International Journal of Surgery 52 (2018) 82–88

Contents lists available at ScienceDirect

International Journal of Surgery

journal homepage: www.elsevier.com/locate/ijsu

Review

Early results of magnetic sphincter augmentation versus fundoplication for gastroesophageal reflux disease: Systematic review and meta-analysis

Alberto Aiolfi, Emanuele Asti, Daniele Bernardi, Gianluca Bonitta, Emanuele Rausa, Stefano Siboni, Luigi Bonavina*

University of Milan, Department of Biomedical Sciences for Health, Division of General Surgery, IRCCS Policlinico San Donato, Italy

ARTICLE INFO

Keywords:
Gastroesophageal reflux disease (GERD)
Laparoscopic fundoplication
Magnetic sphincter augmentation
LINX

ABSTRACT

Background: Laparoscopic Nissen and Toupet fundoplication (LF) are currently considered gold-standard surgical treatment for Gastroesophageal Reflux Disease (GERD). Magnetic Sphincter Augmentation (MSA) is an innovative surgical procedure that has been showed to be effective to control GERD symptoms and to reduce esophageal acid exposure. The aim of this systematic review and meta-analysis was to compare early outcomes of LF and MSA.

Materials and methods: PubMed, MEDLINE, Embase, and Cochrane databases were consulted matching the terms "Gastroesophageal reflux or heartburn", "LINX or magnetic sphincter augmentation" and "fundoplication". Pooled effect measures were calculated using an inverse-variance weighted or Mantel-Haenszel in random effects meta-analysis. Heterogeneity was evaluated using I^2-index and Cochrane Q-test. Meta-regression was used to address the effect of potential confounders.

Results: Seven observational cohort studies, published between 2014 and 2017, matched the inclusion criteria. Overall, 1211 patients, 686 MSA and 525 LF, were included. Postoperative morbidity ranged from 0 to 3% in the MSA group and from 0 to 7% in the LF group, and there was no mortality. Dysphagia requiring endoscopic dilatation occurred in 9.3% and 6.6% of patients respectively (OR = 1.56, 95% CI = 0.61–3.95, p = 0.119). The pooled OR of gas/bloat symptoms, ability to vomit, and ability to belch were 0.39 (95% CI 0.25–0.61; p < 0.001), 10.10 (95% CI 5.33–19.15; p < 0.001), and 5.53 (95% CI 3.73–8.19; p < 0.001), respectively. The postoperative GERD-HRQL was similar (p = 0.101). The pooled OR of PPI suspension, endoscopic dilation, and reoperation were similar in the two patients groups (p = 0.548, p = 0.119, p = 0.183, respectively).

Conclusion: Both anti-reflux procedures are safe and effective up to 1-year follow-up. PPI suspension rate, dysphagia requiring endoscopic dilatation, and disease-related quality of life are similar in the two patient groups. MSA is associated with less gas/bloat symptoms and increased ability to vomit and belch.

1. Introduction

Gastroesophageal reflux disease (GERD) affects up to 25% of the Western population and the prevalence is increasing [1]. First-line treatment of GERD consists of lifestyle modification and medical therapy with proton pump inhibitors (PPI). Although PPI are effective in the majority of patients, 30–40% of individuals on PPI therapy report persistent symptoms [2]. In addition, the therapeutic gain of PPI for the relief of regurgitation is modest and considerably lower than for heartburn in GERD patients [3].

Laparoscopic fundoplication (LF) is the gold-standard treatment for medically refractory GERD [4]. Evidence shows that LF surgery is more effective than PPI in the short/medium term follow-up, but surgical patients more often complain of dysphagia [5,6]. A multicenter randomized clinical trial has shown that laparoscopic antireflux surgery compared to optimized medical therapy are equivalent and most patients remain in remission at 5 years [7]. However, the extensive surgical dissection associated with LF and the technical variability of the procedure may result in significant postoperative morbidity including dysphagia and gas bloat [8,9]. As a consequence, both LF procedures and long-term therapy with PPI have come under scrutiny because of the potential associated side effects.

The magnetic sphincter augmentation (MSA) device was approved by FDA in 2012 and has emerged as a valuable therapeutic alternative in patients with GERD. Several single-arm trials have established consistent and long-term improvement of GERD symptoms scores and

* Corresponding author. Piazza E. Malan, 1, 20097 San Donato Milanese, Milano, Italy.
E-mail addresses: alberto.aiolfi86@gmail.com (A. Aiolfi), Emanuele.Asti@grupposandonato.it (E. Asti), dani_02@hotmail.it (D. Bernardi), bbonit@icloud.com (G. Bonitta), emarausa@yahoo.it (E. Rausa), stesibo@gmail.com (S. Siboni), luigi.bonavina@unimi.it (L. Bonavina).

https://doi.org/10.1016/j.ijsu.2018.02.041
Received 12 December 2017; Received in revised form 16 January 2018; Accepted 15 February 2018
Available online 20 February 2018
1743-9191/

