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ORIGINAL SCIENTIFIC REPORT

Laparoscopic Anterior Versus Posterior Fundoplication for Gastro-esophageal Reflux Disease: A Meta-analysis and Systematic Review

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Abstract

Objectives Although laparoscopic posterior fundoplication (LPF) i.e., Nissen or Toupet have the proven efficacy for controlling gastro-esophageal reflux surgically, there remain problems with postoperative dysphagia and gas bloat syndrome. To decrease some of these postoperative complications, laparoscopic anterior fundoplication (LAF) was introduced. The aim of this study was to conduct a meta-analysis and systematic review of randomized controlled trials (RCTs) to investigate the merits and drawbacks of LPF versus LAF for the treatment of gastro-esophageal reflux disease (GERD).

Data Sources, Study Selection, and Review Methods A search of Medline, Embase, Science Citation Index, Current Contents, PubMed, ISI Web of Science, and the Cochrane Database identified all RCTs comparing different types of LPF and LAF published in the English Language between 1990 and 2013. The meta-analysis was prepared in accordance with the Preferred Reporting Items for Systematic reviews and Meta-analyses (PRISMA) statement. Data was extracted and analyzed on ten variables which include dysphagia score, heartburn rate, redo operative rate, operative time, overall complications, rate of conversion to open, Visick grading of satisfaction, overall satisfaction, length of hospital stay, and postoperative 24-h pH scores.

Data Synthesis Nine trials totaling 840 patients (anterior = 425, posterior = 415) were analyzed. There was a significant reduction in the odds ratio for dysphagia in the LAF group compared to the LPF group. Conversely, significant reduction in the odds ratio for heartburn was observed for LPF compared to LAF. Comparable effects were noted for both groups for other variables which include redo surgery, operating time, overall complications, conversion rate, Visick's grading, patients' satisfaction, length of hospital stay, and postoperative 24-h pH scores.

Conclusions Based on this meta-analysis, LPF compared to LAF is associated with significant reduction in heartburn at the expense of higher dysphagia rate on a short- and medium-term basis. We therefore conclude that LPF is a better alternative to LAF for controlling GERD symptoms.

Introduction

Gastro-esophageal reflux disease (GERD) is a condition which occurs when an abnormal amount of gastric juice

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refluxes into the esophagus causing symptoms such as heartburn, regurgitation, acid brash, and water brash with or without associated esophageal mucosal injury. The open and laparoscopic Nissen fundoplication and its modifications have been employed to treat moderate to severe GERD for almost six decades now [1]. Although Nissen fundoplication (360° wrap) achieves good control of GERD, some patients may experience troublesome postoperative side effects such as dysphagia (5–12 %), inability to vomit or belch, abdominal bloating (gas bloat syndrome—19 %), and excessive flatulence [2–7]. To alleviate these problems, partial posterior and anterior fundoplications were introduced where the wrap extended from 90° to 270° either posteriorly or anteriorly. The question of which technique offers the best results in terms of control of GERD with minimal side effects remains controversial. Many uncontrolled single-center series claim good results with partial posterior [8, 9] and anterior fundoplication [10–12]. However, there have been few RCTs undertaken to address this controversial issue in an evidence-based manner [13–21]. The problem is further compounded by the fact that only a few of these RCTs have long-term follow-up. The aim of this meta-analysis was to investigate the benefits and risks of LAF (180°, 120°, 90°) versus LPF (Nissen and Toupet) for the treatment of GERD.

Materials and Methods

Eligibility criteria

All RCTs of any size that compared any type of LAF with LPF for the treatment of GERD, and were published in full in peer-reviewed journals in the English language between January 1990 and the end of July 2013 were included (Fig. 1; Table 1). Studies must have reported on at least one clinically relevant outcome for inclusion. Unpublished studies and abstracts presented at national and international meetings were excluded to prevent duplication and reporting of interim results.

Outcome assessed

Ten outcome variables, which were considered to exert either direct or indirect influence over practical aspects of surgical practice and policy decisions within institutions, were chosen for analysis and included:

1. Postoperative dysphagia score
2. Postoperative heartburn rate (recurrence of symptoms)
3. Redo operative rate
4. Operative time
5. Overall complications
6. Rate of conversion to open
7. Visick grading of satisfaction
8. Overall satisfaction
9. Length of hospital stay
10. Postoperative 24-h pH scores

All studies with reporting on any number of postoperative outcomes were considered eligible and final analyses were run on outcome variables where numbers were sufficient to allow statistical analysis. Where required, authors were contacted for clarification of data or additional information. However, the response was extremely poor from the authors.

Information sources and search

Trials were identified by conducting a comprehensive search of Medline, Embase, Science Citation Index, Current Contents, PubMed, ISI Web of Science, and the Cochrane Database, using medical subject headings

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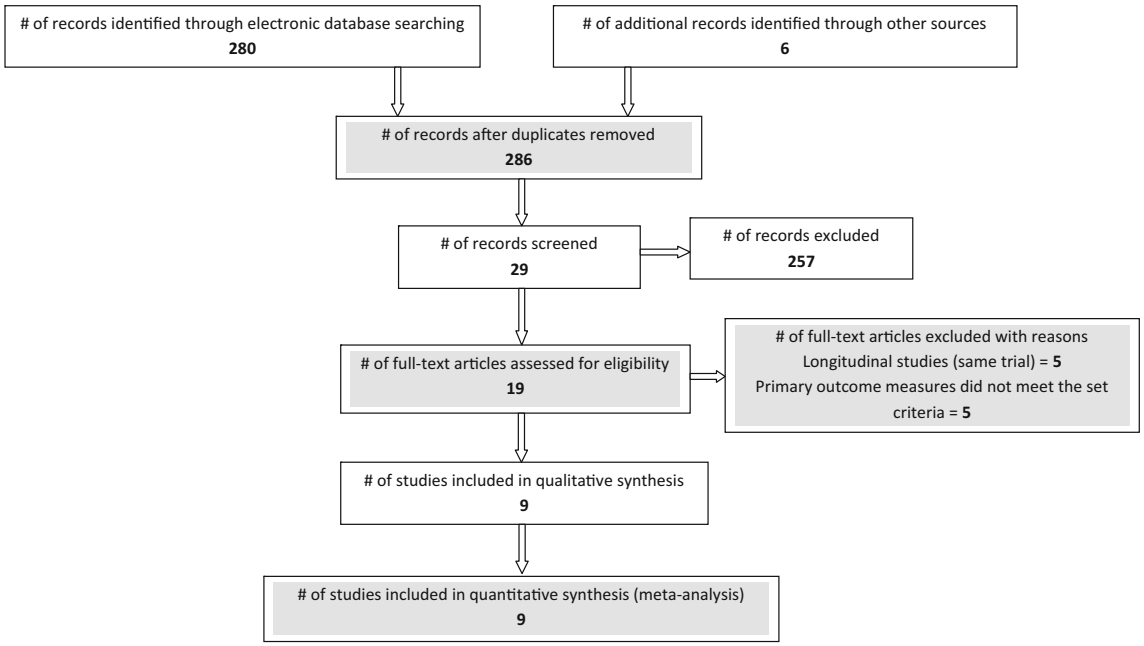

Fig. 1 Flow chart providing information through the different phases of systematic review

"fundoplication," "anti-reflux," "posterior fundoplication," "Nissen fundoplication," "Toupet fundoplication," "anterior antireflux surgery," "Watson's fundoplication," "Dor fundoplication," "gastro-esophageal reflux disease", "comparative studies," "prospective studies," "randomised/randomized controlled trials," "random allocation," and "clinical trial." Manual search of the bibliographies of relevant papers was also carried out to identify trials for possible inclusion.

Data collection process and study selection

Data extraction and critical appraisal were carried out by three authors (MSS, BM, and MAM) for compliance with inclusion criteria and methodological quality. Standardized data extraction forms [22] were used by authors to independently and blindly summarize all the data available in the RCTs meeting the inclusion criteria. The authors were not blinded to the source of the document or authorship for the purpose of data extraction. The data were compared and discrepancies were addressed with discussion until consensus was achieved. The meta-analysis was prepared in accordance with the PRISMA Statement [23].

Methodological quality

Evaluation of the methodological quality of identified studies was conducted using the Jadad scoring system [24] in which each study was assigned a score of between zero (lowest quality) and 5 (highest quality) based on reporting of randomization, blinding, and withdrawals occurring within the study (Table 1).

