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META-ANALYSIS

Is Dor fundoplication optimum after laparoscopic Heller myotomy for achalasia? A meta-analysis

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Abstract

AIM: To compare the outcome of acid reflux prevention by Dor fundoplication after laparoscopic Heller myotomy (LHM) for achalasia.

METHODS: Electronic database PubMed, Ovid (Evidence-Based Medicine Reviews, EmBase and Ovid MEDLINE) and Cochrane Library were searched between January 1995 and September 2012. Bibliographic citation management software (EndNote X3) was used for extracted literature management. Quality assessment of random controlled studies (RCTs) and non-RCTs was performed according to the Cochrane Handbook for Systematic Reviews of Interventions 5.1.0 and a modification of the Newcastle-Ottawa Scale, respectively. The data were analyzed using Review Manager (Version 5.1), and sensitivity analysis was performed by sequentially omitting each study.

RESULTS: Finally, 6 studies, including a total of 523 achalasia patients, compared Dor fundoplication with other types of fundoplication after LHM (Dor-other group), and 8 studies, including a total of 528 achalasia patients, compared Dor fundoplication with no fundoplication after LHM (Dor-no group). Dor fundoplication was associated with a significantly higher recurrence rate of clinical regurgitation and pathological acid reflux compared with the other fundoplication group (OR = 7.16, 95%CI: 1.25-40.93, P = 0.03, and OR = 3.79, 95%CI: 1.23-11.72, P = 0.02, respectively). In addition, there were no significant differences between Dor fundoplication and no fundoplication in all subjects. Other outcomes, including complications, dysphagia, postoperative physiologic testing, and operation-related data displayed no significant differences in the two comparison groups.

CONCLUSION: Dor fundoplication is not the optimum procedure after LHM for achalasia. We suggest more attention should be paid on quality of life among different fundoplications.

Key words: Laparoscopic Heller myotomy; Dor fundoplication; Gastroesophageal reflux; Achalasia; Meta-analysis

Core tip: Laparoscopic Heller myotomy (LHM) is commonly used to treat achalasia and an antireflux procedure is added after LHM for prevention of gastroesophageal reflux (GER). However, there is no consensus on whether Dor fundoplication is the optimum procedure after LHM for the prevention of GER. We conducted this meta-analysis to assess Dor fundoplication com-

pared with non-fundoplication surgery or other types of fundoplication surgery for achalasia. The results indicated higher recurrence rate of clinical regurgitation and pathological acid reflux in Dor fundoplication indicating that Dor fundoplication is not the optimum procedure for the prevention of GER after LHM in achalasia patients.

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INTRODUCTION

Achalasia has generally been accepted as an autoimmune esophageal motility disorder resulting from the loss of inhibitory nerve endings in the myenteric plexus of the esophagus[1]. Pathophysiologically characterized by poor relaxation of lower esophageal sphincter (LES) and aperistalsis of the esophageal body, achalasia presents mainly relevant symptoms such as dysphagia, regurgitation, heartburn, and chest pain. The commonly used treatment of achalasia involves medicine therapy, endoscopic pneumatic dilation, and surgical myotomy with the aim of eliminating the high LES pressure. Previous studies have reported better long-term satisfaction with surgical myotomy than with drug medicine therapy or pneumatic dilation[2-4]. Kostic and colleagues in 2007 also demonstrated the superiority of laparoscopic Heller myotomy (LHM) to pneumatic dilation for achalasia patients[5]. As a result, LHM is routinely considered an option for achalasia patients.

However, although LHM has been previously demonstrated to have positive long-term outcomes for achalasia patients, gastroesophageal reflux (GER) after LHM is commonly regarded as one of the main failures of surgical treatment. For this reason, many surgeons suggest the addition of a fundoplication to LHM for the prevention of acid reflux, and anterior 180° Dor fundoplication is currently well recognized as the best choice[6]. Recently, in 2012, a review conducted by Mayo reconfirmed the efficacy of anti-acid reflux fundoplication following LHM both on pH monitoring and symptom relief; however, the clinical differences between Dor fundoplication and posterior 270° Toupet fundoplication have not been verified. In addition, the Mayo review provides limited evidence without pooling available data from the included studies[7]. Thus, it also remains controversial that Dor fundoplication is the optimum procedure for the prevention of postoperative GER after LHM in achalasia patients.

To address these issues, our team conducted the following meta-analysis to compare Dor fundoplication plus LHM with LHM alone (Dor-no group) and LHM plus other types of fundoplication (Dor-other group), namely, 270° Toupet and 360° Nissen fundoplication. The assessed outcomes included: (1) the primary endpoints of postoperative GER, dysphagia, and perforation; and (2) the secondary endpoints of other symptoms, quality of life, operation-related data, complications, and postoperative physiologic testing.

MATERIALS AND METHODS

This meta-analysis was conducted following the Cochrane Handbook for Systematic Reviews of Interventions 5.1.0 (updated March 2011) to ensure data quality (http://www.cochrane.org/training/cochrane-handbook).

Search for studies

Electronic databases PubMed, Ovid (EBM Reviews, EmBase and Ovid MEDLINE) and Cochrane Library were searched. Moreover, previously published reviews on the topic of interest were obtained and checked. We traced the reference list of relevant articles and used Google Scholar to find potential studies. The search terms were as follows: combined terms of "fundoplication" and "achalasia" using [Mesh] or [Keyword]. The electronic search was up to September 2012 from January 1995 with no limitation on language.

Study selection

Study designs included random controlled studies (RCTs), clinical controlled studies, cohort studies, case-control studies, and case series.

The inclusion criteria were as follows: (1) diagnosis of achalasia confirmed in an adult patient; (2) the surgical procedure compares Dor fundoplication with other fundoplication types (none, Toupet and Nissen); (3) laparoscopic Heller myotomy; and (4) available data for each comparison. We excluded: studies including (1) achalasia in children and pregnancy; (2) one type of fundoplication; (3) special surgical procedure such as anterior 120° wrap or Watson wrap[8]; and (4) studies lacking available data.