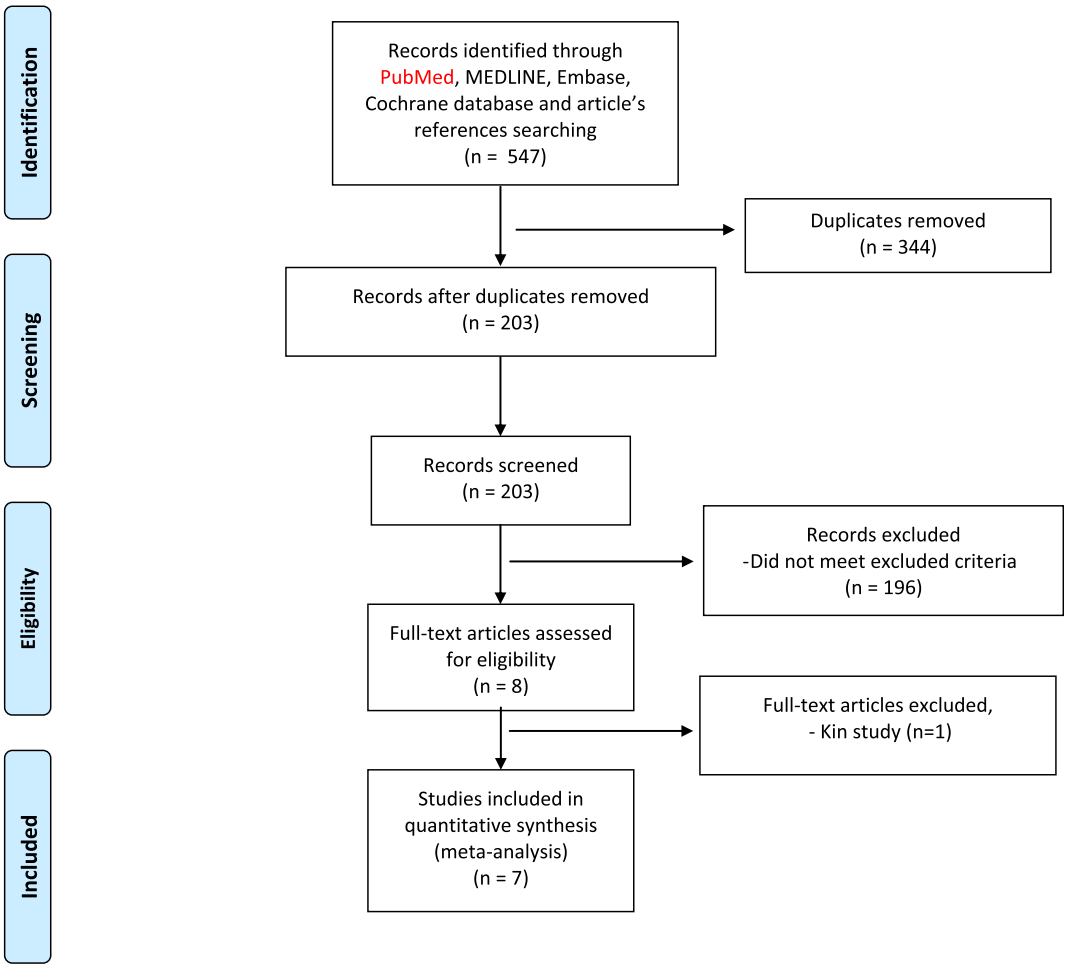

Fig. 1. PRISMA diagram.

esophageal acid exposure, and decreased use of PPI. No studies have directly compared MSA with pharmacological therapy [10–13]. Aim of this systematic review and meta-analysis was to compare early outcomes of MSA and LF.

2. Materials and methods

We conducted this study according to the Preferred Reporting Items For Systematic Reviews and Meta-analyses (PRISMA) statement [14]. An extensive literature search was conducted by all independent authors to identify the English-written published series on studies comparing MSA and LF. PubMed, MEDLINE, Embase, and Cochrane databases were consulted matching the terms "Gastroesophageal reflux or heartburn" and "LINX or endoluminal or magnetic" and "fundoplication" with "AND" and "OR". The search was completed by consulting the listed references of each article.

All articles comparing MSA and laparoscopic partial or total fundoplication were included in the systematic review (Fig. 1). Three authors (AA, EA, DB) independently extracted data from eligible studies. Data extracted included study characteristics (first author name, year and journal of publication), number of patients included in the series, time frame, clinical and demographic characteristics of patients' population, type of surgical procedure, and postoperative outcomes. Disagreements between authors were resolved by consensus; if no agreement could be reached, a fourth senior author (LB), made the decision.

Three investigators independently assessed the methodological quality of the papers using the Newcastle-Ottawa Scale (NOS) [15]. Each study is judged on a "star system" based on the selection of the study groups and the ascertainment of outcome of interest. Each study could earn a maximum of 9 stars.

2.1. Statistical analysis

The results of the systematic review were summarized qualitatively into Frequentist meta-analysis. For pooled measure of effect size an inverse-variance weighted or Mantel-Haenszel random effects meta-analysis was performed, as appropriate [16]. Zero cell count are accounted according to Yusuf et al. [17]. Heterogeneity among the studies was evaluated by I^2–index and Cochran Q test [18]. Statistical heterogeneity was considered significant when $p < 0.10$ or I^2–index was $> 50\%$ [19]. Wald type 95% confidence interval were computed for pooled measure, otherwise 95% confidence interval for I^2–index were calculated according Higgins and Thompson [20]. Small study and publication bias effects were assessed by *Trim and Fill* method [21]. Egger tests were applied [22]. Prediction interval for treatment effect of a new study is calculated according to Borestein [18]. As sample size is not the same in all studies, we performed a sensitivity analysis by excluding one study each time and rerunning the analysis to verify the robustness of the overall results. Z-score test was performed. Two sided p-value were considered statistically significant when < 0.05. All analyses and figures were carried out using R version 3.2.2 software [23].

Table 1
Demographic and clinical data of 1211 patients undergoing Magnetic Sphincter Augmentation (MSA) or fundoplication. nr: not reported.

