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Laparoscopic Anterior 180˚ *versus* Nissen Fundoplication for Gastroesophageal Reflux Disease

Systematic Review and Meta-analysis of Randomized Clinical Trials

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Running head

Anterior 180˚ *versus* Nissen fundoplication for GERD: a meta-analysis

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Mini-Abstract

Systematic review and meta-analysis demonstrating that laparoscopic anterior 180˚ fundoplication (180˚ LAF) reduces short and longer-term dysphagia and gas-related symptoms compared to laparoscopic Nissen fundoplication, with similar reflux control, dilatations and reoperation rate. These results lend level 1a support for the use of 180˚ LAF for the surgical treatment of GERD.

Structured abstract

Objective: To compare short and longer-term outcome after laparoscopic anterior 180˚ fundoplication (180˚ LAF) *versus* laparoscopic Nissen fundoplication (LNF).

Summary of background data: LNF is currently the most frequently performed surgical therapy for GORD. Alternatively, 180˚ LAF has been alleged to reduce troublesome dysphagia and gas-related symptoms, with similar reflux control.

Methods: MEDLINE, EMBASE, Cochrane Library and ISI web of Knowledge CPCI-S were searched for randomized clinical trials (RCTs) comparing primary 180˚ LAF *versus* LNF. The methodological quality was evaluated to assess bias risk. Primary outcomes were esophageal acid exposure, esophagitis, heartburn score, dilatation for dysphagia, modified Dakkak dysphagia score [0-45] and reoperation rate. Meta-analysis was conducted at one and five years.

Results: Five distinct RCTs comparing 180˚ LAF (n=227) *versus* LNF (n=231) were identified. At one year, the Dakkak dysphagia score (2.8 vs 4.8; weighted mean difference (WMD) -2.25; 95% CI [-2.66, -1.83]; P<0.001), gas bloating (11% vs 18%; relative risk (RR) 0.59; 95% CI [0.36,0.97]; P=0.04), flatulence (14% vs 25%; RR 0.57; 95% CI [0.35,0.91]; P=0.02), inability to belch (19% vs 31%; RR0.63 ;95% CI [0.40,0.99]; P=0.05) and inability to relieve bloating (34% vs 44%; RR 0.74; 95% CI [0.55,0.99]; P=0.04) were lower after 180˚ LAF. Esophageal acid exposure (standardized mean difference (SMD) 0.19; 95% CI [-0.07,0.46]; P=0.15), esophagitis (19% vs 13%; RR 1.42; 95% CI [0.69, 2.91]; P=0.34), heartburn score (SMD 1.27; 95% CI [-0.36,2.90]; P=0.13), dilatation rate (1.4% vs 2.8%; RR 0.60; 95% CI [0.19,1.91]; P=0.39), reoperation rate (5.7% vs 2.8%; RR 2.08; 95% CI [0.80,5.41]; *P*=0.13), perioperative outcome, regurgitation, PPI use, LES pressure and patient satisfaction were similar after 180˚ LAF and LNF. At 5 years, the Dakkak dysphagia

score, flatulence, inability to belch and inability to relieve bloating remained lower after 180˚ LAF. The five-year heartburn score, dilatation rate, reoperation rate, PPI use and patient satisfaction were similar.

Conclusions: At one and five years, dysphagia and gas-related symptoms are lower after 180˚ LAF compared with LNF, and esophageal acid exposure and esophagitis are similar, with no differences in heartburn scores, patient satisfaction, dilatations and reoperation rate. These results lend level 1a support for the use of 180˚ LAF for the surgical treatment of GERD.

Introduction

Laparoscopic fundoplication is the surgical approach of choice for gastroesophageal reflux disease (GERD). Total fundoplication according to Nissen provides excellent reflux control and is the most frequently performed operation for GERD.[1-3] However, laparoscopic Nissen fundoplication (LNF) is followed by a significant incidence of troublesome dysphagia and gas-related symptoms.[4-6] Partial fundoplications have been developed as alternatives and aim to reduce the incidence of these postfundoplication symptoms.

A fundoplication is created by wrapping the fundus of the stomach anteriorly or posteriorly around the esophagus. Total fundoplication according to Nissen is an example of a posterior fundoplication. Commonly used partial fundoplications are posterior 270˚ fundoplication, anterior 90˚ fundoplication and anterior 180˚ fundoplication.[7] Several randomized clinical trials (RCTs) have evaluated whether partial wraps reduce postfundoplication symptoms and whether this is associated with inferior reflux control compared to LNF.[7] Systematic reviews have been performed to combine the results of these RCTs. Two meta-analyses have compared LNF to the pooled results of various types of partial fundoplications[5,6] and another review combined a mixture of posterior fundoplications and compared them to the pooled results of anterior fundoplications.[8] However, this year the long-term results of randomized trials demonstrated that 180˚ laparoscopic anterior fundoplication (LAF) offers similar reflux control compared to LNF, whereas reflux control after 90˚ LAF is less effective than after LNF.[9] Therefore, generalizing these two fundoplication types into one category in the setting of a meta-analysis is probably not appropriate. Comparing one partial fundoplication type head-to-head to LNF increases the validity of the analysis and facilitates application of the results in clinical practice. This study aims, therefore, to systematically review all RCTs comparing 180˚ LAF and LNF for GERD and to generate the highest level of evidence.

Methods

Study selection

A systematic literature search with predefined search terms (Figure 1) was carried out in MEDLINE (from 1960),[10] EMBASE (from 1980),[11] Cochrane Library (issue 1, 2012) and the ISI Web of Knowledge Conference Proceedings Citation Index - Science (CPCI-S; from 1990) databases on April 14th, 2012 (Figure 1). All identified articles were screened for cross-references. Language restrictions were not applied.

Inclusion criteria

Title and abstract of all identified articles were screened and selected according to the following inclusion criteria: study population - adult patients with established GERD undergoing primary antireflux surgery; intervention - clearly documented surgical technique of laparoscopic anterior 180˚ fundoplication[12] and laparoscopic Nissen fundoplication[13], irrespective of division of the short gastric vessels;[5] study outcomes - at least one of the outcome measures reported below; study design - patients assigned to either 180˚ LAF or LPF by random allocation; publication - published as a full article in a peer-reviewed journal.

Exclusion criteria

Studies were excluded from analysis if they did not meet the inclusion criteria, or if the corresponding author was not able to provide data requested and it was impossible to extract or calculate appropriate data from the published results. Abstracts of RCTs were excluded as the fundoplication circumference, surgical technique, methodological quality and the risk of bias of these studies could not be assessed.

