Meta-analysis

Systematic review and meta-analysis of laparoscopic Nissen (posterior total) *versus* Toupet (posterior partial) fundoplication for gastro-oesophageal reflux disease

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Background: **Laparoscopic Nissen fundoplication (LNF) is currently considered the surgical approach of choice for gastro-oesophageal reflux disease (GORD). Laparoscopic Toupet fundoplication (LTF) has been said to reduce troublesome dysphagia and gas-related symptoms. A systematic review and meta-analysis of randomized clinical trials (RCTs) was performed to compare LNF and LTF.**

Methods: **Four electronic databases (MEDLINE, Embase, Cochrane Library and ISI Web of Knowledge CPCI-S) were searched and the methodological quality of included trials was evaluated. Outcomes included recurrent pathological acid exposure, oesophagitis, dysphagia, dilatation for dysphagia and reoperation rate. Results were pooled in meta-analyses as risk ratios (RRs) and weighted mean differences.**

Results: **Seven eligible RCTs comparing LNF ($n = 404$) with LTF ($n = 388$) were identified. LNF was associated with a significantly higher prevalence of postoperative dysphagia (RR 1·61 (95 per cent confidence interval 1·06 to 2·44); $P = 0·02$) and dilatation for dysphagia (RR 2·45 (1·06 to 5·68); $P = 0·04$). There were more surgical reinterventions after LNF (RR 2·19 (1·09 to 4·40); $P = 0·03$), but no differences regarding recurrent pathological acid exposure (RR 1·26 (0·82 to 1·95); $P = 0·29$), oesophagitis (RR 1·20 (0·78 to 1·85); $P = 0·40$), subjective reflux recurrence, patient satisfaction, operating time or in-hospital complications. Inability to belch (RR 2·04 (1·19 to 3·49); $P = 0·009$) and gas bloating (RR 1·58 (1·21 to 2·05); $P < 0·001$) were more prevalent after LNF.**

Conclusion: **LTF reduces postoperative dysphagia and dilatation for dysphagia compared with LNF. Reoperation rate and prevalence of gas-related symptoms were lower after LTF, with similar reflux control. These results provide level 1a support for the use of LTF as the posterior fundoplication of choice for GORD.**

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Introduction

Laparoscopic Nissen fundoplication (LNF) is the most frequently performed operation for gastro-oesophageal reflux disease (GORD). Accepted indications for antireflux surgery are persistent regurgitation despite adequate medical therapy, incomplete response to acid-suppressing drugs in patients with proven reflux, and unwillingness to take lifelong medication[1–3]. Several randomized studies have demonstrated that LNF has similar 5-year[4] and 10-year[5] rates for disease control, and fewer incisional hernias, compared with open fundoplication. LNF has been recommended as the surgical therapy of choice by the European Study Group for Antireflux Surgery[6] and the Society of American Gastrointestinal Endoscopic Surgeons[7].

Although LNF ensures long-term reflux control, postfundoplication symptoms may occur[8–11]. Some 8–12 per cent of patients develop severe dysphagia[12–15] and 19 per cent suffer from gas-related symptoms[16]. Laparoscopic Toupet fundoplication (LTF) has been proposed as an alternative operation. LTF differs from

LNF by a partial posterior instead of a circumferential posterior fundoplication, with a different method of fixation[17]. It has been suggested that LTF reduces the prevalence of postoperative dysphagia[18,19] and gas-related symptoms[20,21] compared with LNF. Despite these potential benefits, LTF is not widely used, probably because uncontrolled studies have reported less effective reflux control compared with LNF[22–27]. Partial fundoplication was then proposed as potentially the better procedure for patients with preoperative oesophageal motility disorders to minimize postfundoplication complaints, until randomized clinical trials (RCTs) demonstrated no increase in symptoms following total fundoplication in these patients[28–31].

In the past 2 years, large RCTs comparing LNF with LTF have been published. Results of these individual RCTs have not provided a definitive answer. Most trials do not show significant differences. The present study aimed systematically to review and perform meta-analyses of all RCTs comparing LNF with LTF for GORD, and to generate the highest level of evidence to determine which procedure should be regarded as the surgical therapy of choice.

Methods

Study selection

A systematic literature search with predefined search terms was carried out in MEDLINE (1960 to 2009)[32], Embase (from 1980)[33], Cochrane Library (issue 1, 2009) and the ISI Web of Knowledge Conference Proceedings Citation Index – Science (CPCI-S; from 1990) databases for articles published to 30 December 2009 (*Fig. 1*). All identified articles were screened for cross-references. Language restrictions were not applied.

Inclusion criteria

Titles and abstracts of all identified articles were screened for the following inclusion criteria: study population – adult patients with established GORD undergoing primary antireflux surgery; intervention – clearly documented surgical technique of LNF as laparoscopic Nissen or posterior total (360°) fundoplication, irrespective of division of the short gastric vessels[16], and of LTF as laparoscopic Toupet or posterior partial fundoplication covering the oesophagus 200–270°; study outcomes – at least one of the outcome measures reported below; study design – patients assigned to either LNF or LTF by random allocation; publication – published as an article in a peer-reviewed journal.

Exclusion criteria

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

Outcomes of interest and definitions

Outcome measures examined were: recurrent or persistent pathological acid exposure on pH monitoring, endoscopic oesophagitis, dysphagia, postoperative dilatation for dysphagia, reoperation rate, inability to belch, gas bloating, hyperflatulence, subjective reflux persistence and/or recurrence (defined as postoperative heartburn on a dichotomous scale or unchanged to worsened reflux symptoms compared with the preoperative state[34]), satisfaction with the intervention, mean lower oesophageal sphincter (LOS) pressure on manometry, operating time, mortality and in-hospital complications, and length of hospital stay. Short-term clinical outcomes were excluded and results acquired after at least 1 year of follow-up were pooled.

