Robot-Assisted Laparoscope Fundoplication for Gastroesophageal Reflux Disease: A Systematic Review of Randomized Controlled Trials

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Key Words

Robotics · Laparoscopy · Fundoplication · Gastroesophageal reflux disease

Abstract

Objective: To evaluate the efficacy and safety of robot-assisted fundoplication (RAF) for treating gastroesophageal reflux disease (GERD). **Methods:** Randomized controlled trials (RCTs) or quasi-RCTs were searched for in PubMed, EM-BASE, the Cochrane Library, SCI, Chinese Biomedical Database, China Academic Journals Full-Text Database, Chinese Scientific Journals Database, China online journals, and related journals. We evaluated the quality of the included studies by using the 5.0.1 Cochrane Handbook standards and analyzed the data using the Cochrane Collaboration's RevMan 5.0. **Results:** Five studies (n = 181) were included. A meta-analysis showed that besides the time taken to carry out fundoplication ($p < 0.00001$), both RAF and conventional laparoscopic fundoplication (CLF) were similar in postoperative antisecretory medication ($p = 1.0$), intraoperative conversion to open surgery ($p = 0.94$), postoperative dysphagia ($p = 1.0$), pneumothorax ($p = 1.0$), total intraoperative complications ($p = 0.24$), the time of hiatal dissection ($p = 0.98$), the time of incision to completion of sutures ($p = 0.95$), total operation time ($p = 0.16$), hospital stay ($p = 0.97$), and total cost ($p = 0.25$). **Conclusions:** The current evidence dem-

onstrates that RAF is safe and effective in treating GERD. The weakness of this treatment method is that it prolongs the time necessary to carry out fundoplication. However, RAF should be the future trend for treating GERD.

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Introduction

Gastroesophageal reflux disease (GERD) is one of the most common health problems, and it affects more than 50% of the world's population [1]. Both medical and surgical treatments have shown outstanding results in treating this disease [2]. At present, the routine treatment is the administration of proton pump-inhibiting drugs. Antireflux surgery appears to be an interesting treatment alternative because of the adverse effects and the unwillingness of some patients to be involved in long-term medical therapy. Typically, conventional laparoscopic fundoplication (CLF) is the preferred surgical option. However, as attractive as minimally invasive surgery is, there are several limitations that CLF has as traditional laparoscopy.

First, it is limited by 2-dimensional imaging and restricted instrument motion, and it leads to ocular fatigue, headaches, and nausea in surgeons [3–6]. Second, haptic feedback (force and tactile), natural hand-eye coordina-

tion, and dexterity are not necessary. Third, physiologic tremors of the surgeon are readily transmitted through the length of rigid instruments. These limitations make more delicate dissections and anastomoses difficult [7].

During the last few years, 'experimental approach' minimally invasive robot-assisted surgery has continued to expand into more and more realms of surgery. The motivation to develop surgical robots is rooted in the desire to overcome the limitations of current laparoscopic technologies and to expand the benefits of minimally invasive robot-assisted surgery. For example, the benefits include three-dimensional images, which allow surgeons to operate with superior visibility; furthermore, the robotic system has a 360° range of motion, maintains steadiness, and uses more sophisticated surgical tools with greater degrees of freedom [8]. Since the first report of robot-assisted fundoplication (RAF) published in 1997, computer-assisted fundoplication has become increasingly popular. Consequently, more authors have reported their experience with these devices in antireflux surgery [9]. But controversy remains regarding the preferred surgical technique for the treatment of GERD.

Current studies show that some people think that RAF has emerged as a promising technical innovation [10, 11]. On the other hand, others say it adds to the operation time and increases the cost [12–15]. The tangible benefits of integrating robotics into surgical fundoplication practice remain unclear. To explore this issue, we use the method of the Cochrane systematic review to conduct a comprehensive evaluation of the relevant trials in order to provide the best clinical evidence.

