

Online Submissions: http://www.wjgnet.com/1007-9327office wjg@wjgnet.com doi:10.3748/wjg.v16.i24.3063 World J Gastroenterol 2010 June 28; 16(24): 3063-3071 ISSN 1007-9327 (print) © 2010 Baishideng. All rights reserved.

BRIEF ARTICLE

# Evidence-based appraisal in laparoscopic Nissen and Toupet fundoplications for gastroesophageal reflux disease

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Telephone: +86-21-81885801 Fax: +86-21-63729800 Received: January 20, 2010 Revised: February 20, 2010 Accepted: February 27, 2010 Published online: June 28, 2010

# Abstract

**AIM:** To demonstrate the optimal surgical procedure for gastroesophageal reflux disease.

**METHODS:** The electronic databases of Medline, Elsevier, Springerlink and Embase over the last 16 years were searched. All clinical trials involved in the outcomes of laparoscopic Nissen fundoplication (LNF) and laparoscopic Toupet fundoplication (LTF) were identified. The data of assessment in benefits and adverse results of LNF and LTF were extracted and compared using meta-analysis.

**RESULTS:** We ultimately identified a total of 32 references reporting nine randomized controlled trials, eight prospective cohort trials and 15 retrospective trials. These studies reported a total of 6236 patients, of whom 4252 (68.18%) underwent LNF and 1984 (31.82%) underwent LTF. There were no differences between LNF and LTF in patients' satisfaction, perioperative complications, postoperative heartburn, reflux

recurrence and re-operation. Both LNF and LTF enhanced the function of lower esophageal sphincter and improved esophagitis. The postoperative dysphagia, gas-bloating syndrome, inability to belch and the need for dilatation after LNF were more common than after LTF. Subgroup analyses showed that dysphagia after LNF and LTF was similar in patients with normal esophageal peristalsis (EP), but occurred more frequently in patients with weak EP after LNF than after LTF. Furthermore, patients with normal EP after LNF still had a higher risk of developing dysphagia than did patients with abnormal EP after LTF.

CONCLUSION: Compared with LNF, LTF offers equivalent symptom relief and reduces adverse results.

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Key words: Laparoscopic fundoplication; Nissen, Toupet; Gastroesophageal reflux disease; Anti-reflux surgery; Esophageal peristalsis; Meta-analysis

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Shan CX, Zhang W, Zheng XM, Jiang DZ, Liu S, Qiu M. Evidence-based appraisal in laparoscopic Nissen and Toupet fundoplications for gastroesophageal reflux disease. *World J Gastroenterol* 2010; 16(24): 3063-3071 Available from: URL: http://www.wjgnet.com/1007-9327/full/v16/i24/3063.htm DOI: http://dx.doi.org/10.3748/wjg.v16.i24.3063

# INTRODUCTION

Gastroesophageal reflux disease (GERD) is a chronic acid-peptic disorder characterized by the spontaneous and involuntary retrograde flow of stomach contents into esophagus mainly due to functional defect of the lower esophageal sphincter (LES)<sup>[1]</sup>. Acid reflux into the esophagus may cause esophagitis, tracheobronchitis,



stricture, Barrett's esophagus and even esophageal cancer, all of which affect a sizeable portion of patients, particularly in the USA and Europe<sup>[2-5]</sup>. Symptomatic GERD has fundamental effects on the quality-of-life (QOL) of patients. However, the complex pathophysiology of GERD<sup>[4]</sup> and limitation of the medicine<sup>[6]</sup> always make it extremely difficult to get a satisfactory efficacy under individual anti-acid medication in the long term.

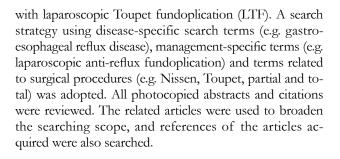
Surgery is discussed as a very effective treatment for GERD which imparts a mechanical solution<sup>[6]</sup>. Surgical treatment was initially introduced by Rudolph Nissen<sup>[7]</sup> in 1956 and subsequently was developed as a safe and effective procedure by Dallemagne in 1991 through a minimal invasive approach<sup>[8]</sup>. Laparoscopic fundoplication has been established as the "gold standard" in the surgical treatment for GERD because of its immense success. There are two major anti-reflux procedures: 360° total (Nissen) fundoplication and 270° partial (Toupet) fundoplication. The superiority of one over the other is a matter of debate. The supporters of partial fundoplication argue that partial and total wrap construction offer equally effective forms of therapy for GERD<sup>[9-11]</sup>. To avoid the major postoperative complication, dysphagia, preoperative esophageal motility should be considered, and partial funduplication has the advantage of reducing this complication<sup>[12,13]</sup>. The proponents of total fundoplication propose that: (1) the 270° wrap provides a weaker anti-reflux barrier, and is therefore insufficient for reflux control<sup>[14,15]</sup>; (2) the prevalence of postoperative dysphagia after Nissen fundoplication is overestimated; and (3) motility disorders are not correlated with postoperative dysphagia<sup>[16]</sup>, suggesting that the so-called "tailored procedure" should be abandoned<sup>[17,18]</sup>. Many crucial issues related to the mechanism of GERD, such as whether esophageal dysmotility is a consequence of GERD or just another component (along with LES dysfunction) of a complex foregut motor disease, have not been elucidated<sup>[19,20]</sup>, so the controversy regarding the optimal surgical technique continues<sup>[21,22]</sup>.

Meta-analysis is a powerful tool with an attempt to overcome the problem of reduced statistical power in studies with small sample sizes and to control variations between studies. The goal of surgical treatment for GERD is to provide optimal reflux control while minimizing adverse results. We focused this current systemic review on comparing which procedure was more effective in improving the QOL of patients while producing less adverse results. We attempted to depict a more comprehensive picture of the feature of laparoscopic anti-reflux operation, thus offering guidance for clinical practice.

# MATERIALS AND METHODS

## Search strategy

The electronic databases of Medline, ScienceDirect (Elsevier), Springerlink and Embase over the last 16 years from January 1994 to November 2009 were searched by two authors (Shan CX and Zhang W) to identify all clinical trials comparing laparoscopic Nissen fundoplication (LNF)



## Selection criteria

Abstracts or full-text articles were initially screened, and then selected or rejected by the two reviewers (Shan CX and Zhang W) on the basis of the inclusion and exclusion criteria described below. A flow chart representing selection of clinical trials is shown in Figure 1.

Inclusion criteria: (1) Comparative clinical trials, including randomized and non-randomized controlled trials, involved in the efficacy and adverse results of different types of laparoscopic anti-reflux surgery (LARS); and (2) The exact data of dichotomous-type information and continuous-type information as well as standard deviation should be provided so as to integrate each single weight in each study.

**Exclusion criteria:** (1) Comparative trials between total and non-posterior partial fundoplication (e.g. total *vs* anterior partial fundoplication); (2) Fundoplications were carried out with laparotomy; (3) Trials involving children or patients younger than 16 years; and (4) Studies published repeatedly by different journals.

## Data extraction

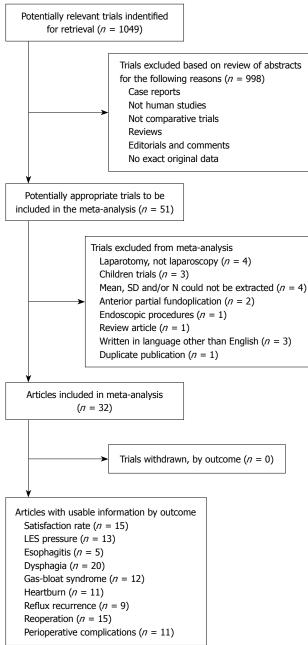
The two reviewers independently extracted details from selected studies which comprised (1) information and quality of the research: first author, year of publication, comparative design, sample capacity, follow-up duration; and (2) outcome analysis, including beneficial and adverse results. The specific rules of data extraction were listed below.

