



New technology minimally invasive for the treatment of gastro-esophageal reflux disease: LINX

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Abstract: Gastroesophageal reflux disease (GERD) is a common disorder worldwide (10–30% of adults); lifestyle modifications and PPI therapy (the gold-standard medical treatment for GERD) work in many patients with GERD but in 30–40% of them symptoms persist. Anti-reflux surgery is indicated, with moderate level of evidence, in PPI-resistant GERD patients and with low level of evidence in erosive GERD patients on long term PPI treatment. LINX Reflux Management System (Torax Medical, Maple Grove, MN) is a device for magnetic sphincter augmentation (MSA) and is gaining interest as a valuable surgical alternative approach in patients with GERD, compared to laparoscopic Nissen fundoplication (LNF) which is nowadays the gold-standard surgical technique. In this brief review of current literature in order to compare LINX to the gold-standard surgical procedure for GERD, we analyzed two reviews and three meta-analyses. Each Authors confirmed the efficacy and safety of both techniques. LINX seems to have shorter operative time, shorter length of stay and fewer complications of gas and bloating, if compared to standard surgical procedure. In all analyzed studies the presence of hiatal hernia (HH) larger than 3 cm was often an exclusion criterion for LINX. No RCTs are currently available in literature in order to compare LNF *vs.* LINX and future researches are needed.

Keywords: Gastroesophageal reflux disease (GERD); LINX; magnetic sphincter augmentation (MSA)

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Introduction

The clinical syndrome called gastroesophageal reflux disease (GERD) is caused by the reflux of stomach content into the esophagus or also oral cavity and it develops several annoying symptoms and complications (1). GERD negatively affects patients' quality of life and it is associated with an increased work absenteeism, a low score in sleep scale and a decrease in productivity and physical functioning (2). The prevalence of the disease is higher in western countries compared to Asia: it has been estimated at 20–30% in USA and less than 10% in Japan (3–5). The heartburn is a retrosternal burning feeling, while regurgitation is the perception of refluxed gastric contents

into the mouth. They are symptoms sufficiently descriptive to be diagnostic for GERD. Endoscopy can further classify GERD in erosive reflux disease (ERD) and non-erosive reflux disease (NERD).

The primary aim of the GERD therapy is to control symptoms and increase the patients' Quality of Life (QOL). Furthermore, long-term control of the disease prevents the complications: esophageal stenosis, Barrett's esophagus and adenocarcinoma (6–9).

Medical treatments are the mainstream for therapy and Proton Pump Inhibitors (PPI) are the first line drugs. Despite the good results with an oral PPI therapy for 8 weeks, several patients experience the PPI-resistant GERD, a condition in which reflux symptoms caused by

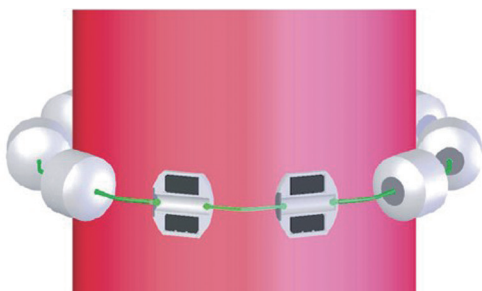


Figure 1 LINX device is made of titanium magnetic beads connected each other by an independent wire (19).

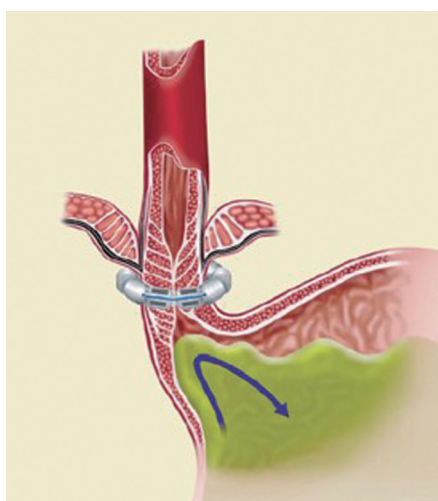


Figure 2 Implantation area (19).

GERD are not adequately mitigated or esophageal mucosa break did not heal after medical therapies (10). Another possibility for GERD treatment is surgery. Anti-reflux surgery is indicated with moderate level of evidence in PPI-resistant GERD patients and with low level of evidence in erosive GERD patients on long term PPI treatment (10). In western countries several clinical trials have been done to compare surgery and medical treatment and they show an improvement of QOL for at least 1 year, reduction of gastric content reflux and a low rate of Barrett's esophagus in patients treated with surgery (11-14).

