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# Laparoscopic magnetic sphincter augmentation versus fundoplication for gastroesophageal reflux disease: systematic review and pooled analysis

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SUMMARY. Magnetic sphincter augmentation (MSA) has been proposed as a less invasive, more appealing alternative intervention to fundoplication for the treatment of gastroesophageal reflux disease (GERD). The aim of this study was to evaluate clinical outcomes following MSA for GERD control in comparison with laparoscopic fundoplication. A systematic electronic search for articles was performed in Medline, Embase, Web of Science, and Cochrane Library for single-arm cohort studies or comparative studies (with fundoplication) evaluating the use of MSA. A random-effects meta-analysis for postoperative proton pump inhibitor (PPI) use, GERD-health-related quality of life (GERD-HROOL), gas bloating, ability to belch, dysphagia, and reoperation was performed. The systematic review identified 6 comparative studies of MSA versus fundoplication and 13 single-cohort studies. Following MSA, only 13.2% required postoperative PPI therapy, 7.8% dilatation, 3.3% device removal or reoperation, and esophageal erosion was seen in 0.3%. There was no significant difference between the groups in requirement for postoperative PPI therapy (pooled odds ratio, POR = 1.08; 95%CI 0.40-2.95), GERD-HRQOL score (weighted mean difference, WMD = 0.34; 95%CI -0.70-1.37), dysphagia (POR = 0.94; 95%CI 0.57-1.55), and reoperation (POR = 1.23; 95%CI 0.26–5.8). However, when compared to fundoplication MSA was associated with significantly less gas bloating (POR = 0.34; 95%CI 0.16–0.71) and a greater ability to belch (POR = 12.34; 95%CI 6.43–23.7). In conclusion, magnetic sphincter augmentation achieves good GERD symptomatic control similar to that of fundoplication, with the benefit of less gas bloating. The safety of MSA also appears acceptable with only 3.3% of patients requiring device removal. There is an urgent need for randomized data directly comparing fundoplication with MSA for the treatment of GERD to truly evaluate the efficacy of this treatment approach.

KEY WORDS: fundoplication, gastroesophageal reflux disease, magnetic sphincter augmentation.

# INTRODUCTION

Gastroesophageal reflux disease (GERD) represents a significant burden on the Western health-care system, affecting up to 20% of adults, with the incidence on the increase.<sup>1,2</sup> Not only does this have a negative impact on a patient's health-related quality of life, but GERD has also been associated with a significant increase in risk of developing esophageal adenocarcinoma.<sup>3</sup> Traditional management of GERD incorporates lifestyle and dietary modification, followed

by antireflux medication (proton pump inhibitors, PPIs, or histamine antagonists) and culminates in surgery for incessant symptoms or pathological complications.<sup>4</sup> The REFLUX randomized clinical trial suggested that surgery offers the most effective symptom control at five years of follow-up, as well as being the most cost-effective treatment strategy.<sup>4–5</sup> Recent evidence has also emerged that suggests that the long-term use of antireflux medication may be associated with dementia, renal pathology, and fractures.<sup>6</sup>

Laparoscopic fundoplication is currently the gold standard of surgical treatment for managing GERD, which can be performed either as a 360° (Nissen) or a partial (Toupet or anterior) fundoplication. According to guidelines from the Society of American Gastrointestinal and Endoscopic Surgeons and the European Association of Endoscopic Surgery, there is no convincing evidence at present to suggest one surgical procedure is superior to the

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other.<sup>7,8</sup> These procedures entail disruption of normal anatomy to produce a competent lower esophageal sphincter using the patient's gastric fundus.<sup>7,9</sup> This form of antireflux surgery has an excellent safety profile with a 30-day mortality risk of 0.03%.<sup>10</sup> Complications of the surgery can be classified as either early (bleeding (<1%), perforation (0–4%), dysphagia (10– 50%), pneumothorax (0-10%), vomiting (2-5%)) or late, including gas bloating in up to 85% of patients, dysphagia (3-24%), diarrhea (18-33%), and recurrence of symptoms (10-62%).<sup>9</sup> In addition to these complications, a proportion of patients may also require surgical reintervention, and some patients may develop recurrent GERD and require the sustained use of antireflux medication postoperatively.<sup>11</sup> Current evidence suggests that 3.6% of patients undergoing fundoplication in England may require surgical reintervention and 59.9% of patients may require antireflux medication at more than 6 months post operatively.<sup>10</sup>

