

Whether robot-assisted laparoscopic fundoplication is better for gastroesophageal reflux disease in adults: a systematic review and meta-analysis

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Abstract

Background Although laparoscopic fundoplication is an effective, minimally invasive surgical technique for gastroesophageal reflux disease (GERD) that failed to be treated with medicine, with wide implementation its technical limitations have become increasingly clear. Recently, robot-assisted laparoscopic fundoplication (RALF) was considered a new approach that makes up for the deficiency of conventional laparoscopic fundoplication (CLF). This systematic review aimed to assess the feasibility and efficiency of robot-assisted laparoscopic fundoplication for GERD.

Methods Two reviewers independently searched and identified seven randomized controlled trials (RCTs) and four clinical controlled trials (CCTs) of RALF versus CLF for GERD in the Cochrane database, Medline, Embase, and Science citation index between 2001 and 2009. The main outcomes were operating time, complication rate, hospital stay, and costs. The meta-analysis was performed by Review Manager 5.0 software. The effect size of the clinical outcomes was evaluated by odds ratio (OR), weighted mean difference (WMD), and standard mean difference (SMD) according to different data type. Heterogeneity and sensitivity analysis were used to account for rationality of pooling data and sources of heterogeneity.

Results Of 483 studies found, a total of 11 trials were included in this review; among 533 patients, 198 patients underwent RALF and 335 patients underwent CLF. The results of meta-analysis showed that the postoperative

complication rate (OR = 0.35, 95% CI = [0.13, 0.93], $p = 0.04$) is lower for RALF, but the total operating time (WMD = 24.05, 95% CI = [5.19, 42.92], $p = 0.01$) is longer for RALF compared with those for CLF. Statistically, there was no significant difference between the two groups with regard to perioperative complication rate (OR = 0.67, 95% CI = [0.30, 1.48], $p = 1.00$) and length of hospital stay (WMD = 0.00, 95% CI = [-0.25, 0.26], $p = 0.04$).

Conclusions Systematic review of the literature indicates that RALF is a feasible and safe alternative to surgical treatment of GERD. However, since it lacks obvious advantages with respect to operating time, length of hospital stay and cost, RALF has limitations for its extensive application in clinics.

Keywords Systematic review · Meta-analysis · Gastroesophageal reflux disease (GERD) · Robot-assisted · Laparoscopy · Fundoplication

Gastroesophageal reflux disease (GERD) is one of the most common gastrointestinal diseases and is associated with a broad spectrum of symptoms that may be typical or atypical of the disease and accompanied by erosive esophagitis. The incidence of GERD generally ranges from 10 to 20% in Western countries, whereas the incidence is less than 5% in Asia [1]. Patients with GERD often need to take a proton pump inhibitor (PPI) to relax and control reflux symptoms. It is a cost-effective, long-lasting medicine-based treatment. However, 50% of GERD patients fail to respond to the drug and get symptoms under control; this indicates a need for surgical management [2].

Laparoscopic Nissen fundoplication, first reported by Dallemagne in 1991 [3], is the major effective minimally

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invasive procedure for controlling severe GERD. It has relatively good outcomes, including relief of reflux symptoms and medication dependence, and patient satisfaction according to short- and long-term follow-up [4, 5]. With its wide use in the last decade, conventional laparoscopic Nissen fundoplication (CLF) was seen as the standard surgical treatment for GERD [6, 7]. However, the inherent limitations of this conventional laparoscopic technique have become clear in clinical practice, especially when accurate and fine procedures are required in limited operative space. Clinical study has demonstrated that due to lack of dexterity, lack of tactile sense, magnification of natural tremor, and surgeons with rigid instruments, there is reduced precision and accuracy of the operation [8]. In addition, the two-dimensional visualization caused surgeons to not adapt to the new operative field and have a longer learning curve [9–11]. Finally, poor ergonomic position increased the surgeon's workload during a long procedure [12]. Laparoscopic fundoplication is no exception. To improve the technical limitations of CLF, computer technology was developed and introduced into the field of laparoscopic surgery in the late 1990s. A robot-assisted system could simulate the fluid motions of a surgeon's wrist to overcome the motion limitations of straight laparoscopic instruments and provide a stable camera platform, three-dimensional imaging, and the surgeon with a comfortable, ergonomically optimal operating position [13].

The first robot-assisted Nissen fundoplication (RALF) was reported by Cadiere in 1999 [14]. Three years later, Cadiere published a prospective randomized study on the application of robotics in antireflux surgery and noted that robot-assisted Nissen fundoplication was feasible, but there was no obvious added benefit in the use of this new technique [15]. Since then, some clinical trials of RALF versus CLF for GERD and their clinical results and different conclusions have been described.

Recently, there has been a heated debate about which approach is optimal for GERD. In order to ascertain whether RALF was a safe, effective alternative to CLF, a systematic review of the literature was conducted to evaluate the safety and efficacy of robot-assisted versus traditional laparoscopic fundoplication for the surgical treatment of GERD.

Materials and methods

Study selection

We searched for all comparative studies of RALF versus CLF for GERD through Medline, Embase, Cochrane database, and Science Citation Index without language restriction. Given the paucity of available evidence from

randomized controlled trials (RCTs), clinical controlled trials (CCTs) and comparative trials were included in this review as well. The following terms and search strategy were used: (((Gastroesophageal Reflux OR gastro* reflux disease OR GORD OR GERD) OR laparoscop*) AND fundoplication AND (remote operations OR telerobotics OR computer-assisted OR robot-assisted OR robot assisted OR robotics)). The “*” symbol means all suffix variations of a root word, which differ in different databases. Both the “related-articles” feature of PubMed and references in found articles were also applied to expand the search's scope by hand. All published and unpublished studies comparing RALF with CLF for GERD were included if they met the study selection criteria. Authors were contacted if any missing data were needed for further inclusion and/or analysis. Two reviewers resolved inconsistency of study inclusion by means of full discussion and review. The latest date for updating the search was September 10, 2009.