We imported the search results into bibliographic citation management software (EndNote X3). Two reviewers independently screened studies by reading titles and abstracts to roughly identify potential reports. The full texts of articles for all references identified as matching the inclusion criteria were obtained. Inclusion criteria were applied to the full texts. Disagreement was resolved through discussion and asking for advice from corresponding authors. The flow chart of study selection was made following the PRISMA statement (http://prisma-statement.org/statement.htm).

Data extraction and quality assessment

Two reviewers independently extracted data from eligible studies, and any disagreement was adjudicated by discussion or consulting the corresponding author. Base-

Table 1 Checklist of quality assessment and scoring of non-random controlled studies

Checklist
Selection
Is the subject definition adequate or described? (if yes, one star)
Were the subjects representative of the total population? (one star, if truly or obviously; no stars if subjects were selected group or not described)
Comparability
Did the study have no differences between Dor fundoplication and no fundoplication or other types of fundoplication? Major factors for consideration were age, gender, symptoms, preoperative therapy (pneumatic dilation and botulin toxin injection), and preoperative diagnostic test (endoscopy parameter and barium swallow) (if yes, two stars; one star if there were no other differences between the two groups even if one or more of these five characteristics was not reported; no star was assigned if the two groups differed)
Outcome assessment
Clearly defined outcome of interest (if yes, one star)
Adequacy of follow-up (one star if less than 20% of achalasia patients lost to follow-up, otherwise no stars)

line information included first author, published year, fundoplication type, study design, region, numbers of cases, and mean age among other parameters. Furthermore, the following outcome data were extracted: (1) the primary outcomes of GER-related clinical regurgitation and pathological acid reflux, dysphagia, and perforation; and (2) the secondary endpoints included other symptoms, quality of life, operation-related data (operation time and hospital stay time), complications, postoperative physiologic testing (LES pressure, DeMeester score and percent total time pH $\leqslant$ 4).

Quality assessment of RCTs was performed by two reviewers according to the Cochrane Handbook for Systematic Reviews of Interventions 5.1.0 based on the following aspects: random sequence generation, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, selective reporting, and other sources of bias. Three bias levels including low risk, high risk and unclear were assigned to every study aspect. Studies with more "low risk" bias assignations were recognized as superior. For non-random controlled studies, a modification of the Newcastle-Ottawa Scale (NOS)[9,10] was used as an assessment tool for selection, comparability and outcome assessment. Out of a total of six scores, studies valued more than four stars were recognized as being moderate to high quality. The detailed checklist is shown in Table 1.

Statistical analysis

The data were analyzed using Review Manager (Version 5.1). OR or RD and MD were used for analyzing dichotomous data and continuous data, respectively. Heterogeneity was measured with the I^2 index and P value. A random effect model was used when $I^2 > 50\%$. Otherwise, a fixed-effect model was considered. SD was estimated by a formula when only a range was reported: Estimate SD = Range/4 ($15 < n < 70$); Range/6 ($n > 70$)[11]. The value of $P < 0.05$ was considered to indicate statistical significance. Sensitivity analysis was performed by sequentially omitting each study.

RESULTS

Characteristics of pooled studies

A total of 731 potential abstracts were identified in the primary search of the electronic databases. A flow diagram of the detailed selection process is shown in Figure 1. Finally, 6 studies (2 RCTs and 4 non-RCTs), including a total of 523 achalasia patients, compared Dor fundoplication with other types of fundoplication (Toupet and Nissen fundoplication) after LHM, and 8 studies (3 RCTs and 5 non-RCTs), including a total of 528 achalasia patients, compared Dor fundoplication with no fundoplication after LHM[12-24]. In the 5 RCTs, two reported the same population group but differed in the main outcomes. Thus, we just extracted useful data integrated from both articles[19,23]. In addition, in the 8 non-RCTs, two studies were conducted by the same research group, who reported on the achalasia population with short- and long-term outcomes, and we chose the latter for our meta-analysis[15,24]. In one non-RCT, we divided the pooled data into two comparisons from the three reported subgroups[20]. In terms of non-Dor fundoplication, surgical fundoplication included 2 studies that used Nissen fundoplication, 4 studies with Toupet fundoplication and no fundoplication was used in the other studies. Table 2 offers the baseline characteristics of all studies.

Quality judgments of studies

In the pooled studies, 5 were RCTs, and 8 were non-RCTs. We used two methods to assess the quality of RCTs and non-RCTs, respectively. Table 3 lists the quality of RCTs according to the Cochrane Handbook for Systematic Reviews of Interventions 5.1.0. All the studies described the random sequence generation method used. Two studies generated sequence using a permuted block size of 4. Two used computer-generated random numbers, and 1 used a random number table generated in Microsoft Excel. In regards to allocation concealment, 3 studies used sealed opaque envelopes, 1 used Random Allocation Software version 1.0, and 1 study was unclear about the allocation concealment method used. In term of blinding, double blinding is difficult, and risks were judged by whether the outcome was likely influenced by the lack of blinding. In the 5 RCTs, only two trials reported double blinding of all recruited patients and researchers involved in the evaluation. Concerning selective reporting, although the protocol of each study was unavailable, the published outcomes included all the outcomes detailed in the method. Other sources of bias

Table 2 Basic characteristics of all pooled studies in the meta-analysis (Dor-other/no group)