Outcomes of interest and definitions

Primary outcomes were: esophageal acid exposure on pH monitoring (total esophageal acid exposure time or DeMeester score[14]), endoscopic esophagitis, presence of heartburn, severity of heartburn (an analog score (0=no heartburn; 10=severe heartburn), dilatation for

dysphagia, presence of dysphagia, severity of dysphagia (validated modified Dakkak dysphagia score: 0, no dysphagia; 45, severe dysphagia)[15] and reoperation rate. Secondary outcomes included operating time, conversion rate, in-hospital complications, length of hospital stay, regurgitation, PPI use, inability to belch, gas bloating, ability to relieve bloating and increased flatulence. Patient satisfaction was scored using an analog score (0=dissatisfied; 10=satisfied), the percentage of patients that was satisfied with outcome, a Visick score (1= no symptoms; 2= mild symptoms; 3= moderate symptoms; 4= moderate symptoms interfering with life; 5= symptoms as bad or worse after surgery)[16] and willingness to undergo surgery again. One-year results (6-18 months), five-year outcome and results at 5 years and beyond were pooled separately in meta-analysis.

Data extraction

Titles and abstracts of all retrieved records, and subsequently full-text articles, were examined independently by two authors (JAB, DJR) according to the Quality of Reporting of Meta-analyses (QUOROM) guidelines.[17-19] The following data were extracted separately by the same two authors (JAB, DJR) for all studies meeting the inclusion criteria: reference of study, study population characteristics, study design, inclusion and exclusion criteria and number of participating subjects for each endpoint. For dichotomous outcomes, the number of events was recorded and for continuous outcomes means and standard deviations (SDs) were registered. In case of discrepancies, a third author (UAA) was consulted and agreement was reached by consensus.

Authors of all the original RCTs were contacted and agreed to provide missing data. When authors could not provide missing data, the following methods of handling missing data were applied. If the number of patients per arm was missing for an outcome, an equal distribution between both arms was assumed. Missing standard deviations (SDs) were either imputed based on ranges when available[20] or based on the average SDs reported by other RCTs for the same outcome.[10] If both means and SDs were missing, they were imputed

based on the medians and ranges[20] or based on medians and interquartile ranges[10], according to availability.

Risk of bias assessment

Risk of bias was assessed of all articles using both the Cochrane Collaboration's tool for assessing risk of bias[10] and the Jadad scoring system.[21]

Statistical analysis

Statistical analyses were performed following the recommendations of the Cochrane Collaboration and QUOROM guidelines.[17-19] Outcomes reported by two or more studies were pooled in meta-analyses. Short and long-term results were analyzed separately. Dichotomous and continuous outcomes were presented as risk ratios (RRs) and weighted mean differences (WMDs), respectively. Results were pooled using standardized mean differences (SMDs) if trials reported different scales for a continuous outcome measure. Data were pooled using the Mantel-Haenszel and the inverse-variance method for dichotomous outcomes and for continuous outcomes, respectively. Trials with zero events in both arms were excluded from meta-analysis. Trials with zero events in one arm were included in the analysis by adding a continuity correction of 0.5 to all cells in the 2x2 table of that study. As a robustness assessment, meta-analyses with RCTs with zero events in one arm were also performed using risk differences in a sensitivity analysis. For all analyses the 95% confidence interval (CI) was calculated.

Heterogeneity was calculated using Higgins χ^2 test,[22] and inconsistency in study effects was quantified by I^2 values.[10,23] The fixed-effects model was used if no heterogeneity was present (χ^2 *P* value > 0.100 and I^2 < 50%). If excessive heterogeneity was present, data were first re-checked and the DerSimonian random-effects model was used when heterogeneity persisted.[24] Funnel plots were used to help identify the presence of publication or other types of bias.[25-27] Review Manager software (RevMan© v. 5.0.16) provided by The Cochrane Collaboration was used for data management and statistical analyses.

Results

Description of studies

A total of 188 potential relevant publications were identified (Figure 1). Twenty-four papers comparing 180˚ LAF vs. LNF were identified. Nine studies did not randomly allocate patients. An Italian trial randomly allocated patients with achalasia to Heller myotomy followed by either 180˚ LAF or LNF.[28] This trial was excluded since the indication for surgery was not primary fundoplication for established GERD. One potentially relevant RCT that had been published as an abstract only without a peer-reviewed publication was excluded.[29] Finally, 8 publications from five original RCTs[30-34] comparing laparoscopic anterior *versus* posterior fundoplication were identified. Five publications reported one-year results,[30-34] three papers evaluated five-year outcome[9,31,35] and there was one trial[36] with ten-year follow-up (Figure 1).

The five included trials were published between 1999 and 2012, all with at least 6 months of follow-up. A total of 458 fundoplications (180˚ LAF n=227; LNF n=231) were performed. In all patients hiatal repair was performed, followed by either a standardized LAF with a circumferential range of 180º and fixation to right crus or a standardized LNF with a circumference of 360º. One trial divided the short gastric vessels in the LNF group (Table 1).[33] Patient characteristics are listed in Table 2. All patients had proof of GERD on upper endoscopy and/or 24h pH-monitoring. Two trials enrolled some patients with esophageal dysmotility and these patients were divided equally between both arms.[31,34]

Methodological quality of included studies

The trials had good methodological quality, with a mean Jadad score of 4 (range 2-5) (Table 3). All trials had adequate sequence generation. Two trials[31,32] did not report double blinding and allocation concealment and one of these did not report loss to follow-up[32]. Two trials reported a sample size calculation.[33,34]

One-year outcome

One-year outcome as available for 448 out of 458 [97.8%] of the patients. All primary and secondary outcome measures were reported by three or more trials. Operating time, in-hospital complications and length of hospital stay were similar for both groups (Table 4). The included trials reported no mortality. The prevalence (15% vs 27%; RR 0.56; 95% CI [0.38,0.81]; P=0.002; Fig. 2A) and severity (2.8 vs 4.8; WMD -2.25; 95% CI [-2.66,-1.83] ; P<0.001 Fig. 2B) of dysphagia were lower after 180˚ LAF than after LNF. Esophageal acid exposure on 24-hour pH monitoring (SMD 0.19; 95% CI [-0.07,0.46]; P=0.15; Fig. 3A) and prevalence of esophagitis (19% vs 13%; RR 1.42; 95% CI [0.69,2.91]; P=0.34; Fig. 3B) were similar after both procedures. This was accompanied by a comparable prevalence (10% vs 6%; RR 1.39; 95% CI [0.43,4.46]; P=0.58; Fig. 4A) and severity of heartburn (SMD 1.27; 95% CI [-0.36,2.90]; P=0.13 Fig. 4B), prevalence of regurgitation and PPI use (Table 4). Dilatation (1.4% vs 2.8%; RR 0.60; 95% CI [0.19,1.91]; P=0.39; Fig. 5A) and reoperation rates were similar (5.7% vs 2.8%; RR 2.08; 95% CI [0.80,5.41]; *P*=0.13; Fig. 5B).