Statistical analysis, summary measures, synthesis of results, risk of bias across studies

Meta-analyses were performed using odds ratios (ORs) for binary outcomes and standardized mean differences (SMDs) for continuous outcome measures. However for the sake of simplicity, ORs have been used throughout this manuscript, both for descriptive analysis and when creating the Forrest plots for all the variables. A slightly amended estimator of OR was used to avoid the computation of the reciprocal of zeros among observed values in the calculation of the original OR [25]. Random effects models, developed using the inverse-variance weighted method approach were used to combine the data [26]. Heterogeneity among studies was assessed using the Q statistic proposed by Cochran [26, 27] and I^2 index introduced by Higgins and Thompson [28, 29]. If the observed value of Q is larger than the critical value at a given significant level, in this case 0.05, we conclude that the outcome variable is statistically significant. For the computations of the confidence intervals, estimates of mean and standard deviation are required. However, some of the published clinical trials did not report the mean and standard deviation, but rather reported the size of the trial, the median, and range. From these available statistics, estimates of the

Table 1 Study details

Authors/year/country	Methods	Characteristics	Interventions	Outcomes	Jadad score
Watson et al. (1999)/Australia [13]	Sealed opaque envelops	Single center RCT	54 LAF 180°	Primary: postop dysphagia and heartburn	2
	Patients and assessors blinded		53 Lap	Secondary: complication, conversion, Hosp stay, redo surgery, Visick grading and overall patient's satisfaction	
	Intention to treat—yes		Nissen		
	FU: 6 months				
Hagedorn et al (2002)/Sweden [14]	Allocation sequence not stated	Single center RCT	47 LAF 120°	Primary: postop dysphagia and reflux	2
	Unclear blinding		48 Lap	Secondary: redo surgery	
	Intention to treat—yes		Toupet		
	FU: 12 months				
Watson et al. (2004)/Australia [15]	Sealed opaque envelops	Multicenter RCT	60 LAF 90°	Primary: postop dysphagia and heartburn	2
	Patients and assessor blinded		52 Lap	Secondary: complication, conversion, Hosp stay, redo surgery, Visick grading and overall patient's satisfaction	
	Intention to treat—yes		Nissen		
	FU: 6 months				
Chrysos et al. (2004)/Greece [16]	Computer generated sequence	Multicenter RCT	12 LAF 180°	Primary: postop dysphagia and reflux	2
	Blinding not mentioned		12 Lap	Secondary: manometric measurements	
	Intention to treat—yes		Nissen		
	FU: 5 months				
Baigrie et al. (2005)/South Africa [17]	Sealed opaque envelops	Single center RCT	79 LAF 180°	Primary: postop dysphagia and heartburn	2
	Patients and assessors blinded		84 Lap	Secondary: complication, conversion, Hosp stay, redo surgery, Visick grading and overall patient's satisfaction	
	Intention to treat—yes		Nissen		
	FU: 24 months				
Spence et al. (2006)/Australia [18]	Sealed opaque envelops	Single center RCT	40 LAF 90°	Primary: postop dysphagia and heartburn	2
	Patients and assessors blinded		39 Lap	Secondary: Complication, conversion, Hosp stay, redo surgery, Visick grading and overall patient's satisfaction	
	Intention to treat—yes		Nissen		
	FU: 12 months				
Khan et al. (2010)/UK [19]	Sealed opaque envelops	Single center RCT	53 LAF 120°	Primary: postop dysphagia and heartburn	3
	Patients and assessors not blinded		50 Lap	Secondary: complication, conversion, Hosp stay, redo surgery, Visick grading and overall patient's satisfaction	
	Intention to treat—yes		Nissen		
	FU: 12 months				

Table 1 continued

Authors/year/country	Methods	Characteristics	Interventions	Outcomes	Jadad score
Raue et al. (2011)/Germany [20]	Computer generated sequence	Single center RCT	30 LAF 180°	Primary: postop dysphagia and heartburn and postop QOL	5
	Patients and assessors blinded		27 Nissen	Secondary: complication, conversion, Hosp stay, redo surgery, Visick grading and overall patient's satisfaction	
	Intention to treat—yes				
	FU: 18 months				
Cao et al. (2012)/China [21]	Computer generated sequence	Single center RCT	50 LAF 180	Primary: postop dysphagia, flatulence and heartburn	4
	Assessors blinded		50 Lap Nissen	Secondary: redo surgery and maintenance of proton pump inhibitor	
	Intention to treat—yes				
	FU: 60 months				

mean and standard deviation were obtained using formulas proposed by Hozo [30]. Funnel plots were synthesized in order to determine the presence of publication bias in the meta-analysis. Both total sample size and precision (1/standard error) were plotted against the treatment effects (OR for binary variables and SMD for continuous variables) [26, 31]. All estimates were obtained using computer programs written in R [32]. All plots were obtained using the 'rmeta' package [33]. In the case of tests of hypotheses, the paper reports p values for different study variables. In general, the effect is considered to be statistically significant if the p value is small. If one uses a 5 % significance level then the effect is significant only if the associated p value is less than or equal to 5 %.

Results

Study selection/characteristics

There was almost a perfect agreement ($\kappa = 0.99$) between the three authors (MSS, BM, MAM) regarding the inclusion and exclusion of various RCTs. Based on this agreement, a total of nine RCTs [13–21] involving a total of 840 patients (LAF = 425, LPF = 415) were considered suitable for meta-analysis. Except for three trials [19–21], none of the other trials achieved the Jadad score of more than 2 (Table 1).

Clinical outcomes

A statistically significant reduction for dysphagia score was noted favoring LAF (SMD −2.31, CI −3.19, −1.43, $p < 0.001$) (Fig. 2). In contrast, there was a significant reduction in the odds ratio for heartburn (OR 1.90, CI 1.04, 3.49, $p = 0.037$) (Fig. 3). Comparable effects were seen for LPF and LAF for other variables which include redo surgery (OR 1.66, CI 0.91, 3.04, $p = 0.1$) (Fig. 4), operating time (SMD −0.30, CI −1.00, 0.40, $p = 0.39$) (Fig. 5), overall complications (OR 1.07, CI 0.45, 2.53, $p = 0.88$) (Fig. 6), conversion rate (OR 1.32, CI 0.45, 3.91, $p = 0.61$) (Fig. 7), Visick grading (OR 0.96, CI 0.50, 1.87, $p = 0.91$) (Fig. 8), patient satisfaction (SMD 0.69, CI −0.69; 2.08, $p = 0.32$) (Fig. 9), length of hospital stay (SMD 0.07, CI −0.18, 0.33, $p = 0.58$) (Fig. 10), and 24-h pH study (SMD 1.82, CI −0.70, 4.35, $p = 0.15$) (Fig. 11). These results are summarized in Table 2.

Heterogeneity

The Q test and I^2 Index are commonly used methods in meta-analysis for detecting heterogeneity. In general, there was a high degree of heterogeneity detected only for four

variables i.e. dysphagia, operation time, overall satisfaction and postoperative 24-h pH scores (Table 2).

Publication bias

Some of the funnel plots demonstrate asymmetry and thus suggest the presence of publication bias for variables like dysphagia score, operating time, satisfaction score, and postoperative 24-h pH study (Fig. 12). However, the number of studies included for all these variables were too few to sensitively detect publication bias.

Discussion

Although laparoscopic fundoplication is often the treatment of choice for moderate to severe GERD, controversy remains as to which fundoplication technique offers the best clinical and functional outcomes with the least side effects. Whereas laparoscopic Nissen fundoplication is traditionally associated with higher rates of dysphagia at least in the short term, any modification of Nissen is allegedly associated with less than satisfactory reflux control. Therefore, various modifications have concentrated on the degree of wrap e.g., 90°, 120°, 180°, 270°, and 360°, location of the wrap such as posterior or anterior, length of wrap, and gaging the tightness of the wrap by calibrating it with intragastric bougies with or without the division of the short gastric vessels.

The assumption that laparoscopic Nissen is associated with better reflux control at the expense of more obstructive symptoms compared to LAF was supported objectively by Anderson et al. [34]. Nissen fundoplication was associated with a greater elevation of resting and residual lower esophageal sphincter pressures compared to LAF. The drawback of this study was that it was carried out soon after the surgery, and therefore, the results may not be applicable in the long term (e.g., 6 months or longer).

The second assumption that laparoscopic partial posterior fundoplication (i.e., Toupet) will reduce troublesome postoperative side effects such as dysphagia and gas bloat syndrome. Although most of the RCTs comparing LAF vs LPF have addressed the issue of dysphagia, no such data is available for gas bloat syndrome. One of the earliest prospective studies [8] concluded erroneously that an excessively high rate of dysphagia and gas bloat syndrome was mainly due to preservation of the short gastric vessels in the Rosetti-Nissen group, a view which has been discarded now. A 10-year follow-up result of a RCT [35] comparing laparoscopic Toupet (180° posterior, $n = 72$) and Nissen fundoplication (360°, $n = 65$), showed no difference in the rate of dysphagia (41 vs. 38 %). These authors [36] have recently published an 18-year analysis of the same patients and concluded that both types of posterior fundoplications i.e., Nissen and Toupet provided excellent reflux control after 2 decades. Moreover, the previously reported differences in gas bloat syndrome and excessive rectal flatulence in favor of the Toupet group seemed to disappear over time. A recent systematic review and meta-analysis [37] of laparoscopic Nissen ($n = 404$) versus Toupet fundoplication found a significantly higher prevalence of postoperative dysphagia (13.5 vs 8.6 %) and dilatation for dysphagia (6.9 vs 2.7 %) in Nissen's patients although there were issues with the methodological quality of the included studies and the short-term follow-up which may have resulted in overestimating the benefits of one procedure over the other in such a situation.