Currently laparoscopic Nissen fundoplication (LNF) is the gold-standard surgical treatment for GERD.

Unfortunately, laparoscopic fundoplication is influenced by surgical experience and skill and the achievement of a secure anti-reflux effect must be balanced with the onset of complications such as dysphagia and bloating (15,16). LINX

Reflux Management System (Torax Medical, Maple Grove, MN) is a device for magnetic sphincter augmentation (MSA) appeared in 2008 (17) and approved by FDA in 2012. It has emerged as a valuable alternative surgical approach in patients with GERD (18) instead of LNF.

The aim of this study is to elucidate the indication, surgical implantation and provide a brief review of current literature regarding LINX system and its comparison with the gold-standard surgical technique: LNF.

Device features

The LINX SYSTEM is an alternative way to surgical fundoplication. It's implantable through a minimal invasive and reversible procedure. During the operation there is no need of an extensive dissection so the anatomical disruption is minimal and the fundic area is spared. The sizing of the device is customizable and adaptable to a wide range of esophagus diameter.

The LINX SYSTEM is manufactured with titanium beads that contain magnetic cores and are linked together using a titanium wire forming a flexible circular ring (*Figure 1*). This device, after the implantation, rests around the lower esophageal sphincter (LES) (*Figure 2*). The magnetic cores of the beads are conceived to increase the sphincter's resistance to opening from gastric pressures (20).

The augmentative force of the device doesn't decrease over time. When implanted, at rest, there is no compression of the esophageal wall and all the beads are touching each other. During swallowing a bolus can freely pass because the transport force allows the beads to separate and breaks temporarily the attraction bond between magnetic beads because of separation distance. When all beads are separated, the diameter of LINX is almost double. The magnetic attraction force that must be overcome to allow separation of the beads is the same regardless of the number of beads (21).

The LINX SYSTEM is available in various lengths, with different number of beads (from 10 to 18 beads). The device is sized for each patient based on the measurement of the circumference of the esophagus at the gastroesophageal junction (GEJ) (19).

Technical features

Preoperative evaluation

The Gastroesophageal Reflux Disease-Health Related

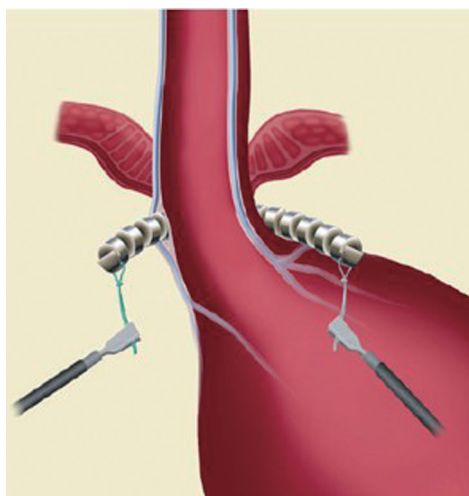


Figure 3 Implant around the esophagus (19).

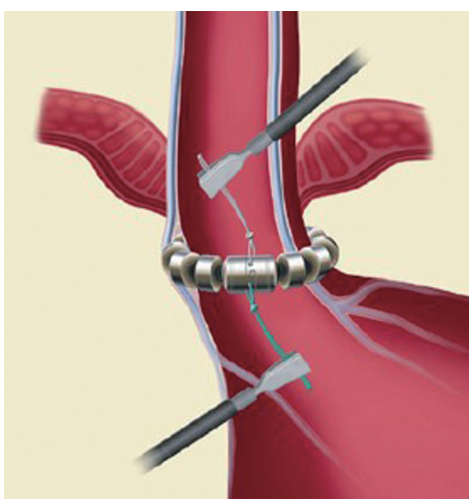


Figure 4 Ends engaged (19).

Quality of Life (GERD-HRQL) questionnaire is still the best preoperative evaluation in order to assess the impact of GERD on patients' everyday life. It is administered off PPI therapy, prior to any diagnostic test (22).

Through esophagogastroduodenoscopy we can verify the presence of esophagitis (Los Angeles classification) and, if present, the length of hiatal hernia (HH; measuring it between the proximal limit of the gastric folds and the crural impression).