Data extraction

Titles and abstracts of all retrieved records, and subsequently full-text articles, were examined independently by two authors (J.A.J.L.B., F.A.M.) according to the Quality of Reporting of Meta-analyses (QUOROM) guidelines[35]. The following data were extracted separately by the same two authors for all studies meeting the inclusion criteria: reference of study, study population characteristics, study design, inclusion and exclusion criteria, number of participating subjects and events for each endpoint. In case of discrepancies, a third author (U.A.A.) was consulted and agreement reached by consensus. Authors of the original RCTs were contacted to provide missing data; total numbers of patients for each outcome parameter and standard deviations of continuous outcomes were determined.

Risk of bias assessment

Risk of bias was assessed of all articles using both the Cochrane Collaboration's tool for assessing risk of bias[32] and the Jadad scoring system[36].

Statistical analysis

Statistical analyses were performed following the recommendations of the Cochrane Collaboration and

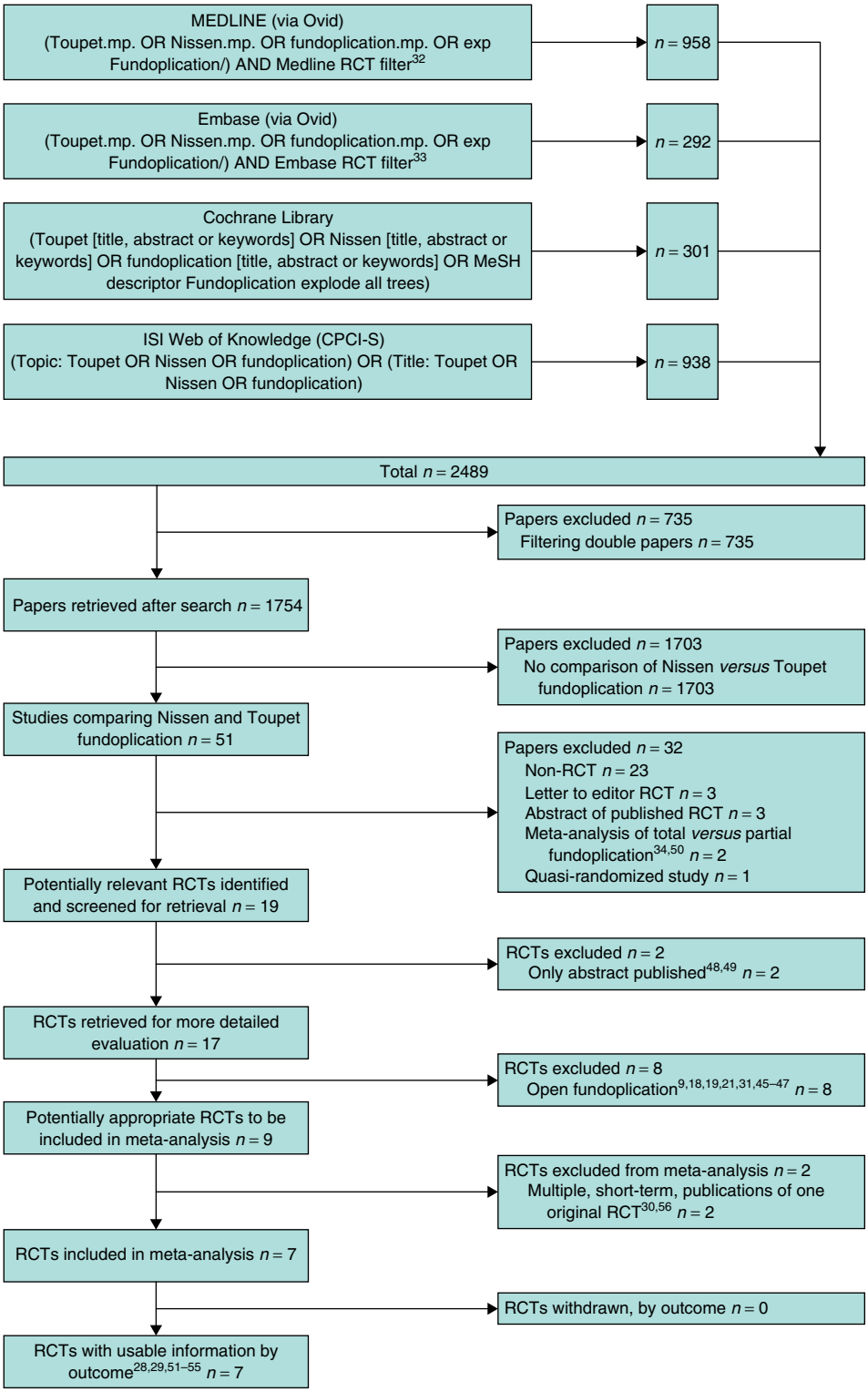

Fig. 1 Flow chart illustrating details of the search strategy and the study selection process according to the QUOROM statement[35]. RCT, randomized clinical trial; MeSH, Medical Subject Heading; CPCI-S, Conference Proceedings Citation Index – Science

QUOROM guidelines[35,37,38]. Outcomes reported by two or more studies were pooled in meta-analyses. Dichotomous and continuous outcomes were presented as risk ratios (RRs) and weighted mean differences (WMD) respectively. Data were pooled using the Mantel–Haenszel and the inverse variance method for dichotomous and continuous outcomes respectively. 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 two by two table for that study. Trials with zero events in both arms were excluded from meta-analysis. For all analyses the 95 per cent confidence interval (c.i.) was calculated.

The fixed-effects model was used if no heterogeneity was present (χ^2 *P* value greater than 0·100 and I^2 less than 50 per cent); otherwise the DerSimonian random-effects model was used[39]. Heterogeneity was calculated using Higgins χ^2 test[40], and inconsistency in study effects was quantified by I^2 values[32,41]. If excessive heterogeneity was present, data were first rechecked. When heterogeneity persisted, subgroup or sensitivity analyses were used to explore its causes. Funnel plots were used to help identify the presence of publication or other types of bias[42–44]. Data management and statistical analyses were conducted using the Review Manager software (RevMan© version 5.0.16) provided by the Cochrane Collaboration.