Watson et al. [13] introduced laparoscopic anterior partial fundoplication with a view to reduce these obstructive symptoms. The results of their RCT comparing Nissen and LAF showed equivalent control of reflux with fewer side effects at 6 months. The Adelaide group [38, 39], published their 5- and 10-year follow-up data on Nissen vs LAF patients using a standard clinical questionnaire. They found no difference in functional and clinical outcome (i.e., control of reflux or dysphagia) in both groups. However, their findings were based on the subjective data. They [40] recently published objective outcomes 14 years after 180° LAF versus Nissen fundoplication on a subgroup of 18 patients. This study showed superiority of Nissen fundoplication in terms of total esophageal acid exposure time and total number of acid and weakly acid reflux episodes which were found to be higher after LAF. The authors concluded that 180° LAF offers less effective reflux control compared to Nissen fundoplication.

The Adelaide group also reported on two further RCTs [15, 18] comparing laparoscopic Nissen versus laparoscopic anterior 90° fundoplication to further reduce the incidence of postoperative dysphagia and gas bloat syndrome. Five-year follow-up of a multicenter RCT [41] revealed superior control of reflux symptoms in the laparoscopic Nissen group compared to LAF. The authors felt that these results have impacted the practice of anti-reflux surgery in their hospital. This in turn has led to surgeons based outside of Adelaide reverting back to performing laparoscopic Nissen compared to either partial anterior or posterior fundoplication.

In our meta-analysis, six [13–15, 17, 18, 21] out of the nine studies reported the dysphagia score (Fig. 2). Pooling of the available data revealed a statistically significant reduction in dysphagia score in the LAF group compared to the LPF. It is worth noting that our pooled data has provided results for dysphagia scores which were reported between 6 and 24 months for most of these RCTs except for one [21] which may have prejudiced the results. The

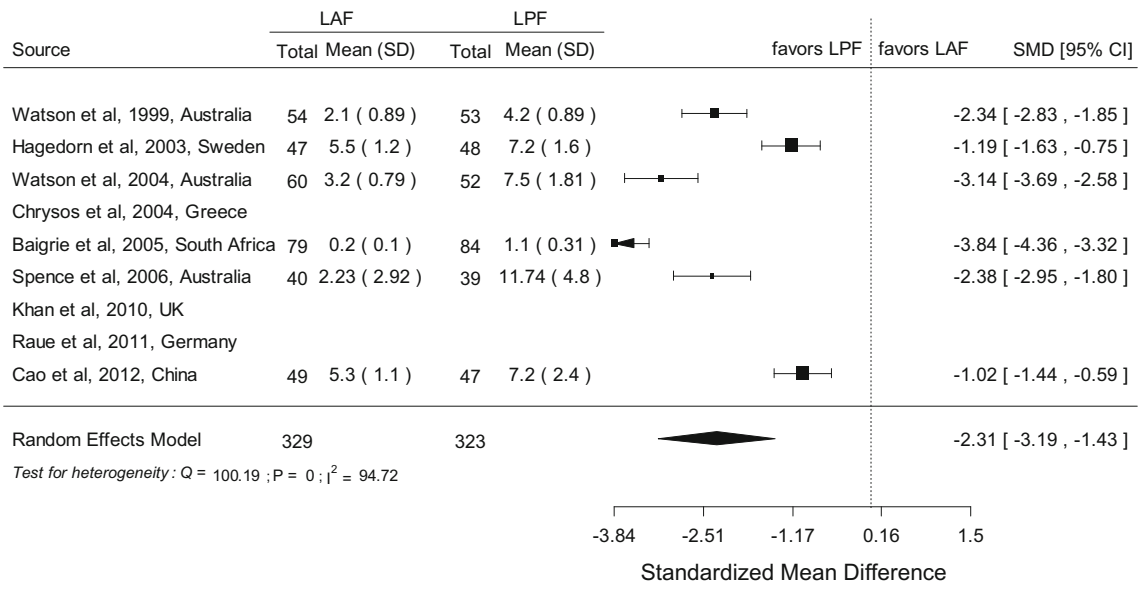

Fig. 2 Forest plot of dysphagia for LAF versus LPF using standardized mean difference (SMD). Forest plots draw the 95 % confidence intervals for odds ratios (OR) or standardized mean differences (SMD) as *horizontal lines*. *Lines* representing confidence intervals show arrows when they exceed specified limits. In the forest plot, *squares* indicate the estimated treatment effects with the size of the *squares* representing the weight attributed to each study. The pooled estimated OR/SMD is obtained by combining all the ORs or SMDs of the studies using the inverse-variance weighted method, represented by the *diamond* and the width of the *diamond* depicts the 95 % confidence interval. For binary outcomes the pooled OR line is drawn at one and for continuous outcome, the pooled SMD line is drawn at zero

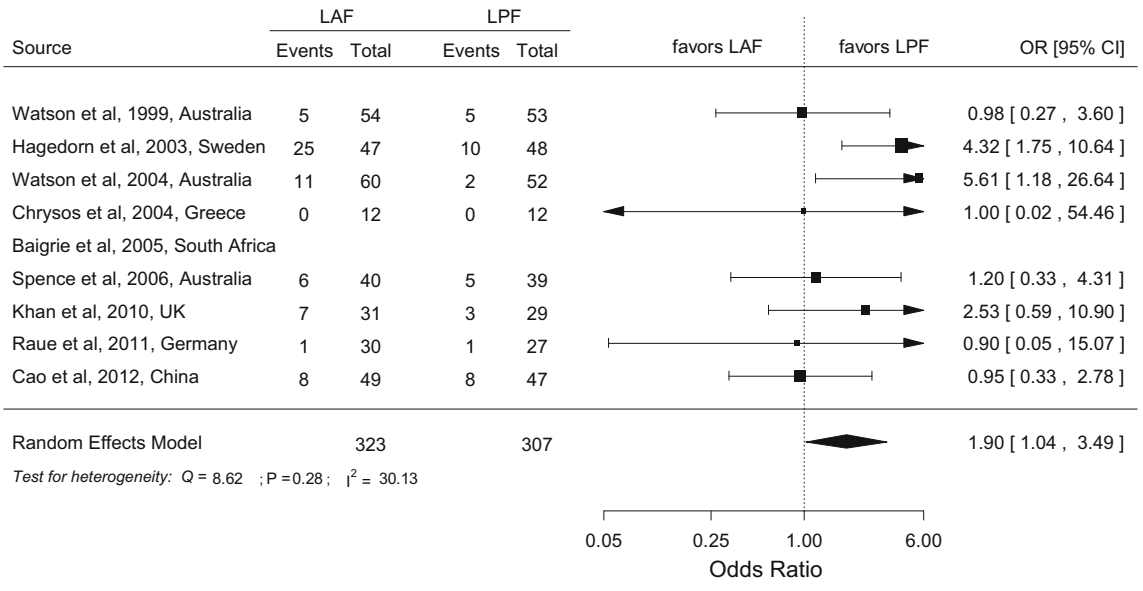

Fig. 3 Forest plot of heartburn for LAF versus LPF using odds ratio (OR)

long-term results for dysphagia scores are only available from four RCTs i.e., Swedish [42], Adelaide [39, 40] and Chinese [21] groups. No statistically significant difference in the dysphagia scores for both liquids and solids were noted either for Nissen or LAF at 5 or 10 years from either Swedish or Adelaide groups. However, the dysphagia score was significantly less in LAF compared to Nissen in the Chinese RCT. Nonetheless persistent dysphagia is a rarity even after laparoscopic Nissen fundoplication as evident by some long-term longitudinal studies. Therefore, the

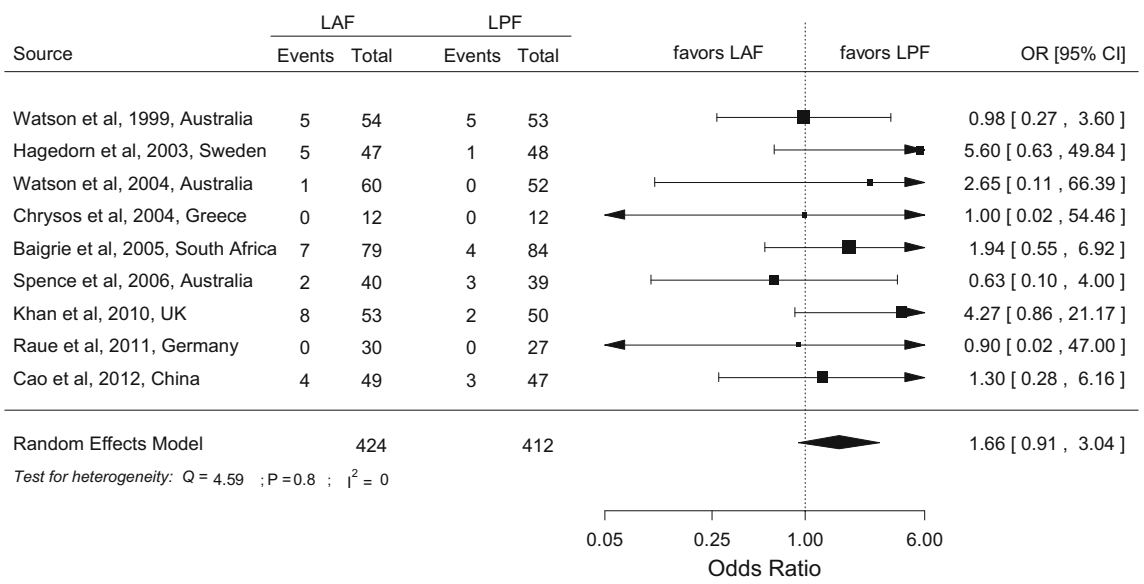

Fig. 4 Forest plot of redo surgery for LAF versus LPF using odds ratio (OR)