In 2007, a magnetic sphincter augmentation device was introduced as a less invasive, more appealing alternative intervention to fundoplication.<sup>12</sup> The LINX device is placed around the distal esophagus and comprises titanium beads with magnets in the center that augment lower esophageal tone and thus prevent reflux.<sup>13</sup> The device is commonly placed laparoscopically and does not require the same extensive dissection required for fundoplication.<sup>14</sup> The most common complication of the LINX device is dysphagia in 33.9-38% requiring dilatation at the site of the device to relieve symptoms in 5–11% of patients. There have been a few reports of endoluminal erosions that required removal of the device, although no long-term sequalae have been noted.<sup>14</sup> A previous randomized trial comparing the LINX device to increased doses of PPIs demonstrated that patients receiving the LINX device had improved GERD-health-related quality of life (GERD-HRQOL) scores compared to those in the PPI group.<sup>15</sup> Patients also report favourable outcomes with LINX compared to fundoplication, particularly related to the ability to vomit and belch as needed. The LINX device is appealing in terms of its ease of insertion, apparent symptom control, and reduced intra- and postoperative time.<sup>16</sup>

This systematic review and meta-analysis primarily intends to compare clinical outcomes of laparoscopic fundoplication in comparison to the insertion of a LINX device in managing GERDassociated symptoms and complications. The secondary objective is to evaluate the current literature published on the LINX device in substantial case series, in order to identify the true rate of complications, specifically focusing on erosion caused by the device.

# METHODS

# Literature search strategy

An electronic literature search was undertaken using Embase, Medline, and Web of Science databases up to January 2019. The search terms 'linx', 'magnetic sphincter augmentation', 'fundoplication', 'laparoscopy', 'gastroesophageal reflux disease', and Medical Subject Headings (MeSH) 'gastroesophageal reflux' and 'fundoplication' were used in combination with the Boolean operators AND or OR. Two authors (TW and NG) performed the literature search in January 2019. The electronic literature search was supplemented by a hand-search of published abstracts from meetings of the International Society of Diseases of Esophagus (2016 and 2018), European Society of Diseases of the Esophagus (2014, 2015, 2016, and 2017), and European Association of Endoscopic Surgery (2014, 2015, 2016, 2017, and 2018). The reference lists of articles obtained were also searched to identify further relevant citations. Abstracts of the articles identified by the electronic search were scrutinized by two authors (TW and NG) to determine their suitability for inclusion in the pooled analysis.

Publications were included if they were cohort or comparative studies investigating magnetic sphincter augmentation for the treatment of gastroesophageal reflux disease including more than 20 patients. Comparative studies were included in a pooled analysis that compared magnetic sphincter augmentation with fundoplication (partial or total) for the treatment of gastroesophageal reflux disease. Studies were excluded if they included less than 20 patients receiving magnetic sphincter augmentation, or for comparative studies if magnetic sphincter augmentation was not compared to fundoplication.

# **Outcome measures**

*Pooled analysis*: The primary outcome measure was postoperative requirement for PPI therapy. Secondary outcome measures included postoperative GERD-HRQOL score, gas bloating, ability to belch, dysphagia, and need for reoperation.

# Statistical analysis

Data from eligible trials was entered into a computerized spreadsheet for analysis. Statistical analysis was performed using StatsDirect 2.5.7 (Stats-Direct, Altrincham, UK). Weighted mean difference (WMD) was calculated for the effect size of the LINX device upon continuous variables. Pooled odds ratios (PORs) were calculated for the effect of the LINX device on discrete variables (with LINX as

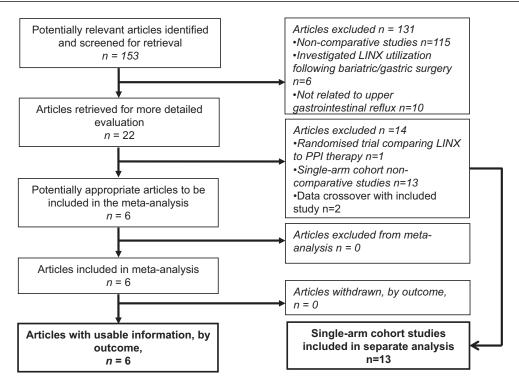


Fig. 1 PRISMA flowchart.

exposure and fundoplication considered as control). All pooled outcome measures were determined using random-effects models as described by DerSimonian & Laird.<sup>17</sup> Heterogeneity among trials was assessed by means of Cochran's Q statistic, a null hypothesis in which P < 0.05 is taken to indicate the presence of significant heterogeneity. The Egger test was used to assess the funnel plot for significant asymmetry, indication of possible publication, or other biases.

