Systematic Review and Meta-Analysis

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Laparoscopic Nissen (total) versus anterior 180° fundoplication for gastro-esophageal reflux disease

A meta-analysis and systematic review

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Abstract

Background: Laparoscopic Nissen fundoplication (LNF) has been the gold standard for the surgical management of Gastro-esophageal reflux disease (GERD). Laparoscopic anterior 180° fundoplication (180° LAF) is reported to reduce the incidence of postoperative complications while obtaining similar control of reflux. The present meta-analysis was conducted to confirm the value of the 2 techniques.

Methods: PubMed, Medline, Embase, Cochrane Library, Springerlink, and China National Knowledge Infrastructure Platform databases were searched for randomized controlled trials (RCTs) comparing LNF and 180° LAF. Data regarding the benefits and adverse results of 2 techniques were extracted and compared using a meta-analysis.

Results: Six eligible RCTs comparing LNF (n = 266) and 180° LAF (n = 265) were identified. There were no significant differences between LNF and 180° LAF with regard to operating time, perioperative complications, length of hospital stay, patient satisfaction, willingness to undergo surgery again, quality of life, postoperative heartburn, proton pump inhibitor (PPI) use, postoperative DeMeester scores, postoperative lower esophageal sphincter (LES) pressure, postoperative gas-bloating, unable to belch, diarrhea, or overall reoperation. LNF was associated with a higher prevalence of postoperative dysphagia compared with 180° LAF, while 180° LAF was followed by more reoperation for recurrent reflux symptoms.

Conclusion: LNF and 180° LAF are equally effective in controlling reflux symptoms and obtain a comparable prevalence of patient satisfaction. 180° LAF can reduce the incidence of postoperative dysphagia while this is offset by a higher risk of reoperation for recurrent symptoms. The risk of recurrent symptoms should need to be balanced against the risk of dysphagia when surgeons choose surgical procedures for each individual with GERD.

Abbreviations: 180° LAF = laparoscopic anterior 180° fundoplication, GERD = gastro-esophageal reflux disease, LES = lower esophageal sphincter, LNF = laparoscopic Nissen fundoplication, LTF = laparoscopic Toupet fundoplication, PPI = proton pump inhibitor, RCTs = randomized controlled trials.

Keywords: anterior fundoplication, gastro-esophageal reflux disease, laparoscopic fundoplication, meta-analysis, Nissen fundoplication

1. Introduction

Gastro-esophageal reflux disease (GERD) is a very common disorder with increasing prevalence, leading a considerable healthcare burden and affecting quality of life.[1–3] Since the first laparoscopic Nissen fundoplication (LNF) was described in 1991,[4] extensive studies regarding laparoscopic antireflux surgery have been reported, demonstrating an established role of fundoplication for the treatment of GERD.[5–7] As the most widely used surgical treatment of GERD, LNF is associated with some unwanted functional disorders, such as dysphagia, gas-bloating syndrome. To minimize the risk of these complications, a variety of modifications of LNF have been launched.[8–10] Division of the short gastric vessels is one such strategy. However, the results of randomized controlled trials (RCTs)[9,11] failed to demonstrate any advantage of such strategy in reducing side-effects.

Constructing a posterior partial fundoplication is an alternative approach. The outcomes of RCTs[12,13] and a meta-

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analysis[14] we conducted previously have not shown a significant reduction in postoperative dysphagia following posterior partial fundoplication and "tailored therapy" has not been supported based on preoperative esophageal motility.

Anterior fundoplication, another alternative surgical treatment of GERD, has been recommended by some surgeons. Compared with LNF, uncontrolled prospective studies[15,16] have suggested that laparoscopic anterior 180° fundoplication (180° LAF) can reduce the incidence of postoperative complications while having a comparable control of reflux symptoms. But, several other RCTs have not shown a significant difference between 2 techniques.[17,18] To provide evidence for optimal clinical practice, we performed a meta-analysis of published RCTs.

2. Methods

This meta-analysis was conducted and the results were described according to the PRISMA statement.[19]

2.1. Search strategy

The following electronic databases were searched till February 2017: PubMed, Medline, Embase, Cochrane Library (issue 2, 2017), Springerlink, and China National Knowledge Infrastructure Platform (CNKI; http://www.cnki.net) databases. A manual search was also performed to identify trials in the reference lists of the articles acquired. Language restrictions were not applied. A search strategy using disease-specific terms (e.g., gastro-esophageal reflux disease), management-specific terms (e.g., laparoscopic antireflux fundoplication), and terms related to surgical procedures (e.g., Nissen, anterior, total, and partial) were adopted.