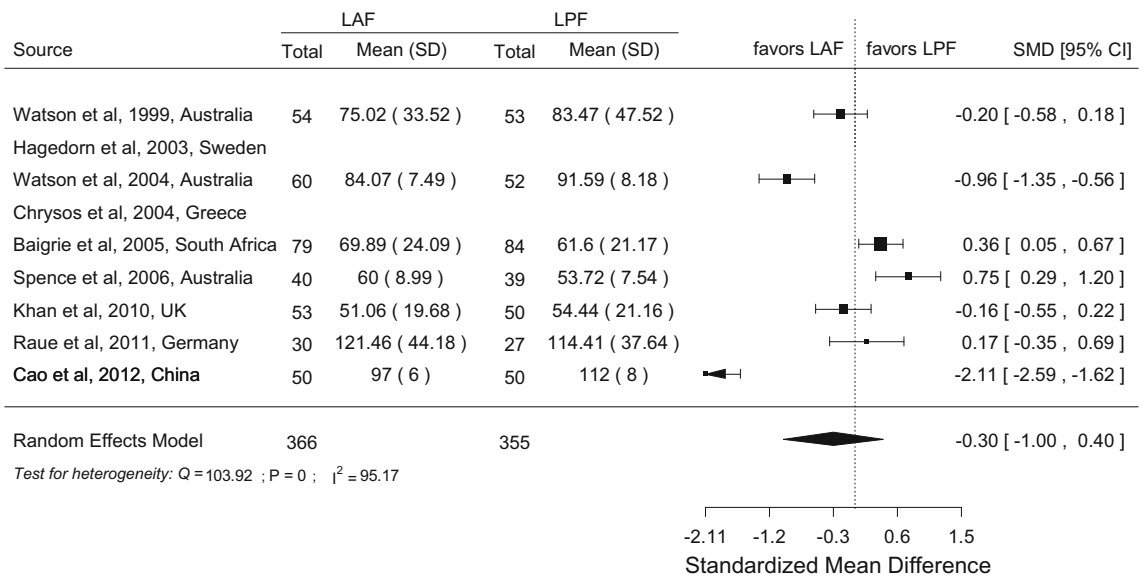

Fig. 5 Forest plot of operation time for LAF versus LPF using standardized mean difference (SMD)

assumption that LAF leads to significant less dysphagia needs to be re-evaluated based on recent long-term analysis of some of these studies.

Does LPF (total or partial) have a better control of reflux than LAF? This issue is addressed by all the RCTs [13–21]. Even the short-term data shows significantly better reflux control in LPF patients compared to their LAF counterpart (Fig. 3). One can therefore postulate that the long-term results would be even worse in the LAF group. In the RCT by the Adelaide group [38], at 5 years there was a higher number of patients with heartburn in the LAF group (20 %) compared to their LPF counterpart (10 %). Moreover, there were no differences in the use of proton pump inhibitors in both groups. Furthermore, at 10 years [39], there were no significant differences in mean heartburn scores, number of patients reporting heartburn, or consumption of proton pump inhibitors based on telephone interviews. However, a 14-year follow-up longitudinal objective study on a subgroup of 18 patients comparing 180° LAF versus Nissen by the same group [40] showed superiority of Nissen in terms

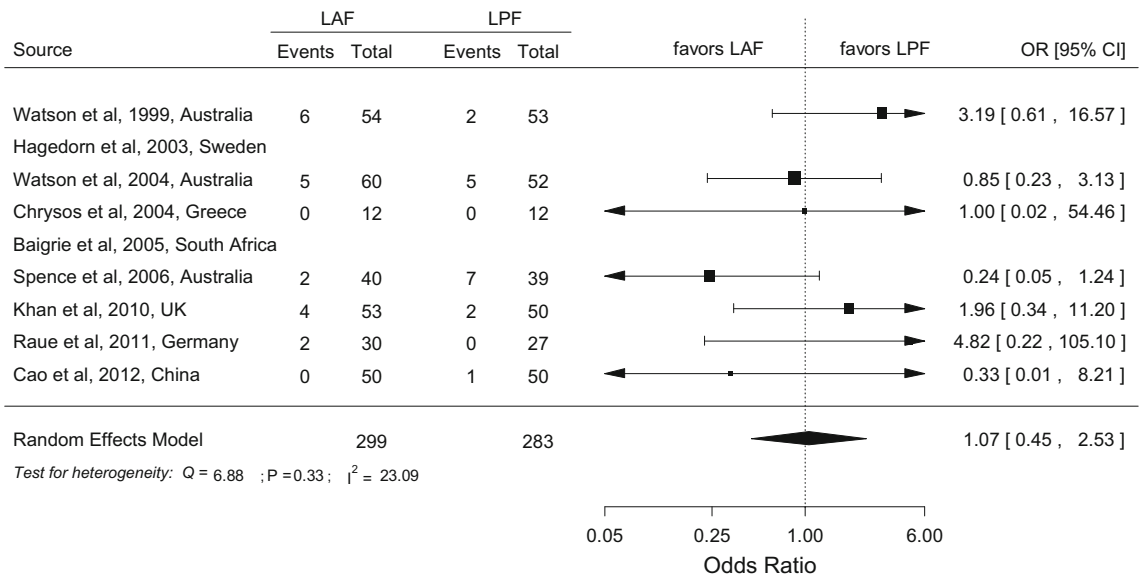

Fig. 6 Forest plot of overall complications for LAF versus LPF using odds ratio (OR)

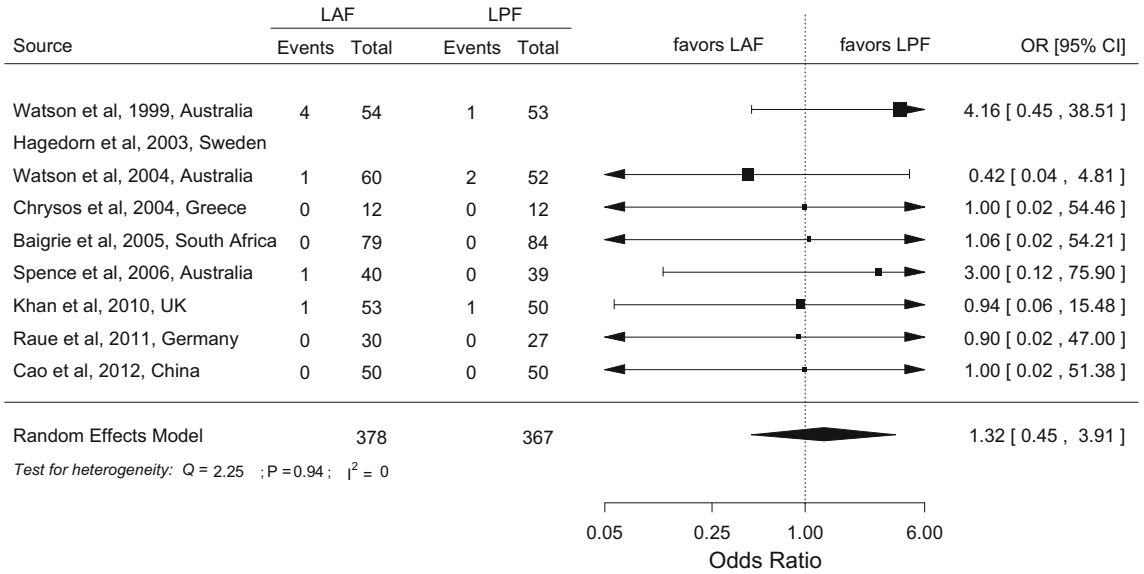

Fig. 7 Forest plot of conversion rate for LAF versus LPF using odds ratio (OR)

of total esophageal acid exposure time and total number of acid and weakly acid reflux episodes which were found to be higher after LAF. Furthermore, the number of liquid and mixed reflux episodes were also higher after LAF leading to higher clinical heartburn scores. A 5-year follow-up result of Swedish trial [42] showed that 82.2 % has no acid regurgitation in the LPF group in comparison to only 34.9 % in the LAF group. Only 7 % in the LPF group as compared to 23.3 % in the LAF group used antisecretory medication on a daily basis to control reflux-like symptoms. Lastly, far more people were satisfied with the overall outcome of their operation in the LPF group (93 %) compared to the LAF group (59 %). Similar poor results were reported by Watson's group [15, 41]. A 10-year retrospective study from Fein [43] involving 120 patients also showed that regurgitation persisted in only 15 % LPF patient compared to 44 % LAF patient. It is therefore evident from the various RCTs that LPF (Nissen and Toupet) produces far superior reflux control compared to LAF. In our meta-analysis all nine RCTs [13–21] reported the number of patients experiencing heartburn following their anti-reflux surgery (Fig. 3). Pooling of the available