### RESULTS

### Literature search (Fig. 1; PRISMA flowchart)

The systematic review identified 6 cohort studies <sup>18–23</sup> that directly compared magnetic sphincter augmentation with fundoplication, comprising 1099 patients, 632 receiving magnetic sphincter augmentation and 467 receiving fundoplication. This systematic review also included 13 single-arm cohort studies, <sup>14,24–35</sup> comprising 11,598 patients, evaluating clinical outcomes from magnetic sphincter augmentation. Follow-up protocols varied between studies, and the time period of follow-up for each study is detailed in Tables 1 and 2.

### Cohort studies and outcome measures (Table 1)

From the 13 single-arm cohort studies, magnetic sphincter augmentation resulted in good control of GERD, as illustrated by only 13.2% (138 out

of 1043 reported patients) requiring postoperative proton pump inhibitor therapy. Further postoperative dilatation was performed in 7.8% (164 out of 2112 reported patients) and device removal or reoperation was required in 3.3% (69 out of 2098 reported patients). From these published single-arm cohort series, the overall rate of esophageal erosion was 0.3%(31 out of 11,530 reported patients).

### Pooled analysis (Table 2)

### Postoperative requirement for PPI therapy (Fig. 2)

Five studies reported the requirement for postoperative PPI therapy. There was no significant difference between the groups in the number of patients requiring postoperative PPI therapy (POR = 1.08; 95%CI 0.40 to 2.95; P = 0.877). There was evidence of significant statistical heterogeneity (Cochran Q = 14.27; P = 0.007,  $I^2 = 72\%$ ), however no significant evidence of bias (Egger = 0.30; P = 0.895).

### Postoperative GERD-HRQOL score (Fig. 3)

Three studies reported the postoperative GERD-HRQOL score. There were no significant differences between the groups in postoperative GERD-HRQOL score (WMD = 0.34; 95%CI -0.70 to 1.37; P = 0.525). There was evidence of significant statistical heterogeneity (Cochran Q = 6.79; P = 0.033,  $I^2 = 70.6\%$ ); however, there was insufficient data to calculate statistical bias.

11-J - 14	N = 9453		Buckley $N = 200$	Czosnyka N = 102	$\underset{N=100}{\text{Ganz}}$			N = 47	N = 47	N = 33	N = 33 $N = 68$	N = 66	Tatum $N = 182$
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PPI use	I	15(15%)	9 (4.5%)	) г	14 (14%)	I	26 (13%)	8 (17%)	5 (10.6%)	4	8 (1	11 (1	38 (20.9%)
Gas bloat	I	2 (2%)	I	I	I	I	32 (16%)	Ι	I	I	I	Ι	Ι
Ability to belch	I	(%66) 66	I	I	I	I	198 (99%)	I	I	I	I	I	I
Abuity to vomit Dilatation		(0/66) 66	- 19/9 50%)	- (% 8%)	- 19 (19%)		13(65%)	2 (4 3%)	6 (12 8%)		- 0 0%)	_ 4 (ہے 1%)	- 20 (15 9%)
Reintervention	I	$\frac{2}{3}(3\%)$	2 (1%)	1 (1%)	4 (4%)	36 (3.6%)	5 (2.5%)	(0/C···) 4	2 (4.3%)	) 3 (9.1%)		0	11 (6%)
Erosion	29 (0.3%)	0	0	0	0	1(0,1%)	1 (0.5%)	0	0			0	
Dysphagia		2 (2%)	12 (6%)	9 (8.8%)	68 (68%)		30(15%)	I	I	I	14(20.6%)	- (	9 (4.9%)
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Outcomes	$\frac{\text{Linx}}{N = 135}$	nx Fundo 135 $N = 103$	$\underset{N=34}{\text{Linx}}$	Fundo $N = 32$	Linx N = 48	Fundo $N = 59$	do 59 Linx N	= 202	Fundo $N = 47$ N	$\begin{array}{cc} \text{Linx} & \mathbf{I} \\ N = 12 & 1 \end{array}$	Fundo $N = 12$ Li	$\operatorname{Linx} N = 201$	Fundo $N = 214$
Mean follow-up	44	4 42	9	10	12	12		12	12	7	7	12	12
(Inolluns) GERD-HRQL score PPI lise		3 3 18 CT· 0 81–1 70	50	5.1 1.(3.1%)	4 7 (14 6%)	5 5 (8 5%)		39 (19 3%) 18 (3	3,5 18 (38 2%) 3	3 (25%) 2	- 16 7%	6 24 (11 9%)	5 12 (5 6%)
Gas bloat	OR 0	OR 0.69 CI: 0.21–2.28	0			616						55 (27.4%)	73 (34.1%)
Ability to vomit			10(4/.170		46 (95.8%)	-			42 (09.4%) 21 (44.7%)	1 1		194 (90.3%) 192 (95.5%)	92 (43%)
Dilatation Reintervention	HR 0	HR 0.77 CI 0.234–2.57	1 (2.9%) 0	1 (3.1%)	9 (18.8%)	o) 8 (13.6%)		8 (4%) 3 (6	3 (6.4%) 6	- 6 (50%)	. 0 0	2 (1%) 2 (1%)	2 (0.9%) 2 (0.9%)
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Odds ratio meta-analysis plot (random effects)