2.2. Inclusion criteria and exclusion criteria

Inclusion criteria were: RCTs comparing efficacy and adverse outcomes of LNF and 180° LAF; age ≥16 years; laparoscopic procedure was carried out in all patients; raw data could be extracted from studies to calculate outcomes; patients with established GERD undergoing primary antireflux surgery.

Exclusion criteria were: non-RCTs; trials comparing total and non-180° LAF (e.g., total versus anterior 90° fundoplication); fundoplications were carried out with laparotomy; studies published repeatedly in different journals; studies for which raw data could not be extracted to obtain pooled results and the corresponding author could not provide data requested.

2.3. Outcomes of interest

Subjective evaluation included patient satisfaction with the intervention, presence of postoperative heartburn, dysphagia, gas-bloating, unable to belch, and diarrhea. Objective evaluation consisted of DeMeester scores on 24-hour pH monitoring, lower esophageal sphincter (LES) pressure, and endoscopic esophagitis. Prevalence of perioperative complications, postoperative dilatation for dysphagia, quality of life, reoperation, number of willingness to undergo surgery again, postoperative proton pump inhibitor (PPI) use, operating time, duration of hospitalization, and mortality were also evaluated. Among the outcomes mentioned above, patient satisfaction, postoperative heartburn, postoperative esophagitis, and dysphagia were regarded as primary outcome parameters, and the others were regarded as secondary outcome.

2.4. Data extraction

Two independent reviewers (XD and FW) extracted details from selected studies independently. Data comprised information provided and the quality of the research: first author, publication year, study population characteristics, study design, sample size, follow-up duration, and inclusion/exclusion criteria; and outcomes analysis, including beneficial and adverse results. Disagreements between reviewers were resolved by a third author (CZ). Outcomes of interest of repeated RCTs in which the study population arose from the same cohort published in different journals at different phases were extracted based on the article that was published most recently. For dichotomous outcomes, the number of events was recorded and for continuous outcomes, the mean and standard deviations (SDs) were registered. If data were missing, the authors of the original studies were contacted to provide the relevant information. If the authors could not provide missing mean and SDs, they were imputed on the basis of the medians and ranges.[20]

2.5. Statistical analysis

Data extracted from eligible trials were integrated with Review Manager 5.3 provided by the Cochrane Collaboration, following the recommendation of The Cochrane Collaboration and Quality of Reporting of Meta-analyses guidelines.[21,22] Outcomes reported by 2 or more studies were pooled in the meta-analysis. Dichotomous and continuous outcomes were presented as risk ratio (RR) and weighted mean difference respectively. Results were pooled using standardized mean difference (SMD) if a continuous outcome was reported by different scales. Dichotomous outcomes were pooled using the Mantel–Haenszel method, while continuous outcomes were pooled using the inverse variance method. The fixed-effects model was used if heterogeneity was absent (χ^2 test, $P > .1$ and $I^2 < 50\%$).[23,24] If excessive heterogeneity was present, data were first rechecked and the random-effects model was used when heterogeneity persisted.[25] Subgroup analysis was performed to assess the impact of follow-up duration. Funnel plots were used to identify the presence of publication bias.[26]

2.6. Quality assessment

According to Cochrane criteria guidelines, all included studies were evaluated to ascertain if methodological bias was present.[27]

2.7. Ethical approval and patient consent

Ethical approval and patient consent were not necessary because the study was a systematic review of previous published studies and did not involve patient consent.

3. Results

3.1. Description of the studies

After screening of trials according to inclusion and exclusion criteria, 6 RCTs[17,18,28–31] published between 2004 and 2015 were identified, including 531 patients, of whom 266 (50. 1%) underwent LNF and 265 (49.6%) underwent 180° LAF, one of which was published in Chinese and obtained from Chinese databases[31] (Fig. 1). Duration of follow-up ranged from 5 to 120 months. Hiatal repair was performed in all the patients, followed by either a standardized 180° LAF or a standardized