Gas bloating (11% vs 18%;RR 0.59; 95% CI [0.36,0.97]; P=0.04), flatulence (14% vs 25% RR 0.57; 95% CI [0.35,0.91]; P=0.02), inability to belch (19% vs 31%; RR 0.63; 95% CI [0.40,0.99]; P=0.05) and inability to relieve bloating (34% vs 44%; RR 0.74; 95% CI [0.55,0.99]; P=0.04) were lower after 180˚ LAF (Table 4). Mean LES resting and relaxation pressure were similar (Table 4). There were no differences in the number of patients that was satisfied with outcome, satisfaction scores, willingness to undergo surgery again and the percentage of patients with resolved or mild symptoms (Table 4). Sensitivity analysis of outcomes with zero events in one arm (dilatation, in-hospital complications) yielded similar results. Funnel plots did not demonstrate evidence of publication bias (Fig. 6).

Five-year outcome

Five-year outcome as available for 347 out of 370 [93.8%] patients. At five years, PPI use and the number of patients that was satisfied with intervention were reported by two trials. All

the remaining primary and secondary outcome measures were reported by three or more trials. In line with the one-year results, the prevalence (21% vs 33%; RR 0.67 95% CI [0.47,0.94]; Fig. 7A) and severity (5.0 vs 8.3; WMD -2.33; 95% CI [-3.32,-1.34]; P<0.00; Fig. 7B) of dysphagia remained lower after 180˚ LAF than after LNF. The prevalence (17% vs 12%; RR 1.40; 95% CI [0.83,2.36]; Fig.8A) and severity (1.7 vs 1.5; WMD 0.13; 95% CI [-0.19,0.46]; P=0.43; Fig. 8B) of heartburn and PPI use were comparable. Dilatation (2.4% vs 5.6%; RR 0.44; 95% CI [0.15,1.30]; P=0.14; Fig. 9A) and reoperation rates (9.5% vs 6.2%; RR 1.53; 95% CI [0.73,3.19]; P=0.26; Fig. 9B) were similar.

Flatulence (37% vs 50%; RR 0.75; 95% CI [0.60,0.94]; P=0.01), inability to belch (16% vs 34%; RR 0.47; 95% CI [0.32,0.70]; P<0.001) and inability to relieve bloating (31% vs 44%; RR 0.69; 95%CI [0.53,0.92]; P=0.01) remained lower after 180˚ LAF. The difference in gas bloating that was identified at one year, was no longer present at 5 years (Table 5). Again, there were no differences in the number of patients that was satisfied with outcome, satisfaction scores, willingness to undergo surgery again and the percentage of patients with resolved or mild symptoms (Table 5). Sensitivity analysis of outcomes with zero events in one arm (dilatation) yielded similar results.

Outcome at five years and beyond

One trial reported both 5 and 10 year results.[35,36] An additional analysis was performed based on the latest follow-up of the three trials that reported outcome at five years and beyond. Outcome at five years and beyond was available for 335 out of 370 [90.5%] patients. This analysis yielded similar results compared with the 5-year analysis. The only discrepancy was that the difference in inability to relieve bloating which was identified by the 5-year analysis, was no longer present in the analysis that included 10-year data (table 6). Sensitivity analysis of outcomes with zero events in one arm (dilatation) yielded similar results.

Discussion

Antireflux surgery aims to provide durable reflux control with minimal postoperative dysphagia and gas-related symptoms. Partial fundoplications have been proposed to reduce the risk of side effects that are associated with LNF. In 2010, American guidelines for surgical treatment of GERD have evaluated partial and Nissen fundoplication. These guidelines concluded that there is "paucity of long-term follow-up data" and recommended "controlled studies with long-term follow-up".[7] Posterior 270˚ fundoplication, anterior 90˚ and anterior 180˚ fundoplication have all been described.[7] Earlier this year the long-term results of randomized trials demonstrated that 180˚ LAF offers similar reflux control compared to LNF, whereas reflux control after 90˚ LAF is less effective than after LNF.[9] A systematic review that directly compared posterior 270˚ fundoplication to LNF concluded that it reduces dysphagia and gas-related symptoms compared LNF, with similar reflux control up to 5 years.[4] A similar meta-analysis comparing outcome after 180˚ LAF and LNF has not been reported previously.

In the past year, two RCTs[31,33] have been published comparing 180˚ LAF to LNF in addition to the three trials[30,32,34] that had been reported earlier, with 5-year results of two of these trials reported as well.[9,31] Some of these individual trials were inconclusive as they were underpowered, and hence too small to identify significant differences regarding the most important determinants of successful antireflux surgery: objective reflux control, dilatations for dysphagia and the need for surgical reintervention. The results from all of these trials, however, have not been previously pooled in meta-analysis comparing 180˚ LAF to LNF. The current meta-analysis aims to provide this evidence.

The methodological quality of the five RCTs included in the current meta-analysis was good, with a mean Jadad score of 4. Surgical techniques of the included trials were standardized and similar. In all patients hiatal repair was performed, followed by either 180º LAF with fixation to right hiatal pillar or LNF. One trial divided the short gastric vessels in the LNF group.[33] This is not likely to introduce any bias since it has previously been demonstrated that division of the short gastric vessels does not influence outcome.[5] Two

trials enrolled an equal number of patients with esophageal dysmotility in both arms.[31,34] The current study analyzed patients with and without esophageal dysmotility together, as four RCTs have shown that outcome of fundoplication is similar in patients with normal and abnormal esophageal motility[37-40]. Study population and surgical interventions were similar between trials in all other aspects.

There are no significant differences in perioperative outcome measures. The one-year outcomes demonstrate that 180º LAF is followed by less dysphagia and gas-related symptoms compared to LNF. Both procedures similarly increased LES pressure, which was accompanied by comparable subjective and objective reflux control. Patient satisfaction, endoscopic dilatation and reoperation rates are similar in the short-term as well. The 5-year outcomes show that the differences in dysphagia and gas-related symptoms persist at longer-term follow-up. Extension of follow-up to 5 years does not demonstrate differences in reflux symptoms, PPI use, patient satisfaction, dilatation or reoperation rates.

The reduction in gas-related symptoms after 180º LAF, with similar reflux control at up to 5 years compared with LNF, is supported by a study that has evaluated the physiological effects of fundoplication. It is commonly assumed that impairment of ventilation of swallowed air from the stomach causes gas bloating and flatulence after fundoplication.[41] The first author recently reported that air venting is easier after partial than Nissen fundoplication.[42] In addition, partial and Nissen fundoplication were found to reduce acid and weakly acidic reflux to a similar extent.[42] These results are in line with the current observation that reflux control is similar after 180º LAF and LNF at one and five years. This is in contrast with findings of RCTs that report that 90º LAF and 120º LAF are associated with inferior reflux control in both the short[43-45] and the long-term.[9,46] The two main differences between 90º LAF and 120º LAF *versus* 180º LAF are the reduced circumference of the wrap and the lack of fixation of the wrap to the right hiatal pillar. Fixation to the right hiatal pillar is probably the main factor that accounts for differences in the risk of recurrent reflux between various anterior fundoplications and probably accounts for the good results following 180º LAF demonstrated by this meta-analysis. Supporting this is the experience of some of us when undertaking

revision surgery for recurrent reflux. During revision for recurrent reflux an anterior 180˚ fundoplication always remains securely attached to the right hiatal pillar and failure is due to proximal migration of the gastroesophageal junction, whereas with lesser degrees of anterior partial fundoplications such as 90˚ and 120˚ the fundoplication seem to unravel and loosen in some patients. Hence, tt seems reasonable to speculate that this is due to the lack of anchorage of the fundus to the right hiatal pillar.

