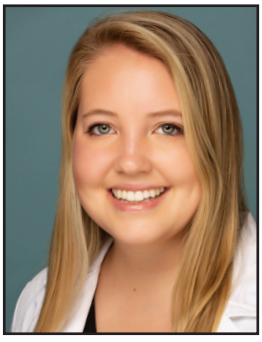
Patient-Related Adverse Events and Clinical Device Failures Associated with the Linx Magnetic Sphincter Augmentation Device: A MAUDE Database Analysis



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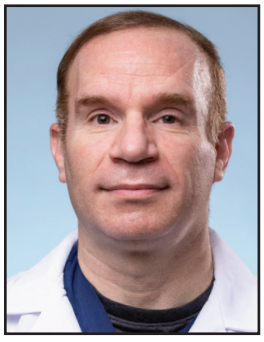

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Abstract

Introduction: The Linx Medical Sphincter Augmentation Reflux Management System is a surgical option for the treatment of chronic gastroesophageal reflux disease (GERD). However, real life data regarding device failures and patient-related adverse events is lacking.

Methods: We analyzed device failures and patient-related adverse events reported to the FDA Manufacturer and User Facility Device Experience (MAUDE) database related to the Linx device from January 2011 to October 2021.

Results: We identified 499 reports describing 918 patient-related adverse events and 101 device failures with two duplicates excluded. The most reported patient-related adverse events were dysphagia in 275 patients (30%), odynophagia in 271 patients (29.5%), GERD in 135 patients (14.7%), adverse events not otherwise specified in 39 patients (4.2%) and erosion in 38 patients (4.1%). The most reported device failures were device removal for recurrence of symptoms in 61 patients (60.4%), Linx device opening unexpectedly in 14 patients (13.9%), Linx device removed without additional information reported in 9 patients (8.9%), Linx bead separation in 7 patients (6.9%) and device migration from the original site of implantation in 7 patients (6.9%).

Conclusion: Linx device implantation offers an alternative to other surgical and medical therapies in the treatment of refractory GERD; however, additional investigation of both short and long-term device failures and patient-related adverse events is necessary.

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ABSTRACT

The Linx Medical Sphincter Augmentation Reflux Management System is a surgical option for the treatment of chronic gastroesophageal reflux disease (GERD). However, data regarding device failures and patient-related adverse events is lacking. We analyzed Linx device failures and patient-related adverse events reported to the FDA Manufacturer and User Facility Device Experience (MAUDE) database from January 2011 to October 2021. We describe 101 device failures and 918 patient-related adverse events in detail, providing valuable information for clinicians and patients considering Linx implantation.

INTRODUCTION

The Linx Medical Sphincter Augmentation Reflux Management System (Ethicon, Bridgewater, NJ) is a device created as a surgically-implanted option for the treatment of chronic gastroesophageal reflux disease (GERD). Linx was approved in 2012 by the U.S Food and Drug Administration (FDA) as a safe alternative to fundoplication for the treatment of patients with GERD.[1] Compared to the previous surgical gold standard of Nissen fundoplication, the Linx device is designed to be implanted laparoscopically without altering foregut anatomy and is reversible via device removal.[2] Prior to antireflux surgery, increasing the dose of proton pump inhibitors in patients with GERD is a common treatment option to suppress acid secretion; however, some patients continue to have insufficient symptom control after dose adjustments.[2,3] The magnetic sphincter augmentation (MSA) device was developed as a long-term solution for GERD due to its specific design to augment lower esophageal sphincter length and provide support to patients with LES failure.[4]

The Linx device is a ring composed of interlinked titanium beads with magnetic cores that is surgically implanted around the gastroesophageal junction to reduce and/or prevent acid from entering the esophagus. The beads can temporarily separate in the context of ring expansion to allow food or liquid to pass into the stomach as well as belching and vomiting.[5] The magnetic attraction between the beads allows the lower esophageal sphincter to remain closed and protect the esophagus from acid reflux and mucosal injury. The magnetic force when the beads are closed is 40 grams and when the beads are separated falls to 7 grams.[6] Linx device implantation via laparoscopy occurs under general anesthesia and patients are able to return to a regular diet shortly after the procedure.[7]

According to Duke Health, approximately 6,000 Linx devices had been implanted globally by 2017 with the number of explants not reported.[8] A study of the safety of magnetic sphincter augmentation published in 2021 noted 30,000 Linx devices have been implanted worldwide with a 7-year cumulative removal of 4.81%.[9] The likelihood of removal was felt to be related to device size, with devices composed of a lower number of magnetic beads having a higher rate of removal.[9] Due to the relative lack of data regarding Linx device failures and clinical adverse events, we undertook an analysis of the MAUDE database to assess these outcomes.