Ref.	Patients (*n*)		Follow-up (mean ± SD or range)		Age (mean ± SD or range)	Type of fundoplication in control group	Study design	Country
	Dor group	Control group	Dor group	Control group				
Di Martino *et al*[13], 2011	30	26	24	24	42.8 ± 14.7	Other[1]	Prospective	Italy
Oelschlager *et al*[15], 2003	52	58	46 (1-85)	16 (1-38)	42.6 ± 15.5	Other[2]	Retrospective	United States
Rawlings *et al*[17], 2012	36	24	12	12	48.8 ± 13.0	Other[2]	RCT	United States
Rebecchi *et al*[18], 2008	72	72	125 (60-168)	125 (60-168)	49 (11-80)	Other[1]	RCT	Italy
Richardson *et al*[20], 2006	18	20	37 (2-97)	37 (2-97)	69 (15-80)	Other[2]	Retrospective	United States
Wright *et al*[24], 2007	52	63	46 ± 24	45 ± 17	42.5 (15.4)	Other[2]	Retrospective	United States
Dempsey *et al*[12], 2004	22	29	39 ± 22	26 ± 19	47.5 (12.6)	No	Retrospective	United States
Finley *et al*[14], 2007	71	24	6.9 ± 3.5	6.9 ± 3.5	47.9 (16-84)	No	Retrospective	Canada
Ramacciato *et al*[16], 2005	17	15	12	12	42.0 (14-77)	No	Retrospective	Italy
Richards *et al*[19], 2004	22	21	6	6	50 ± 12.7	No	RCT	United States
Richardson *et al*[20], 2006	18	14	37 (2-97)	37 (2-97)	69 (15-80)	No	Retrospective	United States
Simić *et al*[21], 2010	36	22	36	36	49.6 ± 29.2	No	RCT	Serbia
Tapper *et al*[22], 2008	75	99	8.4 ± 12.0	48.7 ± 34.6	47.0 ± 16.8	No	Prospective	United States
Torquati *et al*[23], 2006	22	21	NA	NA	50 ± 12.7	No	RCT	United States

[1]Other: Nissen fundoplication; [2]Other: Toupet fundoplication. NA: Not available; RCT: Random controlled trail.

Table 3 Quality assessment of random controlled studies in the meta-analysis based on the Cochrane Handbook version 5.1.0

Ref.	Random sequence generation	Allocation concealment	Blinding of participants and personnel	Blinding of outcome assessment	Incomplete outcome data	Selective reporting	Other sources of bias
Rawlings *et al*[17], 2012	Low	Unclear	High	Low	Low	Low	Unclear
Rebecchi *et al*[18], 2008	Low	Low	High	Low	Low	Low	Unclear
Richards *et al*[19], 2004	Low	Low	Low	Low	Low	Low	Unclear
Simić *et al*[21], 2010	Low	Low	High	High	Unclear	low	Unclear
Torquati *et al*[23], 2006	Low	Low	Low	Low	Low	Low	Unclear

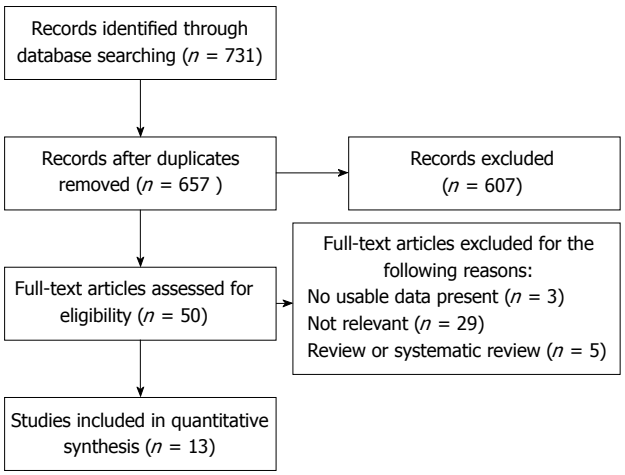


Figure 1 Flow diagram of meta-analysis study selection process.

were unclear in the included RCTs.

In term of the 8 non-RCTs, Table 4 lists the evaluation stars of each study followed by the modified NOS. In the selection of patients, one study included patients without continuity, which could hardly represent the total population[22]. Three studies (two studies reported the same patients group) received no stars in the domain of adequacy of follow-up, with a follow-up of 63.7%[20] and 30% (postoperative manometer), respectively[15,24]. Overall, all studies were evaluated as being moderate to high quality.

Outcomes in the Dor-other group

Primary endpoints: With respect to clinical regurgitation, 3 non-RCTs reported the available number of achalasia patients[13,18,20], and a fixed-effect model was used in the subgroup meta-analysis. Dor fundoplication was appraised to have a significantly higher recurrence rate of clinical regurgitation compared with other types of fundoplication (OR = 7.16, 95%CI: 1.25-40.93, P = 0.03 and heterogeneity I^2 = 0%) (Figure 2A). One study, which did not have an available number of achalasia patients, reported no significant difference in regurgitation frequency score (P = 0.546)[24].

In the pathological acid reflux analysis, 1 RCT and 2 non-RCTs were pooled, and a fixed-effect model was used[13,17,18]. The odds ratio was 3.79 in the Dor fundoplication group compared with the other fundoplication group (95%CI: 1.23-11.72, P = 0.02 and heterogeneity I^2 = 0%).

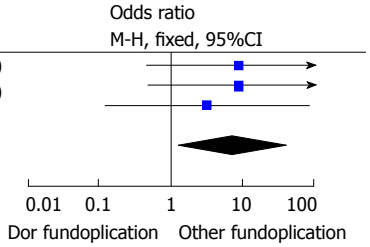
Perforation was estimated in 2 RCTs and 1 non-RCT, and a fixed-effect model was used. The subgroup analysis indicated no significant differences in the Dor-other group (RD = -0.00, 95%CI: -0.04-0.04, P = 0.94, heterogeneity I^2 = 0%) (Figure 2A).