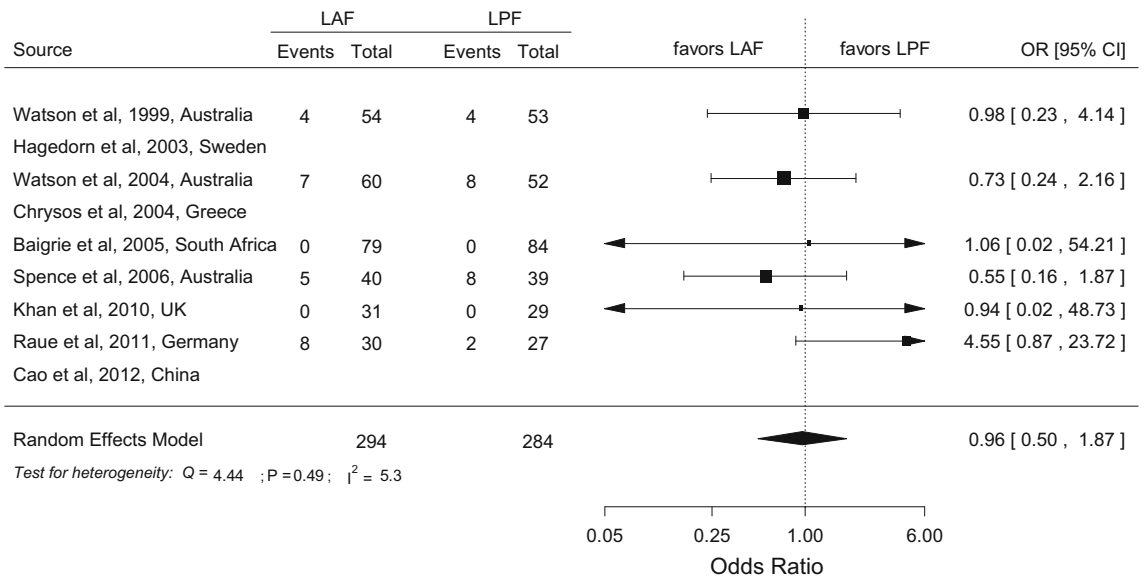

Fig. 8 Forest plot of Visick Grading for LAF versus LPF using odds ratio (OR)

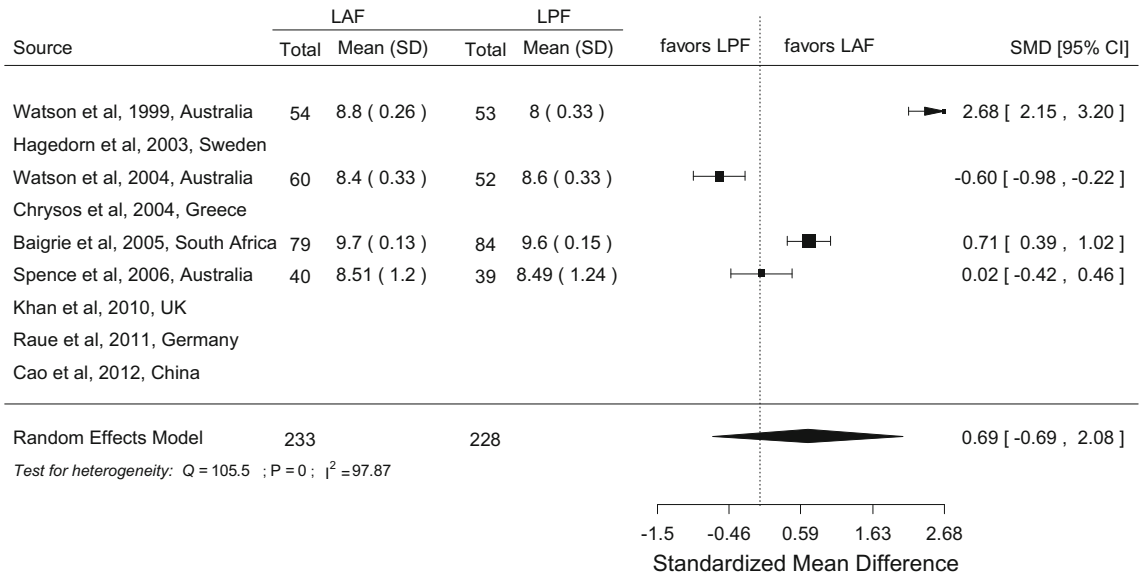

Fig. 9 Forest plot of patient's satisfaction for LAF versus LPF using standardized mean difference (SMD)

data revealed a statistically significant reduction of heartburn by the patients who have undergone LPF group compared to LAF. This has implications for both the utilization of regular proton pump inhibitors (long-term medical therapy) and redo surgery to control persistent reflux. This in turn has cost implications for patients and health services, an issue not addressed by any of these trials (cost vs benefit analysis).

The two main causes for redo surgery are dysphagia and recurrence of reflux symptoms. Overall the surgery for recurrence of reflux symptoms following LAP is far more prevalent than for dysphagia following LPF. A 10-year follow-up of RCT of laparoscopic Nissen versus LAF [39] showed that five patients in each group had revisional surgery. In the LAF group five patients had their 180° anterior wrap converted to Nissen fundoplication for persistent reflux. In the LPF, three patients had their Nissen converted to Toupet repair for persistent dysphagia, one had its Nissen fundoplication refashioned and another one had its hiatus tightened for persistent reflux. It is worth noting that none of the LPFs were converted to LAF. In the Swedish trial [42] at 5-year follow-up, five LAF patients

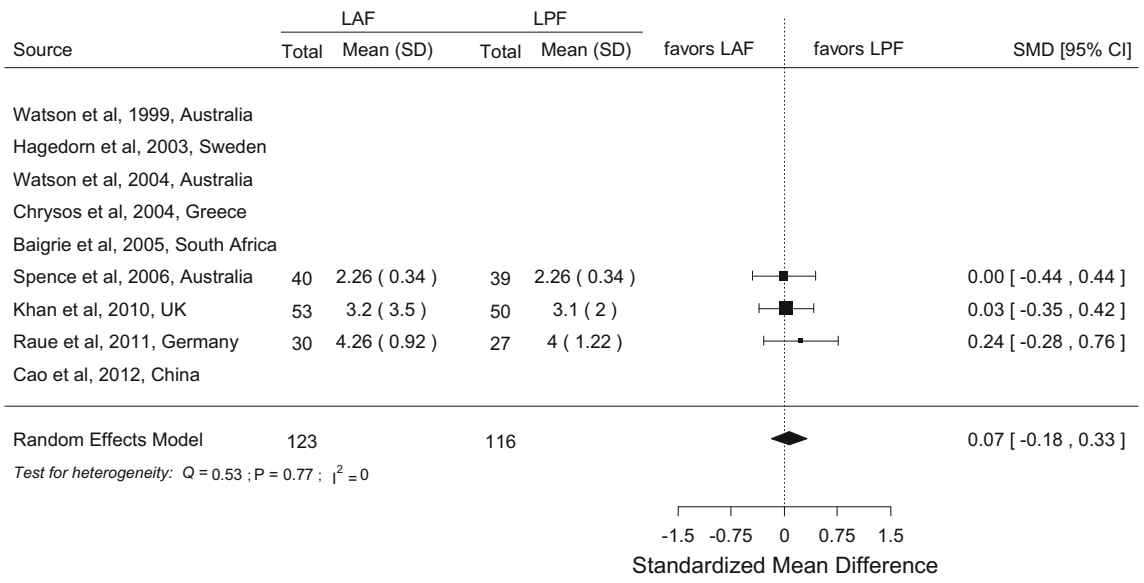

Fig. 10 Forest plot of length of hospital stay for LAF versus LPF using standardized mean difference (SMD)

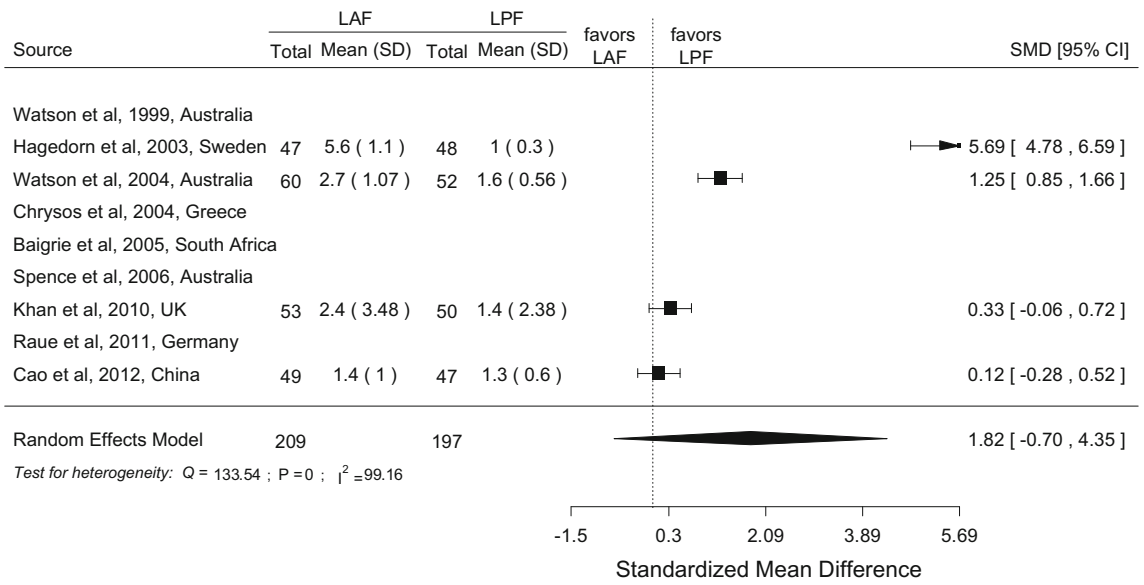

Fig. 11 Forest plot of 24-h pH for LAF versus LPF using standarized mean difference (SMD)