Results

Description of studies

A total of 2489 potential relevant publications were identified. *Fig. 1* outlines the search strategy. Fifty-one relevant papers were identified. Twenty-four studies did not randomly allocate patients. Eight RCTs[9,18,19,21,31,45–47] were excluded because an open surgical approach had been used, and two trials[48,49] were published only as abstracts. Two papers reported meta-analyses comparing both laparoscopic and open, as well as total *versus* various types of anterior and posterior partial fundoplication[16,50]. Finally, seven original randomized trials[28,29,51–55] comparing laparoscopic Nissen with Toupet fundoplication were identified (*Fig. 1*).

Included trials were published between 1997 and 2010. They presented outcomes after different times but with at least 12 months of follow-up. In total, 792 antireflux operations (404 LNF; 388 LTF) were performed. In all patients, a standardized total (360°) LNF or a LTF with a circumferential range of 200–270° was created. In all trials the length of the fundoplication was similar in both arms, but the fundoplication length differed from 1 to 4 cm between trials. The only exception was the study by Shaw and colleagues[54], who performed a 1-cm LNF wrap and a 2-cm LTF wrap. Laws and co-workers[52] did not perform routine posterior crural repair in the LTF group (*Table 1*). The trials enrolled patients with and without oesophageal dysmotility, with no differences between the arms of each trial. Patient characteristics and indications for surgical treatment are listed in *Table 2*.

Methodological quality of included studies

The methodological quality of the included trials ranged from poor to excellent, with a median Jadad score of 2 (range 1–5) (*Table 3*). This resulted from poor description of randomization methods, lack of double-blinding, and

Table 1 Details of included randomized clinical trials comparing laparoscopic Nissen and Toupet fundoplication

Reference	Period	Method	*n*	PF (°)	Crural repair	Bougie (Fr)	DSGV	Fixation*	Wrap length (cm)	Follow-up (months)
Booth (2008)[28]	1998–2001	Nissen	64		Yes	56	Yes	Yes	2	12
		Toupet	63	270	Yes	56	Yes	Yes	2	
Chrysos (2003)[29]	NR	Nissen	14		Yes	None	No	Yes	3–4	12
		Toupet	19	270	Yes	None	No	Yes	3–4	
Guérin (2007)[51]	1998–2002	Nissen	77		NR	34	Yes	Yes	3	12
		Toupet	63	270	NR	NR	Yes	Yes	NR	
Laws (1997)[52]	NR	Nissen	23		Yes	30–40	Yes	Yes	2·2	27
		Toupet	16	200–270	No	NR	Yes	Yes	NR	
Mickevicius (2008)[53]	2000–2003	Nissen	76		Yes	52	Yes	Yes	1·5/3	12
		Toupet	77	200–270	Yes	52	Yes	Yes	1·5/3	
Shaw (2010)[54]	1997–2001	Nissen	50		Yes	52	Yes	Yes	1	60
		Toupet	50	270	Yes	52	Yes	Yes	2	
Strate (2008)[30,55,56]	1999–2000	Nissen	100		Yes	36	Yes	Yes	2	24
		Toupet	100	270	Yes	NR	Yes	Yes	NR	

*Fixation of fundoplication to anterior wall of oesophagus. PF, partial fundoplication (circumference of Toupet wrap); DSGV, division of short gastric vessels; NR, not reported.

Table 2 Patient characteristics

Reference	Method	Mean age (years)	Sex ratio (M : F)	Oesophageal dysmotility	Indication for surgical treatment
Booth *et al.*[28]	Nissen Toupet	45·3 44·2	41 : 23 43 : 20	26 of 64* 26 of 63*	GORD proven on 24-h pH monitoring; refractory to PPI therapy (94) or patient preference (33)
Chrysos *et al.*[29]	Nissen Toupet	59·2 61·7	7 : 7 11 : 8	14 of 14† 19 of 19†	GORD requiring daily PPI therapy, proven on 24-h pH monitoring
Guérin *et al.*[51]	Nissen Toupet	NR NR	54 : 23 32 : 31	0 of 77‡ 0 of 63‡	GORD requiring daily PPI therapy, proven on upper endoscopy
Laws *et al.*[52]	Nissen Toupet	45·5 55·5	10 : 13 9 : 7	0 of 23 0 of 16	GORD proven on upper endoscopy
Mickevicius *et al.*[53]	Nissen Toupet	51·5 53·6	34 : 42 40 : 37	NR* NR*	GORD requiring daily PPI therapy, proven on upper endoscopy
Shaw *et al.*[54]	Nissen Toupet	45·2 45·6	31 : 19 29 : 21	14 of 50§ 11 of 50§	GORD proven on upper endoscopy
Strate *et al.*[30,55,56]	Nissen Toupet	56.0	121 : 79	50 of 100§ 50 of 100§	GORD requiring daily PPI therapy, proven on 24-h pH monitoring or upper endoscopy

*At least 30 per cent of swallows non-transmitted or distal amplitude less than 30 mmHg; †distal amplitude less than 30 mmHg; ‡at least 30 per cent of swallows non-transmitted; §at least 60 per cent of swallows non-transmitted or distal amplitude less than 40 mmHg. GORD, gastro-oesophageal reflux disease; PPI, proton pump inhibitor; NR, not reported.