Methods

We performed an analysis of the FDA Manufacturer and User Facility Device Experience (MAUDE) database to report the device failures and clinical adverse events following Linx device implantation. The MAUDE database contains medical device reports submitted to the FDA by voluntary reporters, patients and healthcare professionals, or mandatory reporters, such as manufacturers; however, the medical device reports cannot be solely used to establish rate of events. The FDA works to include all reports received and updates the MAUDE database monthly. The database is available to the public at accessdata.fda.gov/scripts/cdrh/cfdocs/cfmaude/search.cfm. We searched the MAUDE database from January 2011 to October 2021 for all reports related to the Linx device. The medical device reports were downloaded and individual reports were analyzed for device failures and clinical adverse events.

The event descriptions for each report were individually analyzed and categorized and data was collected on the type of device failure and clinical adverse events. Each device failure and clinical adverse event were assigned a number. When appropriate, some of the clinical adverse events

Table 1. Clinical Adverse Events Following Linx Implantation

Dysphagia	275
Odynophagia	271
GERD	135
Adverse Event Not Otherwise Specified	39
Abdominal Pain	38
Erosion Secondary to Device	38
Pain (Location Unspecified)	24
Vomiting	16
Chest Pain	16
Hiatal Hernia	14
Nausea	7
Anxiety	4
Headache	3
Muscle Spasm	3
Weight Change	3
Flatus	3
Inflammation	2
Fatigue	2
Allergy	2
Aspiration	2
Diarrhea	2
Ulcer	2
Infection	2
Perforation	2
Hemorrhage	2
Pneumothorax	1
Muscle Weakness	1
Eructation	1
Abscess	1
Laceration of Esophagus	1
Adhesion	1
Constipation	1
Hypertension	1
Obstruction	1
Cardiac Arrest	1
Dry Mouth/Xerostomia	1
Scar Tissue Formation	1
Foreign Body Sensation	1

were reclassified to correct for some differences in nomenclature. For example, pyrosis, regurgitation and heartburn were all classified under GERD. As the individual reports were analyzed, the numbers representing each device failure and clinical adverse event were assigned to the report. The total number of device failures and clinical adverse events associated with each report were calculated and organized into two tables.

Results

Our search of the MAUDE database identified 499 reports describing 918 patient-related adverse events and 101 device failures from January 2011 to October 2021 with two duplicates excluded.

Patient-related Adverse Events

Patient-related adverse events following Linx implantation are detailed in Table 1. The most reported patient-related adverse event following Linx implantation was dysphagia, which was reported in a total of 275 patients (30%). This was followed by odynophagia in 271 patients (29.5%) and GERD in 135 patients (14.7%). Thirty-nine patients (4.2%) had adverse events not otherwise specified in the event descriptions associated with the report. Erosion secondary to the device occurred in 38 patients (4.1%). Reports of erosion secondary to Linx device implantation include one or more of the magnetic beads eroding through the esophageal lumen. Thirty-eight patients (4.1%) experienced abdominal pain and 24 patients (2.6%) reported pain but the location was unspecified. Vomiting occurred in 16 patients (1.7%). Additionally, sixteen patients (1.7%) had chest pain while 14 patients (1.5%) reported a hiatal hernia. Nausea occurred in 7 patients (0.7%) and anxiety in 4 patients (0.4%). Three patients (0.3%) experienced headaches. Muscle spasms, weight change and flatus each occurred in 3 patients (0.3%). Inflammation, fatigue, allergy, aspiration, diarrhea, ulcer, infection, perforation and hemorrhage were reported for 2 patients (0.2%) each. The remaining adverse events each occurred in 1 patient (0.1%); pneumothorax, muscle weakness, eructation, abscess, laceration of the esophagus, adhesion, constipation, hypertension, obstruction, cardiac arrest, scar tissue formation, foreign body sensation and dry mouth.

