to eat. There was a variable onset of dysphagia with 60.5 per cent of patients experiencing dysphagia immediately after surgery. A total of 37.2 per cent of patients were initially able to tolerate a regular diet before experiencing dysphagia symptoms beginning at one to three weeks after surgery. One patient had no symptoms of dysphagia until 12 weeks after placement of the LINX. A total of 79.1 per cent of patients had spontaneous resolution of their dysphagia by 12 weeks after surgery with a median time to resolution of eight weeks. Eight patients underwent intervention consisting of one or two endoscopies with balloon dilation up to 18 mm for persistent dysphagia lasting more than eight weeks. One patient had complete resolution of symptoms and the other seven patients experienced significant improvement but continue to report occasional mild dysphagia symptoms.

On subset analysis, there was no significant difference in the percentage of patients who experienced dysphagia based on inclusion/exclusion of the posterior vagus nerve in the LINX device or repair of a hiatal hernia with crural closure (Table 1).

Discussion

Our study confirms the pre-FDA approval data that laparoscopic MSA is safe and effective in controlling GERD symptoms.¹¹ Predominantly mild dysphagia is present in the majority of patients initially but resolves

TABLE 1. *Dysphagia Outcomes According to Operative Technique*

	+ Vagus	- Vagus	P
+ HHR, no.	1	9	
Dysphagia, no. (%)	1 (100)	7 (77.8)	0.59
- HHR, no.	13	29	
Dysphagia, no. (%)	12 (92.3)	23 (79.3)	0.29
All cases	14	38	
Dysphagia, no. (%)	13 (92.9)	30 (78.9)	0.24
+ HHR		- HHR	
+ Vagus, no.	1	13	
Dysphagia, no. (%)	1 (100)	11 (84.6)	0.67
- Vagus, no.	9	29	
Dysphagia, no. (%)	7 (77.8)	23 (79.3)	0.92
All, no.	10	42	
Dysphagia, no. (%)	8 (80)	35 (83.3)	0.80

+ Vagus, posterior vagus encircled by LINX; - vagus, posterior vagus dissected posteriorly and excluded from LINX; + HHR, hiatal hernia repaired with crural closure, - HHR, no hiatal hernia repair or crural closure.

in eight to 12 weeks in most. Although LNF is very effective in eliminating GERD symptoms, for many patients, the side effects, including persistent dysphagia, gas bloat, and the inability to belch or vomit, are unacceptable. The LINX RMS is a safe and effective alternative to LNF, but its use has several limitations. At this time it is not recommended in patients with large hiatal hernias (more than 3 cm), esophageal motility disorders, or in patients with more advanced GERD including those with severe esophagitis (Los Angeles Grade C or D), Barrett's esophagus, esophageal stricture, or gross anatomic abnormality.¹⁰ The LINX RMS has not been tested in this group of patients and therefore the results and potential complications are unknown.

On our subset analysis we looked for a difference in the frequency of dysphagia symptoms in patients who required repair of their hiatal hernia with crural closure. We did not see a significant difference; however, given the small number of patients who underwent hiatal hernia repair, our study may not have the power to detect a difference.

A larger multicenter study designed as part of the FDA approval process is following 100 patients implanted with the LINX device for five years.¹² Three-year results from that study were recently published. Fifty-eight per cent of patients had normalization of esophageal pH exposure and 64 per cent had at least a 50 per cent reduction in esophageal acid exposure at 3 years. Ninety-two per cent of patients had at least a 50 per cent reduction in GERD-HRQL score from baseline at three years and 93 per cent of patients had at least a 50 per cent reduction in PPI use at three years. Dysphagia was seen in 68 per cent of patients with residual symptoms in 11 per cent at one year and four per cent at three years. Nineteen patients required endoscopic dilation with improvement in 16 patients. There were six

device explants, three for persistent dysphagia, one for persistent GERD, one for persistent chest pain, and one for nausea and vomiting of unclear origin.¹²