Considering dysphagia, no significant symptom relief benefit was found for Dor fundoplication compared with other types of fundoplication, and a random-effect model was used (OR = 1.19, 95%CI: 0.16-8.67, P = 0.86 and heterogeneity I^2 = 77%) (Figure 2B). One study that lacked information on the number of acha-

A Clinical regurgitation

Study or subgroup	Dor fundoplication Events	Total	Other fundoplication Events	Total	Weight	Odds ratio M-H, fixed, 95%CI
Di Martino *et al*, 2011	4	30	0	26	33.1%	9.00 (0.46, 175.59)
Rebecchi *et al*, 2008	4	71	0	67	34.9%	9.00 (0.48, 170.44)
Richardson *et al*, 2006	1	12	0	12	32.0%	3.26 (0.12, 88.35)
Total (95%CI)		113		105	100.0%	7.16 (1.25, 40.93)
Total events	9		0			

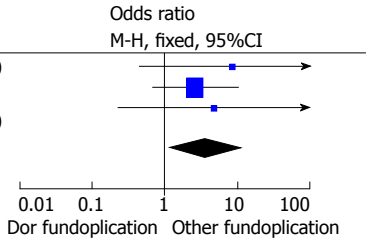
Heterogeneity: χ^2 = 0.26, *df* = 2 (*P* = 0.88); I^2 = 0%
Test for overall effect: Z = 2.21 (*P* = 0.03)



Pathological acid reflux

Study or subgroup	Dor fundoplication Events	Total	Other fundoplication Events	Total	Weight	Odds ratio M-H, fixed, 95%CI
Di Martino *et al*, 2011	4	30	0	26	12.8%	9.00 (0.46, 175.59)
Rawlings *et al*, 2012	10	24	4	19	73.2%	2.68 (0.68, 10.53)
Rebecchi *et al*, 2008	2	71	0	67	14.0%	4.86 (0.23, 103.03)
Total (95%CI)		125		112	100.0%	3.79 (1.23, 11.72)
Total events	16		4			

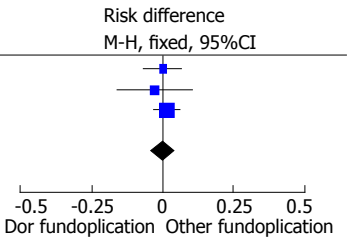
Heterogeneity: χ^2 = 0.60, *df* = 2 (*P* = 0.74); I^2 = 0%
Test for overall effect: Z = 2.32 (*P* = 0.02)



Perforation

Study or subgroup	Dor fundoplication Events	Total	Other fundoplication Events	Total	Weight	Odds ratio M-H, fixed, 95%CI
Di Martino *et al*, 2011	0	30	0	26	21.7%	0.00 (-0.07, 0.07)
Rawlings *et al*, 2012	2	36	2	24	22.4%	-0.03 (-0.16, 0.11)
Rebecchi *et al*, 2008	2	72	1	72	56.0%	0.01 (-0.03, 0.06)
Total (95%CI)		138		122	100.0%	0.00 (-0.04, 0.04)
Total events	4		3			

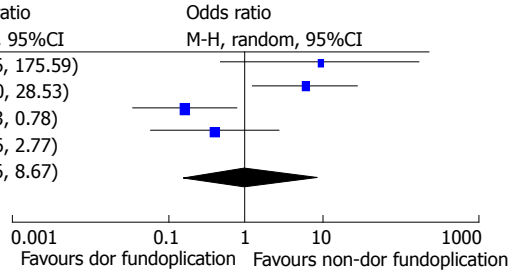
Heterogeneity: χ^2 = 0.46, *df* = 2 (*P* = 0.80); I^2 = 0%
Test for overall effect: Z = 0.07 (*P* = 0.94)



B Other fundoplication

Study or subgroup	Dor fundoplication Events	Total	Other fundoplication Events	Total	Weight	Odds ratio M-H, fixed, 95%CI
Di Martino *et al*, 2011	4	30	0	26	19.1%	9.00 (0.46, 175.59)
Oelschlager *et al*, 2003	9	52	2	58	27.6%	5.86 (1.20, 28.53)
Rebecchi *et al*, 2008	2	71	10	67	27.8%	0.17 (0.03, 0.78)
Richardson *et al*, 2006	2	12	4	12	25.4%	0.40 (0.06, 2.77)
Total (95%CI)		165		163	100.0%	1.29 (0.16, 8.67)
Total events	17		16			

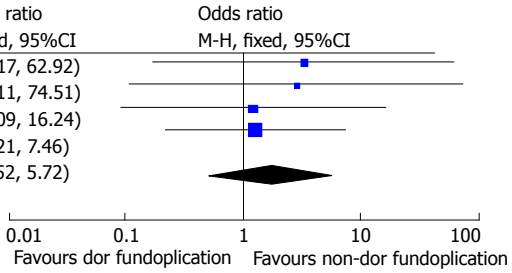
Heterogeneity: Tau^2 = 3.06; χ^2 = 12.91, *df* = 3 (*P* = 0.005); I^2 = 77%
Test for overall effect: Z = 0.17 (*P* = 0.86)



No fundoplication

Study or subgroup	Dor fundoplication Events	Total	Other fundoplication Events	Total	Weight	Odds ratio M-H, fixed, 95%CI
Finley *et al*, 2007	4	71	0	24	15.7%	3.27 (0.17, 62.92)
Ramacciato *et al*, 2005	1	17	0	15	10.9%	2.82 (0.11, 74.51)
Richardson *et al*, 2006-2	2	12	1	7	23.7%	1.20 (0.09, 16.24)
Simić *et al*, 2010	4	36	2	22	49.7%	1.25 (0.21, 7.46)
Total (95%CI)		136		68	100.0%	1.73 (0.52, 5.72)
Total events	11		3			

Heterogeneity: χ^2 = 0.46, *df* = 3 (*P* = 0.93); I^2 = 0%
Test for overall effect: Z = 0.89 (*P* = 0.37)



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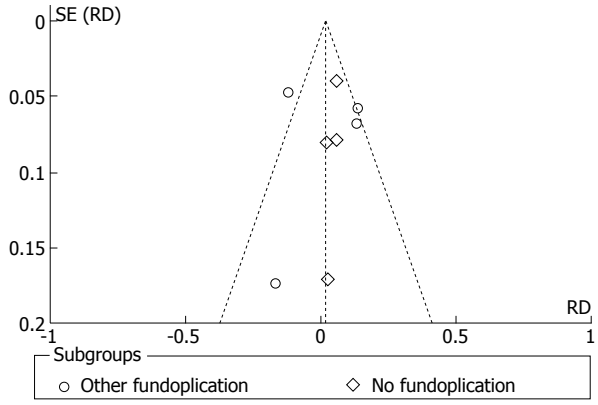

Figure 2 Forest plot. A: Forest plot of the major outcomes in the Dor-other group; B: Forest plot of dysphagia symptoms in both the Dor-other and Dor-no groups; C: Funnel plot of dysphagia symptoms in both the Dor-other and Dor-no groups.