First, the assessment data of repeated trials published in different journals at different phases was extracted based on the latest article. For example, the results in the studies of Strate *et al*<sup>16</sup>, Fibbe *et al*<sup>23</sup> and Zornig *et al*<sup>24</sup> were highly homologous, containing identical study objects and design protocol. Thus, the source of data extraction was focused on the latest citation of Zornig *et al*<sup>24</sup>.

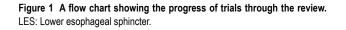
Second, the assessment data of trials containing multiple groups were initially divided into single groups, and then extracted individually. For example, the research of Mickevicius *et al*<sup>22]</sup> included two subgroups of LARS with a 1.5-cm wrap fundoplication and 3.0-cm wrap. We split it into two independent trials according to the wrap length.

And third, the evaluation indices of surgical efficacy and incidence of postoperative morbidities were subject to the final updates based on long-term follow-up results. For example, Chrysos *et al*<sup>25]</sup> reported the 3- and 12-mo incidences of postoperative dysphagia in their









article. We ultimately extracted the information on the 12-mo incidence of dysphagia after LARS and integrated it into the total meta-analysis.

## Statistical analysis

All individual outcomes were integrated with the metaanalysis software: Review Manager Software 5.0 (Cochrane Collaborative, Oxford, England). Results were analyzed with the random-effect method if significant heterogeneity (P < 0.05 was used to define statistically significant heterogeneity) was detected among studies. Otherwise, a fixed-effect model was adopted. The odds ratio (OR) and the weighted mean difference were calculated for dichotomous data and continuous data, respectively. In addition, subgroup analyses were done to estimate if the results of postoperative dysphagia would change after LARS with respect to preoperative esophageal motility (EM). Thus, three subgroups were established. Subgroup 1: all patients underwent LNF or LTF and had normal esophageal peristalsis (EP); subgroup 2: all patients underwent LNF or LTF and had abnormal EP; and subgroup 3: LNF for patients with normal EP vs LTF for patients with abnormal EP.

# RESULTS

Identification and characteristics of studies and patients We ultimately identified 32 references reporting 29 independent controlled studies published between January 1994 and November 2009. Nine randomized controlled trials<sup>[10,16,21-27]</sup>, eight prospective cohort trials<sup>[11,17,28-33]</sup> and 15 retrospective trials<sup>[9,12,20,33-45]</sup> met the selection criteria reporting 6236 patients, of whom 4252 (68.18%) underwent LNF and 1984 (31.82%) underwent LTF. Twenty studies provided the sex and 11 trials provided the age of included patients. The percentage of males varied from 39.39% to 70.13% in the LNF group, and from 39.53% to 66.67% in the LTF group. The mean age ranged from 45.2 to 59.2 years in the LNF group and from 44.2 to 61.7 years in the LTF group. The details of these studies are shown in Table 1.

# Subjective assessment: Satisfaction rate

Fifteen studies assessed patient satisfaction as the major efficacy of LARS. In addition, patient satisfaction with the outcome of surgery was always expressed by Visick scores evaluating QOL. After follow-up, each single research suggested that > 90% patients were satisfied with postoperative outcomes after LNF or LTF, and 91.78% (1674/1824) of patients in the LNF group and 91.33% (938/1027) in the LTF group reported excellent or good results after LARS. There was no statistically significant difference between the two groups (OR 0.96, 95% CI: 0.72 - 1.28, P = 0.77).

## **Objective evaluation**

LES pressure: The change in LES pressure after LARS was investigated in 13 trials. The mean preoperative LES pressure was 3.1-12.8 mmHg in the LNF group, and about 2.3-13.6 mmHg in the LTF group, and increased significantly to 10.3-26 mmHg after LNF and 11-18 mmHg after LTF, respectively. Moreover, 360° total fundoplication could form a relatively stronger anti-reflux barrier than 270° partial funduplication because the amplitude of LES pressure increase was significantly higher after LNF than after LTF (OR 2.76, 95% CI: 1.57-3.95, *P* < 0.05).

Esophagitis: Five authors outlined the improvement of preoperative esophagitis after LARS by endoscopy. Esophagitis severity was graded according to the Savary-Miller classification in most studies. Remission of moderate-to-severe esophagitis was observed by endoscopic re-examination after anti-reflux procedures; there was a reduction in case number from 87/210 to 12/191 in the



## Shan CX et al. Laparoscopic Nissen and Toupet fundoplication

Data source	source Design PF (°) Sample capacity (LNF/LTF)		Group or subg. depend on EM	Follow-up (mo)	Level of evidence	
Mickevicius <i>et al</i> <sup>[22]</sup> , 2008 Fibbe <i>et al</i> <sup>[23]</sup> , 2001	RCT	200-270	76/77	No detail	12	1b Level A
Zornig <i>et al</i> <sup>[24]</sup> , 2002 Strate <i>et al</i> <sup>[16]</sup> , 2008	RCT	270	100/100	More subgroups	24	1b Level A
Chrysos <i>et al</i> <sup>[25]</sup> , 2003	RCT	270	14/19	Both abnormal	12	2b Level B
Guérin <i>et al</i> <sup>[26]</sup> , 2007	RCT	270	77/63	77/63 Normal-Nissen/Abnormal-Toupet		1b Level A
Laws <i>et al</i> <sup>[10]</sup> , 1997	RCT	200	23/16	Both normal	27.2	2b Level B
Shaw <i>et al</i> <sup>[27]</sup> , 2010	RCT	270	50/50	No detail	> 55	1b Level A
Booth <i>et al</i> <sup>[21]</sup> , 2008	RCT	270	64/63	No detail	12	1b Level A
Coster <i>et al</i> <sup>[28]</sup> , 1997	PCT	No detail	125/101	No detail	12	2b Level B
Granderath et al <sup>[29]</sup> , 2007	PCT	270	28/28	Both normal	3	3b Level B
Wykypiel <i>et al</i> <sup>[30]</sup> , 2008	PCT	300	20/20	Normal-Nissen/Abnormal-Toupet	6	3b Level B
Hunter <i>et al</i> <sup>[31]</sup> , 1996	PCT	180-300	101/83	Both normal	3	3b Level B
Bessell <i>et al</i> <sup>[17]</sup> , 2000	PCT	200-270	761/85	More subgroups	12	2b Level B
Radajewski <i>et al</i> <sup>[32]</sup> , 2009	PCT	No detail	51/43	No detail	12	2b Level B
Kamolz <i>et al</i> <sup>[33]</sup> , 2000 Kamolz <i>et al</i> <sup>[11]</sup> , 2002	PCT	No detail	107/68	No detail	60	2b Level B
Sgromo <i>et al</i> <sup>[34]</sup> , 2008	RT	No detail	150/116	No detail	72	2b Level B
Erenoğlu <i>et al</i> <sup>[35]</sup> , 2003	RT	270	118/26	Normal-Nissen/Abnormal-Toupet	27.5	2b Level B
Herbella <i>et al</i> <sup>[20]</sup> , 2007	RT	240	55/16	More subgroups	16	3b Level B
Wetscher et al <sup>[12]</sup> , 1997	RT	No detail	17/32	Normal-Nissen/Abnormal-Toupet	15	3b Level B
Fernando <i>et al</i> <sup>[36]</sup> , 2002	RT	270	163/43	No detail	19.7	2b Level B
Wykypiel <i>et al</i> <sup>[37]</sup> , 2005	RT	300	77/132	Normal-Nissen/Abnormal-Toupet	52	2b Level B
McKernan et al <sup>[38]</sup> , 1994	RT	180-200	14/14	No detail	> 3.4	3b Level B
Fein <i>et al</i> <sup>[45]</sup> , 2008	RT	No detail	88/10	Normal-Nissen/Abnormal-Toupet	120	2b Level B
Patti et al <sup>[39]</sup> , 2004	RT	240	216/141	More subgroups	> 23	2b Level B
Zügel <i>et al</i> <sup>[9]</sup> , 2002	RT	270	40/122	No detail	19	2b Level B
Pessaux et al <sup>[40]</sup> , 2000	RT	180	1078/392	No detail	24	2b Level B
Bell et al <sup>[41]</sup> , 1996	RT	180	11/11	No detail	13	4 Level C
Lund <i>et al</i> <sup>[42]</sup> , 1997	RT	270	16/46	Both abnormal	6	3b Level B
Farrell <i>et al</i> <sup>[43]</sup> , 2000	RT	270	293/52	More subgroups	12	3b Level B
Heider <i>et al</i> <sup>[44]</sup> , 2003	RT	270	15/4	Both abnormal	29.5	4 Level C

# Table 1 LNF and LTF in treatment of patients with gastroesophageal reflux diseas

LNF: Laparoscopic Nissen fundoplication; LTF: Laparoscopic Toupet fundoplication; PF: Circumferential degrees of the partial wrap; Subg.: Subgroup; EM: Esophageal motility; RCT: Randomized controlled trial; PCT: Prospective controlled trial; RT: Retrospective trial.