Data extraction and analysis

Two reviewers independently extracted the following data from each included study: first author, publication date, country, population characteristics, operating time, complication rates, cost, and follow-up. All the extracted data were tabulated and the methodological homogeneity between studies was evaluated (Tables 1–3). The study was not included in the pool if severe heterogeneity was found.

Quality assessment of retrieved trials

Methodological quality of clinical trials was anonymously evaluated by two reviewers independently according to the evidence grade for Evidence-based Medicine from Oxford Centre [16]. The standard is stated as follows: level 1a, systematic review of RCTs; level 1b, individual RCT (with narrow confidence interval); level 2a, systematic review of cohort studies; level 2b, individual cohort study (including low-quality RCT); level 3a, systematic review of case-control studies; level 3b, individual case-control study; level 4, case series; level 5, expert opinion.

Statistical analysis

Meta-analyses were performed for the three primary outcome parameters: operating time, complication rates, length of hospital stay by using Review Manager software (RevMan 5.0) of the Cochrane Collaboration. For dichotomous outcomes (complication rates) and continuous outcomes (operating time and hospital stay), we calculated the odds ratio (OR) and weighted mean difference (WMD) or

Table 1 Baseline characteristics of included studies

Study ref. no.	Year	Study type	Level of evidence	Number		Mean age (years)		BMI (kg/m ²)		Robotic system	Fundoplication	Country	Follow-up (months)
				RALF	CLF	RALF	CLF	RALF	CLF				
[15]	2001	RCT	1b	10	11	40.0	38.0	23.7	28.5	Mona	Nissen	Belgium	–
[31]	2006	RCT	1b	25	25	48.0	52.0	25.6	28.7	Da Vinci	Nissen	Netherlands	6
[25]	2002	RCT	2b	15	15	–	–	–	–	Aesop	Nissen	USA	–
[32]	2006	RCT	1b	25	25	43.0	46.3	25.5	26.1	Da Vinci	Nissen	Italy	12
[30]	2007	RCT	1b	20	20	49.6	50.5	29.2	26.2	Da Vinci	Nissen	Germany	1,12
[27]	2009												
[33]	2006	RCT	1b	9	11	44.0	48.0	25.3	24.8	Da Vinci	Nissen	Belgium	32
[34]	2002	CCT	2b	20	20	49.6	42.9	–	–	Da Vinci	Nissen	USA	6.7
										Toupet			
[26]	2007	CCT	2b	11	11	39	41	25.1 ^a	27.68 ^a	Da Vinci	Nissen	Netherlands	–
[29]	2009	CCT	2b	18	62	57	53	27.2	30.0	Da Vinci	Dor	Germany	48
[28]	2009	CCT	2b	45	135	55	54	28	27.1	Da Vinci	Nissen	Italy	43

RALF robot-assisted Nissen fundoplication, CLF conventional laparoscopic fundoplication; –, not reported

^a BMI: was calculated

Table 2 Quality assessment of included studies

Study ref. no.	Random sequence generation	Allocation concealment	Blinding of participants, personnel, and outcome assessors	Incomplete outcome data	Selective outcome reporting	Free of baseline imbalance	Free of source of founding bias
[15]	Not stated	Unclear	Unclear	Yes	Yes	Yes	Unclear
[31]	Not stated	Unclear	Unclear	Yes	Yes	Yes	Unclear
[25]	Not stated	Unclear	Unclear	Yes	Yes	Yes	Unclear
[32]	Yes	yes	Unclear	Yes	Yes	Yes	Unclear
[27, 30]	Yes	Yes	Yes	Yes	Yes	Yes	Unclear
[33]	Yes	Yes	Unclear	Yes	Yes	Yes	Unclear
[34]	No	No	No	Yes	Yes	Yes	Unclear
[26]	No	No	No	Yes	Yes	Yes	Unclear
[29]	No	No	No	Yes	Yes	Yes	Unclear
[28]	No	No	No	Yes	Yes	Yes	Unclear

Yes = low risk of bias; No = high risk of bias; Unclear = uncertain risk of bias

standard mean difference (SMD) with 95% confidence intervals (CI), respectively. For continuous data that provided only median and range values, mean and SD were calculated by using formulas proposed by Hozo et al. [17]. Heterogeneity between studies was first assessed with χ^2 ($p < 0.01$) and I^2 ($I^2 > 50\%$) by using a fixed-effect model. A random effect model would be used in statistical analysis if heterogeneity was not found and vice versa. Sensitivity and subgroup analyses were simultaneously applied to explore the reasons for heterogeneity as well. In addition, the subgroup analysis was divided into high-quality study (level 1b) and lower-quality study (level 2b). Statistical difference of the overall effect was considered valid when $p < 0.05$. The forest plot was used to show outcome parameters, but the funnel plot was not used to evaluate

publication bias because of the small number of studies included in the meta-analysis. Since certain data were unsuitable for meta-analysis, we assessed only with systematic description.