Table 4 Quality assessment of non-random controlled studies in the meta-analysis based on modified Newcastle-Ottawa Scale judgment

Ref.	Selection		Comparability	Outcome assessment		Quality judgment
	1	2	3	4	5	
Dempsey *et al*[12], 2004	*	*	**	*	*	******
Di Martino *et al*[13], 2011	*	*	**	*	*	******
Finley *et al*[14], 2007	*	*	*	*	*	*****
Oelschlager *et al*[15], 2003	*	*	*	*	--	****
Ramacciato *et al*[16], 2005	*	*	*	*	*	*****
Richardson *et al*[20], 2006	*	*	**	*	--	*****
Tapper *et al*[22], 2008	*	--	*	*	*	****
Wright *et al*[24], 2007	*	*	*	*	--	****

Table 5 Pooled outcomes of random controlled studies and non-random controlled studies for postoperative physiological testing and operation-related data

	Studies (*n*)	Participants		Test of heterogeneity		MD (95%CI)	*P* value for effect size
		Dor group	Control group	I^2	*P* value		
LES pressure							
Dor-other group	2	47	43	94%	< 0.0001	-1.02 (-9.90, 7.86)	0.82[1]
Dor-no group	2	58	43	65%	0.09	1.97 (-0.93, 4.86)	0.18[2]
DeMeester score							
Dor-other group	2	40	39	48%	0.17	-7.13 (-18.37, 4.12)	0.21[2]
Dor-no group	1	21	18	Not applicable		-25.00 (-58.40, 8.40)	0.14
Percent total time pH ⩽ 4							
Dor-other group	4	154	142	63%	0.05	0.96 (0.00, 1.91)	0.05[1]
Dor-no group	1	21	18	Not applicable		-7.20 (-13.34, -1.06)	0.02
Surgery time							
Dor-other group	3	138	122	14%	0.31	-5.37 (-7.71, -3.03)	< 0.00001[2]
Dor-no group	2	39	36	0%	0.35	24.14 (7.21, 41.08)	0.005[2]
Hospital stay time							
Dor-other group	4	171	176	94%	< 0.00001	0.10 (-0.59, 0.80)	0.77[1]
Dor-no group	1	22	21	Not applicable		0.00 (-0.15, 0.15)	1.00

[1]Random-effect model; [2]Fixed-effect model. RCT: Random controlled trial.

lasia patients reported no significant difference in the dysphagia frequency score and a significant difference in the dysphagia severity score ($P = 0.465$ and $P = 0.003$, respectively)[24]. No publication bias was observed in the funnel plot of studies when reporting dysphagia in the two comparisons (Figure 2C).

Secondary endpoints: In regards to the other symptoms, one study reported bloating, chest pain, and heartburn recurrence frequency score without any significance difference in the Dor-other group[24]. With regard to quality of life, one multicenter RCT assessed the outcome using an SF-36 questionnaire and ten health-related domains[17]. No significant score difference was observed in the Dor fundoplication group compared with the other fundoplication group in five and seven domains of the total ten domains, respectively. Another prospective study in the Dor-other group reported that the SF-36 score ranged from 0-100, and the two compared types of fundoplication scored 70.5 ± 4.06 and 72.3 ± 4.53 each with a *P* value > 0.5[13].

Postoperative physiologic testing including LES pressure, DeMeester score, and percent total time pH ⩽ 4 displayed no obvious significant difference in the Dor-other group. Considering the relatively high heterogeneity, the random effect model was applied in all three outcomes. In the subgroup analysis of surgery time, Dor fundoplication took significantly less time than the other types of fundoplication, and the estimated hospital stay time was not different in the comparison group. The details are shown in Table 5.

In addition to perforation, other complications were described as follows: Di Martino *et al*[13] reported intra-operatively 1 mucosal tear and 2 cervical subcutaneous emphysema occurrences and postoperatively reported 2 pulmonary atelectasis occurrences in the Dor fundoplication group, intra-operatively 1 pneumothorax occurrence, and postoperatively 1 urinary retention occurrence in the other fundoplication group. Wright *et al*[24] reported 1 urinary retention occurrence in the Dor fundoplication group compared with none in the other fundoplication group. Another 2 studies reported no complications in either group[17,18].

Outcomes in the Dor-no group

Primary endpoints: With respect to clinical regurgitation, two non-RCTs were validly pooled without displaying any significant difference in the Dor-no group (OR = 0.51, 95%CI: 0.09-2.92, $P = 0.32$ and heterogeneity $I^2 = 0\%$)[16,20]. A fixed-effect model was applied in this

analysis. Two studies without an available number of achalasia patients reported no significant differences of dysphagia severity score[14,22].

In the pathological acid reflux analysis, one RCT indicated that Dor fundoplication was associated with an obviously lower pathological acid reflux rate than no fundoplication (OR = 0.11, 95%CI: 0.02-0.59, $P = 0.01$)[19].

Perforation was estimated in 1 RCT and 3 non-RCTs, and a fixed-effect model was used[12,14,16,19]. Subgroups were evaluated with no significant differences in Dor-no group (RD = 0.02, 95%CI: -0.04-0.07, $P = 0.59$ and heterogeneity $I^2 = 0\%$) observed.