had a reoperation due to persistent reflux compared to only one for LPF for dysphagia. In the South African trial [17], four patients with dysphagia after Nissen fundoplication required revisional surgery. In LAF, ten patients had persistent reflux however only seven underwent revisional surgery. In a trial by Spence et al. [18], at 1-year follow-up, two patients in LAF were converted to laparoscopic Nissen fundoplication for recurrent reflux. In laparoscopic Nissen fundoplication, three patients underwent further surgery for dysphagia. In all three patients the hiatus was widened and in only one patient, Nissen was converted to Toupet. In the Sheffield trial [19], eight patients required reoperation in the LAF group due to recurrence of reflux symptoms whereas in LPF group two patients required reoperation for similar reasons. There was not a single patient in LPF who underwent surgery for dysphagia. In our meta-analysis all studies [13–21] (Fig. 4) reported on reoperation rate, the pooled data of which revealed 1.66 % lower risk of reoperation in the LPF group compared to the LAF counterpart, although this difference did not reach statistical

Table 2 Summary of pooled data comparing LPF and LAF using OR and SMD for various outcomes variables

Outcome variables	RCTS	Patients	Pooled OR [95 % CI][a] SMD [95 % CI][b]	Test for overall effect		Test for heterogeneity		
	n	*n*		*Z*	*p*	*Q*	*p*	*I* [CI]
Dysphagia	6	652	−2.31 [−3.19, −1.43][b]	−5.156	<0.001	100.189	<0.001	94.72 [86.45,99.12]
Heartburn	8	630	1.90 [1.04,3.49][a]	2.082	0.037	8.616	0.281	30.13 [0, 76.40]
Redo surgery	9	836	1.66 [0.91, 3.04][a]	1.644	0.100	4.589	0.801	0 [0,50.95]
Operation time	7	721	−0.30 [−1.00, 0.40][b]	−0.849	0.396	103.92	<0.001	95.17 [88.26,99.03]
Overall complications	7	582	1.07 [0.45,2.53][a]	0.144	0.886	6.876	0.332	23.09 [0,81.83]
Conversion rate	8	745	1.32 [0.45, 3.91][a]	0.505	0.614	2.251	0.945	0 [0, 16.81]
Visick grading	6	578	0.96 [0.50, 1.87][a]	−0.110	0.913	4.443	0.488	5.30 [0,78.99]
Satisfaction	4	461	0.69 [−0.69,2.08][b]	0.9805	0.327	105.495	<0.001	97.87 [93.29,99.85]
Length of hospital stay	3	239	0.07 [−0.18,0.33][b]	0.552	0.581	0.533	0.766	0 [0,92.01]
24 h pH	4	406	1.82 [−0.70, 4.35][b]	1.416	0.157	133.542	<0.001	99.16 [98.62, 99.99]

[a] OR [95 % CI] stands for odds ratio [95 % confidence interval]

[b] SMD [95 % CI] stands for standarized mean differences [95 % confidence interval]

significance. Except for the Adelaide group [39–41] which provided 5, 10, and 14-year follow-up results, all the other studies have provided either a short-term or medium-term follow-up which may not reflect the true state of affair in terms of recurrent reflux symptoms. It is entirely possible that a proportion of patients requiring further medical or surgical treatment for these symptoms may increase with time and only long-term follow-up of all these trials will provide us with some clarity on this issue.

Seven of the nine RCTs [13, 15, 17–21] provided data on operating times (Fig. 5). None of the individual trials showed any major differences in the operating time between the two groups. Pooling of the data furthermore did not show any preference for either group.

Complication rates for the two treatment groups were provided by seven of the nine RCTs [13, 15, 16, 18–21] (Fig. 6). Our analysis failed to show any difference between the two groups. Table 3 provides details of various complications most of which were treated conservatively.

Conversion from laparoscopic procedure to an open procedure was reported in eight of the nine RCTs [13, 15–21] (Fig. 7). The analysis showed no difference between LAF and LPF. The reasons for conversion were varied and included obesity, large left lobe of the liver, large paraesophageal hiatus hernia causing difficulty in esophageal dissection, intra-abdominal adhesions, bowel injury, liver bleeding, esophageal perforation, and intra-abdominal bleeding (not specified).

Only six of the nine RCTs reported the duration of hospital stay [13, 15, 18–21] (Fig. 10). Pooling of the data did not reveal any difference for either group. The only two factors which seem to have any major impact on the hospital stay are complication rate and conversion to an open procedure which do not differ between the two groups.

Visick grading based on subjective evaluation of patients symptoms postoperatively was reported by six out of nine RCTs [13, 15, 17–20] (Fig. 8). Pooling of this data did not reveal any statistical difference between the two groups. Unfortunately, the subjective outcome has not being substantiated objectively using endoscopy, manometry, or postoperative 24-h pH monitoring by many trials because there remains poor patient compliance especially when the patients are asymptomatic [14, 18]. Furthermore, funding may also be an issue in a research setting. The absence of correlation between reduction of esophageal acid exposure using 24-h postoperative ambulatory pH monitoring and heartburn, esophagitis, dysphagia, and quality of life to investigate the efficacy of various anti-reflux surgical procedures is an important one. In the absence of such objective information and simple reliance on questionnaire or interview (subjective) data to grade patient's postoperative satisfaction, there remains a real danger that such assessment may overestimate the benefit of anti-reflux surgery when such does not exist. However, data on patient satisfaction in one or other form was provided by only four [13, 15, 17, 18] out of nine trials (Fig. 9) which failed to show any difference between the two types of fundoplication. Also postoperative 24-h pH scores were provided by seven [13–16, 18, 19, 21] (Fig. 11) out of nine trials once again failed to show any difference between the two groups. However, this data may be flawed because of the very low number of patients accepting this postoperative investigation and the ones accepting this investigation may be a self selected group of individuals who either are symptomatic or wanted to know if their operation has been successful therefore further biasing the results. Lastly, because the number of patients participating in this investigation is quite low, the real difference may be either

Table 3 Summary perioperative complications

Authors (year)	No of patients		Complications	
	LAF	LPF	(*n*)LAF	LPF
Watson et al. (1999) [13]	54	53	1 Urinary retention	1 Subphrenic abscess
			1 Atelectasis	1 Postoperative dysphagia
			1 Pneumothorax	
			1 Acute postoperative paraesophageal herniation	
			1 Severe postoperative dysphagia	
			1 Esophageal perforation	
			1 Liver bleeding	
Hagedorn et al. (2003) [14]	47	48	N/A	N/A
Watson et al. (2004) [15]	60	52	1 Small bowel injury	1 Splenic infarction
				1 Pneumothorax
			1 Pneumothorax	1 Urinary retention
			1 Pulmonary embolus	1 Respiratory infection
			1 Wound infection	1 Bleeding
			1 Urinary retention	
Chrysos et al. (2004) [16]	12	12	No complications	No complications
Baigrie et al. (2005) [17]	79	84	N/A	N/A
Spence et al. (2006) [18]	40	39	1 Paraesophageal hernia	1 Respiratory infection
			1 Umbilical port site hernia	1 Cervical subcutaneous emphysema
			3 Pneumothorax	
			1 Urinary retention	
			1 Excessive retching	
Khan et al. (2010) [19]	53	50	1 Respiratory tract infection	1 Respiratory tract infection
			1 Acute renal failure	
			2 Cardiovascular complications	1 Pulmonary embolus
Raue et al. (2011) [20]	30	27	1 Serious bleeding	No complications
			1 Wound infection leading to port site hernia	
Cao et al. (2012) [21]	50	50	No complication	Posterior esophageal perforation

obscured or exaggerated by the relatively small sample size.

Limitations

There are a number of limitations both statistical and clinical in this paper. Firstly, publication bias was detected on funnel plot analysis for the outcomes of dysphagia score, operating time, satisfaction score, and postoperative 24-h pH scores [44, 45] (Fig. 12). A second possible limitation within this meta-analysis is the presence of heterogeneity detected within several outcomes. Although some degree of heterogeneity is inevitable in a medical meta-analysis due to the realities of clinical practice [44, 46], the degree of between-study heterogeneity present may undermine the quality and legitimacy of the results obtained [47]. Thirdly, the exclusion of studies published in languages other than English is another potential limitation to the present work. The impact of the inclusion of English only studies was also challenged by re-running the search terms without this limit applied—no eligible studies in languages other than English were located. Next the small number of studies included in this meta-analysis remains a largely unavoidable limitation of this and many other meta-analyses conducted in surgical fields [48, 49]. Lastly, pooling of different types of LAF and LPF (360°, 270°, 180°, 120°, and 90°) [13–21] may be considered a potential limitation.