Device Failures

Device failures following Linx implantation are detailed in Table 2. The most reported device failure, affecting 61 patients (60.4%), was device removal for recurrence of original symptoms such as dysphagia, odynophagia and GERD. This was followed by the Linx device opening unexpectedly through the interlinked titanium beads and/or the locking clasp, after implantation around the lower esophageal sphincter in a total of 14 patients (13.9%). Nine patients (8.9%) had the Linx device removed without additional information reported in the event description associated with the report. Seven patients (6.9%) experienced Linx bead separation, where a magnetic bead disconnects from an adjacent wire link, after device implantation. Device migration from the original site of implantation occurred in 7 patients (6.9%). The reports include Linx device movement below the diaphragm or around the stomach leading to device removal. Unintended movement of the Linx device also occurred due to a hiatal hernia. In 1 patient (1.0%), the Linx locking device (a multi-directional locking clasp) mechanism failed. Additionally, in 1 patient (1.0%), there was a sizing tool failure during the procedure, which is used to approximate the Linx device to the circumference of the distal esophagus. Lastly, 1 patient (1.0%) experienced an implantation failure due to findings of impaired esophageal peristalsis during a motility study.

Table 2. Device Failures Following Linx Implantation

Device Removed for Recurrence of Original Symptoms	61
Linx Device Opened Unexpectedly	14
Device Removed Without Additional Information	9
Linx Bead Separation	7
Device Migration	7
Linx Locking Device Mechanism Failed	1
Implantation Failure	1
Sizing Tool Failure	1

Discussion

This analysis of the MAUDE database over a 10-year period reveals a variety of device failures and patient-related adverse events reported after Linx implantation. This is the first study exploring device failures and patient-related adverse events reported to the MAUDE database. One previous MAUDE analysis of the Linx device reported solely on the single and specific adverse event of erosion.[10] Their study evaluated 9,453 Linx device implantations from 2007 to 2017 and included 29 reported cases of erosion with most patients experiencing new-onset dysphagia.[10] In our study, removal of the Linx device for recurrence of original symptoms and the Linx device opening unexpectedly were the most common reported device failures.

A study on Linx explantation in 435 devices from 2009 to 2017 from a single institution concluded that the most common reason for device removal in patients was recurrent GERD, which parallels our MAUDE database finding of removal for recurrence of the patient's original symptoms.[11] Additionally, a review on magnetic sphincter augmentation for GERD noted postoperative dysphagia is a common reason for device removal.[12] In our study, dysphagia, odynophagia and GERD were the most commonly reported patient-related adverse events.

A literature review on the Linx device concluded that dysphagia was the most common patient related adverse event following MSA.[13] In addition, Linx device erosion through the esophageal lumen was reported as the most significant adverse event of the device due to its potential morbidity.[13] Further, a safety analysis of the first 1000 patients treated with the MSA device for GERD also concluded dysphagia was the primary reason for device removal.[14] In our study, dysphagia was also the most reported patient-related adverse event in 275 patients (30%). Further, our study revealed erosion secondary to Linx device implantation was a significant adverse event, occurring in 38 patients (4.1%).

MAUDE database medical device reports have limitations. Not all reports contain complete data regarding the device failure or patient related adverse event. For this reason, some of the device failures were reported without specific information on the type of device failure. Those entries were categorized in our study as devices removed

without additional information. Additionally, patient related adverse events that were reported without further details were classified as adverse events not otherwise specified. Other MAUDE database limitations include lack of information on the frequency of device use and the potential for under-reporting of events.

With 101 device failures and 918 patient-related adverse events, our study highlights the importance of awareness of the potential adverse outcomes of Linx device implantation. Early reviews assessing the efficacy of the Linx device concluded that the device is a well-tolerated option for the treatment of GERD but also note the long-term safety of the device was, at that time, undetermined.[15,16,17] A more recent review stated the adverse event of esophageal endoluminal erosion was not fully appreciated in previous reviews and Linx device implantation should be used with restraint with regards to this potential injury.[13]

Although Linx device implantation has its own risks, laparoscopic removal of the device can be performed safely as a 1-stage procedure even within the context of esophageal erosion.[18] Endoscopic removal of the Linx device is considered safe; however, potential complications from device implantation still need to be considered. A case report on esophageal penetration of the MSA device analyzed two cases of severe dysphagia due to migration of the device into the esophagus after implantation.[19] The report concluded that the Linx device may migrate into the esophagus as seen in the two cases, yet the authors felt that the device was considered an effective treatment option for GERD and device removal is generally without diffculty.[19] In our study, device migration from the original site of implantation occurred in 7 patients (6.9%) leading to device explantation.