Results

We first identified a total of 483 comparative studies through combined search strategies. Two reviewers independently excluded 42 reviews and 423 clearly irrelevant articles by browsing titles and abstracts. Eighteen references were retrieved for further assessment. Eleven trials in English met the predefined inclusion criteria and were included in this systematic review. Seven studies, including

Table 3 Standardized data extract form for current systematic review

Study ref. no.	Intervention	No. of cases [n (M/F)]	Total operative time (min)	Setup time	Effective operative time	Perioperation complications (case)	Postoperation complications (case)	In-hospital stay (days)	In-hospital costs (€)	Satisfaction scores	
										Nurse	Surgeon
[15]	RALF	10 (7/3)	76 ± 3.3* (59–130)	–	–	1	0	1.75 ± 0.97* (1–4)	–	–	–
	CLF	11 (8/3)	52 ± 2.0* (45–62)	–	–	0	1	1.85 ± 1.25* (1–18)	–	–	–
[31]	RALF	25 (16/9)	125 ± 25* (80–180)	10 (3–15)	–	4	0	3.5 ± 1* (2–6)	–	–	–
	CLF	25 (17/8)	115 ± 37.5* (60–210)	–	–	9	3	4.5 ± 3* (1–13)	–	–	–
[25]	RALF	15 (–)	–	–	–	–	–	–	–	9.2	9.0
	CLF	15 (–)	–	–	–	–	–	–	–	5.3	5.1
[32]	RALF	25 (19/6)	131.1 ± 18.3 (90–162)	23.1 ± 6.5 (12–39)	78.0 ± 17.5 (48–104)	1	0	3.0 ± 0.9* (2–7)	3157	–	–
	CLF	25 (18/7)	91.1 ± 10.6 (72–16)	–	63.5 ± 13.3 (46–84)	0	0	2.9 ± 0.8* (2–6)	1527	–	–
[27, 30]	RALF	20 (10/10)	88 ± 18 (60–150)	23 ± 5 (14–35)	65 ± 18 (40–130)	1	16	2.9 ± 0.8	3244 ± 512 (1511–3970)	–	–
	CLF	20 (12/8)	102 ± 19 (75–152)	20 ± 3 (15–30)	82 ± 18 (55–130)	2	18	3 ± 0.8	2743 ± 483 (1892–3763)	–	–
[33]	RALF	9 (6/3)	137 ± 12	23 ± 4	–	1	0	4.4 ± 0.2	6973 ± 99	–	–
	CLF	11 (8/3)	96 ± 5	–	–	0	4	4.1 ± 0.3	5167 ± 168	–	–
[34]	RALF	20 (13/7)	133.6 ± 18.5* (99–173)	–	–	–	–	1	–	–	–
	CLF	20 (7/13)	101.8 ± 30.75* (45–168)	–	–	–	–	1	–	–	–
[26]	RALF	11 (7/4)	191	15	176	–	3	–	4363.82	–	–
	CLF	11 (7/4)	155	20	135	–	3	–	3376.35	–	–
[29]	RALF	18 (9/9)	207 ± 45	–	–	0	–	7.2 ± 5.8	–	–	–
	CLF	62 (30/32)	116 ± 63	–	–	1	–	6.3 ± 2.3	–	–	–
[28]	RALF	45 (25/22)	65 ± 15* (40–105)	–	–	1	–	3.04 ± 0.5* (2–4)	–	–	–
	CLF	137 (61/76)	85 ± 14.2* (45–130)	–	–	8	–	3.19 ± 0.67* (2–6)	–	–	–

–, Not reported

* Mean ± SD was calculated

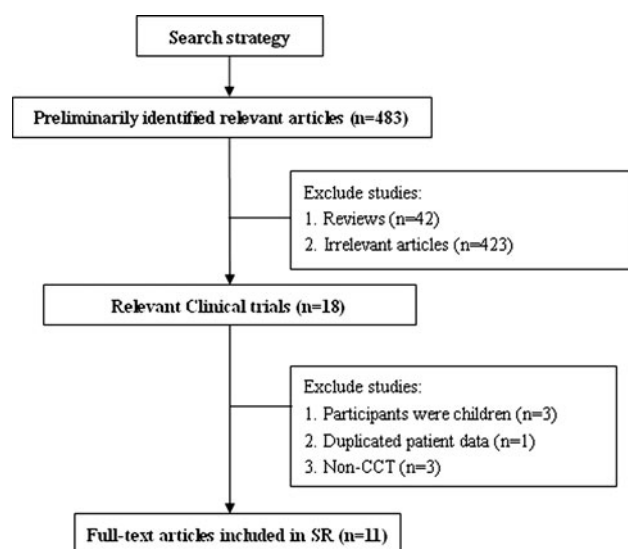


Fig. 1 Search strategy

three children-based trials [18–20], three non-CCTs [21–23], and 1 duplicated study [24] were excluded (Fig. 1).

The 11 included trials were published between October 2001 and June 2009. These trials involved 533 patients, with 198 undergoing robot-assisted surgery and 335 patients undergoing laparoscopic surgery for GERD. The baseline characteristics of the included studies are given in Table 1. Because the remaining trials had similar inclusion and exclusion criteria, a relative homogeneity to the patients recruited was confirmed. Included patients were those with a diagnosis of GERD, age over 16, and eligible for surgical treatment. Patients with a history of previous gastric surgery, giant hiatal hernia, general contraindications for laparoscopy, and psychiatric diseases were excluded from the studies.

There are three RCTs that provided the criteria for relatively adequate methodological information. Morino et al. [32] reported that “computer-generated random numbers” and “sealed opaque envelopes” were used. Muller-Stich et al. [27, 30] provided methodological information that “only patients were blinded” from the full text, and via e-mail they stated: “We performed a computer randomization with differing block sizes. The conceal allocation was with envelopes. Patients and assessors of the follow-up were blinded for the method applied.” Nakadi et al. [33] mentioned “randomized by envelopes” in the original article and “The randomization was done using an informatics random number generator” in an e-mail. Unfortunately, the other three RCTs and four CCTs did not provide methodological information on the randomization method, concealment, and blindedness. The methodological quality of the trials is summarized in Table 2.