Nissen group, and from 99/218 to 17/197 in the LTF group. There was no significant difference in remission rate between the two groups (6.28% *vs* 8.63%, OR 0.72, 95% CI: 0.59-1.33, P = 0.42).

## Adverse results: Perioperative complications

Eleven studies reported the surgical complications in 1622 patients with LNF and 836 patients with LTF. Both techniques entailed a low (but definite) risk of surgical morbidity which occurred in 1.30%<sup>[26]</sup>-14.28%<sup>[25]</sup> of the population after Nissen fundoplication and in  $2.46^{\circ}$ <sup>[9]</sup>-15.63<sup>\%</sup><sup>[12]</sup> of the population after Toupet fundoplication. Lacerations of the gastric fundus and spleen, bleeding from the spleen or short gastric blood vessels and pneumothorax were the main disease categories. However, surgical mortality was also a natural sporadic event. Only two patients died: one on the 15th day after LNF due to secondary peritonitis from necrosis of the wrap<sup>[40]</sup>, and the other died of esophageal perforation and mediastinitis<sup>[22]</sup>. The cumulative prevalence of perioperative complications after LNF and LTF was 4.01% and 5.14%, respectively, with no significant difference between the groups (4.01% vs 5.14%, OR 0.73, 95% CI: 0.47-1.12, *P* = 0.15).

#### Postoperative symptoms

Dysphagia and need for bougie dilatation: Twentyfour studies assessed the outcome of dysphagia after LARS. Various questionnaires were used to define dysphagia severity, ranging from no symptoms to very severe episodes at the end of follow-up. The overall prevalence of dysphagia after LNF was significantly higher than after LTF (14.29% vs 11.00%, OR 1.68, 95% CI: 1.12-2.52, P = 0.01) (Figure 2A). A similar result was also obtained if only patients with moderate-to-severe dysphagia were included (12.30% vs 2.74%, OR 3.11, 95% CI: 1.94-5.00, P < 0.01). For patients with severe symptoms needing bougie dilatation, prevalence was still significantly higher after LNF than after LTF (7.91% vs 1.44%, OR 3.67, 95% CI: 1.90-7.09, P < 0.01). We thought it necessary to carry out subgroup analyses because preoperative EM was an important variable in the choice of surgical procedure and may have an effect on the analyses. Defining esophageal dysmotility was not consistent in the surgical literature. Most surgeons would agree that a distal esophageal amplitude > 40 mmHg and peristaltic contraction of the esophageal body of at least 70% indicate normal motility<sup>[18]</sup>. As described above, subgroup 1 analysis showed that the surgical procedure had no effect on the occurrence of

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# Shan CX et al. Laparoscopic Nissen and Toupet fundoplication