LES pressure and length can be tested using esophageal manometry with a station pull-through method: five wet swallows are needed to measure LES relaxation and ten wet

swallows for esophageal contractility (5 mL for each swallow, every 30 seconds). The esophageal motility is abnormal when the average contraction amplitude is 30 mmHg or less and/or when there are at least 30% of simultaneous, interrupted or dropped waves.

Intraoperative

The intraoperative conduction is well described in a previous paper by Bonavina *et al.* (18). Under general anesthesia, the device is implanted laparoscopically.

The exposure of anterior esophageal wall is possible by the dissection of the visceral peritoneum localized on the anterior surface of GEJ. After this, the anterior vagal trunk is detected and preserved in its intramuscular location. The retro-esophageal dissection is performed starting from the anterior border of the right crus, just cephalad to decussation of the crura. In this phase we can identify the posterior vagal trunk. Then the dissection takes place also on diaphragm's left crus. The procedure goes on with the retro-esophageal opening and with the creation of a tunnel between the posterior vagal trunk and the posterior esophageal wall and then with the placement of a 6 mm Penrose drain encircling the esophagus. Since there are different sizes of LINX, we encircle the esophagus with the measurement tool to select the device suitable for the patient and then the LINX is placed into the tunnel and so it encircles the esophagus (*Figure 3*). At the end LINX lies in the incision made previously in the visceral peritoneum at the level of GEJ (*Figure 4*). Both ends of the LINX are securely sutured with a Ti-Knot® (LSI Solutions, Victor, NY, USA). Endoscopically the location of the implant is the Z line (*Figure 5*).

Postoperative period

Oral refeeding starts on postoperative day 1 and the discharge takes place in postoperative day 1 or 2. The follow up is strongly recommended according to the center's protocols.

Indications for use

The LINX Reflux Management System is used to minimize or eliminate GERD related symptoms despite maximum medical therapy.

Pathologic GERD is defined by abnormal Ph testing.

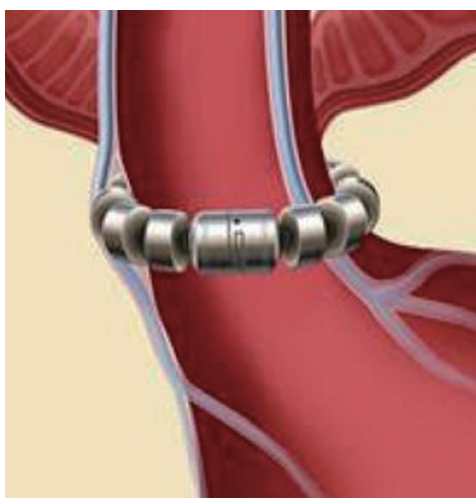


Figure 5 Trimmed suture ends (19).

Contraindication

Allergies to titanium, nickel, ferrous or stainless steel material.

Precautions

- (I) LINX device is labeled for use by physician only.
- (II) For single use only. Do not sterilize.
- (III) The LINX device has not been evaluated in case of HH >3 cm. The use of the device in this subgroup of patients depends on medical history and severity of symptoms.
- (IV) Safety and effectiveness have not been evaluated for other several conditions:
 - (i) Barrett's esophagus grade B and C (LA Classification), grade IV (Savary-Miller) esophagitis.
 - (ii) Patients with defibrillator, pacemaker or other metallic abdominal implants.
 - (iii) Patients with major motility disorders, stricture or anatomic abnormalities (Schatzki's ring).
 - (iv) Patients with scleroderma.
 - (v) Patients with suspected or confirmed esophageal or gastric cancer.
 - (vi) Distal esophageal motility less than 35 mmHg peristaltic amplitude or <70% propulsive peristaltic waves.
 - (vii) achalasia, nutcracker esophagus, diffuse esophageal spasm or hypertensive LES.
 - (viii) Prior gastric or esophageal surgery.

- (ix) Variceal disease.
- (x) Morbid obesity.
- (xi) Lactating, pregnant or plan to become pregnant (21).

Conclusions

GERD is a common disorder worldwide (10–30% of adults); lifestyle modifications and PPI therapy work in many patients with GERD but in 30–40% of them symptoms persist. Patients can become candidate for surgery because of partial control of symptoms with medication, non-compliance with oral treatment, request to avoid long-term PPI therapy, complications or side effects related to PPIs, cost of medical therapy, symptoms with large HH (23).

Currently LNF is the gold-standard surgical treatment for GERD. Magnetic sphincter augmentation device of the LES (MSA or LINX® Reflux Management System, Torax Medical) is an upcoming alternative technique described in 2008 and approved by FDA in 2012.