A few studies were excluded from meta-analysis of different outcomes for the following reasons: only

satisfaction scores of physician and nurse between HERMES-assisted and non-HERMES-assisted laparoscopic antireflux surgery were evaluated by Luketich et al. [25], median data without range value were given [26], and only outcomes of midterm follow-up were provided [27].

Total operating time

Nine of the 11 included studies reported total operating time [15, 26, 28–34], and one trial was excluded due to lack of SD [26]. In meta-analysis, statistically significant heterogeneity ($I^2 = 98\%$) was observed among eight trials. However, there was no clinical heterogeneity when we thoroughly reviewed the full text of the studies. The subgroup analysis did not reveal any difference attributable to study quality. The results of pooling data with the random-effect model demonstrated that total operating time in the RALF group was 24.05 min longer than in the CLF group (WMD = 24.05, 95% CI = [5.19, 42.92], $p = 0.01$) (Fig. 2).

Setup time

Five articles described their setup time, which was defined as the time from when the patient entered the operating room to the introduction of the first instrument into the abdominal cavity [26, 30–33]. Only one trial provided the setup times, which were 23 ± 5 min and 20 ± 3 min for RALF and CLF, respectively [30]. No statistical difference was found between the two groups ($p = 0.05$). Four other studies provided the setup time for RALF only. Therefore, the data for setup time was not pooled for meta-analysis.

Effective operating time

Three of the 11 studies reported effective operating time, which was defined as the time between the introduction of the laparoscopic instrument and the completion of the last skin suture [26, 30, 32]. The main meta-analysis with the random-effect model illustrated significant heterogeneity between the two groups ($I^2 = 95\%$); thus, meta-analysis was not allowed to summarize the data. Muller-Stich et al. [30] described that effective operating time for RALF was shorter compared with that for CLF (65 vs. 82 min). However, both Morino et al. [32] and Heemskerk et al. [26] reported that more time was needed for RALF (78 vs. 63.5 min and 176 vs. 135 min, respectively).

Perioperative complication rate

Figure 3 summarizes the results of the meta-analysis of the perioperative complication rate. Significant differences were not found in seven studies (OR = 0.67, 95% CI = [0.30, 1.48], $p = 0.32$) [15, 28–33]. Heterogeneity analysis