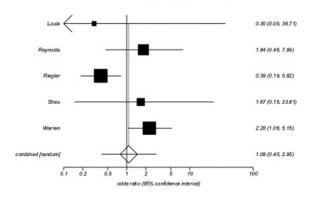


Fig. 2 Forrest plot showing no significant difference between the groups in the number of patients requiring postoperative PPI therapy (POR = 1.08; 95%CI 0.40–2.95; P = 0.877).

Effect size meta-analysis plot [random effects]

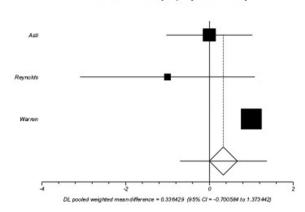
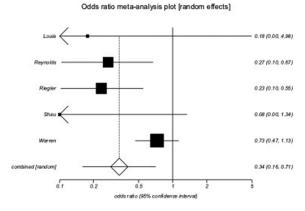


Fig. 3 Forrest plot showing no significant differences between the groups in postoperative GERD-HRQOL score (WMD = 0.34; 95%CI -0.70 to 1.37; P = 0.525).

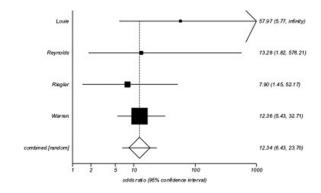


**Fig. 4** Forrest plot showing magnetic sphincter augmentation was associated with a significant reduction in postoperative gas bloating (POR = 0.34; 95%CI 0.16–0.71; P = 0.004).

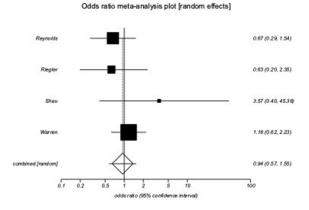
#### Gas bloating (Fig. 4)

Five studies reported the prevalence of postoperative gas bloating. Magnetic sphincter augmentation was associated with a significant reduction in postoperative gas bloating (POR = 0.34; 95%CI 0.16 to 0.71; P = 0.004). There was evidence of significant statistical heterogeneity (Cochran Q = 10.76; P = 0.029,

Odds ratio meta-analysis plot [random effects]



**Fig. 5** Forrest plot showing magnetic sphincter augmentation was associated with a significant increase in the ability to belch postoperatively (POR = 12.34; 95%CI 6.43–23.7; P < 0.001).



**Fig. 6** Forrest plot showing no significant differences between the groups in the prevalence of postoperative dysphagia (POR = 0.94; 95%CI 0.57–1.55; P = 0.822).

 $I^2 = 62.8\%$ ), however no significant evidence of bias (Egger = -1.92; P = 0.149).

#### Ability to belch (Fig. 5)

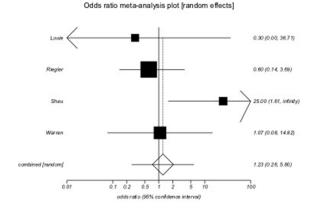
Four studies reported the prevalence of ability to belch postoperatively. Magnetic sphincter augmentation was associated with a significant increase in the ability to belch postoperatively (POR = 12.34; 95%CI 6.43 to 23.7; P < 0.001). There was no evidence of statistical heterogeneity (Cochran Q = 1.46; P = 0.669,  $I^2 = 0\%$ ) or bias (Egger = 0.68; P = 0.504).

#### Dysphagia (Fig. 6)

Four studies reported the prevalence of postoperative dysphagia. There were no significant differences between the groups in the prevalence of postoperative dysphagia (POR = 0.94; 95%CI 0.57 to 1.55; P = 0.822). There was no evidence of significant statistical heterogeneity (Cochran Q = 3.77; P = 0.288;  $I^2 = 20.4\%$ ) or bias (Egger = 0.74; P = 0.725).