Author, year country	Study period	Study design	Procedure	#Pts	Males	Mean age (yr)	Mean BMI (Kg/m2)	Mean Hernia size (cm)	Esophagitis ≥ B	Barrett	Mean OR time (min)	Length of stay (hrs)	Completed 6–12 mo follow-up
Louie 2014 USA [24]	2012–2013	Observational retrospective	MSA	34	18	54	27	1.4	5	nr	73	nr	24
			Nissen	32	13	47	30	1.5	7	nr	118	nr	17
Reynolds 2015 USA [25]	2007–2013	Observational retrospective (propensity score matched)	MSA	50	30	53	26.4	1.5	6	10	nr	nr	47
			Nissen	50	27	54	26.7	1.6	7	11	nr	nr	47
Sheu 2015 USA [26]	2012–2013	Observational retrospective	MSA	12	7	39.3	26.8	nr	nr	nr	63.7	24	12
			Nissen	12	6	43.8	26.8	nr	nr	nr	90.3	26.4	12
Riegler 2015 Europe [27]	2010–2013	Observational prospective (multicenter)	MSA	202	125	46.6	25.7	nr	21	2	nr	nr	202
			Nissen/Toupet	47	28	52.8	26.1	nr	14	9	nr	nr	47
Warren 2016 USA [28]	2007–2014	Observational retrospective	MSA	201	104	54	nr	1	38	36	60	13	169
			Nissen	214	92	52	nr	2	55	66	76	32	185
Reynolds 2016 USA [29]	2010–2013	Observational retrospective	MSA	52	32	53	26	nr	2	16	66	17	48
			Nissen	67	31	53	27	nr	5	18	82	38	59
Asti 2016 Europe [30]	2007–2014	Observational retrospective	MSA	135	44	44	23.9	2	13	6	42	48	135
			Toupet	103	61	50	25.1	2	8	7	87	48	103

3. Results

3.1. Systematic review

Seven studies published between 2014 and 2017 matched the inclusion criteria. The total number of patients was 1211; the sample size of the individual studies ranged from 24 to 415. There were no randomized controlled studies. All reports were observational, cohort studies. There was one prospective and one propensity score matched study. Each study reached a NOS score of 6 or 7 (median 6.8), suggesting a good quality level.

Demographic, clinical, and operative variables of the patient sample are shown in Table 1. All patients were operated through a laparoscopic approach. Overall, 686 patients (56%) were managed with the LINX® (Thorax Medical) Magnetic Sphincter Augmentation (MSA) device while 525 (44%) underwent total (Nissen) or partial (Toupet) fundoplication. The mean age of patients ranged from 39.3 to 54, and half of them were males (51.1%). The mean BMI ranged from 23.9 to 30; the mean hernia size ranged from 1 to 2 cm; esophagitis ≥ grade B was present in 15.4% of patients and Barrett esophagus in 16.2%.

Quantitative data from preoperative esophageal pH monitoring (DeMeester score and/or % esophageal pH $<$ 4) were reported in four studies as mean or median values. In the MSA group, the preoperative DeMeester score and the % pH $<$ 4 ranged from 31.4 to 49.5 and from 8 to 14.8, respectively. In the LF group, the preoperative DeMeester score and the % pH $<$ 4 ranged from 37.6 to 49 and from 8.3 to 13.5, respectively. Only one study examined and compared the effect of both procedures on esophageal acid exposure before and after surgery, and found that reflux control was similar [24]. No manometric data were reported in the reviewed studies.

The operative time ranged from 42 to 73 min in the MSA group and from 76 to 118 in the LF group. No studies reported the number of patients that required crural repair in addition to MSA or LF. The overall postoperative morbidity ranged from 0 to 3% in the MSA group and from 0 to 7% in the LF group. There was no mortality. The hospital length of stay ranged from 13 to 48 h in the MSA group and from 26 to 48 h in the LF group. The postoperative follow-up ranged from 6 to 12 months. Since different validated questionnaires for postoperative dysphagia assessment were used in the studies, we focused the sub group of patients who underwent endoscopic dilation. Endoscopic dilation was required in 9.3% of MSA and 6.6% of LF patients. No data were available on symptom resolution after dilation. Assessment of regurgitation was reported only in two studies. Compared to preoperative baseline, a statistically significant improvement was noted for both procedures [24,27]. Reoperation was required in 13 MSA patients: 12 device removals (1 for erosion) and 1 crural release. There were 11 reoperations in the LF group (herniation of the fundic wrap n = 5, persistent GERD n = 3, retroesophageal abscess n = 2, crural release n = 1).

3.2. Meta-analysis

In addition to a systematic review, we performed a Frequentist meta-analysis. Considering random effect model, the estimated pooled mean difference for postoperative GERD-HRQL from 6 studies, which include a total of 1083 patients, is −0.48 (95% CI -1.05-0.09; p = 0.101). The prediction lower and upper limits are −1.289 and 0.331, respectively. There is no significant heterogeneity (I^2 = 0.0%, 95% CI 0.0–42.3%; p = 0.82). Funnel plot and Egger test (p = 0.758) do not show evidence of publication and small study bias. The adjusted *Trim and Fill* mean difference is −0.83 (95% CI -0.31 to −0.36) is close to the original estimation (Fig. 2).