Table 3 Risk of bias summary

	Booth[28]	Chrysos[29]	Guérin[51]	Laws[52]	Mickevicius[53]	Shaw[54]	Strate[30,55,56]
Adequate sequence generation	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Allocation concealment	Yes	Yes	NR	NR	Yes	Yes	Yes
Blinding (observer)	NR	Yes	NR	Yes	Yes	Yes	Yes
Blinding (patient)	Yes	No	No	No	No	Yes	No
Adequate report on loss to follow-up	No	Yes	No	No	No	Yes	No
Free of other sources of bias	No*	Yes	Yes	No†	Yes	Yes	NR
Jadad score[36]	2	3	1	1	2	5	2

*Baseline imbalance in dysphagia between the two arms; †no crural repair in laparoscopic Toupet fundoplication group. NR, not reported.

absence of explanation for withdrawals and dropouts. In addition, none of the RCTs reported a sample size calculation. In the study of Booth and colleagues[28] there was a significantly higher preoperative prevalence of moderate dysphagia in the LNF group compared with the LTF group. Therefore, new-onset dysphagia or worsening of dysphagia was used to compare this study in a meta-analysis. Five of seven authors of original trials agreed to share missing data[28,29,53–55]. Outcome measures that were missing and completed by the authors were reoperation rate ($n = 1$), recurrent reflux symptoms ($n = 2$), inability to belch ($n = 1$), gas bloating ($n = 2$), patient satisfaction ($n = 2$) and operating time ($n = 1$). Outcome measures that were missing and could not be completed by the authors were recurrent pathological acid exposure ($n = 2$), oesophagitis ($n = 1$), inability to belch ($n = 2$), gas bloating ($n = 1$) and satisfaction with the intervention ($n = 1$).

Results of outcomes

All primary outcomes and all but two secondary outcomes were reported by two or more studies. There were no differences in the percentage of patients with recurrent pathological acid exposure (RR 1·26, 95 per cent c.i. 0·82 to 1·95; $P = 0·29$) (*Fig. 2*) or oesophagitis (RR 1·20, 95 per cent c.i. 0·78 to 1·85; $P = 0·40$) (*Fig. 3*) in LNF and LTF groups. LNF was associated with a significantly higher prevalence of postoperative dysphagia (13·5 *versus* 8·6 per cent; RR 1·61, 95 per cent c.i. 1·06 to 2·44; $P = 0·02$) (*Fig. 4*), or in the percentage that underwent postoperative dilatation for dysphagia (6·9 *versus* 2·7 per cent; RR 2·45, 95 per cent c.i. 1·06 to 5·68; $P = 0·04$) (*Fig. 5*). The number of surgical reinterventions was also higher after LNF (7·0 *versus* 3·1 per cent; RR 2·19, 95 per cent c.i. 1·09 to 4·40; $P = 0·03$) (*Fig. 6*). Gas-related symptoms were more common after LNF. A higher prevalence of inability to belch (RR 2·04, 95 per cent

Reference	Recurrent acid exposure		Weight (%)	Risk ratio
	Nissen	Toupet		
Booth *et al.*[28]	3 of 39	5 of 37	18·7	0·57 (0·15, 2·22)
Shaw *et al.*[54]	3 of 41	5 of 43	17·7	0·63 (0·16, 2·47)
Strate *et al.*[55]	28 of 70	18 of 74	63·6	1·64 (1·00, 2·69)
Total	34 of 150	28 of 154	100·0	1·26 (0·82, 1·95)

Heterogeneity: $\chi^2 = 3{\cdot}42$, 2 d.f., $P = 0{\cdot}18$, $I^2 = 41\%$
Test for overall effect: $Z = 1{\cdot}06$, $P = 0{\cdot}29$

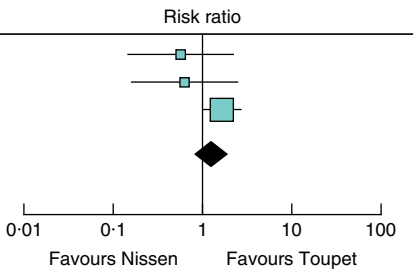

Fig. 2 Meta-analysis of recurrent pathological acid exposure following laparoscopic Nissen and Toupet fundoplication for gastro-oesophageal reflux disease. Risk ratios are shown with 95 per cent confidence intervals (Mantel–Haenszel fixed-effects model)

Reference	Oesophagitis		Weight (%)	Risk ratio
	Nissen	Toupet		
Chrysos *et al.*[29]	5 of 14	8 of 19	22·5	0·85 (0·35, 2·04)
Laws *et al.*[52]	1 of 23	0 of 16	1·9	2·13 (0·09, 49·08)
Mickevicius *et al.*[53]	9 of 76	8 of 77	26·4	1·14 (0·46, 2·80)
Strate *et al.*[55]	20 of 88	15 of 90	49·2	1·36 (0·75, 2·49)
Total	35 of 201	31 of 202	100·0	1·20 (0·78, 1·85)

Heterogeneity: $\chi^2 = 0{\cdot}91$, 3 d.f., $P = 0{\cdot}82$, $I^2 = 0\%$
Test for overall effect: $Z = 0{\cdot}84$, $P = 0{\cdot}40$

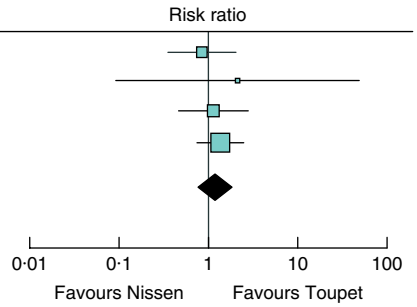

Fig. 3 Meta-analysis of oesophagitis following laparoscopic Nissen and Toupet fundoplication for gastro-oesophageal reflux disease. Risk ratios are shown with 95 per cent confidence intervals (Mantel–Haenszel fixed-effects model)

Reference	Dysphagia		Weight (%)	Risk ratio
	Nissen	Toupet		
Booth *et al.*[28]	14 of 59	9 of 58	29·0	1·53 (0·72, 3·25)
Chrysos *et al.*[29]	2 of 14	3 of 19	8·1	0·90 (0·17, 4·71)
Guérin *et al.*[51]	2 of 64	3 of 57	10·1	0·59 (0·10, 3·43)
Laws *et al.*[52]	0 of 23	0 of 16		Not estimable
Mickevicius *et al.*[53]	11 of 64	8 of 63	25·7	1·35 (0·58, 3·14)
Shaw *et al.*[54]	2 of 47	0 of 48	1·6	5·10 (0·25, 103·57)
Strate *et al.*[55]	19 of 100	8 of 100	25·5	2·38 (1·09, 5·17)
Total	50 of 371	31 of 361	100·0	1·61 (1·06, 2·44)