#### Need for reoperation (Fig. 7)

Four studies reported the prevalence of postoperative reoperation. There were no significant differences



**Fig. 7** Forrest plot showing no significant differences between the groups in the prevalence of postoperative reoperation (POR = 1.23; 95%CI 0.26–5.8; P = 0.797).

between the groups in the prevalence of postoperative reoperation (POR = 1.23; 95%CI 0.26 to 5.8; P = 0.797). There was no evidence of significant statistical heterogeneity (Cochran Q = 5.83; P = 0.12,  $I^2 = 48.5\%$ ) or bias (Egger = 1.65; P = 0.517).

#### DISCUSSION

This systematic review and pooled analysis primarily confirms that magnetic sphincter augmentation is safe, with minimal postoperative complications identified throughout the currently available literature, and only 0.3% of patients experiencing device erosion and 3.3% of patients requiring device removal or reoperation. The current analysis also confirms that magnetic sphincter augmentation is equally as effective as fundoplication in controlling symptoms of GERD. This is demonstrated by the lack of significant statistical difference in the use of PPIs after GERD intervention in the two groups, as well as similar GERD-HRQOL scores between the two interventions postoperatively. One comparative study also performed postoperative pH testing and demonstrated that the DeMeester score and the period that pH was below 4 both normalized following magnetic sphincter augmentation and laparoscopic fundoplication.<sup>19</sup> Importantly, the current analysis also suggests that magnetic sphincter augmentation may be superior to traditional fundoplication in the development of specific symptoms, with reduction in gas bloating and improvement in the ability to belch postoperatively. These are important factors to consider when comparing patient satisfaction between the procedures, as antireflux surgery is primarily an operation for quality of life.

A random-effects model was utilized in the current study to correct for the heterogeneity of the analyzed data. However, there remain several other limitations to consider when interpreting these results. Magnetic sphincter augmentation studies may potentially underreport complications associated with device implantation, leading to publication bias. The reported complications are reliant on health-care professionals efficiently following up patients post device insertion, identifying both early and late complications, and reporting these complications to the device manufacturer. This process evidently has many potential pitfalls. Associated with this potential limitation is the fact that many magnetic sphincter augmentation studies and comparative studies have relatively small recruitment populations, leading to numerous underpowered studies. Reporting bias is also a limitation to consider in the current literature available, as insertion of the magnetic sphincter augmentation device is a novel procedure, which some surgeons may be technically invested in, driving promising outcomes. Meta-analysis of data regarding reoperation rates was based upon comparative studies with limited follow-up, and may be expected to change substantially over time with more extended follow-up. There was also significant variation in the followup protocols and specifically length of follow-up between individual studies. These limitations highlight the need for a well-designed multicenter randomized controlled trial to fully evaluate the effectiveness of MSA in comparison to laparoscopic fundoplication.

The optimal subgroup for magnetic sphincter augmentation appears to be individuals with mild to moderate symptoms of GERD who are not responding to medical management. The device offers a bridging opportunity in GERD management by attempting to resolve symptoms, while leaving the option for reversal or conversion to fundoplication as a future possible intervention if symptoms do not improve or if complications occur postinsertion. Insertion of the magnetic sphincter augmentation device, despite being quick and technically relatively easy to perform, with less operator variability, has its own complications not associated with those of fundoplication. Currently magnetic sphincter augmentation is not licensed for use in large hiatal hernias, dysmotility disorders, or esophageal erosive disease, so in these circumstances fundoplication would still be the mainstay of treatment.<sup>36,37</sup> With specific reference to esophageal motility, there are different thresholds for peristaltic integrity for patients undergoing laparoscopic fundoplication (which may be considered in patients with a degree of esophageal dysmotility) or magnetic sphincter augmentation (where presence of dysmotility is considered a contra-indication). This factor was addressed by some of the studies included in the current analysis where normal esophageal motility was required for inclusion in either treatment group,<sup>18,19,23</sup> but this was not the case in all studies. This highlights the need for a randomized trial between these two treatments with appropriate

exclusion criteria to ensure comparability between groups.

The findings in this systematic review are in keeping with findings in other studies.<sup>12,36,38</sup> At present, magnetic sphincter augmentation offers an appealing alternative to fundoplication in appropriately selected clinical cases. However, the true preference and clinical benefits for device insertion will only be clearly defined once a randomized control study has been performed. The current data confirms the need for such a trial to take place. Studies that have demonstrated positive outcomes at long-term follow-up post device insertion support the premise that such a trial would be safe to perform.<sup>18,32</sup>

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