The 5-year reoperation rates of the current study were 9.5% for 180 degree anterior fundoplication and 6.2% for Nissen fundoplication. Reoperation rates in case series with less than complete follow-up can differ considerably from the randomized controlled trials with high follow-up rates that have been included this review. Publication bias and selection bias probably help to explain the difference in these results. A benchmark meta-analysis of randomized controlled trials demonstrated that 9.6% of patients who had a Nissen fundoplication underwent surgical reintervention at mean follow-up of two-and-a-half years.[5] The reoperation rate in the present study is consistent with these results, especially considering the extended length of follow-up.

The internal validity of the current study is high because the analysis was based on high-quality RCTs, with high follow-up rates and low risk of bias. The fact that the trials were performed across four continents increases the external validity of this meta-analysis. It is notable that the senior authors of every trial agreed to provide both short and long-term missing data. The principal investigators of the South African and Chinese RCT worked with the Australian research group during the first trial[34] and subsequently applied identical surgical techniques and questionnaires for their trials.[30,31] Consequently, a complete set of identical outcome measures and scales could be pooled. These 3 trials comprise 81% of the included patients and reported both one and five-year results. The current analysis is limited by the fact that 5-year follow-up was not yet available for the two remaining trials. However, these two trials were the smallest and of limited size, contributing only 19% of the included patients. Another flaws is that physiological studies were performed in only 50% of patients.

A recent meta-analysis concluded that posterior 270˚ fundoplication offers similar reflux control up to five years, but fewer dysphagia and gas-related compared to LNF.[4] The present study has similar methodology and demonstrates that 180˚ LAF has similar advantages over Nissen fundoplication up to five years. There is one RCT that has compared 180˚ LAF to posterior 180˚ fundoplication for the surgical treatment of GERD, but in this study follow-up was incomplete (57%) and short term.[47] Two parallel RCTs are currently being conducted in Australia and The Netherlands to evaluate differences between 180˚ LAF and posterior 270˚ fundoplication, and it is hoped they will address this question better.

In conclusion, dysphagia and gas-related symptoms are lower after 180˚ LAF compared with LNF at one and five years. Esophageal acid exposure and prevalence of esophagitis are similar after both procedures. Control of reflux symptoms, PPI use, patient satisfaction, dilatations and reoperation rate are similar in both the short and the long-term. These results lend level 1a support for the use of 180˚ LAF for the surgical treatment of GERD.

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Table 1 Details of included RCTs comparing 180˚ LAF *versus* LNF

Author	Year	Period	Method	*n*	Hiatal repair	DSGV	Bougie	Fixation to right crus/ esophagus†	1-year FU	5-year FU
Baigrie[9,30]	'05	'99-'01	180˚ LAF	79	Yes	No	None	Yes/No	12 [30]	60 [9]
			LNF	84	Yes	No	56 Fr	No/No		
Cao[31]	'12	'02-'07	180˚ LAF	50	Yes	No	52 Fr	Yes/Yes	12 [31]	60 [31]
			LNF	50	Yes	No	52 Fr	No/No		
Chrysos[32]	'04	'99-'02	180˚ LAF	12	Yes	No	None	Yes/Yes	6 [32]	
			LNF	12	Yes	No	None	No/Yes		
Raue[33]	'11	'05-'07	180˚ LAF	32	Yes	No	42 Fr	Yes/Yes	18 [33]	
			LNF	32	Yes	Yes	42 Fr	No/Yes		
Watson[34-36]	'99/'04/'08	'95-'97	180˚ LAF	54	Yes	No	None	Yes/Yes	6 [34]	60 [35]
			LNF	53	Yes	No	52 Fr	No/Yes		120 [36]

°, Circumference of the wrap; DSGV, Division of the short gastric vessels; †Fixation of the fundoplication to the right crus/esophagus; FU, Follow-up (months); NR, Not reported; Fr, French

Table 2 Patient characteristics

Author	Method	Age (yr)	Male / female sex	Esophageal dysmotility / total	Indication for surgical treatment
Baigrie[9,30]	180˚ LAF	45	45/34	NR	pH or endoscopically proven GERD
	LNF	43	49/34	NR	
Cao[31]	180˚ LAF	57	16/34	8/50	pH or endoscopically proven GERD
	LNF	59	21/29	6/50	
Chrysos[32]	180˚ LAF	58	4/8	0/12	pH or endoscopically proven GERD
	LNF	52	9/3	0/12	
Raue[33]	180˚ LAF	53	14/16	0/30	pH or endoscopically proven GERD
	LNF	50	16/11	0/27	
Watson[34-36]	180˚ LAF	45	34/30	11/54	pH or endoscopically proven GERD
	LNF	47	36/17	11/53	

GERD, gastroesophageal reflux disease; NR, Not reported; pH or endoscopically proven GERD, GERD proven on upper endoscopy or 24h pH-monitoring

Table 3 Risk of bias summary

	Baigrie[9,30]	Cao[31]	Chrysos[32]	Raue[33]	Watson[34-36]
Adequate sequence generation	Yes	Yes	Yes	Yes	Yes
Allocation concealment	Yes	No	No	Yes	Yes
Blinding (observer)	Yes	Yes	No	Yes	Yes
Blinding (patient)	Yes	No	No	Yes	Yes
Adequate report on loss to follow-up	Yes	Yes	No	Yes	Yes
Free of other sources of bias	Yes	Yes	Yes	Yes	Yes
Jadad score	5	3	2	5	5

Table 4 1-year outcome

	RCT	180˚ LAF	LNF	RR	WMD	95% CI	*P*-value
Operating time (min)	4	79.7 (n=205)	78.8 (n=206)		-1.07	-12.8,10.7	0.86
In-hospital complications	4	8/213 [3.8%]	3/214 [1.4%]	2.18		0.69,6.93	0.19
Length of hospital stay (days)	4	3.1 (n=181)	3.0 (n=182)		0.02	-0.10,0.13	0.76
Regurgitation	3	9/145 [6.2%]	7/142 [4.9%]	1.25		0.48,3.23	0.65
PPI use	3	7/127 [5.5%]	9/121 [7.4%]	0.74		0.29,1.91	0.54
Gas bloating	5	21/196 [11%]	36/201 [18%]	0.59		0.36,0.97	0.04
Increased flatulence	3	19/133 [14%]	33/130 [25%]	0.57		0.35,0.91	0.02
Inability to belch	3	24/124 [19%]	37/120 [31%]	0.63		0.40,0.99	0.05
Inability to relieve bloating	3	39/116 [34%]	54/122[44%]	0.74		0.55,0.99	0.04
LES resting pressure (mm Hg)	4	16.7 (n=123)	20.1 (n=116)		-3.58	-9.93,2.77	0.27
LES relaxation pressure (mm Hg)	3	5.6 (n=94)	7.9 (n=92)		-2.48	-8.48,3.51	0.42
Satisfied with outcome	3	159/177 [90%]	163/183 [89%]	1.01		0.94,1.08	0.84
Satisfaction score	3	9.1 (n=177)	8.9 (n=183)		0.27	-0.52,1.05	0.50
Willingness repeat surgery	3	162/173 [94%]	160/179 [89%]	1.05		0.99,1.12	0.13
Resolved or mild symptoms	4	181/209 [87%]	188/213 [88%]	0.99		0.92,1.06	0.68