Heterogeneity: $\chi^2 = 3{\cdot}42$, 5 d.f., $P = 0{\cdot}64$, $I^2 = 0\%$
Test for overall effect: $Z = 2{\cdot}26$, $P = 0{\cdot}02$

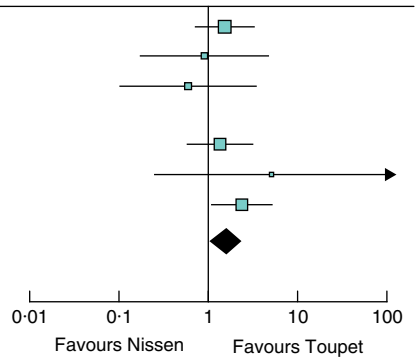

Fig. 4 Meta-analysis of dysphagia following laparoscopic Nissen and Toupet fundoplication for gastro-oesophageal reflux disease. Risk ratios are shown with 95 per cent confidence intervals (Mantel–Haenszel fixed-effects model)

c.i. 1·19 to 3·49; $P = 0{\cdot}009$) (*Fig. 7*) and gas bloating (RR 1·58, 95 per cent c.i. 1·21 to 2·05; $P < 0{\cdot}001$) (*Fig. 8*) was found after LNF. Subjective reflux recurrence (RR 1·11, 95 per cent c.i. 0·75 to 1·63; $P = 0{\cdot}61$) (*Fig. 9*) and satisfaction with the intervention (RR 1·01, 95 per cent c.i. 0·95 to 1·06; $P = 0{\cdot}77$) (*Fig. 10*) were similar for both groups.

Meta-analysis of LOS pressure and operating time showed excessive heterogeneity. Therefore, the random-effects model was used for pooling data. This showed a

Reference	Postop. dilatation for dysphagia: Nissen	Postop. dilatation for dysphagia: Toupet	Weight (%)	Risk ratio
Booth *et al.*[28]	2 of 59	1 of 58	14·0	1·97 (0·18, 21·09)
Chrysos *et al.*[29]	0 of 14	0 of 19		Not estimable
Laws *et al.*[52]	2 of 23	1 of 16	16·4	1·39 (0.14, 14·07)
Mickevicius *et al.*[53]	0 of 64	0 of 63		Not estimable
Strate *et al.*[55]	14 of 100	5 of 100	69·6	2·80 (1·05, 7·48)
Total	18 of 260	7 of 256	100·0	2·45 (1·06, 5·68)

Heterogeneity: $\chi^2 = 0{\cdot}33$, 2 d.f., $P = 0{\cdot}85$, $I^2 = 0\%$
Test for overall effect: $Z = 2{\cdot}09$, $P = 0{\cdot}04$

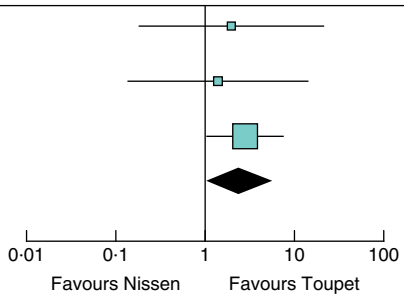

Fig. 5 Meta-analysis of postoperative dilatation for dysphagia following laparoscopic Nissen and Toupet fundoplication for gastro-oesophageal reflux disease. Risk ratios are shown with 95 per cent confidence intervals (Mantel–Haenszel fixed-effects model)

Reference	Reoperation rate: Nissen	Reoperation rate: Toupet	Weight (%)	Risk ratio
Booth *et al.*[28]	1 of 64	1 of 63	9·4	0·98 (0·06, 15·40)
Chrysos *et al.*[29]	0 of 19	0 of 14		Not estimable
Laws *et al.*[52]	0 of 23	1 of 16	16·4	0·24 (0·01, 5·45)
Mickevicius *et al.*[53]	3 of 76	1 of 77	9·3	3·04 (0·32, 28·58)
Shaw *et al.*[54]	4 of 47	3 of 48	27·7	1·36 (0·32, 5·76)
Strate *et al.*[55]	15 of 100	4 of 100	37·3	3·75 (1·29, 10·91)
Total	23 of 329	10 of 318	100·0	2·19 (1·09, 4·40)

Heterogeneity: $\chi^2 = 3{\cdot}73$, 4 d.f., $P = 0{\cdot}44$, $I^2 = 0\%$
Test for overall effect: $Z = 2.19$, $P = 0{\cdot}03$

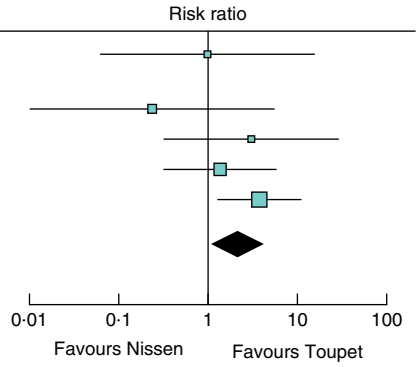

Fig. 6 Meta-analysis of reoperation rate following laparoscopic Nissen and Toupet fundoplication for gastro-oesophageal reflux disease. Risk ratios are shown with 95 per cent confidence intervals (Mantel–Haenszel fixed-effects model)

Reference	Inability to belch: Nissen	Inability to belch: Toupet	Weight (%)	Risk ratio
Booth *et al.*[28]	8 of 59	3 of 58	17·7	2·62 (0·73, 9·40)
Guérin *et al.*[51]	2 of 64	1 of 59	6·1	1·84 (0·17, 19·81)
Strate *et al.*[55]	25 of 100	13 of 100	76·2	1·92 (1·04, 3·54)
Total	35 of 223	17 of 217	100·0	2·04 (1·19, 3·49)