Considering dysphagia, no significant symptom relief benefit was found for Dor fundoplication compared with no fundoplication (OR = 1.73, 95%CI: 0.52-5.72, $P = 0.37$ and heterogeneity $I^2 = 0\%$), and a fixed-effects model was used (Figure 2B). Of two studies that did not provide the number of patients, one reported significantly less severe dysphagia in the Dor fundoplication group[22], and the other reported no difference[12].

Secondary endpoints: Concerning other symptoms, there was no obvious difference in heartburn in the Dor-no group in two studies[12,24] and a lower recurrence rate in Dor fundoplication compared with no fundoplication in one study[22]. No significant difference in chest pain was found in 2 studies[12,22], and 1 study reported vomiting without difference and a lower choking rate in the Dor fundoplication group compared with the no fundoplication group[22]. With regard to symptom satisfaction, Dempsey reviewed the consecutive patients with 86% satisfaction in the Dor-no group, which was not significantly different than the Dor group[12]. Tapper and colleagues selectively reviewed their patients and found a slightly higher satisfaction rate in the no fundoplication group compared with the Dor group (89% and 75%, respectively)[22].

Similar to the results in the Dor-other group, postoperative physiologic testing and hospital stay time displayed no obvious significance in the Dor-no group. In addition, Dor fundoplication took significantly more time than no fundoplication on surgery time ($P = 0.005$). Complications were rarely reported in the Dor-no group, except for 2 studies mentioning no complications in this comparison[14,19].

DISCUSSION

Since the description of minimal invasive treatment for achalasia by Shimi *et al*[25], LHM has gained world-wide popularity and is increasingly regarded as the standard treatment for achalasia by surgeons and gastroenterologists. Furthermore, the routine application of fundoplication following LHM has been identified as useful for protection of postoperative GER[4,6,26]. Dor fundoplication, with the advantage of a simple procedure and covering of the mucosa, is being accepted as the first-line type of fundoplication for achalasia in most regions. However, some opponents of Dor fundoplication have reported no significant benefit with regard to the clinical outcomes when Dor fundoplication was added to LHM, and they recommend posterior or even total fundoplication, such as posterior 270° Toupet fundoplication and total 360° Nissen fundoplication, be added to LHM for better long-term outcome[12,27]. Thus, there is no consensus on whether Dor fundoplication is the optimum procedure after LHM for achalasia.

Our group conducted this meta-analysis to provide evidence for fundoplication choice on achalasia surgery. Finally, we found a significantly higher clinical and pathological acid reflux rate in for Dor fundoplication than for other types of fundoplication, although no significant difference was found between Dor fundoplication and no fundoplication. Our results contradict the conventional concept that Dor fundoplication after LHM is the optimal choice for achalasia. However, caution should be taken care to explain the pooled results because of the limitations of our study.

Postoperative GER was the main evaluation used to assess the efficacy of Dor fundoplication for achalasia. GER includes clinical regurgitation symptoms and pathological acid reflux, which was defined as more than 4.2% total time per 24-h period for which pH $\leqslant$ 4 or as a DeMeester score of $\geqslant$ 18 for 24 consecutive hours. Our results demonstrate that Dor fundoplication provides no beneficial clinical regurgitation palliation compared with fundoplication, and, in addition, it leads to a significantly higher clinical regurgitation rate than the other types of fundoplication examined. These results may be explained by the fact that Dor fundoplication may add less resistance than Toupet or Nissen fundoplication, which allows acid to flow through the loose esophagogastric junction more easily. In addition, though the pH testing in two comparison groups indicated no significant difference, the clinical regurgitation symptoms result is supported by the pathological acid reflux outcome, which also demonstrates that Dor fundoplication resulted in more acid reflux than the other fundoplication types. It should be noted that our pooled clinical regurgitation results exclude one study without available data that might affect the outcome[24].

With regard to dysphagia, Dor fundoplication displayed no significant dysphagia relief difference compared with either the other types of fundoplication or no fundoplication. Campos and colleagues suggested that dysphagia relief is independent of whether a fundoplication is performed[2]. Their conclusion is consistent with our pooled outcome that Dor fundoplication did not produce a lower recurrence of dysphagia than the other types of fundoplication, and we also found no obvious difference in postoperative dysphagia when comparing the Dor and Dor-no groups. The relative lack of change in the mucosa fibrosis around the dissected esophagus between the different types of fundoplication may explain this finding, although we have found no significant difference on LES pressure. As the Heller muscle is dissected whether LHM alone or LHM plus fundoplication

is performed, the pressure changes associated with the follow-up procedure may not be significantly different between fundoplication types. Furthermore, a study designed by Rohof on efficacy of treatment for achalasia indicates distensibility of the esophagogastric junction should recommend as better parameter of treatment for achalasia rather than LES pressure[28].

As the most dangerous and latest complication, perforation is the main outcome we focus on. In the pooled outcomes, we failed to find that Dor fundoplication had a lower perforation rate when used for achalasia treatment. As previous studies have reported, perforation was highly related with perioperative therapy, especially pneumatic dilation, and the occurrence is more predicted by the number and duration of dilations[29]. The restricted number of pooled studies and small participant size might decrease the power of these outcomes. In addition, just the fact that observation studies were included may be somewhat responsible for these results.

The surgery time differences can be easily explained by the fact that the more complex surgical procedures and difficulties associated with the other types of complex fundoplication surgeries require more time to perform than Dor fundoplication. The recovery of achalasia patients accounts for many factors: disease itself, surgery, and complications, among others. Our pooled hospital stay time outcome indicates that surgery type has little influence on recovery. Because of the relatively skillful clinicians and the standardized nature of the surgical procedures, no perioperative surgery-related death was found for any surgical type.

Finally, in the sensitivity analysis, the primary pooled estimation of the outcomes is consistent with that of the sensitivity analysis when one study was extracted out, and this result may indicate our pooled results had good quality.