Considering random effect model, the estimated pooled Odds Ratio of PPI suspension, resulting from 6 studies, which include a total of 1098 patients, is 0.81 (95% CI 0.42–1.58; p = 0.548). The prediction lower and upper limits are 0.11 and 5.80, respectively. The

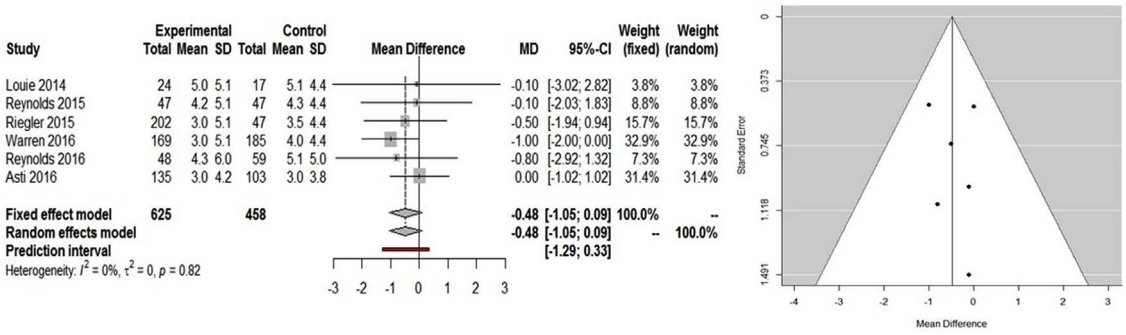

Fig. 2. Forest and Funnel plot of postoperative GERD-HRQL.

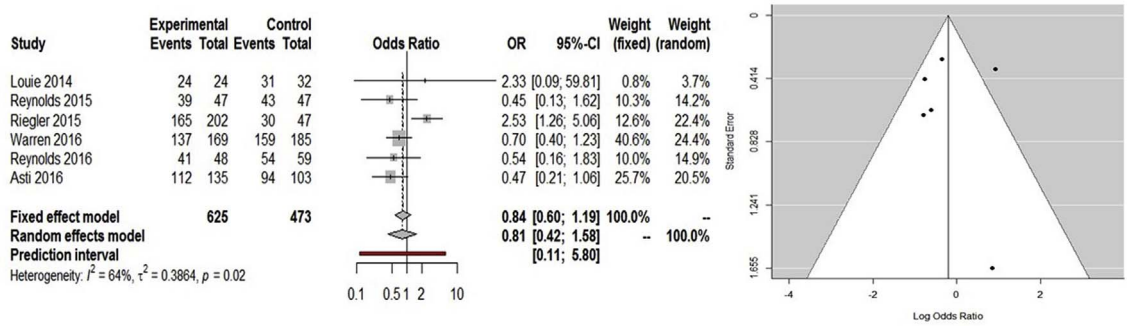

Fig. 3. Forest and Funnel plot of postoperative PPI suspension.

heterogeneity is moderate (I^2 = 63.9%, 95% CI 12.7–85.1%; p = 0.016) and τ^2 = 0.39. Funnel plot shows that publication and small study bias effect could be rejected according to Egger test (p = 0.832). The adjusted *Trim and Fill* Odds Ratio is 0.81 (95% CI 0.41–1.57). The meta-regression using age, BMI, and hernia size as covariates in the univariate model does not significantly reduce the heterogeneity of the study (p < 0.01) (Fig. 3).

Considering random effect model, the estimated pooled Odds Ratio of gas/bloat symptoms, resulting from 5 studies, which include a total of 1042 patients, is 0.39 (95% CI 0.25–0.61; p < 0.001). The prediction lower and upper limits are 0.10 and 1.48, respectively. The heterogeneity is moderate (I^2 = 49.6%, 95% CI 0.0–81.5%; p = 0.09) and τ^2 = 0.12. Funnel plot shows that publication and small study bias effect could not be negligible despite the Egger test is not statistically significant (p = 0.156). The adjusted *Trim and Fill* Odds Ratio that is 0.51 (95% CI 0.32–0.80), that is slight different from the original estimation. The meta-regression using age, BMI, and hernia size as covariates in the univariate model does not significantly reduce the heterogeneity of the study (p < 0.01) (Fig. 4).

Considering random effect model, the estimated pooled Odds Ratio for the ability to vomit, resulting from 6 studies, which include a total of 1048 patients, is 10.10 (95% CI 5.33–19.15; p < 0.001). The prediction lower and upper limits are 1.87 and 54.64, respectively. The heterogeneity is not significant (I^2 = 44%, 95% CI 0.0–78.0%; p = 0.112) and τ^2 = 0.26. Funnel plot shows that publication and small study bias effect could not be negligible despite the Egger test is not statistically significant (p = 0.188). The adjusted *Trim and Fill* Odds Ratio that is 15.58 (95% CI 7.99–30.38), that is different from the original estimation. The meta-regression using age, BMI, and hernia size as covariates in the univariate model does not significantly reduce the heterogeneity of the study (p < 0.01) (Fig. 5).

Considering random effect model, the estimated pooled Odds Ratio for the ability to belch, resulting from 7 studies, which include a total of 1107 patients, is 5.53 (95% CI 3.73–8.19; p < 0.001). The prediction lower and upper limits are 2.87 and 10.65, respectively. The heterogeneity is not significant (I^2 = 8.2%, 95% CI 0.0–73.2%; p = 0.365) and τ^2 = 0.25. Funnel plot and Egger test (p = 0.754) do not show evidence of publication and small study bias. The adjusted *Trim and Fill* Odds Ratio that is 5.54 (95% CI 3.74–8.20), that is close to the original estimation. The meta-regression using age, BMI, and hernia size as covariates in the univariate model does not significantly reduce the heterogeneity of the study (p < 0.01) (Fig. 6).