# A

Shaw <i>et a</i> <sup>[27]</sup> , 2010 Laws <i>et a</i> <sup>[10]</sup> , 1997 Guérin <i>et a</i> <sup>[26]</sup> , 2007 Mickevicius 3.0 <i>et a</i> <sup>[22]</sup> , 2008 Patti <i>et a</i> <sup>[39]</sup> , 2004 Booth <i>et a</i> <sup>[21]</sup> , 2008 Chrysos <i>et a</i> <sup>[25]</sup> , 2003 Strate <i>et a</i> <sup>[16]</sup> , 2008 Mickevicius 1.5 <i>et a</i> <sup>[22]</sup> , 2008 Mickevicius 1.5 <i>et a</i> <sup>[22]</sup> , 2008 McKernan <i>et a</i> <sup>[38]</sup> , 1994 Farrell <i>et a</i> <sup>[43]</sup> , 2000 Wykypiel <i>et a</i> <sup>[43]</sup> , 2000 Wykypiel <i>et a</i> <sup>[43]</sup> , 2008 Hunter <i>et a</i> <sup>[43]</sup> , 2008 Hunter <i>et a</i> <sup>[31]</sup> , 1996 Wetscher <i>et a</i> <sup>[12]</sup> , 1997 Granderath <i>et a</i> <sup>[35]</sup> , 2003 Sgromo <i>et a</i> <sup>[35]</sup> , 2003 Bell <i>et a</i> <sup>[41]</sup> , 1996 Pessaux <i>et a</i> <sup>[40]</sup> , 2000 Fernando <i>et a</i> <sup>[36]</sup> , 2002 Fein <i>et a</i> <sup>[45]</sup> , 2008 Wykypiel <i>et a</i> <sup>[437]</sup> , 2005 Lund <i>et a</i> <sup>[42]</sup> , 1997	3         2           2         8           20         16           2         30           3         2           83         6           7         1	Total 7 23 62 31 216 59 14 100 33 14 293 20 101 17	Events 1 1 0 3 12 5 3 11 5 0 15 2 2 2	Total 8 16 56 30 141 58 19 100 33 14 52 20	(%) 1.9 2.0 1.5 4.0 6.4 5.2 2.9 6.3 3.8 1.4 6.7 2.0	M-H, random (95% CI) 5.25 (0.40-68.95) 1.43 (0.12-17.23) 4.67 (0.22-99.38) 3.13 (0.74-13.20) 1.10 (0.52-2.32) 3.94 (1.34-11.63) 0.89 (0.13-6.18) 3.47 (1.62-7.40) 0.56 (0.12-2.56) 5.80 (0.25-132.56)	concealment? Yes Yes Yes Yes Yes Yes Yes Yes Yes No	M-H, random (95% CI)
Laws <i>et a</i> <sup>(10]</sup> , 1997 Guérin <i>et a</i> <sup>(26]</sup> , 2007 Mickevicius 3.0 <i>et a</i> <sup>(22)</sup> , 2008 Patti <i>et a</i> <sup>(33)</sup> , 2004 Booth <i>et a</i> <sup>(21)</sup> , 2008 Chrysos <i>et a</i> <sup>(22)</sup> , 2003 Strate <i>et a</i> <sup>(16)</sup> , 2008 Mickevicius 1.5 <i>et a</i> <sup>(22)</sup> , 2008 Mickevicius 1.5 <i>et a</i> <sup>(32)</sup> , 2008 Mickevicius 1.5 <i>et a</i> <sup>(32)</sup> , 2008 Mickevicius 1.5 <i>et a</i> <sup>(31)</sup> , 1994 Farrell <i>et a</i> <sup>(43)</sup> , 2000 Wykypiel <i>et a</i> <sup>(30)</sup> , 2008 Hunter <i>et a</i> <sup>(31)</sup> , 1996 Wetscher <i>et a</i> <sup>(12)</sup> , 1997 Granderath <i>et a</i> <sup>(29)</sup> , 2007 Erenoğlu <i>et a</i> <sup>(35)</sup> , 2003 Sgromo <i>et a</i> <sup>(34)</sup> , 2008 Bell <i>et a</i> <sup>(41)</sup> , 1996 Pessaux <i>et a</i> <sup>(40)</sup> , 2000 Fernando <i>et a</i> <sup>(36)</sup> , 2002 Fein <i>et a</i> <sup>(45)</sup> , 2008 Wykypiel <i>et a</i> <sup>(42)</sup> , 1997	2 8 20 16 2 30 3 2 83 6 7 1	23 62 31 216 59 14 100 33 14 293 20 101	1 0 3 12 5 3 11 5 0 15 2	16 56 30 141 58 19 100 33 14 52 20	2.0 1.5 4.0 6.4 5.2 2.9 6.3 3.8 1.4 6.7	1.43 (0.12-17.23) 4.67 (0.22-99.38) 3.13 (0.74-13.20) 1.10 (0.52-2.32) 3.94 (1.34-11.63) 0.89 (0.13-6.18) 3.47 (1.62-7.40) 0.56 (0.12-2.56) 5.80 (0.25-132.56)	Yes Yes Yes Yes Yes Yes Yes	
Guérin <i>et al</i> <sup>(26]</sup> , 2007 Mickevicius 3.0 <i>et al</i> <sup>(22]</sup> , 2008 Patti <i>et al</i> <sup>(39]</sup> , 2004 Booth <i>et al</i> <sup>(21]</sup> , 2008 Chrysos <i>et al</i> <sup>(25]</sup> , 2003 Strate <i>et al</i> <sup>(16]</sup> , 2008 Mickevicius 1.5 <i>et al</i> <sup>(22]</sup> , 2008 Mickerian <i>et al</i> <sup>(38]</sup> , 1994 Farrell <i>et al</i> <sup>(43]</sup> , 2000 Wykypiel <i>et al</i> <sup>(30]</sup> , 2008 Hunter <i>et al</i> <sup>(31]</sup> , 1996 Wetscher <i>et al</i> <sup>(12]</sup> , 1997 Granderath <i>et al</i> <sup>(29]</sup> , 2007 Erenoğlu <i>et al</i> <sup>(33]</sup> , 2008 Bell <i>et al</i> <sup>(41]</sup> , 1996 Pessaux <i>et al</i> <sup>(40]</sup> , 2000 Fernando <i>et al</i> <sup>(36]</sup> , 2002 Fein <i>et al</i> <sup>(45]</sup> , 2008 Wykypiel <i>et al</i> <sup>(47]</sup> , 1997	2 8 20 16 2 30 3 2 83 6 7 1	62 31 216 59 14 100 33 14 293 20 101	0 3 12 5 3 11 5 0 15 2	56 30 141 58 19 100 33 14 52 20	1.5 4.0 6.4 5.2 2.9 6.3 3.8 1.4 6.7	4.67 (0.22-99.38) 3.13 (0.74-13.20) 1.10 (0.52-2.32) 3.94 (1.34-11.63) 0.89 (0.13-6.18) 3.47 (1.62-7.40) 0.56 (0.12-2.56) 5.80 (0.25-132.56)	Yes Yes Yes Yes Yes Yes	
Mickevicius 3.0 <i>et al</i> <sup>(22)</sup> , 2008 Patti <i>et al</i> <sup>(39)</sup> , 2004 Booth <i>et al</i> <sup>(21)</sup> , 2008 Chrysos <i>et al</i> <sup>(22)</sup> , 2003 Strate <i>et al</i> <sup>(16)</sup> , 2008 Mickevicius 1.5 <i>et al</i> <sup>(22)</sup> , 2008 Mickevicius 1.5 <i>et al</i> <sup>(22)</sup> , 2008 Mickerian <i>et al</i> <sup>(38)</sup> , 1994 Farrell <i>et al</i> <sup>(43)</sup> , 2000 Wykypiel <i>et al</i> <sup>(30)</sup> , 2008 Hunter <i>et al</i> <sup>(31)</sup> , 1996 Wetscher <i>et al</i> <sup>(31)</sup> , 1997 Granderath <i>et al</i> <sup>(29)</sup> , 2007 Erenoğlu <i>et al</i> <sup>(35)</sup> , 2003 Sgromo <i>et al</i> <sup>(34)</sup> , 2008 Bell <i>et al</i> <sup>(41)</sup> , 1996 Pessaux <i>et al</i> <sup>(40)</sup> , 2000 Fernando <i>et al</i> <sup>(36)</sup> , 2002 Fein <i>et al</i> <sup>(45)</sup> , 2008 Wykypiel <i>et al</i> <sup>(47)</sup> , 2005 Lund <i>et al</i> <sup>(42)</sup> , 1997	8 20 16 2 30 3 2 83 6 7 1	31 216 59 14 100 33 14 293 20 101	3 12 5 3 11 5 0 15 2	30 141 58 19 100 33 14 52 20	4.0 6.4 5.2 2.9 6.3 3.8 1.4 6.7	3.13 (0.74-13.20) 1.10 (0.52-2.32) 3.94 (1.34-11.63) 0.89 (0.13-6.18) 3.47 (1.62-7.40) 0.56 (0.12-2.56) 5.80 (0.25-132.56)	Yes Yes Yes Yes Yes Yes	
Patti <i>et a</i> <sup>(39]</sup> , 2004 Booth <i>et a</i> <sup>(21)</sup> , 2008 Chrysos <i>et a</i> <sup>(25)</sup> , 2003 Strate <i>et a</i> <sup>(16)</sup> , 2008 Mickevicius 1.5 <i>et a</i> <sup>(22)</sup> , 2008 McKernan <i>et a</i> <sup>(38)</sup> , 1994 Farrell <i>et a</i> <sup>(43)</sup> , 2000 Wykypiel <i>et a</i> <sup>(43)</sup> , 2000 Wukypiel <i>et a</i> <sup>(43)</sup> , 2008 Hunter <i>et a</i> <sup>(41)</sup> , 1997 Granderath <i>et a</i> <sup>(29)</sup> , 2007 Erenoğlu <i>et a</i> <sup>(35)</sup> , 2003 Sgromo <i>et a</i> <sup>(35)</sup> , 2003 Sgromo <i>et a</i> <sup>(35)</sup> , 2003 Bell <i>et a</i> <sup>(41)</sup> , 1996 Pessaux <i>et a</i> <sup>(46)</sup> , 2000 Fernando <i>et a</i> <sup>(36)</sup> , 2002 Fein <i>et a</i> <sup>(45)</sup> , 2008 Wykypiel <i>et a</i> <sup>(43)</sup> , 2005 Lund <i>et a</i> <sup>(42)</sup> , 1997	20 16 2 30 3 2 83 6 7 1	216 59 14 100 33 14 293 20 101	12 5 3 11 5 0 15 2	141 58 19 100 33 14 52 20	6.4 5.2 2.9 6.3 3.8 1.4 6.7	1.10 (0.52-2.32) 3.94 (1.34-11.63) 0.89 (0.13-6.18) 3.47 (1.62-7.40) 0.56 (0.12-2.56) 5.80 (0.25-132.56)	Yes Yes Yes Yes Yes	
Booth <i>et al</i> , <sup>(21)</sup> , 2008 Chrysos <i>et al</i> , <sup>(25)</sup> , 2003 Strate <i>et al</i> , <sup>(16)</sup> , 2008 Mickevicius 1.5 <i>et al</i> , <sup>(22)</sup> , 2008 McKernan <i>et al</i> , <sup>(38)</sup> , 1994 Farrell <i>et al</i> , <sup>(43)</sup> , 2000 Wykypiel <i>et al</i> , <sup>(30)</sup> , 2008 Hunter <i>et al</i> , <sup>(21)</sup> , 1997 Granderath <i>et al</i> , <sup>(22)</sup> , 2007 Erenoğlu <i>et al</i> , <sup>(35)</sup> , 2003 Sgromo <i>et al</i> , <sup>(34)</sup> , 2008 Bell <i>et al</i> , <sup>(41)</sup> , 1996 Pessaux <i>et al</i> , <sup>(40)</sup> , 2000 Fernando <i>et al</i> , <sup>(36)</sup> , 2002 Fein <i>et al</i> , <sup>(45)</sup> , 2008 Wykypiel <i>et al</i> , <sup>(37)</sup> , 2005 Lund <i>et al</i> , <sup>(42)</sup> , 1997	16 2 30 3 2 83 6 7 1	59 14 100 33 14 293 20 101	5 3 11 5 0 15 2	58 19 100 33 14 52 20	5.2 2.9 6.3 3.8 1.4 6.7	3.94 (1.34-11.63) 0.89 (0.13-6.18) 3.47 (1.62-7.40) 0.56 (0.12-2.56) 5.80 (0.25-132.56)	Yes Yes Yes Yes	