There are some limitations in this meta-analysis: (1) some indirect data acquirement methods were used, such as when dealing with the SD from range; (2) relatively high heterogeneity of data was estimated for the secondary outcomes, especially in postoperative physiological testing. This may be derived from differences in technology used in different regions and countries; (3) RCTs and non-RCTs were pooled for some outcomes because of the lack of available data and studies; and (4) though, we searched for studies without language limitation, the pooled studies were all published in English, which may be responsible for part of the observed heterogeneity.

In summary, we identified a significantly higher recurrence rate of clinical regurgitation and pathological acid reflux for Dor fundoplication than for other types of fundoplication after LHM for achalasia, although no significant difference was found between Dor fundoplication and no fundoplication. Therefore, we conclude that Dor fundoplication after LHM is not the optimum procedure for achalasia and suggest that more attention should be paid on quality of life among different fundoplication approaches.

COMMENTS

Background

Achalasia is generally regarded as an autoimmune esophageal motility disorder resulting from the loss of inhibitory nerve endings in the myenteric plexus of the esophagus, and laparoscopic Heller myotomy (LHM) is commonly used as the main surgical treatment. However, although LHM has been previously shown to have positive long-term outcomes for achalasia patients, gastroesophageal reflux (GER) after LHM is often one of the main failures of treatment.

Research frontiers

In recent years, anterior 180° Dor fundoplication has been recommended after LHM for the prevention of acid reflux. However, LHM alone or LHM plus other types of fundoplication (*e.g.*, posterior 270° Toupet and total 360° Nissen fundoplication) have also been reported to have different benefits compared with LHM plus Dor fundoplication. Thus, there is no consensus on whether Dor fundoplication is the optimum procedure after LHM for the prevention of GER.

Innovations and breakthroughs

Dor fundoplication did not display any obvious benefit in relation to dysphagia and other symptoms versus non-fundoplication or other types of fundoplication surgery. Conversely, the pooled Dor fundoplication results indicated a higher recurrence rate for clinical regurgitation and pathological acid reflux compared with other types of fundoplication (95%CI: 1.25-40.93, and $P = 0.03$ and 95%CI: 1.23-11.72, and $P = 0.02$, respectively), although no significant difference was found between Dor fundoplication and no fundoplication. The results of this meta-analysis indicate that Dor fundoplication after LHM should not be routinely recommended for achalasia.

Applications

This present meta-analysis demonstrates that Dor fundoplication after LHM is not the optimum procedure for achalasia. To prevent postoperative GER, complex types of fundoplication, such as Toupet and Nissen fundoplication, may be added after LHM for the treatment of achalasia.

Peer review

LHM is commonly used to treat achalasia, but GER is a frequent side effect, and an antireflux surgical technique is normally used. The aim of this meta-analysis was to assess Dor-fundoplication compared with non-fundoplication surgical techniques and other types of surgical fundoplication. The paper is well designed and demonstrates the difficulty in assessing and standardizing the published data. The paper is slightly difficult to read, but the graphs and tables facilitate comprehension. This meta-analysis gives the readers relevant reliable data for the selection of fundoplication surgical techniques after LHM.

REFERENCES

1 **Zaninotto G**, Rizzetto C. Endoscopic and surgical management of achalasia. *Eur Surg* 2008; **40**: 146-153 [DOI: 10.1007/s10353-008-0413-1]

2 **Campos GM**, Vittinghoff E, Rabl C, Takata M, Gadenstätter M, Lin F, Ciovica R. Endoscopic and surgical treatments for achalasia: a systematic review and meta-analysis. *Ann Surg* 2009; **249**: 45-57 [PMID: 19106675 DOI: 10.1097/SLA.0b013e31818e43ab]

3 **Lopushinsky SR**, Urbach DR. Pneumatic dilatation and surgical myotomy for achalasia. *JAMA* 2006; **296**: 2227-2233 [PMID: 17090769]

4 **Rosemurgy AS**, Morton CA, Rosas M, Albrink M, Ross SB. A single institution's experience with more than 500 laparoscopic Heller myotomies for achalasia. *J Am Coll Surg* 2010; **210**: 637-645, 645-647 [PMID: 20421021 DOI: 10.1016/j.jamcollsurg.2010.01.035]

5 **Kostic S**, Kjellin A, Ruth M, Lönroth H, Johnsson E, Andersson M, Lundell L. Pneumatic dilatation or laparoscopic cardiomyotomy in the management of newly diagnosed idiopathic achalasia. Results of a randomized controlled trial. *World J Surg* 2007; **31**: 470-478 [PMID: 17308851]

6 **Kashiwagi H**, Omura N. Surgical treatment for achalasia: when should it be performed, and for which patients? *Gen*