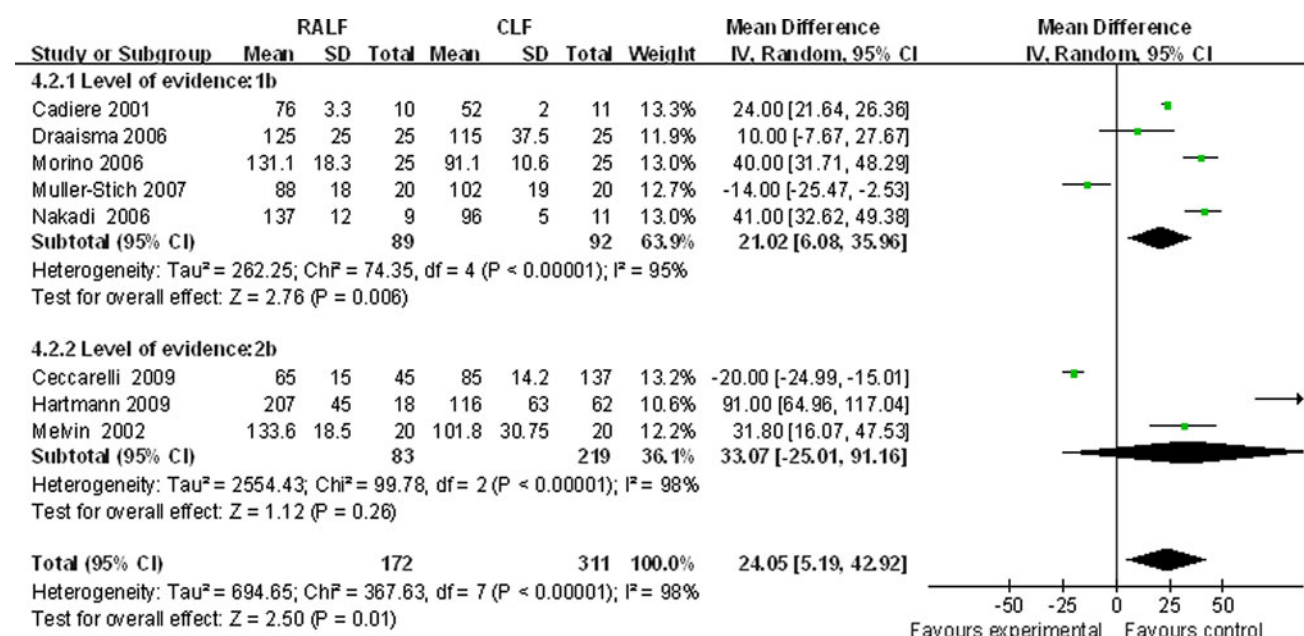


Fig. 2 Meta-analysis of total operating time in RALF vs. CLF

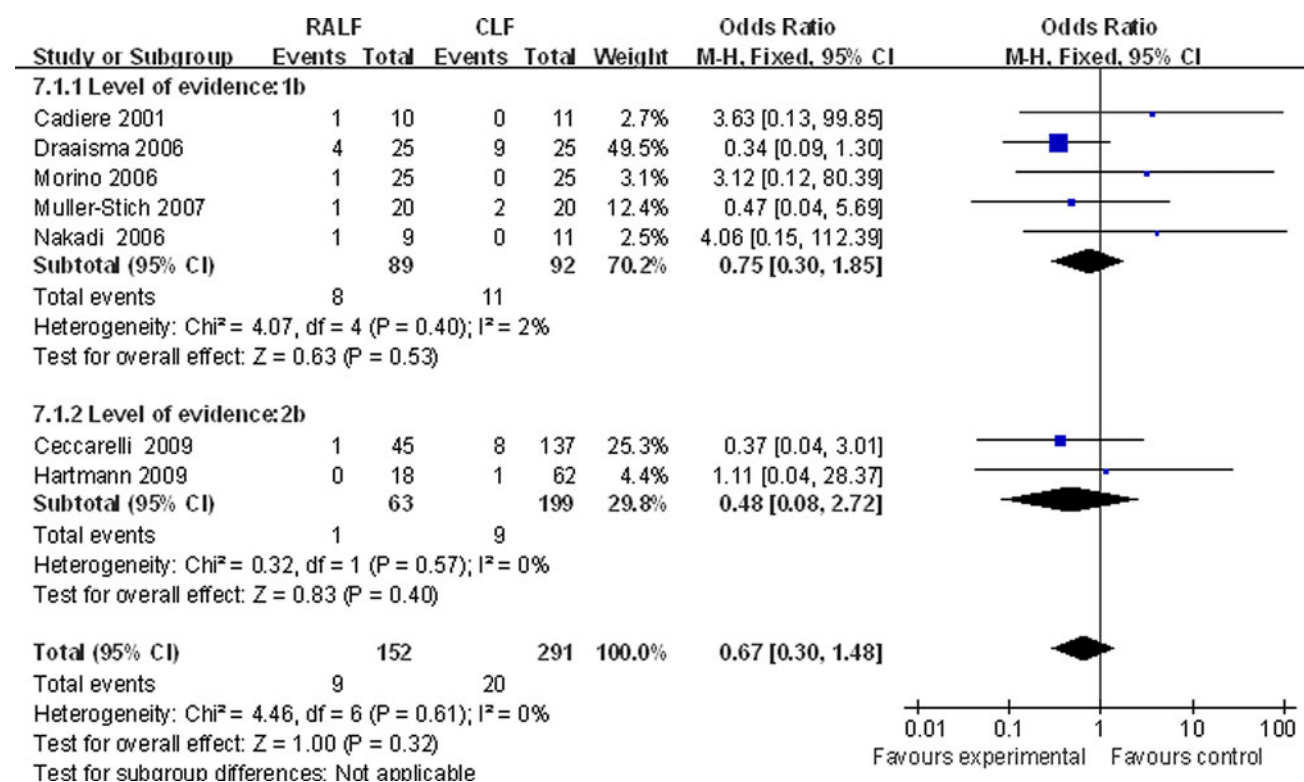


Fig. 3 Meta-analysis of perioperative complication rate in RALF vs. CLF

showed homogeneity ($I^2 = 0\%$) in seven eligible studies. Sensitivity analysis also indicated the stable result with random-effect model. The subgroup analysis also supports the eventual result (Fig. 3).

Postoperative complication rate

Complication after surgery was reported in six publications [15, 26, 27, 31–33]. Muller-Stich et al. [30] described only

Table 4 Summary of complications in included studies

Study ref. no.	Intervention	Patients	Perioperation complications (case)	Details of complication (<i>n</i>)	Postoperation complications (case)	Details of complication (<i>n</i>)
[15]	RALF	10	1	Acute gastric dilation 1	0	–
	CLF	11	0	–	1	Stomach perforation 1
[31]	RALF	25	4	Small liver capsule tears 2, minor bleeding 2	0	–
	CLF	25	9	Pneumothorax 1, small liver capsule tears 4 Small spleen capsule tears 2, conversion to open surgery 2	3	Pneumonia 2, urinary tract infection 1
[32]	RALF	25	1	Conversion to laparoscopic surgery 1	0	–
	CLF	25	0	–	0	–
[27, 30]	RALF	20	1	Pneumothorax 1	16	Mild dysphasia 16
	CLF	20	2	Bleeding 2	18	Mild dysphasia 18
[33]	RALF	9	1	Conversion to laparoscopic surgery 1	0	–
	CLF	11	0	–	4	Dysphasia 2 Flatulence 2
[26]	RALF	11	–	–	3	–
	CLF	11	–	–	3	–
[29]	RALF	18	0	–	–	–
	CLF	62	1	Pneumothorax 1	–	–
[28]	RALF	45	1	Pneumothorax 1	–	–
	CLF	137	8	Liver lobe tear 5, Gastric perforation 1 Pneumothorax 1, spleen injury 1	–	–

–, Not report

mild dysphasia, while five other studies reported moderate to severe complications, which are summarized in Table 4. The results of those studies indicated that the complications rate after surgery by RALF was approximately the same as those by CLF. However, the main meta-analysis with the fixed-effect model indicated a significant reduction of 65% in the relative odds of complication rates for the RALF group compared with those for the CLF group (OR = 0.35, 95% CI = [0.13, 0.93], $p = 0.04$). Heterogeneity is not observed ($I^2 = 0\%$). All six trials that met the predefined inclusion criteria did not report either mortality or treatment-related deaths (Fig. 4; Table 5).