Considering random effect model, the estimated pooled Odds Ratio of endoscopic dilation, resulting from 5 studies, which include a total of

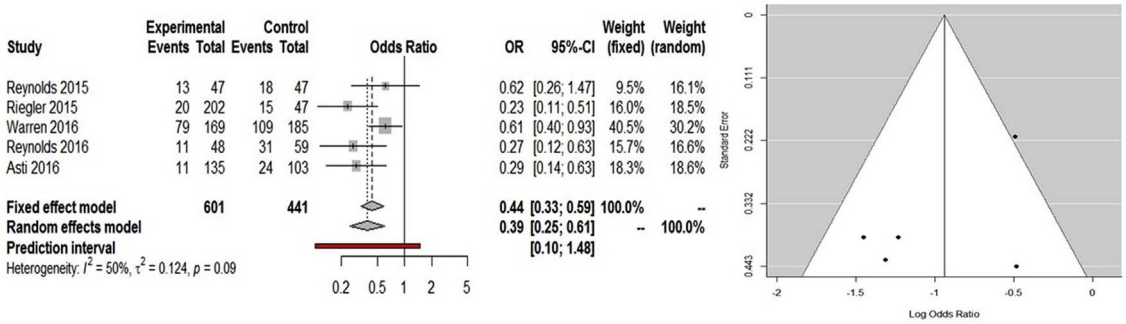

Fig. 4. Forest and Funnel plot of gas/bloat symptoms.

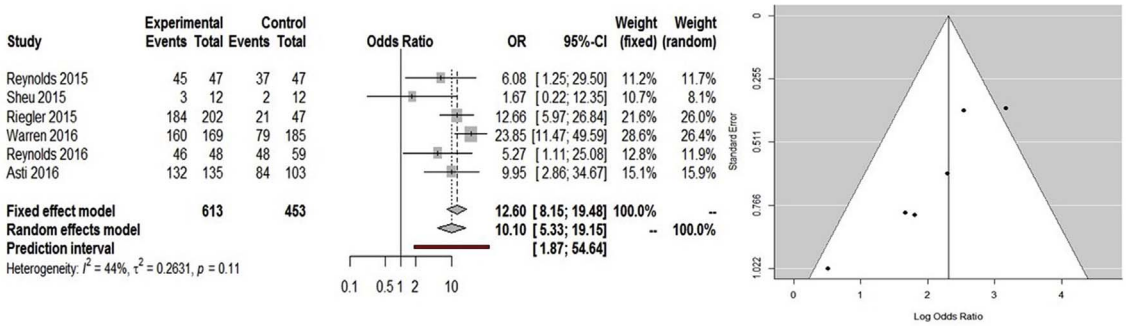

Fig. 5. Forest and Funnel plot of ability to vomit.

535 patients, is 1.56 (95% CI 0.61–3.95; p = 0.119). The prediction lower and upper limits are 0.13 and 18.42, respectively. The heterogeneity is not significant (I^2 = 35%, 95% CI 0.0–75.6%; p = 0.19) and $\tau 2$ = 0.38. Funnel plot shows that publication and small study bias effect could be rejected according to Egger test (p = 0.508). The adjusted *Trim and Fill* Odds Ratio is 1.13 (95% CI 0.42–3.02), that is different from original estimation. The meta-regression using age, BMI, and hernia size as covariates in the univariate model does not significantly reduce the heterogeneity of the study (p < 0.01) (Fig. 7). Furthermore, a potential source of heterogeneity could be the lack of manometric data and information on the effect of crural repair.

Considering random effect model, the estimated pooled Odds Ratio of reoperation, resulting from 3 studies, which include a total of 1187 patients, is 0.54 (95% CI 0.22–1.34; p = 0.183). The prediction lower and upper limits are 0.00 and 191.24, respectively. The heterogeneity is negligible (I^2 = 0.0%, 95% CI 0.0–49; 4.1%; p = 0.814 and $\tau 2$ = 0.0. Funnel plot shows that publication and small study bias effect could not be rejected although Egger test is not significant (p = 0.707). The adjusted *Trim and Fill* Odds Ratio is 0.54 (95% CI 0.23–1.33). The meta-regression using age, BMI, and hernia size as covariates in the univariate model does not significantly reduce the heterogeneity of the study (p < 0.01) (Fig. 8). In addition, the sensitivity analysis showed the robustness of the results for all considered outcomes.

4. Discussion

This systematic review and meta-analysis shows that both LF and MSA are safe and effective up to 1-year follow-up. Preserving the patient ability to belch and vomit and reducing gas-bloat symptoms appear to be the most significant advantage of MSA over LF. Dysphagia requiring endoscopic dilation and reoperation for complications were similar in both patient groups. Quality of life scores, assessed by GERD-HRQL, and the rate of PPI suspension were also similar. In addition, at least up to one year of follow-up, the point estimation of OR relative to reoperation, although not statistically significant, indicates that the risk of redo surgery is about 50% less with MSA compared to LF. Although the OR relative to reoperation is not statistically significant, its magnitude indicates a clinically relevant trend. It is likely that increasing the sample size the result may become statistically significant.