At present, analysis of literature shows two reviews [Zhang *et al.* (24) and Schizas *et al.* (21)] and three meta-analyses [Aiolfi *et al.* (25), Guidozzi *et al.* (26) and Chen *et al.* (27)] comparing LNF and MSA.

Zhang *et al.* (2016) analyzed the data from 15 clinical studies describing the status of MSA or LINX: they concluded that MSA is as effective as the conventional surgical treatment and there are some advantages with MSA such as good control of symptoms, minimal invasion and less severe postoperative complications.

Chen *et al.* (2017) included 4 trials comparing MSA and NF with a total of 624 patients (299 MSA *vs.* 325 NF respectively). This meta-analysis confirmed efficacy and safety of both techniques; it also showed that MSA has shorter operative time, shorter length of stay and fewer complications of gas and bloating than NF.

In the metanalysis of Aiolfi *et al.* (2018) 7 studies have been included with 1,211 total patients (686 MSA *vs.* 525 Nissen or Toupet laparoscopic fundoplication). Also, this study demonstrated that both techniques are safe and effective. Moreover, MSA is a less invasive and more standardized procedure and seems to induce less bloating and flatulence and to facilitate belch and vomiting.

Guidozzi *et al.* (2019) identified 6 studies that compared MSA *vs.* fundoplication, with a total of 1,099 patients (632 *vs.* 467 respectively). This systematic review also included 13 single-arm cohort studies (11,598 total patients) which evaluated clinical outcomes using MSA. This analysis also

confirmed that MSA is as effective as fundoplication in the control of GERD's symptoms and suggested MSA may be superior in reduction of gas bloating and improvement of belching. Guidozi *et al.* expressed the strong need for a randomized clinical trial between these two surgical treatments.

At last, Schizas *et al.* (2020) reviewed 35 studies with 2,511 MSA patients. This paper showed the advantages of MSA: this technique has shorter operative time and it can be performed with less technical variability than LNF. Moreover, during MSA less interventions on normal anatomy are needed and after this procedure the patient has fewer bloating symptoms and a better capacity to belch or vomit.

Therefore, all meta-analyses and reviews confirmed safety and efficacy, considered as cessation of PPI therapy and reduction or elimination of symptoms, of both methods. The rate of complications is similar in the two groups: postoperative morbidity is 0–3% in MSA and 0–7% in LF. The major complication is dysphagia which can be solved with an endoscopic dilation. Both techniques improve the quality of life of patients with reduction of bloating symptoms and improvement of belching ability.

If necessary, LINX device can be removed. The main cause that lead to device removal is recurrence of heartburn or regurgitation, not related to device complications; never this procedure was performed emergently. Indeed, literature confirms the safety of LINX device and MSA technique (21).

Lipham *et al.* (28) in their study showed that only 3.4% of patients were re-operated.

In another study incidence of device removal was 2.7% without complications (29).

Furthermore, in some cases during the procedure the surgeon performed fundoplication, mostly partial, without long-term complications (30); however, there aren't evidences or studies regarding how to proceed after device removal.

BMI >35 kg/m² influences negatively the success of MSA (31) and LINX implantation seems promising in patients who underwent bariatric surgery only after losing weight (32,33). Further studies including this subgroup of patients are needed.

LINX device, according to SAGES technology and value assessment committee (34), can be successfully used in patients with HH <3 cm. The instructions for use (IFU) reports HH >3 cm within the precaution. Despite this, recent studies (35,36) demonstrated promising results in using MSA in patients with HH (HH) >3 cm.

Ayazi *et al.* (37) demonstrated that excellent outcomes after MSA don't depend on the presence or size of HH and that, despite higher rates of recurrence in large HH than in small ones, the rates of postoperative intervention and LINX removal are similar.

In the meta-analyses and reviews previously described, the presence of HH larger than 3 cm was often an exclusion criterion therefore other studies regarding this population of patients are necessary.

Compared to LNF, MSA has a shorter operative time and length of stay that can neutralize the initial higher cost of the device (38). A study published in 2019 (39) demonstrated that payer costs may be compensated by the reduction in the expenses after surgery.

Future researches are needed in order to present long-term outcomes and confirm efficacy and safety profile, in particular in literature there isn't a randomized controlled trial of MSA *vs.* LNF and many authors have expressed the need of it.

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