Chrysos <i>et al</i> <sup>(25)</sup> , 2003 Strate <i>et al</i> <sup>(16)</sup> , 2008 Mickevicius 1.5 <i>et al</i> <sup>(22)</sup> , 2008 McKernan <i>et al</i> <sup>(38)</sup> , 1994 Farrell <i>et al</i> <sup>(43)</sup> , 2000 Wykypiel <i>et al</i> <sup>(30)</sup> , 2008 Hunter <i>et al</i> <sup>(31)</sup> , 1996 Wetscher <i>et al</i> <sup>(12)</sup> , 1997 Granderath <i>et al</i> <sup>(23)</sup> , 2007 Erenoğlu <i>et al</i> <sup>(35)</sup> , 2003 Sgromo <i>et al</i> <sup>(34)</sup> , 2008 Bell <i>et al</i> <sup>(41)</sup> , 1996 Pessaux <i>et al</i> <sup>(40)</sup> , 2000 Fernando <i>et al</i> <sup>(36)</sup> , 2002 Fein <i>et al</i> <sup>(45)</sup> , 2008 Wykypiel <i>et al</i> <sup>(42)</sup> , 1997	2 30 3 2 83 6 7 1	14 100 33 14 293 20 101	3 11 5 0 15 2	19 100 33 14 52 20	2.9 6.3 3.8 1.4 6.7	0.89 (0.13-6.18) 3.47 (1.62-7.40) 0.56 (0.12-2.56) 5.80 (0.25-132.56)	Yes Yes Yes	
Strate <i>et al</i> <sup>(16)</sup> , 2008 Mickevicius 1.5 <i>et al</i> <sup>(22)</sup> , 2008 McKernan <i>et al</i> <sup>(38)</sup> , 1994 Farrell <i>et al</i> <sup>(43)</sup> , 2000 Wykypiel <i>et al</i> <sup>(30)</sup> , 2008 Hunter <i>et al</i> <sup>(31)</sup> , 1996 Wetscher <i>et al</i> <sup>(12)</sup> , 1997 Granderath <i>et al</i> <sup>(29)</sup> , 2007 Erenoğlu <i>et al</i> <sup>(35)</sup> , 2003 Sgromo <i>et al</i> <sup>(34)</sup> , 2008 Bell <i>et al</i> <sup>(41)</sup> , 1996 Pessaux <i>et al</i> <sup>(40)</sup> , 2000 Fernando <i>et al</i> <sup>(36)</sup> , 2002 Fein <i>et al</i> <sup>(45)</sup> , 2008 Wykypiel <i>et al</i> <sup>(37)</sup> , 2005 Lund <i>et al</i> <sup>(42)</sup> , 1997	30 3 2 83 6 7 1	100 33 14 293 20 101	11 5 0 15 2	100 33 14 52 20	6.3 3.8 1.4 6.7	3.47 (1.62-7.40) 0.56 (0.12-2.56) 5.80 (0.25-132.56)	Yes Yes	
Mickevicius 1.5 <i>et al</i> <sup>(22)</sup> , 2008 McKernan <i>et al</i> <sup>(38)</sup> , 1994 Farrell <i>et al</i> <sup>(43)</sup> , 2000 Wykypiel <i>et al</i> <sup>(33)</sup> , 2008 Hunter <i>et al</i> <sup>(31)</sup> , 1996 Wetscher <i>et al</i> <sup>(12)</sup> , 1997 Granderath <i>et al</i> <sup>(29)</sup> , 2007 Erenoğlu <i>et al</i> <sup>(35)</sup> , 2003 Sgromo <i>et al</i> <sup>(34)</sup> , 2008 Bell <i>et al</i> <sup>(41)</sup> , 1996 Pessaux <i>et al</i> <sup>(40)</sup> , 2000 Fernando <i>et al</i> <sup>(36)</sup> , 2002 Fein <i>et al</i> <sup>(45)</sup> , 2008 Wykypiel <i>et al</i> <sup>(42)</sup> , 1997	3 2 83 6 7 1	33 14 293 20 101	5 0 15 2	33 14 52 20	3.8 1.4 6.7	0.56 (0.12-2.56) 5.80 (0.25-132.56)	Yes	
McKernan <i>et al</i> <sup>(38]</sup> , 1994 Farrell <i>et al</i> <sup>(43)</sup> , 2000 Wykypiel <i>et al</i> <sup>(30)</sup> , 2008 Hunter <i>et al</i> <sup>(31)</sup> , 1996 Wetscher <i>et al</i> <sup>(12)</sup> , 1997 Granderath <i>et al</i> <sup>(29)</sup> , 2007 Erenoğlu <i>et al</i> <sup>(35)</sup> , 2003 Sgromo <i>et al</i> <sup>(34)</sup> , 2008 Bell <i>et al</i> <sup>(41)</sup> , 1996 Pessaux <i>et al</i> <sup>(40)</sup> , 2000 Fernando <i>et al</i> <sup>(36)</sup> , 2002 Fein <i>et al</i> <sup>(45)</sup> , 2008 Wykypiel <i>et al</i> <sup>(42)</sup> , 1997	2 83 6 7 1	14 293 20 101	0 15 2	14 52 20	1.4 6.7	5.80 (0.25-132.56)		<b>+</b>
Farrell <i>et al</i> <sup>(43)</sup> , 2000 Wykypiel <i>et al</i> <sup>(30)</sup> , 2008 Hunter <i>et al</i> <sup>(31)</sup> , 1996 Wetscher <i>et al</i> <sup>(12)</sup> , 1997 Granderath <i>et al</i> <sup>(29)</sup> , 2007 Erenoğlu <i>et al</i> <sup>(35)</sup> , 2003 Sgromo <i>et al</i> <sup>(34)</sup> , 2008 Bell <i>et al</i> <sup>(41)</sup> , 1996 Pessaux <i>et al</i> <sup>(41)</sup> , 1996 Persando <i>et al</i> <sup>(36)</sup> , 2000 Fernando <i>et al</i> <sup>(36)</sup> , 2002 Fein <i>et al</i> <sup>(45)</sup> , 2008 Wykypiel <i>et al</i> <sup>(47)</sup> , 2005 Lund <i>et al</i> <sup>(42)</sup> , 1997	83 6 7 1	293 20 101	15 2	52 20	6.7	· · · ·	No	
Wykypiel <i>et al</i> <sup>(30]</sup> , 2008 Hunter <i>et al</i> <sup>(31]</sup> , 1996 Wetscher <i>et al</i> <sup>(12]</sup> , 1997 Granderath <i>et al</i> <sup>(29]</sup> , 2007 Erenoğlu <i>et al</i> <sup>(35]</sup> , 2003 Sgromo <i>et al</i> <sup>(34]</sup> , 2008 Bell <i>et al</i> <sup>(41]</sup> , 1996 Pessaux <i>et al</i> <sup>(40]</sup> , 2000 Fernando <i>et al</i> <sup>(36]</sup> , 2002 Fein <i>et al</i> <sup>(45]</sup> , 2008 Wykypiel <i>et al</i> <sup>(47]</sup> , 2005 Lund <i>et al</i> <sup>(42]</sup> , 1997	6 7 1	20 101	2	20				
Hunter <i>et al</i> <sup>(31]</sup> , 1996 Wetscher <i>et al</i> <sup>(12]</sup> , 1997 Granderath <i>et al</i> <sup>(23]</sup> , 2007 Erenoğlu <i>et al</i> <sup>(33]</sup> , 2003 Sgromo <i>et al</i> <sup>(34]</sup> , 2008 Bell <i>et al</i> <sup>(41]</sup> , 1996 Pessaux <i>et al</i> <sup>(40]</sup> , 2000 Fernando <i>et al</i> <sup>(36]</sup> , 2002 Fein <i>et al</i> <sup>(45]</sup> , 2008 Wykypiel <i>et al</i> <sup>(37]</sup> , 2005 Lund <i>et al</i> <sup>(42]</sup> , 1997	7 1	101				0.97 (0.51-1.87)	No	-+-
Wetscher <i>et a</i> <sup>(12)</sup> , 1997 Granderath <i>et a</i> <sup>(29)</sup> , 2007 Erenoğlu <i>et a</i> <sup>(35)</sup> , 2003 Sgromo <i>et a</i> <sup>(34)</sup> , 2008 Bell <i>et a</i> <sup>(41)</sup> , 1996 Pessaux <i>et a</i> <sup>(40)</sup> , 2000 Fernando <i>et a</i> <sup>(36)</sup> , 2002 Fein <i>et a</i> <sup>(45)</sup> , 2008 Wykypiel <i>et a</i> <sup>(37)</sup> , 2005 Lund <i>et a</i> <sup>(42)</sup> , 1997	1		2		3.3	3.86 (0.67-22.11)	No	
Granderath <i>et al</i> <sup>(29)</sup> , 2007 Erenoğlu <i>et al</i> <sup>(35)</sup> , 2003 Sgromo <i>et al</i> <sup>(34)</sup> , 2008 Bell <i>et al</i> <sup>(41)</sup> , 1996 Pessaux <i>et al</i> <sup>(40)</sup> , 2000 Fernando <i>et al</i> <sup>(36)</sup> , 2002 Fein <i>et al</i> <sup>(45)</sup> , 2008 Wykypiel <i>et al</i> <sup>(37)</sup> , 2005 Lund <i>et al</i> <sup>(42)</sup> , 1997	-	17		83	3.6	3.02 (0.61-14.93)	No	<b>-</b>
Erenoğlu et al <sup>(35)</sup> , 2003 Sgromo et al <sup>(34)</sup> , 2008 Bell et al <sup>(41)</sup> , 1996 Pessaux et al <sup>(40)</sup> , 2000 Fernando et al <sup>(36)</sup> , 2002 Fein et al <sup>(45)</sup> , 2008 Wykypiel et al <sup>(37)</sup> , 2005 Lund et al <sup>(42)</sup> , 1997		1/	1	32	1.6	1.94 (0.11-33.05)	No	
Sgromo <i>et a</i> <sup>[34]</sup> , 2008 Bell <i>et a</i> <sup>[41]</sup> , 1996 Pessaux <i>et a</i> <sup>[40]</sup> , 2000 Fernando <i>et a</i> <sup>[36]</sup> , 2002 Fein <i>et a</i> <sup>[45]</sup> , 2008 Wykypiel <i>et a</i> <sup>[37]</sup> , 2005 Lund <i>et a</i> <sup>[42]</sup> , 1997	0	28	2	28	1.4	0.19 (0.01-4.05)	No	
Bell <i>et al</i> <sup>[41]</sup> , 1996 Pessaux <i>et al</i> <sup>[40]</sup> , 2000 Fernando <i>et al</i> <sup>[36]</sup> , 2002 Fein <i>et al</i> <sup>[45]</sup> , 2008 Wykypiel <i>et al</i> <sup>[37]</sup> , 2005 Lund <i>et al</i> <sup>[42]</sup> , 1997	23	118	5	26	5.2	1.02 (0.35-2.98)	No	
Pessaux <i>et al</i> <sup>(40)</sup> , 2000 Fernando <i>et al</i> <sup>(36)</sup> , 2002 Fein <i>et al</i> <sup>(45)</sup> , 2008 Wykypiel <i>et al</i> <sup>(37)</sup> , 2005 Lund <i>et al</i> <sup>(42)</sup> , 1997	48	99	22	62	6.7	1.71 (0.89-3.29)	No	
Fernando <i>et al</i> <sup>(36)</sup> , 2002 Fein <i>et al</i> <sup>(45)</sup> , 2008 Wykypiel <i>et al</i> <sup>(37)</sup> , 2005 Lund <i>et al</i> <sup>(42)</sup> , 1997	10	11	3	11	2.1	26.67 (2.31-308.00)	No	
Fein <i>et al</i> <sup>[45]</sup> , 2008 Wykypiel <i>et al</i> <sup>[37]</sup> , 2005 Lund <i>et al</i> <sup>[42]</sup> , 1997	57	1078	27	392	7.3	0.75 (0.47-1.21)	No	
Fein <i>et al</i> <sup>(45]</sup> , 2008 Wykypiel <i>et al</i> <sup>(37]</sup> , 2005 Lund <i>et al</i> <sup>(42]</sup> , 1997	17	113	10	29	5.7	0.34 (0.13-0.85)	No	
Lund <i>et al</i> <sup>[42]</sup> , 1997	23	74	3	9	3.9	0.90 (0.21-3.93)	No	
	21	77	6	132	5.6	7.88 (3.01-20.57)	No	
	10	16	10	46	4.7	6.00 (1.75-20.55)	No	<b></b>
Bessell <i>et al<sup>[17]</sup></i> , 2000	87	761	14	85	6.9	0.65 (0.35-1.21)	No	
Total (95% CI)		3365		1482	100	1.68 (1.12-2.52)		▲
Total events 4	481		163			. ,		•
Heterogeneity: Tau <sup>2</sup> = 0.53; $\chi^2$ =	<b>CE 0</b>	4, <i>df</i> = 2	3 ( <i>P</i> < 0.0	0001);	<sup>2</sup> = 65%			
Test for overall effect: $Z = 2.50$ (	= 65.8	-	•	,,				0.001 0.1 1 10 100
		.01)						Favours Nissen Favours Toupet