LF is a notoriously difficult and not standardized procedure with outcomes that are dependent on surgeons' skill and experience [31]. From a technical standpoint, MSA provides the surgeon and the patient with a less invasive and more standardized procedure. MSA eliminates the need for extensive dissection of the esophagus, mobilization of the gastric fundus, and crural repair in selected patients. Less inter-user variability allows more consistent and predictable results in the real world setting as shown in multicenter studies [32,33]. The MSA procedure has provided consistent improvement of moderate/severe regurgitation, GERD-HRQL score, PPI dependency, and esophageal acid exposure, in multiple distinct patient cohorts at various time points [34]. The MSA device can be removed laparoscopically with a 1-stage procedure [35].

The clinical results up to 1 year indicate that both LF and MSA provide satisfactory reflux control in a selected category of patients that is those without large hiatus hernia, severe esophagitis, and Barrett's esophagus. Also the outcome data provided by this meta-analysis suggest that MSA improves the ability to vomit and belch and cause less bloating.

The heterogeneity of GERD-HRQL was low in the meta-analysis thus adding robustness to the results. The heterogeneity of PPI suspension rate, postoperative gas/bloat symptoms and ability to vomit was moderate in the meta-analysis. The meta-regression, adjusted for age, BMI, and hernia size does not explain this heterogeneity. Possible sources of heterogeneity may be related to different types of fundoplication, definition and perception of postoperative symptoms, the lack of validated guidelines on PPI dose and timing of PPI suspension. Interestingly, despite the OR was not statistically significant, the point estimation was in favour of fundoplication regarding PPI discontinuation. On the other hand, the heterogeneity of the estimated pooled Odds Ratio for the ability to belch was negligible.

The heterogeneity of the estimated pooled Odds Ratio of endoscopic dilation was moderate. Again, the meta-regression adjusted for age,

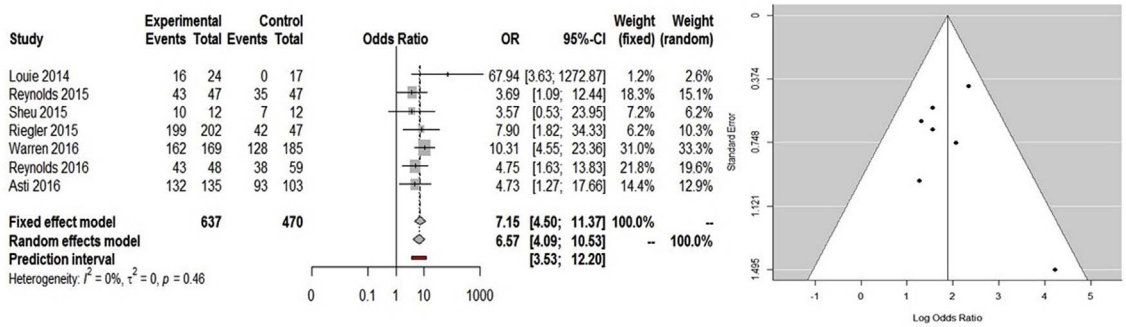

Fig. 6. Forest and Funnel plot of ability to belch.

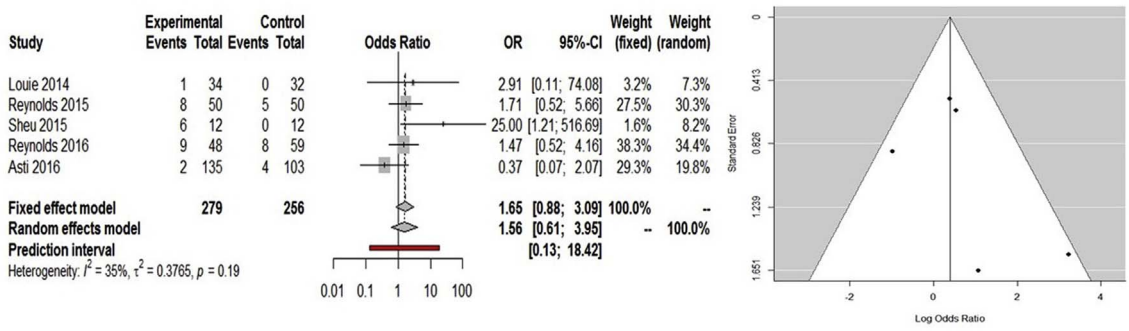

Fig. 7. Forest and Funnel plot of postoperative endoscopic dilation.

BMI, and hernia size does not help to explain this variability. Possible sources of heterogeneity may be the different postoperative dietary regimen in the two groups. The heterogeneity of the estimated pooled Odds Ratio of reoperation was negligible.

To reliably assess the impact of postoperative dysphagia, we focused on the sub-group of patients who required endoscopic dilation during the follow-up. This may have underestimated the overall incidence of dysphagia, but likely represents the expected outcome of any laparoscopic antireflux procedure [36]. Interestingly, given the low heterogeneity, the upper limit of the 95% CI relative to OR, although not statistically significant, is about 4; this may suggest that dysphagia rate after LF is potentially higher due to a greater surgical variability and lack of standardization.

The difference in outcomes between the two patient groups need to be interpreted with caution since no comparative randomized clinical trials exist to provide strong evidence. Furthermore, subgroup analysis according to baseline variables was not possible because all outcomes were aggregated in the analysed studies. However, the sample size of this meta-analysis including over 1200 surgical patients can offer the starting point for planning a randomized clinical trial comparing fundoplication and magnetic sphincter augmentation.

5. Conclusions

Patients with GERD may benefit from both LF and MSA in terms of safety, risk of dysphagia, postoperative disease-related quality of life, and PPI suspension rate at one-year follow-up. MSA appears to induce less bloating and flatulence, and to facilitate belch and vomiting. Whether MSA should be considered a first-line surgical option in appropriately selected patients remains to be determined.