RCT, Randomized clinical trial; RR, Risk ratio; WMD, Weighted mean difference; CI, Confidence interval

Table 5 5-year outcome

	RCT	180˚ LAF	LNF	RR	WMD	95% CI	*P*-value
PPI use	2	7/99 [7.1%]	10/98 [10%]	0.69		0.27,1.75	0.44
Gas bloating	3	61/168 [36%]	86/178 [48%]	0.71		0.41,1.12	0.20
Increased flatulence	3	58/158 [37%]	82/165 [50%]	0.75		0.60,0.94	0.01
Inability to belch	3	27/168 [16%]	61/178 [34%]	0.47		0.32,0.70	<0.001
Inability to relieve bloating	3	52/168 [31%]	78/178 [44%]	0.69		0.53,0.92	0.01
Satisfied with outcome	2	89/99 [90%]	86/98 [88%]	1.01		0.86,1.19	0.91
Satisfaction score	3	8.4 (n=167)	8.3 (n=178)		-0.08	-0.46,0.30	0.69
Willingness repeat surgery	3	151/164 [92%]	154/174 [89%]	1.04		0.97,1.12	0.27
Resolved or mild symptoms	3	138/165 [84%]	144/177 [81%]	1.03		0.93,1.13	0.57

RCT, Randomized clinical trial; RR, Risk ratio; WMD, Weighted mean difference; CI, Confidence interval

Table 6 Outcome at 5 years and beyond

	RCT	180˚ LAF	LNF	RR	WMD	95% CI	*P*-value
Presence dysphagia	3	41/160 [26%]	70/175 [40%]	0.67		0.49,0.90	0.009
Severity dysphagia	3	5.3 (n=159)	8.4 (n=175)		-2.23	-3.23,-1.23	<0.001
Prevalence heartburn	3	26/159 [16%]	23/175 [13%]	1.23		0.74,2.07	0.42
Severity heartburn	3	1.7 (n=159)	1.4 (n=175)		0.17	-0.16,0.49	0.31
Dilatation rate	3	4/160 [2.5%]	10/175 [5.7%]	0.46		0.16,1.35	0.16
Reoperation rate	3	18/160 [11%]	13/175 [7.4%]	1.54		0.78,3.02	0.21
PPI use	2	16/90 [18%]	13/95 [14%]	1.35		0.70,2.62	0.37
Gas bloating	3	58/159 [36%]	62/175 [35%]	1.03		0.59,1.79	0.92
Increased flatulence	3	58/158 [37%]	82/165 [50%]	0.75		0.60,0.94	0.01
Inability to belch	3	31/159 [19%]	63/175 [36%]	0.55		0.38,0.79	0.001
Inability to relieve bloating	3	68/159 [43%]	87/175 [50%]	0.86		0.69,1.07	0.17
Satisfied with outcome	2	84/90 [93%]	91/95 [96%]	0.97		0.91,1.04	0.44
Satisfaction score	3	8.3 (n=158)	8.4 (n=175)		-0.18	-0.56,0.21	0.37
Willingness repeat surgery	3	144/155 [93%]	153/171 [89%]	1.04		0.97,1.11	0.27
Resolved or mild symptoms	3	138/165 [84%]	144/177 [81%]	1.03		0.93,1.13	0.57

RCT, Randomized clinical trial; RR, Risk ratio; WMD, Weighted mean difference; CI, Confidence interval

Figure 1 **Flow-chart illustrating the details of the search strategy and study selection process according to the QUOROM-statement[17-19]**
RTC, Randomized Clinical Trial; MesH, Medical Subject Heading; CPCI-S, Conference Proceedings Citation Index – Science