Methods

Search Strategy and Selection Criteria

We searched PubMed (1966 to Nov. 2008), EMBASE (1974 to Nov. 2008), the Cochrane Library (issue 4, 2008), SCI (1974 to Nov. 2008), Chinese Biomedical Database (1978 to Nov. 2008), China Academic Journals Full-Text Database (1994 to Nov. 2008), Chinese Scientific Journals Database (1989 to Nov. 2008), and China Online Journals (1997 to Nov. 2008) for English language articles using the format: '(telerobotics OR remote operation* OR robot*) AND (laparoscopi* OR peritoneoscop* OR celioscop* OR laparoscopic surgical procedure* OR laparoscopic surger*) AND (fundoplication OR nissen operation OR gastroesophageal reflux disease OR gastro esophageal reflux OR gastro oesophageal reflux OR GER*)'. We also searched some journals that are devoted to laparoscopy and GERD. In addition, we contacted investigators and experts for ongoing and unpublished studies, and scanned references listed in primary studies, review articles, and textbook chapters.

Searches were conducted independently by Dr. Zhang and Dr. Tian. Reference lists from all relevant articles were reviewed to identify additional studies, and the final bibliography was distributed to experts in the field to identify missing or unpublished studies.

We included all randomized controlled trials (RCTs) or quasi-RCTs if they described using RAF versus CLF for the treatment of GERD and reported the surgical complications, operation time, total cost, duration of hospital stay, and other relevant information. All the participants in this study suffered from operable pathologic gastroesophageal reflux which was documented by stereoscopy, 24-hour pH measurements, barium swallow, and esophageal manometry. Studies without raw data available for retrieval and a clearly defined type of dissection were excluded.

Quality Assessment and Data Extraction

The methodological quality of each study was assessed by Dr. Tian and Dr. Sun, using adapted criteria from the Cochrane Handbook version 5.0.1 from the Cochrane Collaboration guidelines [16]. Two reviewers (Dr. Tian and Dr. Li) independently assessed these trials for eligibility and extracted data. Disagreement was solved by discussions with Dr. Yang.

We acquired additional information by interviewing the original authors via telephone. Data was obtained from authors, institutions, study design, patient characteristics, date of publication, and technical features of the studies.

Statistical Analysis

Meta-analyses were carried out by using Review Manager Software (RevMan, version 5.0) provided by the Cochrane Collaboration [17]. If there was no statistically significant heterogeneity in a given set of data, the fixed effects model was used for meta-analysis. If the results of trials showed heterogeneity, the random effects model was used. Statistical heterogeneity between studies was evaluated using the χ^2 test and the I^2 statistic. Potential causes of heterogeneity were explored by carrying out sensitivity and subgroup analyses. Results were expressed as relative risk or mean difference with 95% confidence intervals (CI). $p < 0.05$ was considered statistically significant.

Results

A total of 130 studies were identified using the above-mentioned search strategy, and 125 articles which did not meet the inclusion criteria were subsequently excluded. The baselines of each trial were comparable. Figure 1 details the selection process. A total of 5 studies were included [11–15]. Table 1 shows the characteristics of the studies included in this systematic review. Table 2 includes the quality assessment of studies.

Primary Analysis

Surgical Complications

The fixed effects model was used because there was no heterogeneity in these data sets: postoperative antisecre-

Fig. 1. Selection of study.

tory medication ($I^2 = 0\%$, $p = 0.45$), intraoperative conversion to open surgery ($I^2 = 13\%$, $p = 0.32$), postoperative dysphagia ($I^2 = 0\%$, $p = 0.78$), pneumothorax ($I^2 = 0\%$, $p = 0.33$), and total intraoperative complications ($I^2 = 0\%$, $p = 0.82$). The results showed that there were no significant differences in postoperative antisecretory medication (OR = 1.0, 95% CI: 0.23, 4.29; $p = 1.0$), intraoperative conversion to open surgery (OR = 1.05, 95% CI: 0.23, 4.74; $p = 0.94$), postoperative dysphagia (OR = 1.0, 95% CI: 0.36, 2.74; $p = 1.0$), pneumothorax (OR = 1.0, 95% CI: 0.14, 7.33; $p = 1.0$), and total intraoperative complications (OR = 0.49, 95% CI: 0.15, 1.62; $p = 0.24$) between RAF and CLF (fig. 2).