As the follow-up for most of these RCTs has been short, the true incidence of dysphagia, recurrence of reflux symptoms, patient's satisfaction, and redo surgery is not truly known. Thus, presently we do not know the accurate cost and benefits of LAF versus LPF [50]. Some of the benefits of anti-reflux surgery include cure of GERD and improved quality of life. Cost factors include recurrence of reflux symptoms, reintroduction of proton pump inhibitors after surgery, and redo surgery. Until and unless these factors are analyzed over a certain period of time (e.g., over

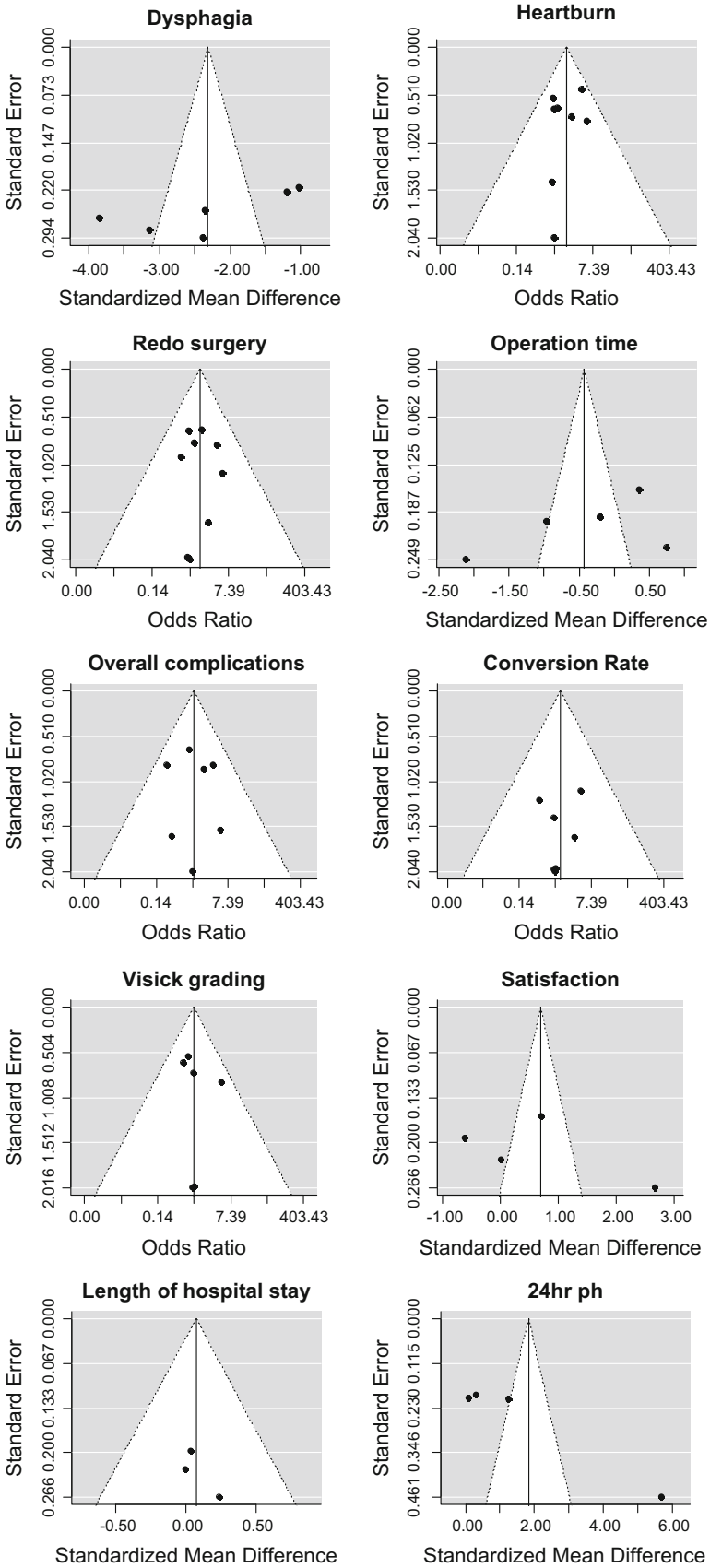

Fig. 12 Funnel plots for the outcome variables. *Funnel plots* represent the scatterplot of the log odds ratios or SMDs against the inverse of their standard errors. A *funnel plot* of inverse standard error versus treatment effect from individual studies in a meta-analysis should like a *funnel* if there is no publication bias. *Funnel plots* for the variables dysphagia, operating time, satisfaction score, and 24-h pH study shows presence of publication bias

5 and 10 years), the true effectiveness of LAF remains speculative and may overestimate some of the parameters associated with anti-reflux surgery. This is seen in two recent publications [36, 41] on anti-reflux surgery where the previously thought mechanical and functional differences of one procedure over other disappeared on long-term follow-up. Therefore, the results of any short-term or medium-term benefits needs to be interpreted with extreme caution.

Lastly, the accurate measurement of clinical and functional outcomes and satisfaction are critical in gaging the benefits of any surgical procedure. The majority of RCTs have reported on subjective outcomes for this purpose. The use of postoperative questionnaires or patient interviews for assessing patients' symptoms or satisfaction in the absence of measurable objective outcomes have multiple problems which include (a) under or overestimation of benefits or drawbacks; (b) poor or incomplete response rate to mail out questionnaire or personal interview; (c) reporting bias especially by a self- selected group of patients; (d) design of questionnaire; and lastly (e) interviewer and interviewee's agenda. The vast majority of RCTs in this meta-analysis lack objective data on both mechanical and functional outcomes and satisfaction score for either procedures. Furthermore, even those RCTs which have reported on these variables have low patient numbers which may have biased the overall results following the anti-reflux surgery [51].

Conclusions

Based on this meta-analysis, LPF is associated with significant reduction of heartburn whereas LAF is associated with a significantly lower incidence of dysphagia. However, it is worth noting that our pooled data has provided results of dysphagia scores which were reported between 6 and 24 months and which may have overestimated dysphagia symptoms. The long-term results for dysphagia from four longitudinal studies [39–42] have shown no difference for this variable between LPF and LAF groups. Furthermore, because of short-term follow-up, the recurrence of reflux symptoms may have been underestimated thereby exaggerating the cure rate for LAF. It is therefore evident that LPF (Nissen and Toupet) seems to provide far more durable and long-lasting relief from GERD compared to LAF. Moreover, the incidence of dysphagia seems to approach the same level as LAF after about 5 years. It is imperative that recurrence of reflux symptoms must be objectively evaluated using ambulatory impendence pH monitoring prior to offering revisional surgery. We feel, based on current scientific data and our meta-analysis, LPF (Nissen and Toupet) as opposed to LAF, should be offered as the first choice of procedure for proven moderate to severe GERD to those patients who choose to undergo surgery following an objective evaluation of their reflux symptoms.

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References

1. Peters MJ, Mukhtar A, Yunus RM, Khan S, Pappalardo J, Memon B, Memon MA (2009) Meta-analysis of randomized clinical trials comparing open and laparoscopic anti-reflux surgery. Am J Gastroenterol 104(6):1548–1561
2. McKenzie D, Grayson T, Polk HC Jr (1996) The impact of omeprazole and laparoscopy upon hiatal hernia and reflux oesophagitis. J Am Coll Surg 183(4):413–418
3. Klaus A, Hinder RA, DeVault KR, Achem SR (2003) Bowel dysfunction after laparoscopic antireflux surgery: incidence, severity, and clinical course. Am J Med 114(1):6–9
4. Spechler SJ (1992) Comparision of medical and surgical therapy for complicated gastroesophageal reflux disease in veterans. The Department of Veterans Affairs Gastroesophageal Reflux Disease Study Group. N Engl J Med 326(12):786–792
5. Bais JE, Bartelsman JF, Bonjer HJ, Cuesta MA, Go PM, Klinkenberg-Knol EC, van Lanschot JJ, Nadorp JH, Smout AJ, van der Graaf Y, Gooszen HG (2000) Laparoscopic or conventional Nissen Fundoplication for gastro-oesophageal reflux disease: randomised clinical trial. The Netherlands Antireflux Surgery Study Group. Lancet 355(9199):170–174
6. Wills VL, Hunt DR (2001) Dysphagia after antireflux surgery. Br J Surg 88(4):486–499
7. Catarci M, Gentileschi P, Papi C, Carrara A, Marrese R, Gaspari AL, Grassi GB (2004) Evidence-based appraisal of antireflux fundoplication. Ann Surg 239(3):325–337
8. Bell RC, Hanna P, Powers B, Sabel J, Hruza D (1996) Clinical and manometric results of laparoscopic partial (Toupet) and complete (Rosetti-Nissen) fundoplication. Surg Endosc 10(7): 724–728
9. O'Reilly MJ, Mullins SG, Saye WB, Pinto SE, Falkner PT (1996) Laparoscopic posterior partial fundoplication: analysis of 100 consecutive cases. Laparoendosc Surg 6(3):141–150
10. Watson A, Jenkinson LR, Ball CS, Barlow AP, Norris TL (1991) A more physiological alternative to total fundoplication for the surgical correction of resistant gastro-oesophageal reflux. Br J Surg 78(9):1088–1094
11. Watson A, Spychal RT, Brown MG, Peck N, Callander N (1995) Laparoscopic 'physiological' antireflux procedure: preliminary results of a prospective symptomatic and objective study. Br J Surg 82(5):651–656
12. Rice S, Watson DI, Lally CJ, Devitt PG, Game PA, Jamieson GG (2006) Laparoscopic anterior 180 degrees partial fundoplication: five-year results and beyond. Arch Surg 141(3):271–275
13. Watson DI, Jamieson GG, Pike GK, Davies N, Richardson M, Devitt PG (1999) Prospective randomized double-blind trial between laparoscopic Nissen fundoplication and anterior partial fundoplication. Br J Surg 86(1):123–130
14. Hagedorn C, Jönson C, Lönroth H, Ruth M, Thune A, Lundell L (2003) Efficacy of an anterior as compared with a posterior laparoscopic partial fundoplication: results of a randomized, controlled clinical trial. Ann Surg 238(2):189–196