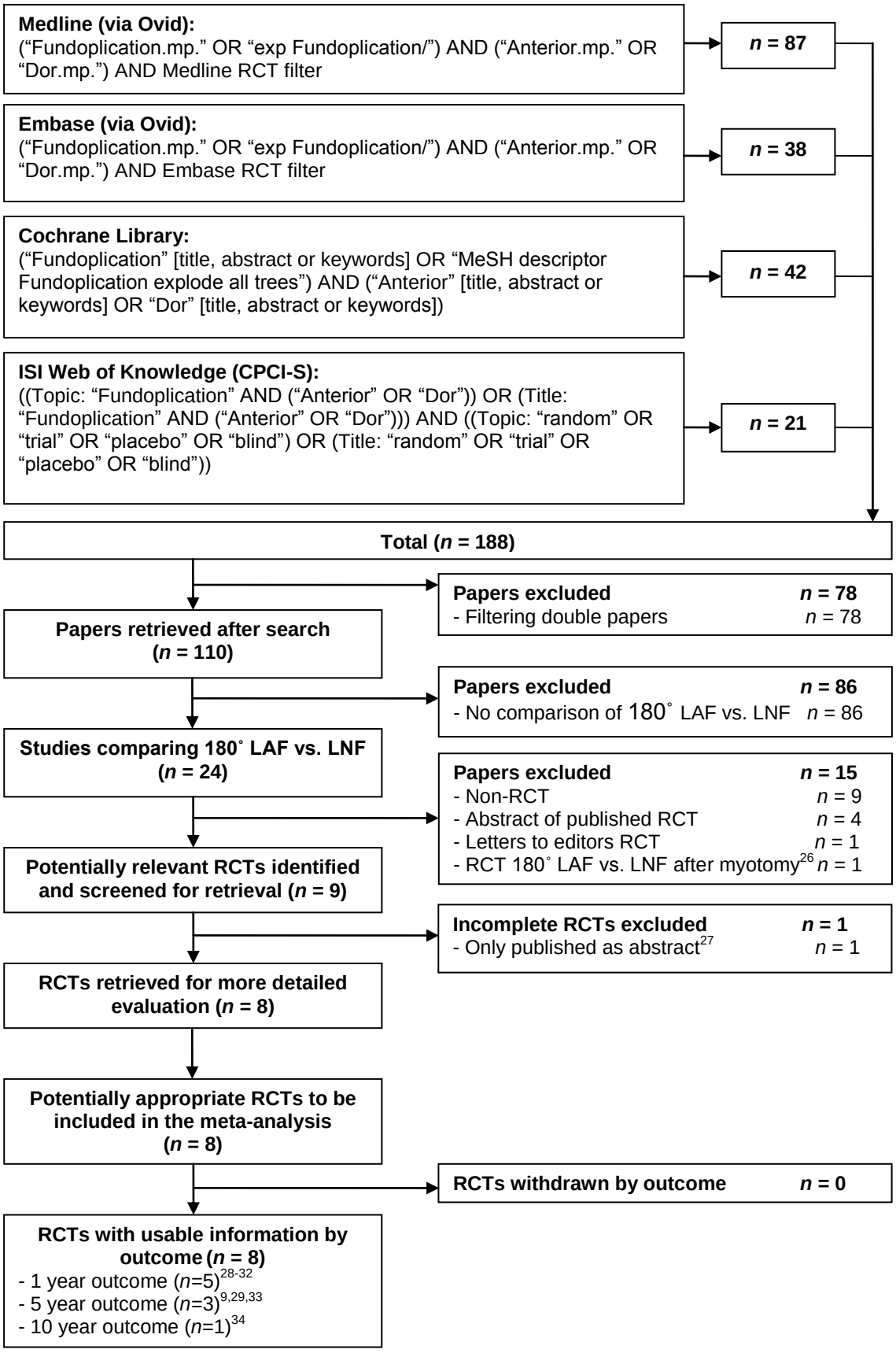
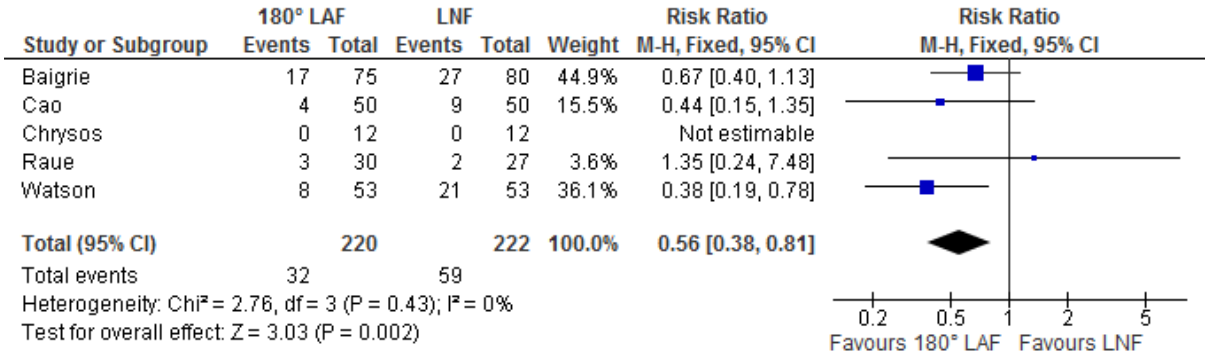


Figure 2 One-year prevalence (A) and severity dysphagia (B)

A



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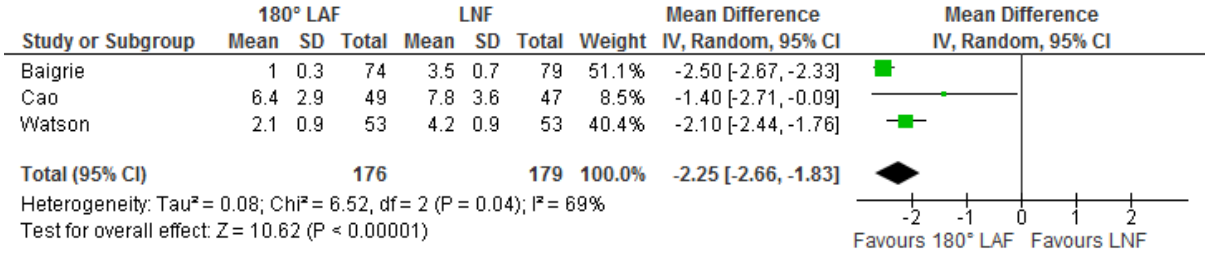
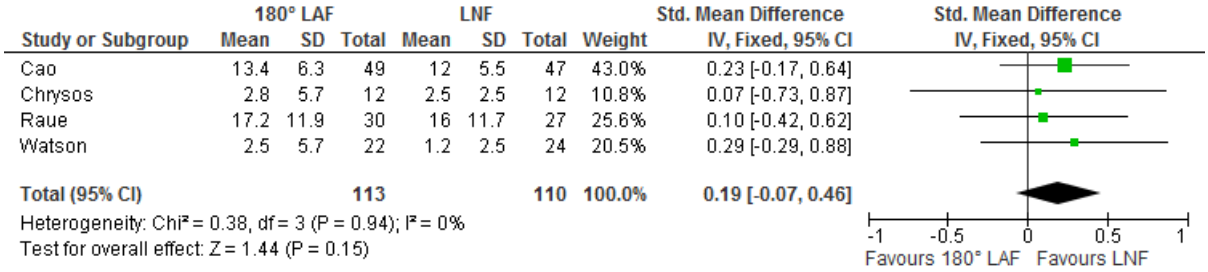


Figure 3 One-year esophageal acid exposure (A) and esophagitis (B)

A



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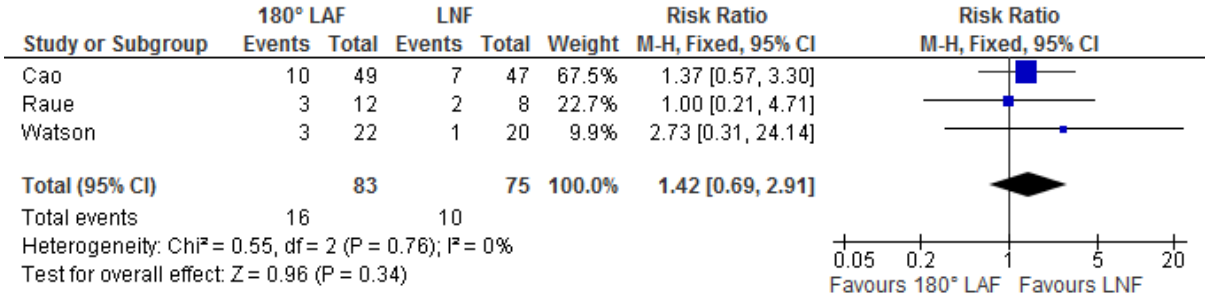
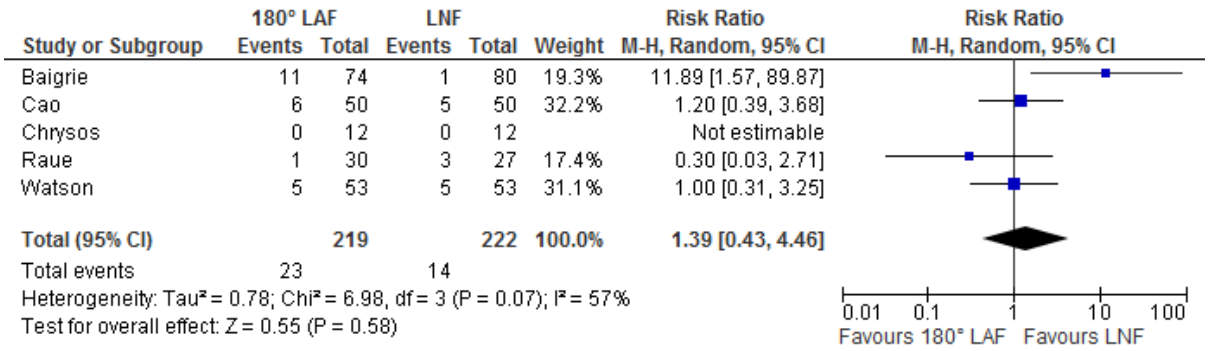