Hospital stay

Seven studies described length of hospital stay [15, 21, 28, 30–33], but one provided only the median so was excluded [34]. Thus, we used seven trials for meta-analysis of length of hospital stay. The random-effect model was applied because of moderate heterogeneity between the two groups ($I^2 = 53\%$). Although two lower-quality studies in the level 2b subgroup increased heterogeneity from 35 to 53%, the result is consistent with that of the level 1b subgroup. The meta-analysis result showed no statistically significant difference, suggesting that the length of hospital stay was

the same for both groups (WMD = 0.00, 95% CI = [–0.25, 0.26], $p = 0.97$) (Fig. 5).

Cost

Four of the 11 studies reported direct medical costs for surgery, including total operative costs, hospital stay expenses, and total costs [26, 30, 32, 33]. There were no other costs (direct nonmedical and indirect costs) stated in the included studies. Total operative costs consisted of personnel, sterilization of reusable instruments, and disposal of instruments, while total costs included total operative costs and hospital stay expenses. Muller-Stich et al. [30] described their direct medical costs, comparing RALF with CLF results. Statistic differences were found for total operative costs and total costs ($p = 0.01$, $p = 0.003$). The results indicated higher costs for RALF than for CLF (€1534 vs. €763 and €3244 vs. €2734, respectively). However, hospital stay costs were similar between RALF and CLF (€1710 vs. €1980). Heemskerk et al. [26] reported that cost consumption was equal between the two groups with increased experience (€4363.82 vs. €3376.35, $p = 0.033$).

The study by Nakadi's group [33] gave relatively good details for costs. Total costs included hospital stay,

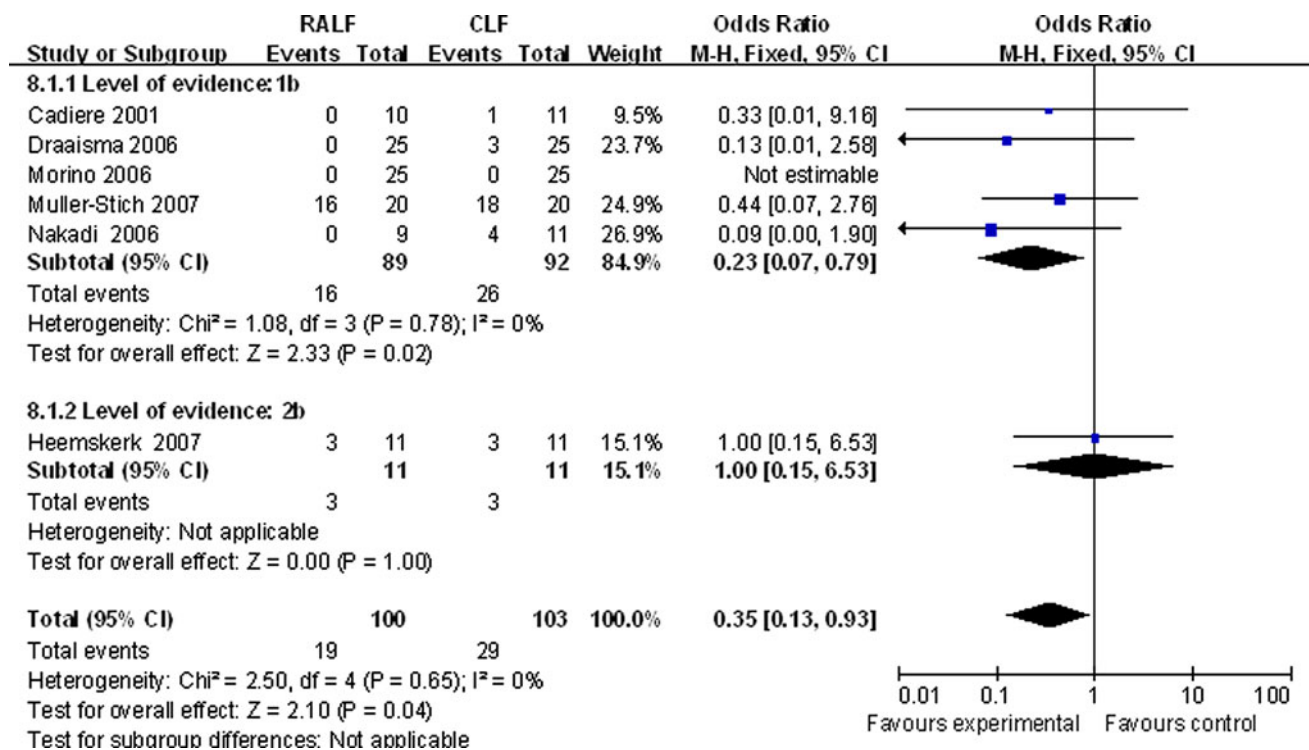


Fig. 4 Meta-analysis of postoperative complication rate in RALF vs. CLF

Table 5 Summary of meta-analysis results of included studies

Outcome	Level of evidence	Studies	Participants	Statistical method	Effect estimate	Overall effect		Heterogeneity	
						Z	p value	p value	I ²
Total operating time	1b	5	181	Mean difference (IV, random, 95% CI)	21.02 [6.08, 35.96]	2.76	<0.001	<0.001	95%
	2b	3	302		33.07 [−25.01, 91.16]	1.12	0.26	<0.001	98%
	Total	8	483		24.05 [5.19, 42.92]	2.50	0.01	<0.001	98%
Perioperative complication rate	1b	5	181	Odds ratio (M-H, fixed, 95% CI)	0.75 [0.3, 1.85]	0.63	0.53	0.4	2%
	2b	2	262		0.48 [0.08, 2.72]	0.83	0.4	0.57	0%
	Total	7	443		0.67 [0.3, 1.48]	1.0	0.32	0.61	0%
Postoperative complication rate	1b	5	181	Odds ratio (M-H, fixed, 95% CI)	0.23 [0.07, 0.79]	2.33	0.02	0.78	0%
	2b	1	22		1.00 [0.15, 6.53]	0	0	Not available	Not available
	Total	6	203		0.35 [0.13, 0.93]	2.1	0.04	0.65	0%
Hospital stay	1b	5	181	Mean difference (IV, random, 95% CI)	0.07 [−0.21, 0.36]	0.5	0.62	0.18	36%
	2b	2	262		−0.15 [−0.33, 0.04]	1.55	0.12	0.45	0%
	Total	7	443		0.00 [−0.25, 0.26]	0.04	0.97	0.05	53%