Heterogeneity: $\chi^2 = 0{\cdot}19$, 2 d.f., $P = 0{\cdot}91$, $I^2 = 0\%$
Test for overall effect: $Z = 2{\cdot}61$, $P = 0{\cdot}009$

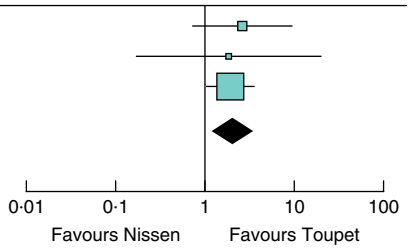

Fig. 7 Meta-analysis of inability to belch following laparoscopic Nissen and Toupet fundoplication for gastro-oesophageal reflux disease. Risk ratios are shown with 95 per cent confidence intervals (Mantel–Haenszel fixed-effects model)

slightly higher mean LOS pressure after LNF (WMD 1·98 (95 per cent c.i. 0·58 to 3·37) mmHg; $P = 0{\cdot}005$, χ^2 $P = 0{\cdot}03$, $I^2 = 62$ per cent) (*Fig. 11*) and no significant difference in operating time between the two techniques (WMD −7·31 (95 per cent c.i. −15·28 to 0·66) min; $P = 0{\cdot}07$, χ^2 $P < 0{\cdot}001$, $I^2 = 80$ per cent) (*Fig. 12*). Exploring possible causes of heterogeneity, taking into account variations in technique concerning division of

Reference	Gas bloating		Weight (%)	Risk ratio
	Nissen	Toupet		
Booth *et al.*[28]	11 of 59	6 of 58	11·2	1·80 (0·71, 4·55)
Chrysos *et al.*[52]	1 of 14	1 of 19	1·6	1·36 (0·09, 19·88)
Mickevicius *et al.*[53]	10 of 64	4 of 63	7·5	2·46 (0.81, 7·44)
Strate *et al.*[55]	63 of 100	43 of 100	79·7	1·47 (1·12, 1.92)
Total	85 of 237	54 of 240	100·0	1·58 (1·21, 2·05)

Heterogeneity: $\chi^2 = 0{\cdot}99$, 3 d.f., $P = 0{\cdot}80$, $I^2 = 0\%$
Test for overall effect: $Z = 3{\cdot}42$, $P < 0{\cdot}001$

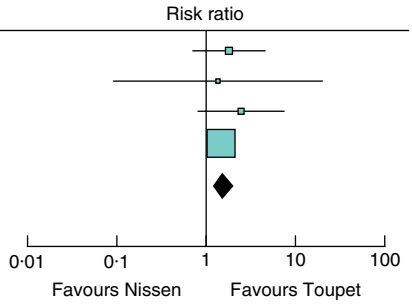

Fig. 8 Meta-analysis of gas bloating following laparoscopic Nissen and Toupet fundoplication for gastro-oesophageal reflux disease. Risk ratios are shown with 95 per cent confidence intervals (Mantel–Haenszel fixed-effects model)

Reference	Subjective reflux recurrence		Weight (%)	Risk ratio
	Nissen	Toupet		
Booth *et al.*[28]	5 of 59	5 of 58	12·2	0·98 (0·30, 3·22)
Guérin *et al.*[51]	0 of 64	3 of 57	9·0	0·13 (0·01, 2·42)
Laws *et al.*[52]	2 of 23	0 of 16	1·4	3·54 (0·18, 69·18)
Mickevicius *et al.*[53]	5 of 76	7 of 77	16·9	0·72 (0·24, 2·18)
Shaw *et al.*[54]	8 of 47	8 of 48	19·2	1·02 (0·42, 2·50)
Strate *et al.*[55]	25 of 100	17 of 100	41·3	1·47 (0·85, 2·55)
Total	45 of 369	40 of 356	100·0	1·11 (0·75, 1·63)

Heterogeneity: $\chi^2 = 4{\cdot}32$, 5 d.f., $P = 0{\cdot}50$, $I^2 = 0\%$
Test for overall effect: $Z = 0{\cdot}51$, $P = 0{\cdot}61$

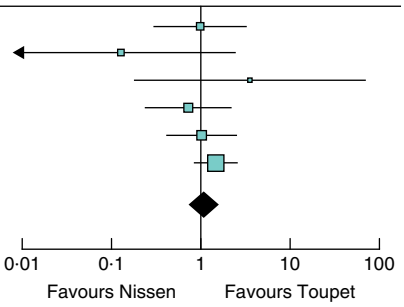

Fig. 9 Meta-analysis of subjective reflux recurrence following laparoscopic Nissen and Toupet fundoplication for gastro-oesophageal reflux disease. Risk ratios are shown with 95 per cent confidence intervals (Mantel–Haenszel fixed-effects model)

Reference	Satisfaction with intervention		Weight (%)	Risk ratio
	Nissen	Toupet		
Chrysos *et al.*[29]	13 of 14	18 of 19	6·1	0·98 (0·82, 1·17)
Guérin *et al.*[51]	63 of 64	56 of 57	23·8	1·00 (0·96, 1·05)
Mickevicius *et al.*[53]	58 of 64	55 of 63	22·3	1·04 (0·92, 1·17)
Shaw *et al.*[54]	34 of 37	33 of 36	13·5	1·00 (0·87, 1·15)
Strate *et al.*[55]	85 of 100	85 of 100	34·2	1·00 (0·89, 1·12)
Total	253 of 279	247 of 275	100·0	1·01 (0·95, 1·06)

Heterogeneity: $\chi^2 = 0{\cdot}40$, 4 d.f., $P = 0{\cdot}98$, $I^2 = 0\%$
Test for overall effect: $Z = 0{\cdot}29$, $P = 0{\cdot}77$