Figure 4 One-year prevalence (A) and severity heartburn (B)

A



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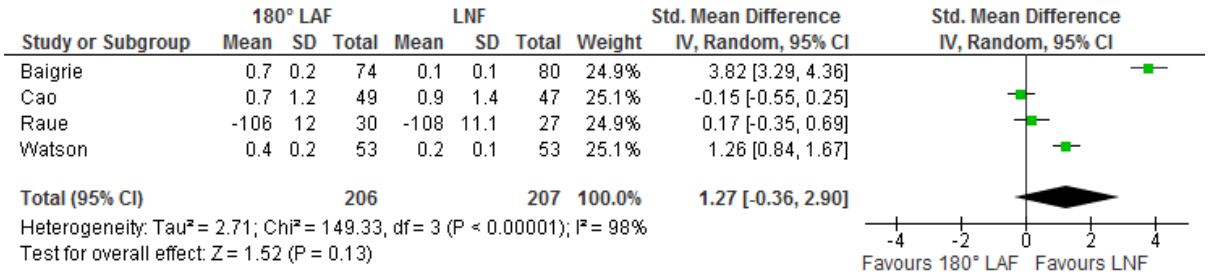
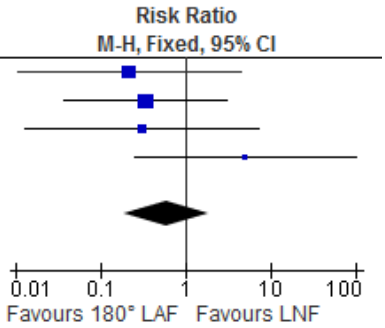


Figure 5 One-year dilatation (A) and reoperation rate (B)

A

Study or Subgroup	180° LAF Events	180° LAF Total	LNF Events	LNF Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Baigrie	0	78	2	83	32.3%	0.21 [0.01, 4.36]
Cao	1	50	3	50	40.0%	0.33 [0.04, 3.10]
Raue	0	30	1	27	21.0%	0.30 [0.01, 7.09]
Watson	2	53	0	53	6.7%	5.00 [0.25, 101.73]
Total (95% CI)		**211**		**213**	**100.0%**	**0.60 [0.19, 1.91]**
Total events	3		6			

Heterogeneity: Chi² = 2.80, df = 3 (P = 0.42); I² = 0%
Test for overall effect: Z = 0.87 (P = 0.39)



B

Study or Subgroup	180° LAF Events	180° LAF Total	LNF Events	LNF Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Baigrie	8	78	4	83	66.0%	2.13 [0.67, 6.79]
Cao	2	50	1	50	17.0%	2.00 [0.19, 21.36]
Raue	0	30	0	27		Not estimable
Watson	2	53	1	53	17.0%	2.00 [0.19, 21.40]
Total (95% CI)		**211**		**213**	**100.0%**	**2.08 [0.80, 5.41]**
Total events	12		6			

Heterogeneity: Chi² = 0.00, df = 2 (P = 1.00); I² = 0%
Test for overall effect: Z = 1.51 (P = 0.13)

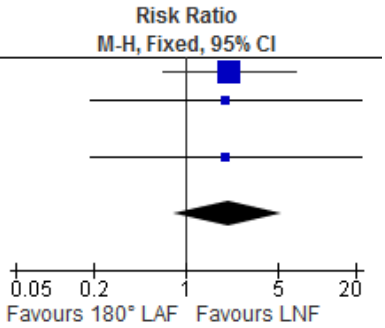


Figure 6 Funnel plot 1 year esophageal acid exposure

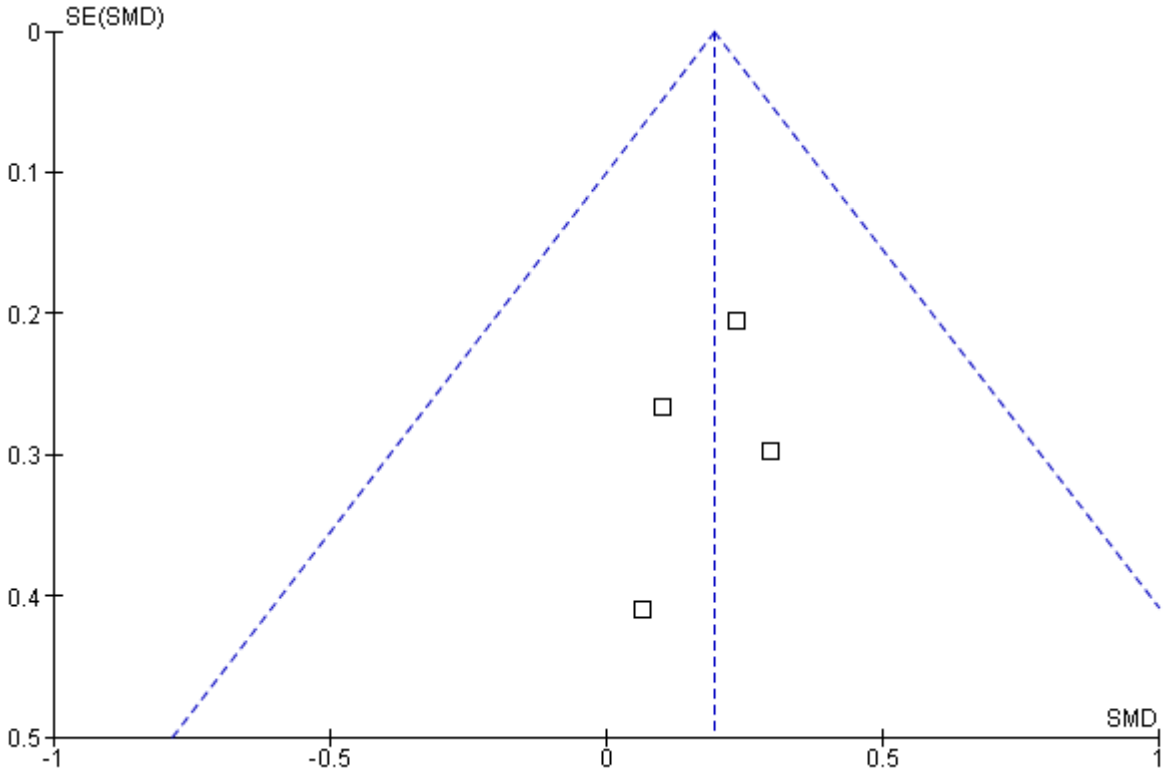
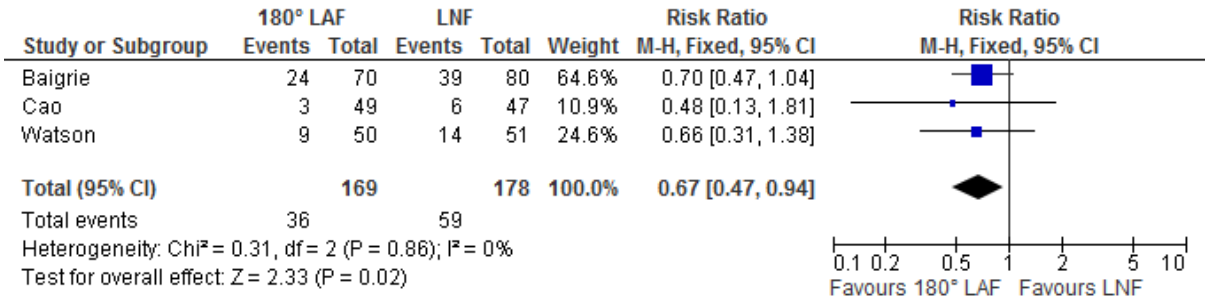