pharmacy, and surgical procedure. The latter included disposable materials, reused materials, nurse's salary, investment, and maintenance. They also calculated annual costs per patient for the investment and maintenance with a 5-year paying-off period and a 5% per year depreciation. Their study showed that the costs of hospital stay,

pharmacy, and surgical procedure were similar between the RALF and CLF groups (€2249 vs. €2242, €167 vs. €202, and €1553 vs. €1525, respectively). Costs of nurse's salary, investment, and maintenance were greater for RALF, but the costs of disposable and reusable materials were higher for CLF. Overall, in their analysis, total costs were still

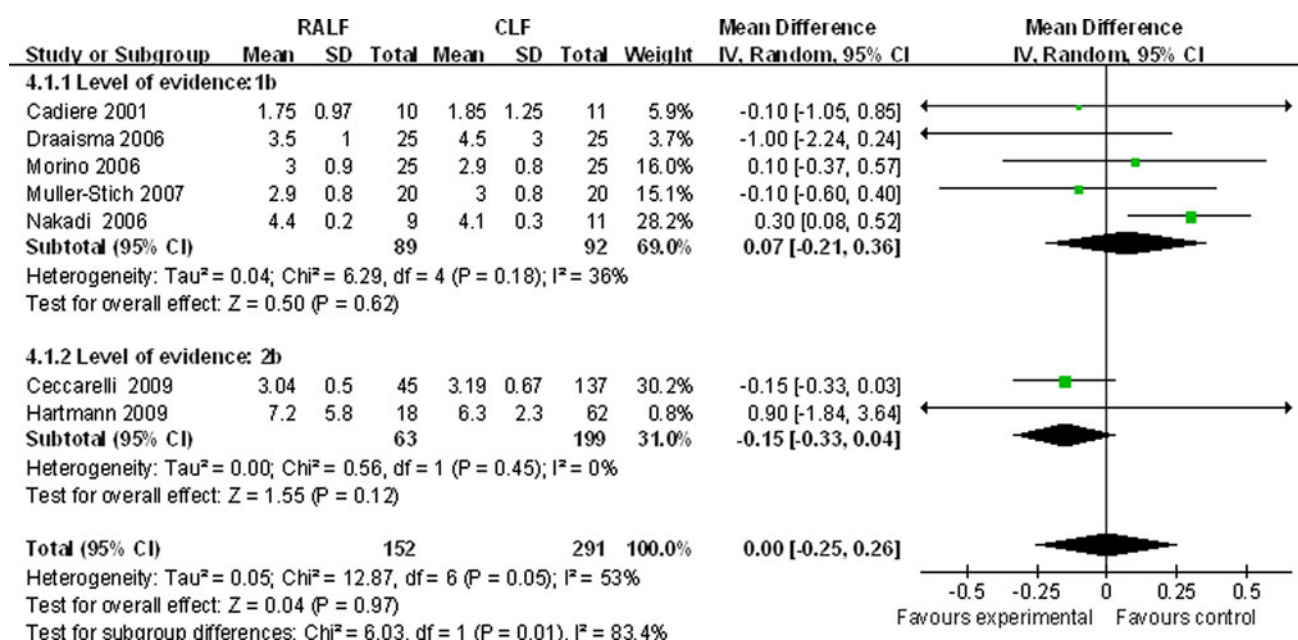


Fig. 5 Meta-analysis of hospital stay in RALF vs. CLF

greater for RALF due to high investment and maintenance fees. Only Morino et al. [32] reported unit costs, while no unit costs were presented in two other studies. Total operative cost was €367 per hour, and hospital stay cost was €300 per hour. The statistic difference was found in disposable instruments and total costs ($p < 0.001$). However, there was no statistic difference in total operative cost and hospital stay expenses.

Follow-up

Of the included trials, eight reported outcomes from follow-up ranging from 1 to 48 months [27–34]. Melvin et al. [34] reported that two cases in each group were lost to follow-up. Half of the 18 CLF patients took daily antisecretory medication during 6 months of follow-up, but none of the 18 RALF patients were observed ($p < 0.001$). There was, however, no difference observed with respect to other outcomes between the two groups. Muller-Stich et al. [30] observed dysphasia scores, endoscopic dilatation, resumed PPI therapy, and mean reflux score at postoperative 1 month. However, there was no statistical difference between two groups. One year later, the authors [27], who observed the Quality of Life in Reflux and Dyspepsia (QOLRAD) score and functional outcomes at the 12-month follow-up, reported that similar effects were concluded from the midterm follow-up. Five other trials also evaluated different outcomes such as 24-h pH, length of stay, esophagitis, and GERD health-related quality of life from 6 to 48 months postoperatively, but the RALF group did not show any additional benefit compared to the CLF group.

Because of the significant clinical heterogeneity of outcome parameters, meta-analysis was not used to pool data.