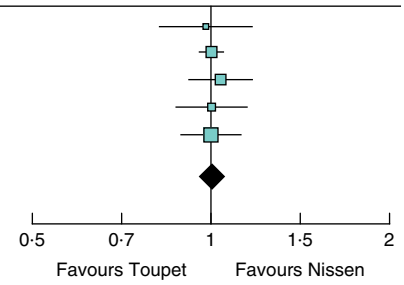

Fig. 10 Meta-analysis of satisfaction with laparoscopic Nissen and Toupet fundoplication for gastro-oesophageal reflux disease. Risk ratios are shown with 95 per cent confidence intervals (Mantel–Haenszel fixed-effects model)

Reference	LOS pressure (mmHg) Nissen	Toupet	Weight (%)	WMD (mmHg)
Booth *et al.*[28]	12·3(4·3) 39	10·5(3·8) 37	21·6	1·80 (–0·02, 3·62)
Chrysos *et al.*[29]	23(6) 14	18(3) 19	11·2	5·00 (1·58, 8·42)
Mickevicius *et al.*[53]	11·4(2·1) 76	11·2(5) 77	27·2	0·20 (–1·01, 1·41)
Shaw *et al.*[54]	15·3(5·3) 41	12·1(6·3) 43	16·4	3·20 (0·71, 5·69)
Strate *et al.*[55]	14·4(4·9) 81	12·5(5·5) 80	23·5	1·90 (0·29, 3·51)
Total	251	256	100·0	1·98 (0·58, 3·37)

Heterogeneity: $\tau^2 = 1{\cdot}48$, $\chi^2 = 10{\cdot}57$, 4 d.f., $P = 0{\cdot}03$, $I^2 = 62\%$
Test for overall effect: $Z = 2{\cdot}78$, $P = 0{\cdot}005$

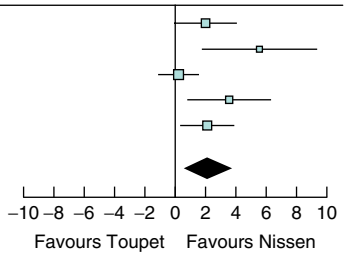

Fig. 11 Meta-analysis of mean(s.d.) lower oesophageal sphincter (LOS) pressure following laparoscopic Nissen and Toupet fundoplication for gastro-oesophageal reflux disease. Weighted mean differences (WMD) are shown with 95 per cent confidence intervals (inverse variance random-effects model). Numbers of patients are also shown

Reference	Operating time (min) Nissen	Toupet	Weight (%)	WMD (min)
DSGV				
Booth *et al.*[28]	81(23) 64	89(20) 63	22·0	–8·00 (–15·47, –0·53)
Mickevicius *et al.*[53]	114(36) 76	116(30) 77	18·5	–2·00 (–12·51, 8·51)
Shaw *et al.*[54]	142(38) 50	145(38) 50	13·8	–3·00 (–18·05, 12·05)
Strate *et al.*[55]	51(12) 100	52(10) 100	26·1	–1·00 (–4·13, 2·13)
Subtotal	290	290	80·4	–2·07 (–4·81, 0·66)
Heterogeneity: $\tau^2 = 0{\cdot}00$, $\chi^2 = 2{\cdot}88$, 3 d.f., $P = 0.41$, $I^2 = 0\%$				
Test for overall effect: $Z = 1{\cdot}48$, $P = 0{\cdot}14$				
No DSGV				
Chrysos *et al.*[29]	67(15) 14	90(12) 19	19·6	–23·00 (–32·53, –13·47)
Subtotal	14	19	19·6	–23·00 (–32·53, –13·47)
Heterogeneity: not applicable				
Test for overall effect: $Z = 4{\cdot}73$, $P < 0{\cdot}001$				
Total	304	309	100.0	–7·31 (–15·28, 0·66)

Heterogeneity: $\tau^2 = 60{\cdot}70$, $\chi^2 = 20{\cdot}00$, 4 d.f., $P < 0{\cdot}001$, $I^2 = 80\%$
Test for overall effect: $Z = 1{\cdot}80$, $P = 0{\cdot}07$
Test for subgroup differences: $\chi^2 = 17{\cdot}11$, 1 d.f., $P < 0{\cdot}001$, $I^2 = 94{\cdot}2\%$

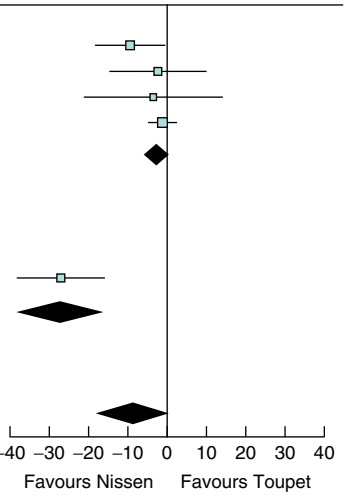

Fig. 12 Meta-analysis of mean(s.d.) operating time for laparoscopic Nissen and Toupet fundoplication for gastro-oesophageal reflux disease. Weighted mean differences (WMD) are shown with 95 per cent confidence intervals (inverse variance random-effects model). Numbers of patients are also shown. DSGV, division of short gastric vessels

Reference	In-hospital complications Nissen	Toupet	Weight (%)	Risk ratio
Booth *et al.*[28]	0 of 64	1 of 63	9·3	0·33 (0·01, 7·91)
Chrysos *et al.*[29]	2 of 14	3 of 19	15·7	0·90 (0·17, 4·71)
Guérin *et al.*[51]	0 of 77	3 of 63	23·7	0·12 (0·01, 2·23)
Laws *et al.*[52]	1 of 23	2 of 16	14·5	0·35 (0·03, 3·52)
Mickevicius *et al.*[53]	2 of 76	5 of 77	30·6	0·41 (0·08, 2·03)
Strate *et al.*[55]	4 of 100	1 of 100	6·2	4·00 (0·46, 35·16)
Total	9 of 354	15 of 338	100·0	0·62 (0·29, 1·32)