Figure 7 Five-year prevalence (A) and severity dysphagia (B)

A



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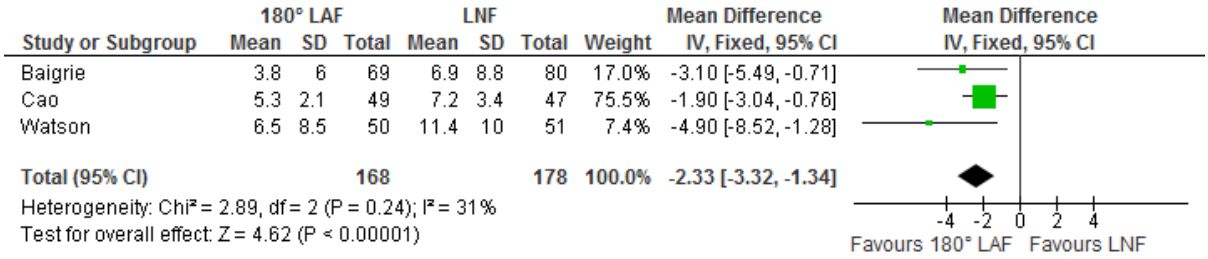
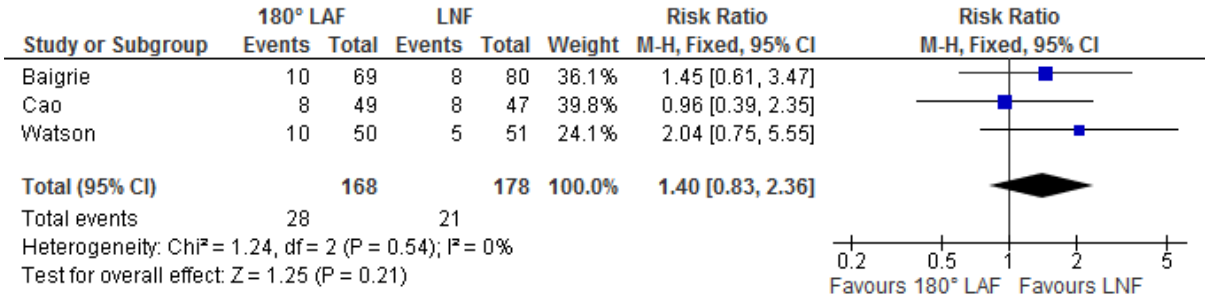


Figure 8 Five-year prevalence (A) and severity heartburn (B)

A



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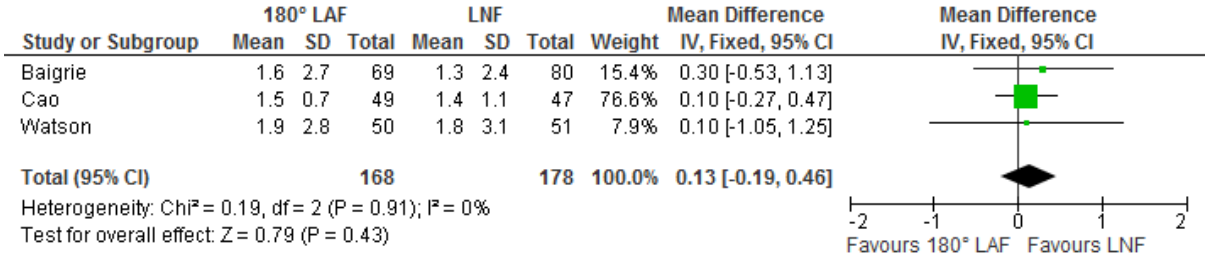
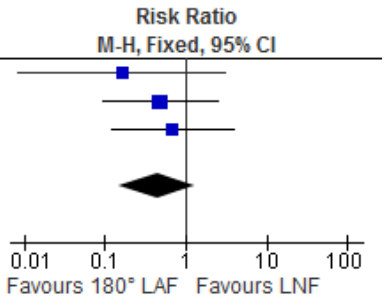


Figure 9 Five-year dilatation (A) and reoperation rate (B)

A

Study or Subgroup	180° LAF Events	Total	LNF Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Baigrie	0	70	3	80	31.7%	0.16 [0.01, 3.10]
Cao	2	49	4	47	39.6%	0.48 [0.09, 2.50]
Watson	2	50	3	51	28.8%	0.68 [0.12, 3.90]
Total (95% CI)		**169**		**178**	**100.0%**	**0.44 [0.15, 1.30]**
Total events	4		10			

Heterogeneity: Chi² = 0.69, df = 2 (P = 0.71); I² = 0%
Test for overall effect: Z = 1.49 (P = 0.14)



B

Study or Subgroup	180° LAF Events	Total	LNF Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Baigrie	7	70	4	80	34.7%	2.00 [0.61, 6.55]
Cao	4	49	3	47	28.5%	1.28 [0.30, 5.41]
Watson	5	50	4	51	36.8%	1.27 [0.36, 4.48]
Total (95% CI)		**169**		**178**	**100.0%**	**1.53 [0.73, 3.19]**
Total events	16		11			

Heterogeneity: Chi² = 0.34, df = 2 (P = 0.85); I² = 0%
Test for overall effect: Z = 1.13 (P = 0.26)