<b>B</b> Study or subgroup	Nic	sen	Tou	ipet	Weight	Odds ratio	Allocation	Odds ratio
Study of Subgroup	Events	Total	Events	Total	(%)	M-H, random (95% CI)	concealment?	M-H, random (95% CI)
	Lvents	Iotai	Lvents	Iotai	(%)		conceannents	
2.2.1 Motility normal (both)								
Strate <i>et al<sup>[16]</sup></i> , 2008	16	50	3	50	16.7	7.37 (1.99-27.32)	Yes	<b>-</b>
aws <i>et al<sup>[10]</sup></i> , 1997	2	23	1	16	7.8	1.43 (0.12-17.23)	Yes	
Bessell <i>et al</i> <sup>[17]</sup> , 2000	58	558	5	21	19.9	0.37 (0.13-1.05)	No	<b>_</b> _
lunter <i>et al</i> <sup>[31]</sup> , 1996	7	101	2	83	13.7	3.02 (0.61-14.93)	No	
ärrell <i>et al</i> <sup>[43]</sup> , 2000	75	267	9	31	22.7	0.95 (0.42-2.17)	No	
ernando <i>et al</i> <sup>[36]</sup> , 2002	14	88	4	7	13.7	0.14 (0.03-0.70)	No	<b>_</b>
Granderath <i>et al<sup>[29]</sup></i> , 2007	0	28	2	28	5.6	0.19 (0.01-4.05)	No	←
Subtotal (95% CI)		1115		236	100	0.93 (0.32-2.64)		-
otal events	172		26					Ť
leterogeneity: Tau <sup>2</sup> = 1.31;	$\chi^2 = 21.6$	6, <i>df</i> = 6	P = 0.00	1); $I^2 =$	72%			
Test for overall effect: $Z = 0$								
2.2.2 Motility abnormal (bot	h)							
Patti <i>et al</i> <sup>[39]</sup> , 2004	9	55	12	141	19.3	2.10 (0.83-5.32)	Yes	+ <b>-</b>
itrate <i>et al<sup>[16]</sup></i> , 2008	14	50	8	50	18.7	2.04 (0.77-5.42)	Yes	<b>_</b>
hrysos <i>et al</i> <sup>[25]</sup> , 2003	2	14	3	19	9.9	0.89 (0.13-6.18)	Yes	<b>_</b>
arrell <i>et al</i> <sup>[43]</sup> , 2000	8	26	6	21	15.6	1.11 (0.31-3.92)	No	<b>_</b>
Bessell <i>et al</i> <sup>[17]</sup> , 2000	29	203	9	64	20.7	1.02 (0.45-2.28)	No	
und <i>et al</i> <sup>[42]</sup> , 1997	10	16	10	46	15.9	6.00 (1.75-20.55)	No	<b>_</b>
Subtotal (95% CI)		364		341	100	1.75 (1.04-2.94)		•
otal events	72		48					•
leterogeneity: Tau <sup>2</sup> = 0.11;	$\chi^2 = 6.78$	, <i>df</i> = 5	(P = 0.24)	$I^2 = 26$	%			
Test for overall effect: $Z = 2$	P = 0	.04)	. ,					
2.2.3 Motility normal (Nisse	n) <i>vs</i> motili	ity abnor	mal (Toupe	et)				
Guérin <i>et al<sup>[26]</sup></i> , 2007	2	62	0	56	6.4	4.67 (0.22-99.38)	Yes	
atti <i>et al<sup>[39]</sup></i> , 2004	18	161	12	141	26.5	1.35 (0.63-2.92)	Yes	_ <b></b>
Vetscher <i>et al</i> <sup>[12]</sup> , 1997	1	17	1	32	7.2	1.94 (0.11-33.05)	No	
Frenoğlu <i>et al</i> <sup>[35]</sup> , 2003	23	118	5	26	22.0	1.02 (0.35-2.98)	No	<b>_</b>
Vykypiel <i>et al</i> <sup>[30]</sup> , 2008	6	20	2	20	14.1	3.86 (0.67-22.11)	No	
Vykypiel <i>et al</i> <sup>[37]</sup> , 2005	21	77	6	132	23.7	7.88 (3.01-20.57)	No	<b></b>
ubtotal (95% CI)		455		407	100	2.47 (1.08-5.68)		▲
otal events	71		26			· · · · · ·		-
leterogeneity: Tau <sup>2</sup> = 0.51;	$\chi^2 = 10.9$	4, <i>df</i> = 5	(P = 0.05)	); $I^2 = 5$	4%			
Test for overall effect: $Z = 2$	<i>,</i> ,,		,	,, -				
								0.01 0.1 1 10 10
								0.01 0.1 1 10 10