Heterogeneity: $\chi^2 = 4{\cdot}92$, 5 d.f., $P = 0{\cdot}43$, $I^2 = 0\%$
Test for overall effect: $Z = 1{\cdot}23$, $P = 0{\cdot}22$

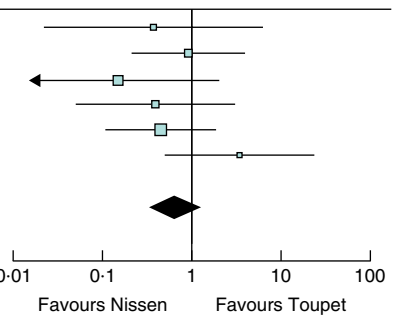

Fig. 13 Meta-analysis of in-hospital complications following laparoscopic Nissen and Toupet fundoplication for gastro-oesophageal reflux disease. Risk ratios are shown with 95 per cent confidence intervals (Mantel–Haenszel fixed-effects model)

the short gastric vessels, reduced the heterogeneity of operating time significantly (4 trials with short gastric vessel division: WMD −2·07 (95 per cent c.i. −4·81 to 0·66) min; $P = 0·14$, χ^2 $P = 0·41$, $I^2 = 0$ per cent) (*Fig. 12*).

One postoperative death occurred after oesophageal perforation during LTF[53]. In-hospital complications (postoperative bleeding, oesophageal and gastric perforation, gastric dilatation, subphrenic abscess, pneumothorax, pneumonia, atelectasis, minor pleural effusion, wound infection, cardiac arrhythmia and thrombophlebitis) were similar for both operations (RR 0·62, 95 per cent c.i. 0·29 to 1·32; $P = 0·22$) (*Fig. 13*). Funnel plots did not demonstrate clear evidence of publication bias.

Discussion

Between 2007 and 2010, five large RCTs were published comparing LTF and LNF[28,51,53–55]. These individual trials were inconclusive in establishing clear differences in outcomes between the two procedures and have not been subjected to meta-analysis.

The methodological quality of the seven RCTs included in the present meta-analysis ranged from poor to excellent. Surgical techniques of the included trials were standardized and generally similar. All patients underwent laparoscopic 360° total or 200–270° partial fundoplication, with all but one trial involving routine use of a bougie, crural repair or fixation of the wrap to the oesophagus. One trial did not routinely divide short gastric vessels, but was included in this review because it has already been shown that there is no difference in outcome after fundoplication with routine *versus* no division of short gastric vessels[16]. The fundoplication length was similar in both arms of all except one trial[54], although the length of fundoplication varied from 1 to 4 cm in the included RCTs. The present meta-analysis included RCTs that enrolled patients with normal and abnormal oesophageal motility as all four RCTs addressing this issue showed that the outcome of Nissen and Toupet fundoplication was similar in patients with normal and abnormal motility[28–31].

The absence of standard crural repair in the LTF group in one study represented a clear difference between the surgical techniques in the two arms and a potential threat to the validity of this RCT[52]. This difference between the arms probably did not cause bias as postoperative subjective and objective reflux recurrence and reoperation rates were not higher in the LTF group. Another potential threat to validity was a significantly higher prevalence of moderate dysphagia in the LNF group at baseline in one study[28]. To exclude this potential source of bias from the meta-analysis, new-onset or worsening dysphagia was analysed for this RCT.

LTF was associated with a significant and clinically relevant reduction in postoperative dysphagia, dilatations for dysphagia, and surgical reinterventions compared with LNF. The lower reoperation rate after LTF was caused partially by the lower prevalence of dysphagia after this procedure, resulting in a lower number of surgical reinterventions to relieve this symptom. LTF significantly reduced inability to belch and gas bloating compared with LNF. In contrast to previous uncontrolled studies[22–27], the present analysis showed that rates of recurrent pathological acid exposure, oesophagitis and reflux symptoms after LTF and LNF were similar. In-hospital complication rates were similar for the two operations. The techniques of LNF and LTF are identical, except for construction of the wrap. In-hospital complications of both techniques might therefore be expected to be similar, except for an increased theoretical risk of perforation due to the greater number of oesophageal and wrap sutures during LTF. The three studies[28,52,53] that specified complications reported one wrap and two oesophageal perforations after LTF, and none after LNF.

Two related meta-analyses have been published previously[16,50]. These reports pooled various types of partial fundoplication, both anterior and posterior with various circumferences, and compared these techniques with total fundoplication. They also included both open and laparoscopic fundoplication techniques. Pooling of these data is questionable, as RCTs have demonstrated important differences in reflux control and reoperation rates between anterior and posterior partial fundoplication techniques[57,58]. Inclusion of open techniques also undermines the generalizability, because laparoscopic fundoplication has become the surgical approach of choice for primary antireflux surgery[5]. In contrast to previous reviews that combined short- and long-term outcomes (range 4–138 months), short-term clinical outcomes were excluded in the present analysis. Outcome was evaluated after at least 12 (range 12–60) months' follow-up, and additional missing data were obtained. Only nine of 59 outcome measures were missing and completed by the authors, and seven outcome measures could not be completed by the authors. Therefore, it is unlikely that addition of the unpublished results would affect the results.

The present study is limited by the methodological quality of the included studies and by the fact that follow-up

was restricted to 1, 2 or 5 years. Long-term results of RCTs comparing open Nissen and Toupet fundoplication have, however, demonstrated that short-term reflux control is durable throughout 5-year[19] and 10-year[45] follow-up. As there were no differences in short-term[15] and long-term[5] reflux control between open and laparoscopic fundoplication, it seems unlikely that differences in reflux control after LNF and LTF will develop with longer follow-up.

LTF is associated with less postoperative dysphagia and need for dilatation for dysphagia compared with LNF, with similar reflux control. The reoperation rate and the prevalence of inability to belch and gas bloating are lower after LTF. There is now level 1a support for the use of LTF as the posterior fundoplication of choice for patients with GORD.

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