Declaration of interest

None.

Meetings

None.

Funding disclosures

None.

Ethical approval

No ethical approval for this review.
Supported by AIRES (Associzione Italiana Ricerca Esofago).

Conflicts of interest

None.

Research registration unique identifying number (UIN)

reviewregistry409.

Author contribution

Study conception and design: AA, LB.
Acquisition of data: AA, EA, SS, ER, DB.
Analysis and interpretation of data: AA, GB, LB.
Drafting of manuscript: AA, GB, LB.
Critical revision: LB.

Guarantor

Prof. Luigi Bonavina.

Acknowledgements

None.

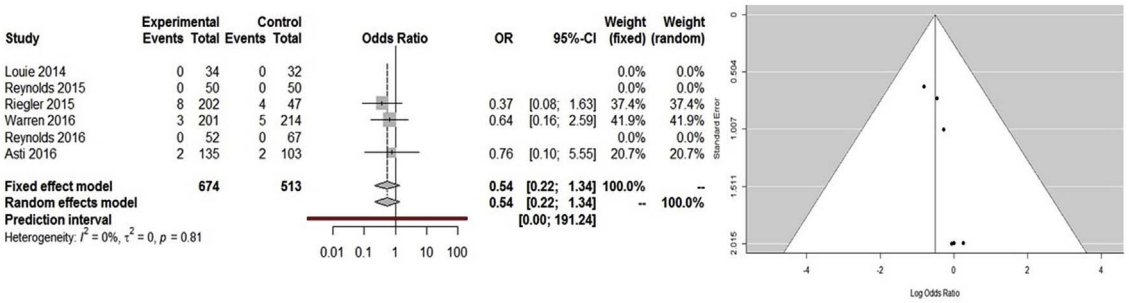

Fig. 8. Forest and Funnel plot of reoperation.

References

[1] H.B. El-Serag, S. Sweet, C.C. Winchester, J. Dent, Update on the epidemiology of gastro-oesophageal reflux disease: a systematic review, Gut 63 (2014) 871–880.

[2] J. Labenz, P. Malfertheiner, Treatment of uncomplicated reflux disease, World J. Gastroenterol. 11 (2005) 4291–4299.

[3] P.J. Kahrilas, C.W. Howden, N. Hughes, Response of regurgitation to proton pump inhibitor therapy in clinical trials of gastroesophageal reflux disease, Am. J. Gastroenterol. 106 (2011) 1419–1425.

[4] P.J. Kahrilas, Gastroesophageal reflux disease, N. Engl. J. Med. 359 (2008) 1700–1707.

[5] S.M. Wileman, S. McCann, A.M. Grant, Z.H. Krukowski, J. Bruce, Medical versus surgical management for gastro-oesophageal reflux disease (GORD) in adults, Cochrane Database Syst. Rev. 17 (2010) CD003243.

[6] D. Mahon, M. Rhodes, B. Decadt, A. Hindmarsh, R. Lowndes, I. Beckingham, B. Koo, R.G. Newcombe, Randomized clinical trial of laparoscopic Nissen fundoplication compared with proton-pump inhibitors for treatment of chronic gastro-oesophageal reflux, Br. J. Surg. 92 (2005) 695–699.

[7] J.P. Galmiche, J. Hatlebakk, S. Attwood, C. Ell, R. Fiocca, S. Eklund, G. Långström, T. Lind, L. Lundell, LOTUS Trial Collaborators, Laparoscopic antireflux surgery vs esomeprazole treatment for chronic GERD: the LOTUS randomized clinical trial, J. Am. Med. Assoc. 305 (2011) 1969–1977.

[8] B. Dallemagne, J. Weerts, S. Markiewicz, J.M. Dewandre, C. Wahlen, B. Monami, C. Jehaes, Clinical results of laparoscopic fundoplication at ten years after surgery, Surg. Endosc. 20 (2006) 159–165.

[9] R.B. Yates, B.K. Oelschlager, Surgical treatment of gastroesophageal reflux disease, Surg. Clin. North. Am. 95 (2015) 527–553.

[10] L. Bonavina, T. DeMeester, P. Fockens, D. Dunn, G. Saino, D. Bona, J. Lipham, W. Bemelman, R.A. Ganz, Laparoscopic sphincter augmentation device eliminates reflux symptoms and normalizes esophageal acid exposure: one- and 2-year results of a feasibility trial, Ann. Surg. 252 (2010) 857–862.

[11] J.C. Lipham, T.R. DeMeester, R.A. Ganz, L. Bonavina, G. Saino, D.H. Dunn, P. Fockens, W. Bemelman, The LINX® reflux management system: confirmed safety and efficacy now at 4 years, Surg. Endosc. 26 (2012) 2944–2949.

[12] L. Bonavina, G. Saino, D. Bona, A. Sironi, V. Lazzari, One hundred consecutive patients treated with magnetic sphincter augmentation for gastroesophageal reflux disease: 6 years of clinical experience from a single center, J. Am. Coll. Surg. 217 (2013) 577–585.

[13] R.A. Ganz, J.H. Peters, S. Horgan, Esophageal sphincter device for gastroesophageal reflux disease, N. Engl. J. Med. 368 (2013) 2039–2040.

[14] D. Moher, A. Liberati, J. Tetzlaff, D.G. Altman, PRISMA Group, Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement, PLoS Med. 6 (2009) e1000097.