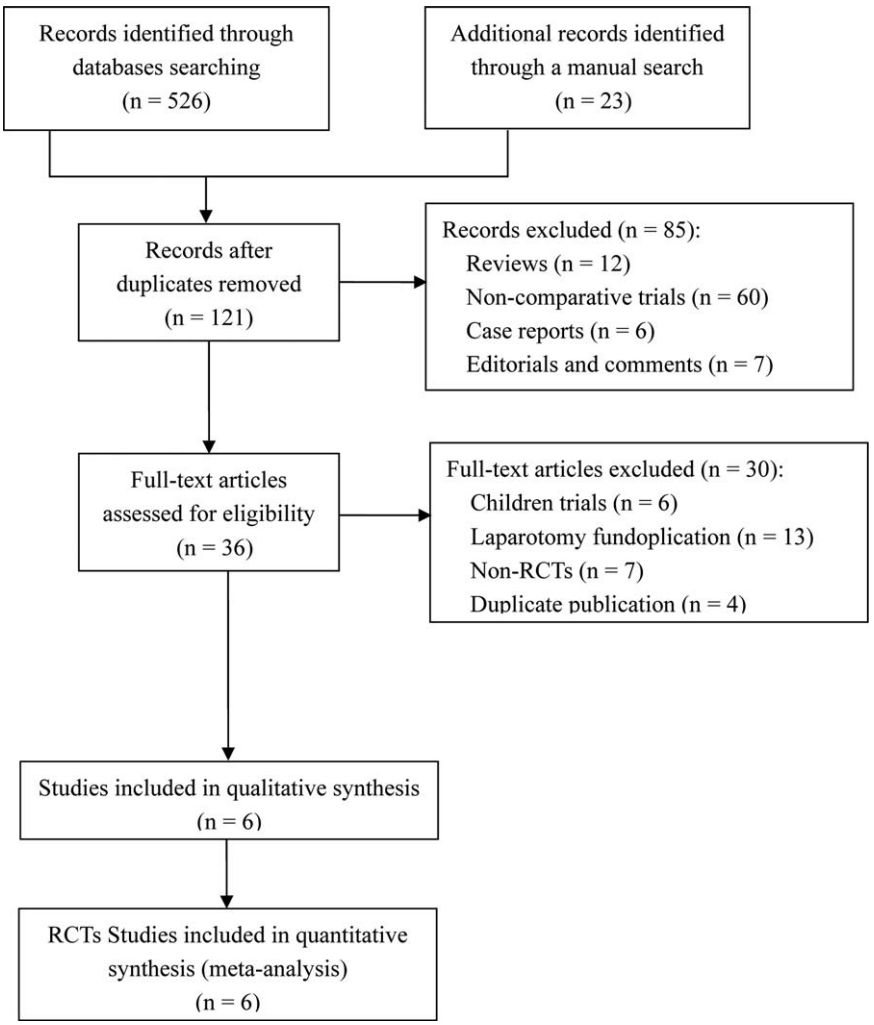

Figure 1. A flowchart showing the process and result of trials screening. RCTs = randomized controlled trials.

LNF. All the patients had proof of GERD on upper gastrointestinal endoscopy and/or 24-hour pH monitoring. The study population of Baigrie et al[29] and Broeders et al[32] came from the same cohort and they reported 24-month and 60-month follow-up outcomes, respectively. Similarly, 3 papers[17,33,34] reported short-term (6 months), mid-term (60 months), and long-term (120 months) results of the same study cohort, respectively. Basic characteristics of included RCTs are listed in Table 1.

3.2. Quality assessment

The methodological quality of included trials is shown in Table 2. Main limitations resulted from poor description of allocation

Table 1

The basic characteristics of included randomized clinical trials.

Source	Country	Method	N	Sex ratio (M/F)	Age, y	Hiatal Repair	Bougie	DSGV	FU
Chrysos 2004[28]	Greece	LAF	12	4/8	58	Yes	No	No	5
		LNF	12	9/3	52	Yes	No	No	
Baigrie 2005[29]	South Africa	LAF	79	45/34	45	Yes	No	No	60
		LNF	84	49/35	43	Yes	56 Fr	No	
Cai 2008[17]	Austria	LAF	54	34/20	45	Yes	No	No	120
		LNF	53	36/17	47	Yes	52 Fr	No	
Raue 2011[18]	Germany	LAF	30	14/16	54	Yes	42 Fr	No	18
		LNF	27	16/11	48	Yes	42 Fr	Yes	
Cao 2012[30]	China	LAF	50	16/34	57	Yes	No	No	60
		LNF	50	21/29	59	Yes	No	Yes	
Diao 2015[31]	China	LAF	40	20/20	45	Yes	No	No	6
		LNF	40	18/22	46	Yes	No	No	

DSGV = division of short gastric vessels, Fr = Frence, FU = follow-up (months), LAF = laparoscopic anterior 180° fundoplication, LNF = laparoscopic Nissen fundoplication, M/F = male/female, NR = not reported.

Table 2

Risk of bias summary.