A series of 100 patients from Italy with five-year follow-up showed similar results to ours with normalization of esophageal pH in 75 per cent of patients at five years and 85 per cent off PPIs at last follow-up.¹³ They did not have any long-term complications such as device migrations or erosions; however, three patients had the device laparoscopically removed for persistent GERD, odynophagia, or dysphagia with subsequent resolution of symptoms.¹³

Although LNF includes an extensive dissection of the left and right crus to detect or reduce a hiatal hernia as well as the complete mobilization of the fundus with taking down of the short gastrics, the laparoscopic MSA procedure is different. It consists of minimal dissection with a surgical goal of altering only the tissue necessary to place the device at the area of the GEJ appropriate for augmenting the LES. To further meet that goal, our technique has changed over the course of the study. Initially the posterior vagus nerve was identified and dissected posteriorly in every patient so the LINX could be placed between the esophagus and the posterior vagus nerve. However, to minimize the amount of dissection done around the esophagus, we are now more liberal regarding the position of the vagus nerve. Our subset analysis did not reveal any significant difference in the frequency of dysphagia in regard to the position of the vagus nerve. However, given the small number of patients who have not had the posterior vagus nerve dissected, our study may be underpowered to detect such a difference.

The sizing device used to determine the number of beads in the device is used in a very standardized method to avoid any variation in how the LINX device fits around the esophagus. Sizing is done twice to ensure the same measurement is obtained each time. At the end of the procedure the device is visually inspected to ensure that it is just approximating the esophagus and not compressing it. Therefore, we do not think that variations in sizing the device contribute to dysphagia.

In our series, there were no intraoperative complications. A careful dissection is necessary and experience in foregut or bariatric surgery is important to safely implant the device. We had no significant postoperative complications. The procedure was well tolerated by patients and all patients were able to resume a diet and be discharged within 36 hours from admission.

Postoperative diets are very different in laparoscopic MSA compared with LNF. All patients have dysphagia immediately after LNF and therefore it is recommended that these patients maintain a liquid diet for ten days before switching to a soft diet and then resume a regular

diet only after being able to tolerate a soft diet without symptoms. This is done to minimize the sensation of postoperative dysphagia. LINX patients, however, are started on a regular diet ideally in the recovery room or as soon as they recover from any anesthesia-induced nausea. They are counseled on the importance of maintaining a regular diet as much as tolerated in the immediate postoperative period because this actuates the beads during the healing process. This is believed to prevent scarring of the device tightly around the esophagus, which would prevent actuation of the beads during normal swallowing. This unrestricted diet may contribute to the reported level of dysphagia.

Although the majority of patients with dysphagia began having mild symptoms immediately after surgery, there was a significant proportion who experienced what we have called a “honeymoon period.” These patients were initially able to eat a normal diet without any pain or difficulty swallowing. However, between one and three weeks after surgery they began having symptoms of dysphagia, which initially worsened and then began to spontaneously resolve, typically between eight and 12 weeks after surgery. We hypothesize that the inflammatory reaction around the LINX device is beginning to scar down and form the capsule around the LINX device at this point and advise patients of the importance of continuing a regular diet as much as possible to continue actuating the beads and prevent capsule formation in the closed position. It is important to note that the vast majority of patients were satisfied with their overall condition, including resolution of reflux symptoms and ability to stop antacid medications despite the presence of dysphagia.

There were eight patients with persistent dysphagia requiring balloon dilation. Discussions with all of these patients has revealed that they did not immediately start a regular diet and continued on liquid or pureed diets for a prolonged period of time. Our thought is that because of the minimal actuation of the beads in these patients, they developed a capsule around the device in the closed position that prohibited the LINX from being able to open. All of these patients had significant improvement from balloon dilation, which likely disrupted the capsule and allowed the beads to again actuate.

Conclusion

MSA with LINX is a safe and effective alternative to fundoplication for treatment of GERD with most patients experiencing minimal and transient postoperative side effects. The most common side effect was dysphagia, which resolves in the vast majority of patients by 12 weeks.

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