Favours Nissen Favours Toupet



## Shan CX et al. Laparoscopic Nissen and Toupet fundoplication

Study or subgroup Nissen Weight Odds ratio Allocation Odds ratio Toupet M-H, random (95% CI) Events Total Events Total M-H, random (95% CI) concealment? (%) 3.3.1 Postoperative gas bloating Chrysos et al<sup>[25]</sup>, 2003 3 19 6.7 1.45 (0.25-8.58) Yes 14 3 Guérin *et al*[26], 2007 1 62 0 56 3.1 2.76 (0.11-69.04) Yes Booth *et al*<sup>[21]</sup>, 2008 11 59 6 58 9.7 1.99(0.68-5.79)Yes Wykypiel *et al*<sup>[37]</sup>, 2005 18 77 6 132 10.1 6.41 (2.42-16.97) No Sgromo *et al*<sup>[34]</sup>, 2008 33 99 23 62 11.5 0.85 (0.44-1.65) No Wykypiel *et al*<sup>[30]</sup>, 2008 6 20 0 20 18.38 (0.96-352.57) 3.6 No Granderath *et al*<sup>[29]</sup>, 2007 17 28 7 28 9.3 4.64 (1.48-14.54) No Fernando *et al*<sup>[36]</sup>, 2002 60 113 18 29 10.8 0.69 (0.30-1.60) No Bell *et al*<sup>[41]</sup>, 1996 Fein *et al*<sup>[45]</sup>, 2008 9 12.00 (1.58-91.08) 11 3 11 5.8 No 63 74 5 9 7.9 4.58 (1.06-19.78) No Coster et al<sup>[28]</sup>, 1997 82 70 38 62 10.9 3.68 (1.66-8.18) No Radajewski et al<sup>[32]</sup>, 2009 29 43 10.6 1.16 (0.48-2.79) 36 51 No Subtotal (95% CI) 690 529 100 2.42 (1.37-4.26) Total events 327 138 Heterogeneity: Tau<sup>2</sup> = 0.55;  $\chi^2$  = 30.48, df = 11 (P = 0.001);  $I^2$  = 64% Test for overall effect: Z = 3.06 (P = 0.002)3.3.2 Postoperative inability to belch Guérin *et al*<sup>[26]</sup>, 2007 0 62 2 56 4.9 0.17 (0.01-3.71) Yes Booth *et al*<sup>[21]</sup>, 2008 34 59 24 58 16.0 1.93 (0.92-4.02) Yes Wykypiel et al<sup>[30]</sup>, 2008 6 20 0 20 5.1 18.38 (0.96-352.57) No Sgromo *et al*<sup>[34]</sup>, 2008 14.9 74 99 55 62 0.38 (0.15-0.93) No Granderath et al<sup>[29]</sup>, 2007 26 28 7 28 10.1 39.00 (7.32-207.87) No Fernando *et al*<sup>[36]</sup>, 2002 22 5 113 29 13.8 1.16(0.40-3.38)No Wykypiel *et al*<sup>[37]</sup>, 2005 26 77 9 132 15.4 6.97 (3.05-15.90) No Coster *et al*<sup>[28]</sup>, 1997 12 82 0 62 5.4 22.16 (1.29-382.06) No Radajewski et al<sup>[32]</sup>, 2009 20 51 7 43 14.4 3.32 (1.24-8.89) No Subtotal (95% CI) 591 490 100 3.02 (1.14-7.95) Total events 220 109 Heterogeneity: Tau<sup>2</sup> = 1.54;  $\chi^2$  = 42.66, df = 8 (P < 0.00001);  $I^2$  = 81% Test for overall effect: Z = 2.23 (P = 0.03) 0.01 0.1 1 10 100 Favours Nissen Favours Tounet

Figure 2 Pooled analysis using the Mantel-Haenszel method and a random-effect model. A: Overall rates of dysphagia after laparoscopic Nissen fundoplication (LNF) and laparoscopic Toupet fundoplication (LTF); B: Subgroup dysphagia depending on preoperative esophageal motility after LNF and LTF; C: Postoperative gas bloating and inability to belch after LNF and LTF.

postoperative dysphagia if preoperative EM was normal (P = 0.89). However, in subgroup 2, patients with abnormal EP, the prevalence of dysphagia after LNF was still more common than after LTF (P = 0.04). In subgroup 3, even though the surgical choice was in accordance with the so-called "tailored procedure", LNF also led to a significantly higher risk of developing postoperative dysphgia than LTF (P = 0.03) (Figure 2B).

**Gas-bloat syndrome or gas-related symptoms:** Gasrelated symptoms ("gas-bloat syndrome") were described in 12 studies involving > 1200 patients. Gas-bloat syndrome included gas bloating, inability to belch, flatulence, postprandial fullness, and epigastric pain. The main objective evaluation of gas-related symptoms was done using a verbal rating scale using the items mentioned above. Overall, 47.39% (327/690) of patients after LNF and 26.09% (138/529) of patients after LTF suffered from gas bloating, whereas 37.22% (220/591) after LNF and 22.24% (109/490) after LTF were unable to belch. Gas bloating and inability to belch were more common in the LNF group and a significant difference between LNF and LTF was also further confirmed to reach a significant level (Figure 2C).