	①	②	③	④	⑤	⑥	⑦
Chrysos 2004[28]	LR	UR	UR	UR	HR	LR	LR
Baigrie 2005[29]	LR	LR	LR	LR	LR	LR	LR
Cai 2008[17]	LR	LR	LR	LR	LR	LR	LR
Raue 2011[18]	LR	LR	LR	UR	LR	LR	LR
Cao 2012[30]	LR	HR	HR	LR	LR	LR	LR
Diao 2015[31]	LR	HR	HR	UR	LR	LR	LR

①: Random sequence generation; ②:Allocation concealment; ③:Blinding of participants and personnel ④:Blinding of outcomes assessment; ⑤:Incomplete outcome data; ⑥:Selective reporting; ⑦: Other bias. HR = high risk, LR = low risk, UR = unclear risk.

concealment and a lack of (or poor description of) double-blinding processes.[28,30,31]

3.3. In-hospital characteristics

Operating time, length of hospital stay, and perioperative complications were similar for both groups (Table 3).

3.4. Patient satisfaction, willingness to undergo surgery again and quality of life

Four trials[17,18,29,30] reported patient satisfaction after LNF and 180° LAF. Meta-analysis revealed no significant difference in this outcome between the 2 arms (RR = 0.95, 95% confidence interval (CI), 0.90–1.01, $P = .10$) (Fig. 2A). Three trials[17,29,30] reported patient's willingness to undergo surgery again after 2 techniques and there was no significant difference in this outcome between the 2 groups (RR = 1.01, 95% CI, 0.96–1.08, $P = .60$) (Table 3). There were 2 trials[18,31] that reported quality of life after 2 techniques and meta-analysis revealed no significant difference in this outcome between the 2 groups (SMD = 0.34, 95% CI, –0.47 to 1.14, $P = .41$) (Table 3).

3.5. Postoperative heartburn and PPI use

All the included studies reported postoperative heartburn after LNF and 180° LAF. Subgroup analysis was conducted according to the duration of follow-up. And both total-group and subgroup analysis found no significant difference in this parameter between the 2 arms (total-group, RR = 1.11, 95% CI, 0.68–1.83, $P = .67$) (Fig. 2B). This was accompanied by a comparable PPI use (Table 3).

3.6. Objective outcomes

Five studies[17,18,28,30,31] reported postoperative DeMeester scores on 24-hour pH monitoring. Meta-analysis revealed no significant difference in this parameter between the 2 arms (weighted mean difference = 0.85, 95% CI, –0.05 to 1.74, $P = .06$) (Fig. 3A). Five studies[17,18,28,30,31] reported postoperative LES pressure. Meta-analysis revealed no significant difference in this parameter between the 2 groups (SMD = –0.74 mm Hg, 95% CI, –1.94 to 0.46 mm Hg, $P = .23$) (Fig. 3b). Three studies[17,18,30] reported postoperative esophagitis after LNF and 180° LAF. Meta-analysis revealed no statistically difference in this parameter between the 2 groups (RR = 2.01, 95% CI, 0.94–4.29, $P = .07$) (Fig. 3C).

3.7. Postoperative complications

All the studies reported the prevalence of postoperative dysphagia, including 3 studies[18,28,31] with duration of follow-up <60 months and 3 studies[17,29,30] with duration of follow-up ≥60 months. In the total-group and subgroup with a follow-up ≥60 months, results favored 180° LAF (total-group, RR = 0.63, 95% CI, 0.47–0.85, $P = .003$; subgroup, RR = 0.67, 95% CI, 0.49–0.90, $P = .009$) (Fig. 4). Nevertheless, in the subgroup with a follow-up <60 months, the prevalence of dysphagia was similar between the 2 groups (RR = 0.39, 95% CI, 0.1–1.33, $P = .13$) (Fig. 4). In addition, postoperative dilatation for dysphagia,

Table 3

Meta-analysis of some outcome parameters after LNF and 180° LAF.

Outcome	n		Heterogeneity test				
	LAF	LNF	I^2 (%)	*P*	Analysis model	SMD (95% CI) or RR (95% CI)	*P*
Operating time	204	203	82	<.001	Random	SMD 0.02 (–0.47, 0.50)	.95
Length of hospital stay	67	70	55	.13	Random	SMD –0.28 (–0.79, 0.23)	.28
Perioperative complication	254	253	0	.42	Fixed	RR 2.18 (0.69, 6.93)	.19
Willingness to undergo surgery again	178	166	14	.31	Fixed	RR 1.01 (0.96, 1.08)	.64
Quality of life	67	70	82	.02	Random	SMD 0.34 (–0.47, 1.14)	.41
PPI use	134	132	0	.85	Fixed	RR 1.25 (0.65, 2.39)	.51
Dilatation for dysphagia	202	190	0	.82	Fixed	RR 0.44 (0.16, 1.22)	.11
Gas-bloating	211	202	73	.01	Random	RR 0.56 (0.17, 1.91)	.36
Unable to belch	147	142	59	.12	Random	RR 1.38 (0.16, 11.99)	.77
Diarrhea	93	94	0	.44	Fixed	RR 1.13 (0.43, 3.00)	.80
Reoperation	206	199	0	.90	Fixed	RR 1.50 (0.76, 2.95)	.24
Reoperation for dysphagia	132	120	0	.95	Fixed	RR 0.28 (0.06, 1.28)	.10
Reoperation for recurrent symptoms	179	169	34	.22	Fixed	RR 3.58 (1.30, 9.88)	.01

LAF = laparoscopic anterior 180° fundoplication, LES = lower esophageal sphincter, LNF = laparoscopic Nissen fundoplication, PPI = proton pump inhibitor, RR = risk ratio, SMD = standard mean difference.