The Linx device is widely used as an alternative to proton pump inhibitors. In a controlled clinical trial in 2012, the Linx device improved the quality of life in patients with GERD in 23 out of 23 patients and decreased dependence on proton pump inhibitors for refractory GERD in 20 out of 25 patients after 4 years.[20] Further, the Linx procedure is minimally invasive and the device can be easily removed, making it a potentially desirable surgical option for patients with chronic GERD.[21] However, the current literature and this analysis suggests that the long-term safety of the device warrants further research.[22]

CONCLUSION

Our study shows that the Linx device has complications which must be thoroughly discussed with patients prior to implantation. Although the Linx device offers patients an alternative to Nissen fundoplication and proton pump inhibitors for the treatment of refractory GERD, additional investigation of both the short and long-term device failures and patient-related adverse events are warranted. ■

References

1. Reynolds JL, Zehetner J, Bildzukewicz N, Katkhouda N, Dandekar G, Lipham JC. Magnetic sphincter augmentation with the LINX device for gastroesophageal reflux disease after U.S. Food and Drug Administration approval. Am Surg. 2014;80(10):1034-1038.
2. Bonavina L, Saino G, Lipham JC, Demeester TR. LINX(®) Reflux Management System in chronic gastroesophageal reflux: a novel effective technology for restoring the natural barrier to reflux. Therap Adv Gastroenterol. 2013;6(4):261-268. doi:10.1177/1756283X13486311
3. Fass R. Alternative therapeutic approaches to chronic proton pump inhibitor treatment. Clin Gastroenterol Hepatol. 2012;10(4):338-e40. doi:10.1016/j.cgh.2011.12.020
4. Reynolds JL, Zehetner J, Wu P, Shah S, Bildzukewicz N, Lipham JC. Laparoscopic Magnetic Sphincter Augmentation vs Laparoscopic Nissen Fundoplication: A Matched-Pair Analysis of 100 Patients. J Am Coll Surg. 2015;221(1):123-128. doi:10.1016/j.jamcollsurg.2015.02.025
5. Bonavina L, DeMeester T, Fockens P, et al. Laparoscopic sphincter augmentation device eliminates reflux symptoms and normalizes esophageal acid exposure: one- and 2-year results of a feasibility trial. Ann Surg. 2010;252(5):857-862. doi:10.1097/SLA.0b013e3181fd879b
6. Schizas D, Mastoraki A, Papoutsi E, et al. LINX® reflux management system to bridge the "treatment gap" in gastroesophageal reflux disease: A systematic review of 35 studies. World J Clin Cases. 2020;8(2):294-305. doi:10.12998/wjcc.v8.i2.294
7. Zimmermann CJ, Lidor A. Endoscopic and Surgical Management of Gastroesophageal Reflux Disease. Gastroenterol Clin North Am.
8. 2021;50(4):809-823. doi:10.1016/j.gtc.2021.07.005 Pittman, Tim, and Tim Pittman. "Novel Procedure Offers Resolution of Reflux Disease." Duke Health Referring Physicians, 17 Jan. 2017, https://physicians.dukehealth.org/articles/novel-procedure-offers-resolution-reflux-disease.
9. DeMarchi J, Schwiers M, Soberman M, Tokarski A. Evolution of a novel technology for gastroesophageal reflux disease: a safety perspective of magnetic sphincter augmentation. Dis Esophagus. 2021;34(11):doab036. doi:10.1093/dote/doab036
10. Alicuben ET, Bell RCW, Jobe BA, et al. Worldwide Experience with Erosion of the Magnetic Sphincter Augmentation Device.