Discussion

This systematic review and meta-analysis comparing RALF with CLF demonstrated that there is a distinct advantage in RALF group with respect to lower postoperative complication rate, while perioperative complication rate and hospital stay were similar except that RALF had longer total operating time. The robot assistants assessed in this review included Da Vinci, Aesop, and Mona surgical systems.

Meta-analysis showed that total operating time was longer by 24.5 min in the RALF group. This is mainly due to the setup time, the time-consuming trocar placement, the unadapted optical system, and camera motion interrupting the surgeon's procedure [33]. Six studies reported a longer operating time for RALF, while two other trials [28, 30] reported the opposite result. In three trials [31–33], setup time for RALF ranged from 3 to 39 min, while CLF did not need any setup time. Nevertheless, another study [30] reported no difference in setup time between the two groups. The different definitions of setup time may explain this difference. Meta-analysis also showed that the data of effective operating time reported by two studies exhibited significant heterogeneity; therefore, pooled data was not appraised [30, 32]. The former [30] found that a shorter time (65 vs. 82 min) was needed in the RALF group, whereas the latter study [32] stated the opposite result (78

vs. 63.5 min). The shorter operating time for RALF was likely because “one single surgeon, highly experienced in robotic surgery, was responsible for all RALF procedures” [30].

Nissen fundoplication, as the standard surgical treatment for GERD, was utilized in most of the included studies. In general, the complications consisted of those that occurred during and after the operation. Perioperative complications were pneumothorax, blood loss, relevant organic injury, and conversion. Postoperative complications included pneumonia, dysphagia, flatulence, and urinary tract infection. Six studies [15, 26, 30–33] similarly showed that no statistical difference was found with respect to complications during and after surgery. Our pooled data indicated that the postoperative complication rate in RALF was lower than in CLF, while the perioperative complication rate was the same. Six clinical trials demonstrated 9 and 20 complications during surgery in RALF and CLF, respectively. All of the included studies indicated no significant difference between the two groups, which is consistent with the result of the meta-analysis. It is noteworthy that there were two conversions from RALF to CLF because of severe obesity or difficult dissection [32, 33]. Two patients were converted from CLF to open surgery due to severe obesity and left lobe hepatomegaly [31]. This suggests that minimally invasive techniques do not have the capacity to overcome severe obesity. With respect to postoperative complications, six studies reported 16 mild dysphagias and 3 other complications in the RALF group. However, there were only 18 mild dysphagias and 10 other complications in the CLF group. Heemskerk et al. [26] reported three complications in each group, but did not give the specific details. A possible explanation for the lower postoperative complication rate in the RALF group is the greater dexterity and accuracy provided by robotic assistance which may decrease the degree of injury and increase the quality of fundoplication in the narrow subphrenic space.

Hospital stay is an important index, too. One study [34] was excluded from meta-analysis for the reason mentioned above. Although the mean hospital stay varied greatly from 1 to 7 days, all included studies showed similar results with no statistical difference between the two groups. Our meta-analysis result agrees with the authors' viewpoint.

One major advantage of robot assistance is the improvement in the surgeon's operative environment which helps in complicated procedures. Thus, the evaluation of the surgeon's satisfaction is necessary. Unfortunately, the satisfaction score for both surgeon and nurse was reported by only one trial [25]. The results showed that the score given by the staff in RALF was higher than that in CLF (surgeon: 9.2 vs. 5.3, nurse: 9.0 vs. 5.1), but method details were not provided in the study.

Four studies included economic evaluations: direct medical costs of short-term outcomes such as total costs, operative costs, and hospital stay expenses. No article focused on costs of long-term outcomes. In the articles' analysis, both total costs and operating costs in RALF are higher because of longer operating time, higher cost of disposable material, investment, and maintenance. Interestingly, total costs in studies from four different countries in Europe varied significantly. For example, overall costs between RALF and CLF in Italy, Germany, Netherlands, and Belgium were €3157 vs. €1527, €3244 vs. €2743, €4363.82 vs. €3376.35, and €6973 vs. €5167, respectively. The reason for the difference among countries is unclear but could be partly explained by different areas and research time.

Seven RCTs and four CCTs were available for inclusion in this systematic review. Baseline patient characteristics, including age, gender, BMI, and symptoms, were similar in these studies of GERD treatment, suggesting that our results are generalizable. Since our inclusion criteria selected RCTs and CCTs for analysis, the methodology had potential flaws. The majority of the included studies were unclear about sequence generation, allocation concealment, blinding, incomplete outcome data, selective outcome reporting, and other potential threats to validity. Three studies had an adequate randomization method and allocation concealment [30, 32, 33]. However, just Muller-Stich et al. [27] performed a blinded outcomes assessment in their research; this may raise the risk of selection bias [35]. Few studies reported data on setup time, effective operating time, satisfaction score, and cost. The shortage of available data restricted the evaluation of the relative efficacy of RALF versus CLF. In addition, the follow-up in eight studies had distinct drawbacks. The time of follow-up ranged from 1 to 48 months and outcomes varied greatly so we could not pool data for meta-analysis.

Overall, the current available evidence from this study remains somewhat limited because of the small number of RCTs and small sample size. With the widespread use and update of RALF, additional randomized clinical trials in accordance with the CONSORT statement revised in 2001 should have a larger sample size, should be multicentered, and particularly focus on long-term follow-up and satisfaction scores of all participants. On account of the limitation of the evidence presented here, our conclusion is only for reference in clinical practice.

The current systematic review indicates that the lower postoperative complication rate with RALF is further proof that robot assistance is a feasible and safe alternative to surgical treatment of GERD. Indeed, it is undeniable that there is no clear advantage to using a robotic assistant because of prolonged operating time and high cost, which limit extensive application of RALF in the clinic.

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