## Recurrence and re-operation

Heartburn and reflux recurrence: Eleven studies investigated the incidence of postoperative heartburn (considered to be the cardinal symptom of GERD recurrence). Heartburn occurred in  $6.45\%^{[26]}$ - $60.29\%^{[43]}$  of the population after LNF, and in  $5.26\%^{[25]}$ - $55.10\%^{[43]}$  after LTF. No statistically significant difference was found between LNF and LTF concerning the cumulative prevalence of heartburn (32.97%, 331/1004 *vs* 31.09%, 157/505, OR 0.83, 95% CI: 0.52-1.33, P = 0.45, respectively).

Nine studies reported the postoperative recurrence of GERD. However, the standard of GERD recurrence was not uniform because some were judged according to symptoms such as reflux, chest pain, and heartburn, whereas others were based on the endoscopic characteristics and 24-h gastric monitoring of pH (e.g. persistent esophagitis, DeMeester score<sup>[46]</sup>). In our analysis, the cumulative prevalence of reflux recurrence was slightly higher after LTF than after LNF, but this difference was not significant (6.50%, 64/985 *vs* 9.42%, 84/892, OR 0.73, 95% CI: 0.35-1.53, P = 0.40).

**Re-operation:** Re-operation prevalence was described in 15 trials involving > 3800 patients. The main causes



of re-operation were persistent dysphagia, severe reflux symptoms, hiatus hernia recurrence, and other severe treatment failures. Although the re-operation rate after LNF was slightly higher than after Toupet fundoplication, 4.40% (115/2616) *vs* 3.68% (47/1276), the difference was not significant (OR 1.29, 95% CI: 0.73-2.29, P = 0.38). The morbidity associated with re-operation after LNF for GERD ranged from 1.56%<sup>[21]</sup> to 27.27%<sup>[41]</sup>, and in the LTF group the rates varied from 1.00%<sup>[28]</sup> to 17.5%<sup>[22]</sup>.

## DISCUSSION

Lower morbidity and mortality, shorter hospitalization and faster convalescence made LARS so attractive to patients with GERD. Since Nissen procedure was first reported a decade ago, it has been adopted as a tremendously successful procedure for reflux control, and it is therefore more often performed than partial fundoplication. However, numerous recent researches witnessed a strong debate between Nissen and Toupet fundoplications<sup>[47]</sup>, shifting the attention to postoperative failures due to mechanical problems (e.g. dysphagia), rather than worries about the recurrence of disease.

Our analysis is a comprehensive and detailed systematic literature review of 32 articles reporting the surgical outcomes of 6236 patients with GERD after LNF and LTF. It demonstrated that the latter is advantageous over the former, showing similar outcomes of satisfaction rate, endoscopic improvement, perioperative complication occurrence, reflux recurrence and re-operation, but a substantially reduced prevalence of postoperative symptoms (e.g. dysphagia, gas-bloat syndrome).

Patient satisfaction is a reasonable and accurate index for assessing the efficacy of surgical treatment for GERD<sup>[11,47]</sup>. In our meta-analysis, > 90% of the study populations reported excellent or good results in the LNF and LTF groups. Bearing in mind that the subjective description of patients was not always in accordance with objective findings<sup>[48]</sup>, we further analyzed the alteration of LES pressure and remission of esophagitis after construction of a mechanical anti-reflux barrier. Elevating the resting pressure of the LES played a crucial role in controlling reflux symptoms, blocking the natural history of Barrett's esophagus and reducing the risk of malignancy. We also found that LNF and LTF could increase the LES pressure and improve preoperative esophagitis. Even though the amplitude of elevation of LES pressure was significantly lower after LTF than after LNF, it seemed that it remained sufficiently powerful to resist the reflux of gastric contents. These subjective assessments and objective evaluations supported the point of view that LTF can control reflux symptoms for GERD.

The prevalence of perioperative complications showed no significant difference between groups, indicating that neither procedure was more technically difficult or more demanding of surgical skills. However, the prevalence of postoperative dysphagia and gas-related symptoms was much higher after LNF than after LTF. Even though the mechanism of gas-related symptoms is unclear<sup>[29]</sup>, these results suggest that wrap type and alteration in LES pressure were the underlying causes.

Dysphagia was still the complication of greatest concern and presented in three scenarios: acute total dysphagia immediately after surgery; mild dysphagia within the first postoperative 6-8 wk; and persistent chronic dysphagia after the postoperative 6-8 wk<sup>[18,49-51]</sup>. Some authors thought that dysphagia converges and the difference normalizes within 12 mo<sup>[52-55]</sup>. This study analyzed the prevalence of chronic dysphagia at the end of follow-up, and the mean duration of follow-up of most included studies was > 12 mo. A subgroup analysis was also executed to incorporate the variable of EM. It seemed that in normal motility patients (subgroup 1), extent of anti-reflux barrier did not affect the possibility of dysphagia. But in patients with abnormal motility (subgroup 2), the higher dysphagia rate after LNF supported that the tailored approach should be preserved. Even using the tailored approach (subgroup 3), the prevalence of dysphagia after LTF was still significantly lower than after LNF. These results indicated that, irrespective of EM status, LTF would be a safer choice in reducing this complication.

Concerns regarding GERD recurrence made surgeons select the Nissen technique rather than the Toupet technique for a long time. The similar prevalence of reflux recurrence between LNF and LTF groups in our analyses appeared to confirm the effectiveness of the Toupet procedure from another viewpoint. However, the value of this index may be slightly inferior. A De-Meester score > 14.7 was a generally accepted criterion, but the standards of GERD recurrence of selected researches were not uniform. Some were judged based on symptoms, some on endoscopic manometry. Furthermore, even though specific pH changes in the gastric environment were related to symptoms to some extent, inconsistency of poor correlation between postoperative reflux symptoms and reflux abnormal DeMeester scores were noted in many instances<sup>[27,45,48]</sup>.

For re-operation, we did not divide subgroups according to causes such as recurrence of reflux or complications. The reason was that they were a miserable experience for the patients and also indicated the failure of primary surgery. The re-operation prevalence between the two groups was comparable. A remarkable phenomenon discovered in some studies<sup>[16,23,24]</sup> was that a large proportion of patients needing re-operation after LNF possessed a intact wrap during surgery with herniation of the wraps into the mediastinum. Nevertheless, it was rarely detected and presented after LTF. The technical issue of a suture between the posterior wall of the wrap and the two crura of the diaphragm, or a suture between the upper portion of the wrap and the anterior edge of the hiatus, has been proposed to maintain the wrap in an adequate abdominal position and to avoid its rotation and migration.

In conclusion, the results of the present meta-analysis suggested that LTF might be the current procedure of choice to treat GERD. It should be advocated as a more physiologic alternative for Nissen repair, allowing a reduced morbidity rate with similar efficacy in reflux control and recurrence. The surgical patterns might be a prior factor to preoperative esophageal motility in affecting the postoperative dysphagia after LARS. More multicenter, randomized controlled trials including objective outcome assessment are required to further confirm the value of LNF and LTF.

# COMMENTS

## Background

The laparoscopic Nissen fundoplication and the laparoscopic Toupet fundoplication are the two major anti-reflux surgical procedures for gastroesophageal reflux disease (GERD). There has been much debate about the superiority of these two techniques.

## **Research frontiers**

A decade ago, Nissen procedure was first reported, then adopted as a tremendous successful procedure for reflux control, and was therefore more often performed than posterior partial fundoplication. However, numerous recent researches witnessed a strong debate about Nissen and Toupet fundoplication, shifting the attention to postoperative failures due to mechanical problems (e.g. dysphagia), rather than worries about the recurrence of disease.

#### Innovations and breakthroughs

To the best of the authors' knowledge, the present study was the most comprehensive and detailed systematic literature review to demonstrate the optimal surgical procedure for GERD.

## Applications

The research showed that laparoscopic Toupet fundoplication might be the current procedure of choice to treat GERD. It should be advocated as a more physiologic alternative for Nissen repair, allowing a reduced morbidity rate with similar efficacy in reflux control and recurrence.

#### Peer review

This article is important and interesting.

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