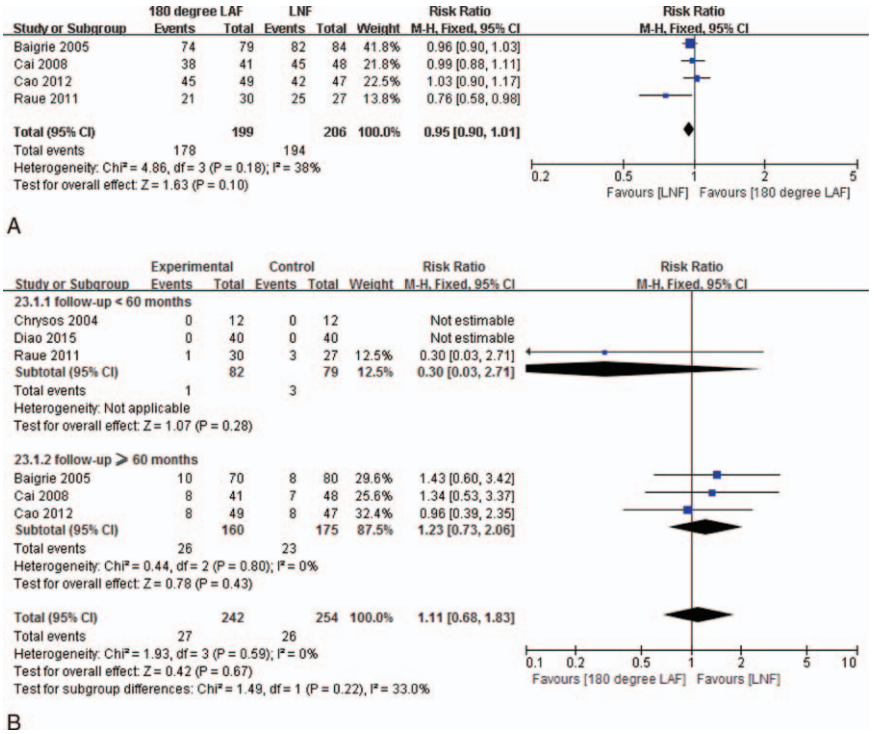

Figure 2. Meta-analysis of patient satisfaction (A) and postoperative heartburn (B) after LNF and180° LAF. LAF = laparoscopic anterior 180° fundoplication, LNF = laparoscopic Nissen fundoplication.

postoperative gas-bloating, unable to belch, and diarrhea were similar between 2 procedures (Table 3).

3.8. Reoperation and mortality

Five studies[17,18,29,30] reported the prevalence of overall reoperation after LNF and 180° LAF. Meta-analysis revealed no significant difference in this parameter between the 2 groups (RR = 1.50, 95% CI, 0.76–2.95, $P = .24$) (Table 3). Subgroup analyses showed reoperation for dysphagia was also similar between 2 groups (RR = 0.28, 95% CI, 0.06–1.28, $P = .10$) (Table 3). However, the reoperation for recurrent symptoms was more prevalent after 180° LAF than LNF (RR = 3.58, 95% CI, 1.30–9.88, $P = .01$) (Table 3).

As there was no death associated with these 2 surgical methods in hospital or during follow-up, the 2 arms could not be compared regarding mortality.

3.9. Publication bias

Funnel plot regarding postoperative dysphagia did not demonstrate obvious evidence publication bias (Fig. 5).