[15] A. Stang, Critical evaluation of the Newcastle-Ottawa scale for the assessment of the quality of nonrandomized studies in meta-analyses, Eur. J. Epidemiol. 25 (2010) 603–605.

[16] R. DerSimonian, N. Laird, Meta-analysis in clinical trials, Contr. Clin. Trials 7 (1986) 177–188.

[17] S. Yusuf, R. Peto, J. Lewis, R. Collins, P. Sleight, Beta blockade during and after myocardial infarction: an overview of the randomized trials, Prog. Cardiovasc. Dis. 27 (1985) 335–371.

[18] M. Borenstein, L.V. Hedges, J.P.T. Higgins, Introduction to Meta-analysis, John Wiley & Sons, Ltd, Chichester, UK, 2009.

[19] J.P. Higgins, S.G. Thompson, J.J. Deeks, D.G. Altman, Measuring inconsistency in meta-analyses, BMJ 327 (2003) 557–560.

[20] J.P. Higgins, S.G. Thompson, Quantifying heterogeneity in a meta-analysis, Stat. Med. 21 (2002) 1539–1558.

[21] J. Anzures-Cabrera, J.P. Higgins, Graphical displays for meta-analysis: an overview with suggestions for practice, Res. Synth. Meth. 1 (2010) 66–80.

[22] M. Egger, G. Davey Smith, M. Schneider, C. Minder, Bias in meta-analysis detected by a simple, graphical test, BMJ 315 (1997) 629–634.

[23] R Development Core Team, A Language and Environment for Statistical Computing, R Foundation for Statistical Computing, Vienna, Austria, 3-900051-07-0, 2015.

[24] B.E. Louie, A.S. Farivar, D. Shultz, C. Brennan, E. Vallières, R.W. Aye, Short-term outcomes using magnetic sphincter augmentation versus Nissen fundoplication for medically resistant gastroesophageal reflux disease, Ann. Thorac. Surg. 98 (2014) 498–504.

[25] J.L. Reynolds, J. Zehetner, P. Wu, S. Shah, N. Bildzukewicz, J.C. Lipham, Laparoscopic magnetic sphincter augmentation vs laparoscopic nissen fundoplication: a matched-pair analysis of 100 patients, J. Am. Coll. Surg. 221 (2015) 123–128.

[26] E.G. Sheu, P. Nau, B. Nath, B. Kuo, D.W. Rattner, A comparative trial of laparoscopic magnetic sphincter augmentation and Nissen fundoplication, Surg. Endoscopy 29 (2015) 505–509.

[27] J.L. Reynolds, J. Zehetner, A. Nieh, N. Bildzukewicz, K. Sandhu, N. Katkhouda, J.C. Lipham, Charges, outcomes, and complications: a comparison of magnetic sphincter augmentation versus laparoscopic Nissen fundoplication for the treatment of GERD, Surg. Endosc. 30 (2016) 3225–3230.

[28] H.F. Warren, J.L. Reynolds, J.C. Lipham, J. Zehetner, N.A. Bildzukewicz, P.A. Taiganides, J. Mickley, R.W. Aye, A.S. Farivar, B.E. Louie, Multi-institutional outcomes using magnetic sphincter augmentation versus Nissen fundoplication for chronic gastroesophageal reflux disease, Surg. Endosc. 30 (2016) 3289–3296.

[29] M. Riegler, S.F. Schoppman, L. Bonavina, D. Ashton, T. Horbach, M. Kemen, Magnetic sphincter augmentation and fundoplication for GERD in clinical practice: one-year results of a multicenter, prospective observational study, Surg. Endosc. 29 (2015) 1123–1129.

[30] E. Asti, G. Bonitta, A. Lovece, V. Lazzari, L. Bonavina, Longitudinal comparison of quality of life in patients undergoing laparoscopic Toupet fundoplication versus magnetic sphincter augmentation: observational cohort study with propensity score analysis, Medicine (Baltim.) 95 (2016) e4366.

[31] L. Bonavina, T.R. DeMeester, R.A. Ganz, LINX(™) Reflux Management System: magnetic sphincter augmentation in the treatment of gastroesophageal reflux disease, Expet Rev. Gastroenterol. Hepatol. 6 (2012) 667–674.

[32] R.A. Ganz, S.A. Edmundowicz, P.A. Taiganides, J.C. Lipham, C.D. Smith, K.R. DeVault, et al., Long-term outcomes of patients receiving a magnetic sphincter augmentation device for gastroesophageal reflux, Clin. Gastroenterol. Hepatol. 14 (2016) 671–677.

[33] G. Saino, L. Bonavina, J.C. Lipham, D. Dunn, R.A. Ganz, Magnetic sphincter augmentation for gastroesophageal reflux at 5 Years: final results of a pilot study show long-term acid reduction and symptom improvement, J. Laparoendosc. Adv. Surg. Tech. A. 25 (2015) 787–792.

[34] R.A. Ganz, A modern magnetic implant for gastroesophageal reflux disease, Clin. Gastroenterol. Hepatology 15 (2017) 1326–1337.

[35] E. Asti, S. Siboni, V. Lazzari, G. Bonitta, A. Sironi, L. Bonavina, Removal of the magnetic sphincter augmentation device: surgical technique and results of a single-center cohort study, Ann. Surg. 265 (2017) 941–945.

[36] S.K. Garg, K.S. Gurusamy, Laparoscopic fundoplication surgery versus medical management for gastro-oesophageal reflux disease (GORD) in adults, Cochrane Database Syst. Rev. 11 (2015) CD003243.