Thorac Cardiovasc Surg 2011; **59**: 389-398 [PMID: 21674305 DOI: 10.1007/s11748-010-0765-x]
7 **Mayo D**, Griffiths EA, Khan OA, Szymankiewicz MA, Wakefield CW, Thompson SK. Does the addition of a fundoplication improve outcomes for patients undergoing laparoscopic Heller's cardiomyotomy? *Int J Surg* 2012; **10**: 301-304 [PMID: 22510440 DOI: 10.1016/j.ijsu.2012.04.002]
8 **Hagedorn C**, Jönson C, Lönroth H, Ruth M, Thune A, Lundell L. Efficacy of an anterior as compared with a posterior laparoscopic partial fundoplication: results of a randomized, controlled clinical trial. *Ann Surg* 2003; **238**: 189-196 [PMID: 12894011]
9 **Athanasiou T**, Al-Ruzzeh S, Kumar P, Crossman MC, Amrani M, Pepper JR, Del Stanbridge R, Casula R, Glenville B. Off-pump myocardial revascularization is associated with less incidence of stroke in elderly patients. *Ann Thorac Surg* 2004; **77**: 745-753 [PMID: 14759484]
10 **Wells GA**, Shea B, O'Connell D, Peterson J, Welch V, Losos M, Tugwell P. The Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomised studies in meta-analyses. Available from: URL: http://www.ohri.ca/programs/clinical_epidemiology/oxford.asp
11 **Hozo SP**, Djulbegovic B, Hozo I. Estimating the mean and variance from the median, range, and the size of a sample. *BMC Med Res Methodol* 2005; **5**: 13 [PMID: 15840177]
12 **Dempsey DT**, Delano M, Bradley K, Kolff J, Fisher C, Caroline D, Gaughan J, Meilahn JE, Daly JM. Laparoscopic esophagomyotomy for achalasia: does anterior hemifundoplication affect clinical outcome? *Ann Surg* 2004; **239**: 779-785; discussion 785-787 [PMID: 15166957]
13 **Di Martino N**, Brillantino A, Monaco L, Marano L, Schettino M, Porfidia R, Izzo G, Cosenza A. Laparoscopic calibrated total vs partial fundoplication following Heller myotomy for oesophageal achalasia. *World J Gastroenterol* 2011; **17**: 3431-3440 [PMID: 21876635 DOI: 10.3748/wjg.v17.i29.3431]
14 **Finley C**, Clifton J, Yee J, Finley RJ. Anterior fundoplication decreases esophageal clearance in patients undergoing Heller myotomy for achalasia. *Surg Endosc* 2007; **21**: 2178-2182 [PMID: 17514394]
15 **Oelschlager BK**, Chang L, Pellegrini CA. Improved outcome after extended gastric myotomy for achalasia. *Arch Surg* 2003; **138**: 490-495; discussion 495-497 [PMID: 12742951]
16 **Ramacciato G**, D'Angelo FA, Aurello P, Del Gaudio M, Varotti G, Mercantini P, Bellagamba R, Ercolani G. Laparoscopic Heller myotomy with or without partial fundoplication: a matter of debate. *World J Gastroenterol* 2005; **11**: 1558-1561 [PMID: 15770738]
17 **Rawlings A**, Soper NJ, Oelschlager B, Swanstrom L, Matthews BD, Pellegrini C, Pierce RA, Pryor A, Martin V, Frisella MM, Cassera M, Brunt LM. Laparoscopic Dor versus Toupet fundoplication following Heller myotomy for achalasia: results of a multicenter, prospective, randomized-controlled trial. *Surg Endosc* 2012; **26**: 18-26 [PMID: 21789646 DOI: 10.1007/s00464-011-1822-y]
18 **Rebecchi F**, Giaccone C, Farinella E, Campaci R, Morino M. Randomized controlled trial of laparoscopic Heller myotomy plus Dor fundoplication versus Nissen fundoplication for achalasia: long-term results. *Ann Surg* 2008; **248**: 1023-1030 [PMID: 19092347 DOI: 10.1097/SLA.0b013e318190a776]
19 **Richards WO**, Torquati A, Holzman MD, Khaitan L, Byrne D, Lutfi R, Sharp KW. Heller myotomy versus Heller myotomy with Dor fundoplication for achalasia: a prospective randomized double-blind clinical trial. *Ann Surg* 2004; **240**: 405-412; discussion 412-415 [PMID: 15319712]
20 **Richardson WS**, Kennedy CI, Bolton JS. Midterm follow-up evaluation after a novel approach to anterior fundoplication for achalasia. *Surg Endosc* 2006; **20**: 1914-1918 [PMID: 16960666]
21 **Simić AP**, Radovanović NS, Skrobić OM, Raznatović ZJ, Pesko PM. Significance of limited hiatal dissection in surgery for achalasia. *J Gastrointest Surg* 2010; **14**: 587-593 [PMID: 20033338 DOI: 10.1007/s11605-009-1135-9]
22 **Tapper D**, Morton C, Kraemer E, Villadolid D, Ross SB, Cowgill SM, Rosemurgy AS. Does concomitant anterior fundoplication promote dysphagia after laparoscopic Heller myotomy? *Am Surg* 2008; **74**: 626-633; discussion 633-634 [PMID: 18646481]
23 **Torquati A**, Lutfi R, Khaitan L, Sharp KW, Richards WO. Heller myotomy vs Heller myotomy plus Dor fundoplication: cost-utility analysis of a randomized trial. *Surg Endosc* 2006; **20**: 389-393 [PMID: 16437281]
24 **Wright AS**, Williams CW, Pellegrini CA, Oelschlager BK. Long-term outcomes confirm the superior efficacy of extended Heller myotomy with Toupet fundoplication for achalasia. *Surg Endosc* 2007; **21**: 713-718 [PMID: 17332964]
25 **Shimi S**, Nathanson LK, Cuschieri A. Laparoscopic cardiomyotomy for achalasia. *J R Coll Surg Edinb* 1991; **36**: 152-154 [PMID: 1833541]
26 **Patti MG**, Herbella FA. Fundoplication after laparoscopic Heller myotomy for esophageal achalasia: what type? *J Gastrointest Surg* 2010; **14**: 1453-1458 [PMID: 20300876 DOI: 10.1007/s11605-010-1188-9]
27 **Falkenback D**, Johansson J, Oberg S, Kjellin A, Wenner J, Zilling T, Johnsson F, Von Holstein CS, Walther B. Heller's esophagomyotomy with or without a 360 degrees floppy Nissen fundoplication for achalasia. Long-term results from a prospective randomized study. *Dis Esophagus* 2003; **16**: 284-290 [PMID: 14641290]
28 **Rohof WO**, Hirsch DP, Kessing BF, Boeckxstaens GE. Efficacy of treatment for patients with achalasia depends on the distensibility of the esophagogastric junction. *Gastroenterology* 2012; **143**: 328-335 [PMID: 22562023 DOI: 10.1053/j.gastro.2012.04.048]
29 **Smith CD**, Stival A, Howell DL, Swafford V. Endoscopic therapy for achalasia before Heller myotomy results in worse outcomes than heller myotomy alone. *Ann Surg* 2006; **243**: 579-584; discussion 584-586 [PMID: 16632991]

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