4. Discussion

Antireflux operations are aimed at creating an effective barrier to reflux at the gastroesophageal junction and thus attempt to improve physiologic and mechanical issues involved in the pathogenesis of GERD.[35] Ideal antireflux surgery should provide durable reflux control with no troublesome functional disorders. However, how to achieve the ideal technique is unknown currently. The small but significant incidence of dysphagia and gas-bloating syndrome associated with LNF has promoted the development of alternative strategies for the treatment of GERD (e.g., posterior and anterior partial fundoplication). The posterior partial fundoplication, mainly laparoscopic Toupet fundoplication (LTF), is to construct 270° wrap of esophagus with the gastric fundus. Nevertheless, no trials have demonstrated a significant reduction in postoperative dysphagia rate or provided clear evidence to support routine application of LTF.[12–14] Memon et al[36] conducted a meta-analysis comparing laparoscopic anterior with posterior fundoplication, and the results of the study suggested laparoscopic anterior fundoplication was a better alternative to laparoscopic posterior fundoplication. However, it is not appropriate to generalize 2 types of partial fundoplication into 1 category and it would reduce the credibility of the results of the meta-analysis above. A meta-analysis was performed to compare outcomes between LNF and 180° LAF in 2013,[37] and a comprehensive study collecting RCTs has not been conducted to date. Therefore, to better weigh the potential benefits against the potential side-effects, reappraisal of data in existing studies is important.

According to the outcomes from our meta-analysis, the conclusions can be drawn as follows. First, patient satisfaction was high (LNF, 94.2%; LAF, 89.4%) and comparable between LNF and 180° LAF. Second, 180° LAF offered similar reflux symptoms control compared with LNF, but with more reoperation for recurrent symptoms. Third, 180° LAF could reduce postoperative dysphagia compared with LNF.

In-hospital characteristics (e.g., operating time, perioperative complications, and length of hospital stay) and reflux symptoms control (measured by heartburn and PPI use) were similar between 2 groups. Subgroup analysis showed that the outcomes regarding postoperative heartburn were not altered by duration of follow-up,