15. Watson DI, Jamieson GG, Lally C, Archer S, Bessell JR, Booth M, Cade R, Cullingford G, Devitt PG, Fletcher DR, Hurley J, Kiroff G, Martin CJ, Martin IJ, Nathanson LK, Windsor JA, International Society for Diseases of the Esophagus-Australasian Section (2004) Multicenter, prospective, double-blind, randomized trial of laparoscopic nissen vs anterior 90 degrees partial fundoplication. Arch Surg 139(11):1160–1167
16. Chrysos E, Athanasakis E, Pechlivanides G, Tzortzinis A, Mantides A, Xynos E (2004) The effect of total and anterior partial fundoplication on antireflux mechanisms of the gastroesophageal junction. Am J Surg 188(1):39–44
17. Baigrie RJ, Cullis SN, Ndhluni AJ, Cariem A (2005) Randomized double-blind trial of laparoscopic Nissen fundoplication versus anterior partial fundoplication. Br J Surg 92(7):819–823
18. Spence GM, Watson DI, Jamiesion GG, Lally CJ, Devitt PG (2006) Single center prospective randomized trial of laparoscopic Nissen versus anterior 90 degrees fundoplication. J Gastrointest Surg 10(5):698–705
19. Khan M, Smythe A, Globe J, Stoddard CJ, Ackroyd R (2010) Randomized controlled trial of laparoscopic anterior versus posterior fundoplication for gastro-oesophageal reflux disease. ANZ J Surg 80(7–8):500–505
20. Raue W, Ordemann J, Jacobi CA, Menenakos C, Buchholz A, Hartmann J (2011) Nissen versus Dor fundoplication for treatment of gastroesophageal reflux disease: a blinded randomized clinical trial. Dig Surg 28(1):80–86
21. Cao Z, Cai W, Qin M, Zhao H, Yue P, Li Y (2012) Randomized clinical trial of laparoscopic anterior 180° partial versus 360° Nissen fundoplication: 5 year results. Dis Esophagus 25(2):114–120
22. Moher D, Cook DJ, Eastwood S, Olkin I, Rennie D, Stroup DF (1999) Improving the quality of reports of meta-analyses of randomised controlled trials: the QUOROM statement. International Society for Diseases of the Esophagus-Australasian Section. Lancet 354(9193):1896–1900
23. Liberati A, Altman DG, Tetzlaff J, Mulrow C, Gøtzsche PC, Ioannidis JP, Clarke M, Devereaux PJ, Kleijnen J, Moher D (2009) The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: explanation and elaboration. J Clin Epidemiol 62(10):1–34
24. Jadad AR, Moore RA, Carroll D, Jenkinson C, Reynolds DJ, Gavaghan DJ (1996) Assessing the quality of reports of randomized clinical trials: is blinding necessary? Control Clin Trials 17(1):1–12
25. Liu IM, Agresti A (1996) Mantel-Haenszel-type inference for cumulative odds ratios with a stratified ordinal response. Biometrics 52(4):1223–1234
26. Sutton AJ, Abrams KR, Jones DR, Sheldon TA, Song F (2000) Methods for meta-analysis in medical research. Wiley, Chichester
27. Hedges LV, Olkin I (1985) Statistical methods for meta analysis. Academic Press, Orlando
28. Higgins JP, Thompson SG (2002) Quantifying heterogeneity in a meta-analysis. Stat Med 21(11):1539–1558
29. Huedo-Medina TB, Sánchez-Meca J, Marín-Martínez F, Botella J (2006) Assessing heterogeneity in meta-analysis: Q statistic or I^2 index? Psychol Methods 11(2):193–206
30. Hozo SP, Djulbegovic B, Hozo I (2005) Estimating the mean and variance from the median, range, and the size of a sample. BMC Med Res Methodol 5(1):13
31. Egger M, Davey Smith G, Schneider M, Minder C (1997) Bias in meta-analysis detected by a simple, graphical test. BMJ 315(7109):629–634
32. Foundation for Statistical computing (2008) R: A language and environment for statistical computing [computer program] Version 2.8.0. Foundation for Statistical computing, Vienna
33. Lumley T (2011) The rmeta Package Version 2.14. http://cran.rproject.org/web/packages/rmeta/index.html (Accessed April 22, 2011)
34. Anderson JA, Myers JC, Watson DI, Gabb M, Mathew G, Jamieson GG (1998) Concurrent fluoroscopy and manometry reveal differences in laparoscopic Nissen and anterior fundoplication. Dig Dis Sci 43(4):847–853
35. Hagedorn C, Lönroth H, Rydberg L, Ruth M, Lundell L (2002) Long-term efficacy of total (Nissen-Rossetti) and posterior partial (Toupet) fundoplication: results of a randomized clinical trial. J Gastrointest Surg 6(4):540–545
36. Mardani J, Lundell L, Engstrom C (2011) Total or posterior partial fundoplication in the treatment of GERD. Results of a randomized trial after 2 decades of follow-up. Ann Surg 253:875–878
37. Broeders JAJL, Mauritz FA, Ahmed Ali U, Draaisma WA, Ruurda JP, Gooszen HG, Smout AJPM, Broeders IAMJ, Hazebrock EJ (2010) Systematic review and meta-analysis of laparoscopic Nissen (posterior total) versus Toupet (posterior partial) fundoplication for gastro-oesophageal reflux disease. Brit J Surg 97(9):1318–1330
38. Ludemann R, Watson DI, Jamieson GG, Game PA, Devitt PG (2005) Five-year follow-up of a randomized clinical trial of laparoscopic total versus anterior 180 degrees fundoplication. Br J Surg 92(2):240–243
39. Cai W, Watson DI, Lally CJ, Devitt PG, Game PA, Jamieson GG (2008) Ten-year clinical outcome of a prospective randomized clinical trial of laparoscopic Nissen versus anterior 180 (degrees) partial fundoplication. Br J Surg 95(12):1501–1505
40. Broeders JA, Broeders EA, Watson DI, Devin PG, Holloway RH, Jamieson GG (2013) Objective outcomes 14 years after laparoscopic anterior 180-degree partial versus Nissen fundoplication. Results from a randomized trial. Ann Surg 258(2):233–239
41. Nijjar RS, Watson DI, Archer S, Bessell JR, Booth M, Cade R, Cullingford GL, Devitt PG, Flecher DR, Hurley J, Kiroff G, Martin IJG, Nathanson LK, Windsor JA, for the International Society for the Diseases of the Esophagus-Australasian Section (2010) Five-year follow-up of multicenter, double-blind randomized clinical trial of laparoscopic Nissen vs anterior 90o partial fundoplication. Arch Surg 145:552–557
42. Engström C, Lönroth H, Mardani J, Lundell L (2007) An anterior or posterior approach to partial fundoplication? Long-term results of a randomized trial. World J Surg 31(6):1215–1221. doi:10.1007/s00268-007-9004-8
43. Fein M, Bueter M, Thalheimer A, Pachmayr V, Heimbucher J, Freys SM, Fuchs KH (2008) Less reflux recurrence following Nissen fundoplication: results of laparoscopic antireflux surgery after 10 years. Chirurg 79(8):759–764
44. Duval S, Tweedie R (2000) Trim and fill: a simple funnel-plot-based method of testing and adjusting for publication bias in meta-analysis. Biometrics 56:455–463
45. Stern JA, Egger M (2001) Funnel plots for detecting bias in meta-analysis: guidelines on choice of axis. J Clin Epidemol 54:1046–1055
46. Ioannidis JP, Lau J (1998) Can quality of clinical trials and meta-analyses be quantified? Lancet 352:590–591
47. Ng TT, McGory ML, Ko CY, Maggard MA (2006) Meta-analysis in surgery: methods and limitations. Arch Surg 141:1125–1130
48. Smith GD, Egger M (1998) Incommunicable knowledge? Interpreting and applying the results of clinical trials and meta-analyses. J Clin Epidemiol 51:289–295
49. Ioannidis JP, Patsopoulos NA, Evangelou E (2007) Uncertainty in heterogeneity estimates in meta-analyses. BMJ 335:914–916
50. Doubilet P, Weinstein MC, McNeal BJ (1986) Use and misuse of the term "cost-effectiveness" in medicine. N Engl J Med 314:253–256
51. Ludemann R, Watson DI, Jamieson GG (2003) Influence of follow-up methodology and completeness on apparent clinical outcome of fundoplication. Am J Surg 186(2):143–147