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SPECIAL ARTICLE

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J Gastrointest Surg. 2018;22(8):1442-1447. doi:10.1007/s11605-018-3775-0
11. Tatum JM, Alicuben E, Bildzukewicz N, Samakar K, Houghton CC, Lipham JC. Removing the magnetic sphincter augmentation device: operative management and outcomes. Surg Endosc. 2019;33(8):2663-2669. doi:10.1007/s00464-018-6544-y
12. Dunn C, Bildzukewicz N, Lipham J. Magnetic Sphincter Augmentation for Gastroesophageal Reflux Disease. Gastrointest Endosc Clin N Am. 2020;30(2):325-342. doi:10.1016/j.giec.2019.12.010
13. Zadeh J, Andreoni A, Treitl D, Ben-David K. Spotlight on the Linx™ Reflux Management System for the treatment of gastroesophageal reflux disease: evidence and research. Med Devices (Auckl). 2018;11:291-300. Published 2018 Aug 31. doi:10.2147/MDER.S113679
14. Lipham JC, Taiganides PA, Louie BE, Ganz RA, DeMeester TR. Safety analysis of first 1000 patients treated with magnetic sphincter augmentation for gastroesophageal reflux disease. Dis Esophagus. 2015;28(4):305-311. doi:10.1111/dote.12199
15. Sheu EG, Rattner DW. Evaluation of the LINX antireflux procedure. Curr Opin Gastroenterol. 2015;31(4):334-338. doi:10.1097/MOG.0000000000000189
16. Bonavina L, Attwood S. Laparoscopic alternatives to fundoplication for gastroesophageal reflux: the role of magnetic augmentation and electrical stimulation of the lower esophageal sphincter. Dis Esophagus. 2016;29(8):996-1001. doi:10.1111/dote.12425
17. Skubleny D, Switzer NJ, Dang J, et al. LINX®magnetic esophageal sphincter augmentation versus Nissen fundoplication for gastroesophageal reflux disease: a systematic review and meta-analysis. Surg Endosc. 2017;31(8):3078-3084. doi:10.1007/s00464-016-5370-3
18. Asti E, Siboni S, Lazzari V, Bonitta G, Sironi A, Bonavina L. Removal of the Magnetic Sphincter Augmentation Device: Surgical Technique and Results of a Single-center Cohort Study. Ann Surg. 2017;265(5):941-945. doi:10.1097/SLA.0000000000001785
19. Salvador R, Costantini M, Capovilla G, Polese L, Merigliano S. Esophageal Penetration of the Magnetic Sphincter Augmentation Device: History Repeats Itself. J Laparoendosc Adv Surg Tech A. 2017;27(8):834-838. doi:10.1089/lap.2017.0182
20. Lipham JC, DeMeester TR, Ganz RA, et al. The LINX® reflux management system: confirmed safety and efficacy now at 4 years. Surg Endosc. 2012;26(10):2944-2949. doi:10.1007/s00464-012-2289-1
21. Asti E, Aiolfi A, Lazzari V, Sironi A, Porta M, Bonavina L. Magnetic sphincter augmentation for gastroesophageal reflux disease: review of clinical studies. Updates Surg. 2018;70(3):323-330. doi:10.1007/s13304-018-0569-6
22. Halpern SE, Gupta A, Jawitz OK, et al. Safety and efficacy of an implantable device for management of gastroesophageal reflux in lung transplant recipients. J Thorac Dis. 2021;13(4):2116-2127. doi:10.21037/jtd-20-3276

Answers to this month's crossword puzzle:

1 D	I	2 G	E	3 S	T	4 I	V	5 E	S	Y	S	6 T	E	7 M
U	■	A	■	I	■	S	■	P	■	■	■	I	■	U
8 C	O	L	I	T	I	S	■	9 I	L	E	I	T	I	S
T	■	L	■	■	■	U	■	D	■	■	■	R	■	C
10 S	U	B	■	11 C	A	E	12 C	U	13 M	■	14 W	A	15 L	L
■	■	L	■	A	■	■	16 O	R	A	L	■	17 T	I	E
■	■	18 A	L	P	H	A	G	A	L	■	19 W	E	T	S
20 A	■	D	■	S	■	■	■	21 L	I	22 N	E	■	■	■
23 S	O	D	I	U	M	■	■	■	24 G	U	T	■	25 U	26 P
Y	■	E	■	L	■	27 A	G	E	N	T	■	28 P	■	A
29 S	U	R	30 G	E	O	N	■	■	31 A	S	P	E	C	T
T	■	■	E	■	■	U	■	■	N	■	■	P	■	T
32 O	X	33 I	M	34 E	T	R	Y	■	35 T	36 I	S	S	U	E
L	■	I	■	P	■	I	■	37 P	■	O	■	I	■	R
38 E	L	I	M	I	N	A	T	I	O	N	■	39 N	O	N