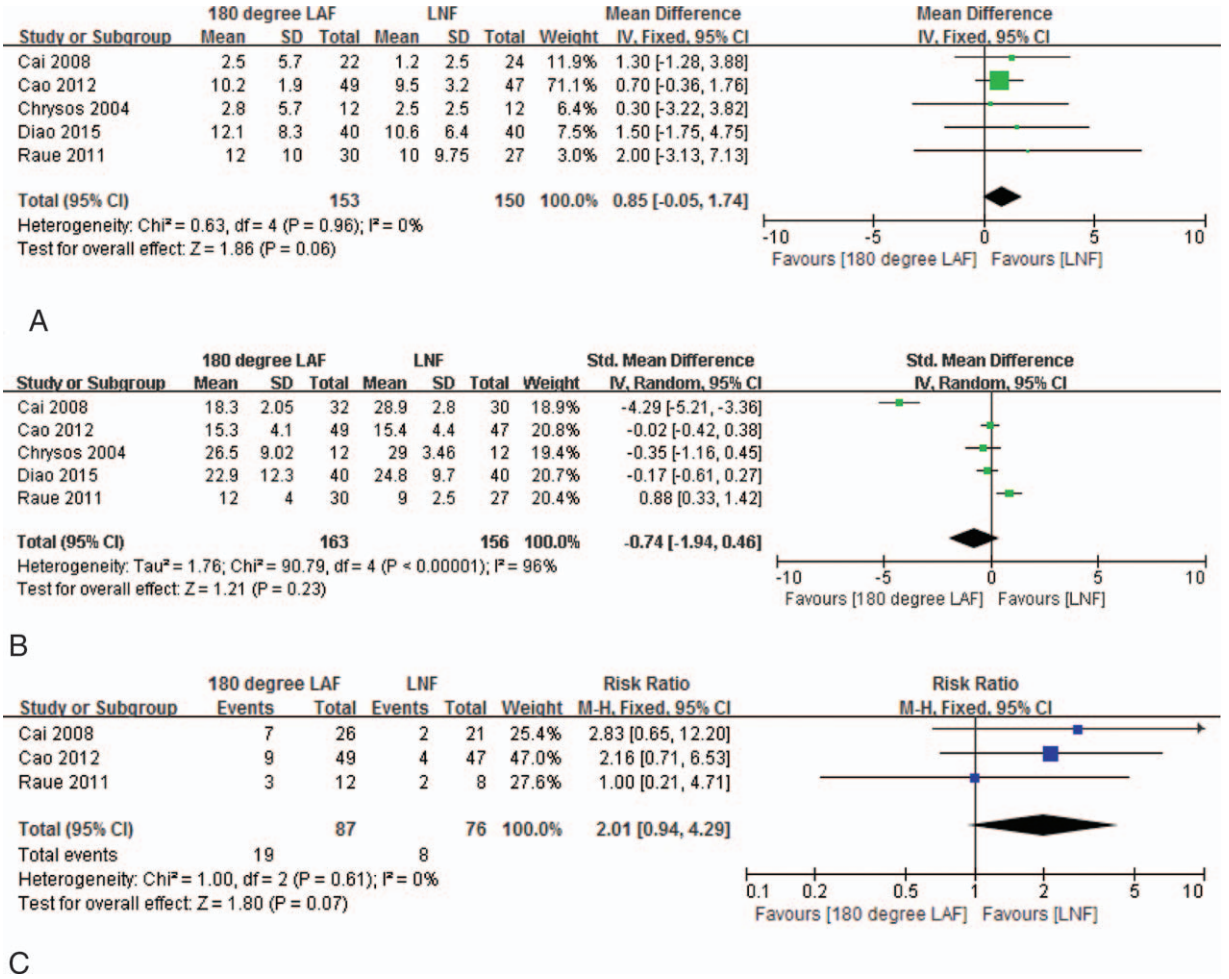

Figure 3. Meta-analysis of postoperative DeMeester scores (A), LES pressure (B), and esophagitis (C) after LNF and 180° LAF. LAF = laparoscopic anterior 180° fundoplication, LES = lower esophageal sphincter, LNF = laparoscopic Nissen fundoplication.

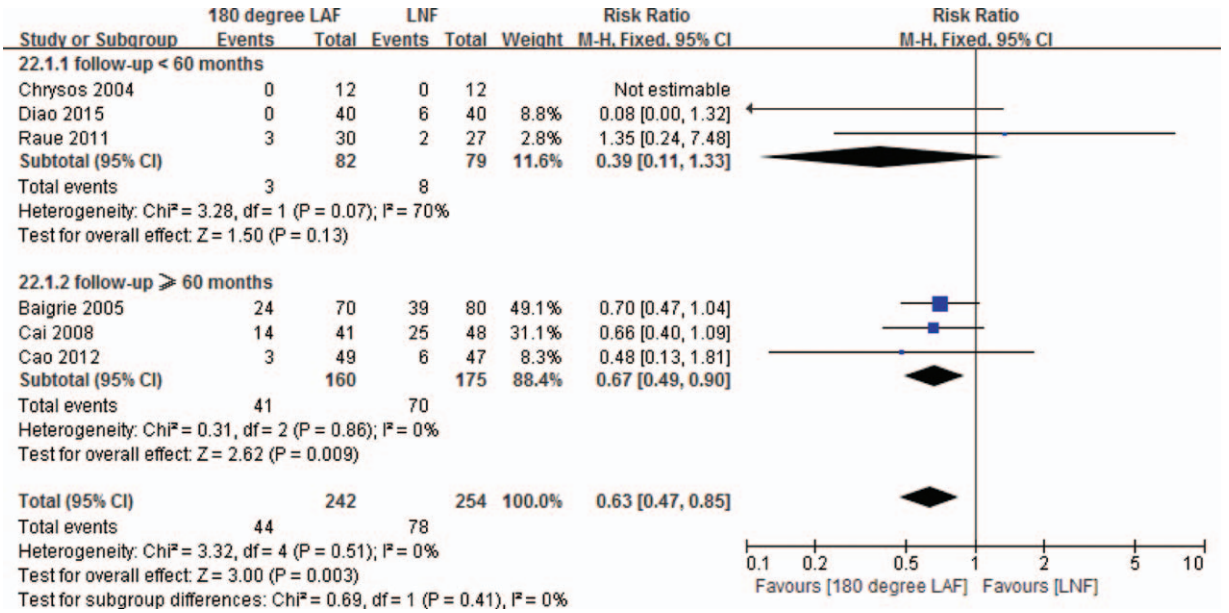

Figure 4. Meta-analysis of prevalence of postoperative dysphagia after LNF and 180° LAF. LAF = laparoscopic anterior 180° fundoplication, LNF = laparoscopic Nissen fundoplication.

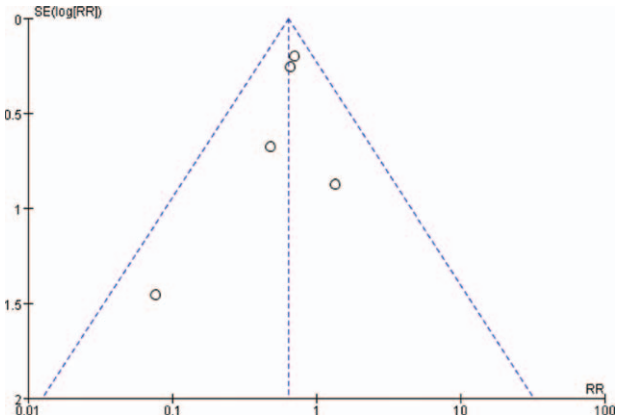

Figure 5. Funnel plot regarding postoperative dysphagia.

indicating that 180° LAF could offer durable reflux control as LNF. However, the use of PPI does not always imply the recurrence of reflux symptoms. And only a small number of patients taking these medicines have abnormal reflux monitoring[38–40] and most of patients undergoing fundoplication use antireflux medication for atypical symptoms different from the original complains.[41] Therefore, the use of antireflux medication should only be regarded as a relative sign of recurrent symptoms.

With respect to objective outcomes, DeMeester scores, LES pressure and the prevalence of esophagitis after operation were both similar between 2 techniques. It should be pointed out that objective follow-up was always less complete than clinical assessment because of the invasiveness of laboratory measurements. From the perspective of patients, successful surgery was determined by symptoms relief rather than the outcomes of objective investigations.[42] That is to say, more objective follow-up data are needed to validate the objective outcomes of 2 procedures.

Gastrointestinal functional disorders, especially dysphagia, are the main side-effects of antireflux procedures, affecting the quality of life of patients undergoing fundoplication. The present meta-analysis revealed that 180° LAF could reduce the prevalence of postoperative dysphagia compared with LNF, and subgroup analysis also showed the similar trend up to 5-year follow-up. However, our report did not find any significant difference regarding postoperative gas-bloating, unable to belch and diarrhea between 2 procedures. As we all know, the way the anterior fundoplication is constructed is different from the posterior fundoplication variants: the gastric fundus is located in front rather than behind the esophagus and the circumference of the wrap is reduced, 2 main factors accounting for the differences between 2 procedures. To investigate the underlying causes of postoperative complains, some studies evaluated physiological effects of fundoplication[43,44] and they found impaired LES relaxation was related to postoperative dysphagia. A systematic review conducted by Broeders et al[45] suggested that LES relaxation was more likely to be incomplete following posterior than anterior fundoplication. The author held the opinion that this might result from placement of the gastric fundus behind the intra-abdominal esophageal and the incompleteness of LES relaxation probably contribute to higher dysphagia rate after LNF, an issue needed to be discussed further. As for postoperative gas-bloating syndrome, it is commonly speculated that impairment of swallowed air venting from the stomach induces gas-bloating and unable to belch after surgery.[46] Broeders et al[47] previously reported that ventilation of air was harder after total fundoplication than partial fundoplication, a potential mechanism accounting for a reduced risk of gas-bloating syndrome. What is more, some surgeons[48] deemed that LNF created an overcompetent valve while partial fundoplication restored the gastro-esophageal junction to a more physiological state.

Our study demonstrated that the patient satisfaction, a reasonable and accurate index for assessing the efficacy of surgical treatment for GERD,[49] was high (nearly 90%) and comparable between the 2 arms. At the same time, patient's willingness to undergo surgery again and quality of life were also similar between the 2 groups.

Despite excellent results of satisfaction, a minority of patients presented with recurrent reflux symptoms, a few of whom required or requested surgical revision for the failed antireflux surgery. To have a successful reoperation, it is key to not only understand the type of anatomical failure but also know the detail of the prior intervention. So, in most cases, the reoperation for the failed antireflux procedure is a touch issue. In the present study, a higher incidence of reoperation for recurrent reflux symptoms was found following 180° LAF (LAF, 15/169; LNF, 4/179), though the overall number of revision procedures was not significantly different after 2 procedures. In addition, LNF was associated with a higher prevalence of dysphagia, but without more reoperation and dilatation for dysphagia and other postoperative complications. From the perspective of the 2 aspects above, 180° LAF was not superior to LNF based on the current evidence.

Strengths of our study are that the meta-analysis was based on the largest sample size (n = 531) and publication bias was not obvious, which ensured high internal validity of the present study. What is more, surgical techniques of the included studies were identical and standardized, including repairment of hiatal hernia and construction of the fundoplication. As for the division of the short gastric vessels, RCTs[9,11] and the meta-analysis we undertook previously[14] showed that it did not alter outcomes. And the subgroup analyses did not support "tailored therapy" according to preoperative esophageal motility.[50]

The limitations of our meta-analysis were: sample size of some included studies was small and few studies reported outcomes beyond 5 years after fundoplication; follow-up outcomes of objective parameters were incomplete (less than 50% of study population). Three RCTs[28,30,31] were not well conducted and the quality of them was low. Further RCTs with large-scale samples and well-designed models are required to validate the value of 2 procedures.

5. Conclusion

LNF and 180° LAF are equally effective in controlling reflux symptoms and obtain a comparable prevalence of patient satisfaction. 180° LAF can reduce the incidence of postoperative dysphagia while this is offset by a higher risk of reoperation for recurrent reflux symptoms. A balance should be achieved between risk of recurrent symptoms and benefits of less dysphagia when surgeons choose surgical procedures for patients with GERD.

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