Operation Times

Figure 3 shows the data for the time necessary to carry out fundoplication ($I^2 = 24\%$, $p = 0.25$) for RAF and CLF, respectively. Two studies [12, 15] were included. The

result showed that RAF prolonged the time necessary to carry out fundoplication [weighted mean difference (WMD) = 3.17, 95% CI: 2.33, 4.00; $p < 0.00001$].

Figures 4–6 show that the data for the time needed for hiatal dissection ($I^2 = 82\%$, $p = 0.02$), the time from incision to completion of sutures ($I^2 = 95\%$, $p < 0.0001$), and the total operation time ($I^2 = 97\%$, $p < 0.00001$) exhibited heterogeneity. For this reason the random effects model was used. The results showed that there were no significant differences in the time needed for hiatal dissection (WMD = -0.10 , 95% CI: -7.25 , 7.09 ; $p = 0.98$), the time from incision to completion of sutures (WMD = -1.04 , 95% CI: -31.31 , 29.82 ; $p = 0.95$), and total operation time (WMD = 22.65 , 95% CI: -8.68 , 53.99 ; $p = 0.16$) between RAF and CLF.

Hospital Stay

Figure 7 shows that the data for duration of hospital stay exhibited heterogeneity ($I^2 = 84\%$, $p = 0.01$); thus the random effects model was used. The results (WMD = -0.01 , 95% CI: -0.70 , 0.67 ; $p = 0.97$) showed there was no significant difference between RAF and CLF.

Total Cost

Figure 8 shows that the data for total cost were heterogeneous ($I^2 = 96\%$, $p < 0.00001$); thus, the random effects model was used. The results (standardized mean difference = 6.39 , 95% CI: -4.61 , 17.39 ; $p = 0.25$) showed that there was no significant difference.

Discussion

This systematic review has demonstrated the apparent feasibility of the robotic procedure. The pooled results of the 5 RCTs showed that no differences were demonstrated between patients who had RAF and CLF regarding surgical complications, time needed for hiatal dissection, time from incision to completion of sutures, total operation time, hospital stay, and total cost. But at the same time, there seem to be some disadvantages, such as prolongation of fundoplication.

Robot-assisted laparoscopic surgery is one of the latest approaches in the evolution of endoscopic surgery. RAF in patients with GERD has been a controversial issue for many years, and several studies have also shown the feasibility and safety of RAF [18–28]. Surgical complications would be the most important outcome of our review. However, there was no clinically significant difference between the surgeries. The reason for this is probably that

Table 1. Basic information of the studies

Study	Body mass index		Cases		Age, years		Sex (male/female)		Outcomes
	RAF	CLF	RAF	CLF	RAF	CLF	RAF	CLF	
Müller-Stich et al. [11], 2007	29.2 (5.83)	26.2 (3.4)	20	20	49.6 (12.0)	50.5 (12.4)	10/10	12/8	operation time, operation costs, complications, hospital stay
Morino et al. [12], 2006	25.5 (2.9)	26.1 (2.3)	25	25	43.0 (12.8)	46.3 (11.3)	16/9	17/8	operation time and costs, complications, postoperative 24-hour pH
Draaisma et al. [13], 2006	25.6 (19.1–37.2)	28.7 (19.5–46.6)	25	25	48.0 (20–74)	52.0 (27–71)	16/9	17/8	operation time, blood loss, complications, hospital stay
Cadière et al. [14], 2001			10	11	40 (29–62)	38 (18–52)	7/3	8/3	operation time, blood loss, complications
Nakadi et al. [15], 2006	25.3 (1.2)	24.8 (0.7)	9	11	44 (4)	48 (4)	6/3	8/3	length of stay, operation time, operation costs

Table 2. Methodological quality of included studies

Study	Assessing risk of bias					
	sequence generation	allocation concealment	blinding	incomplete outcome data	selective outcome reporting	other potential threats to validity
Müller-Stich et al. [11], 2007	unclear	unclear	single blind	yes	yes	unclear
Morino et al. [12], 2006	random numbers	sealed opaque envelopes	unclear	yes	yes	unclear
Draaisma et al. [13], 2006	unclear	unclear	unclear	yes	yes	unclear
Cadière et al. [14], 2001	unclear	unclear	no	yes	yes	unclear
Nakadi et al. [15], 2006	envelopes	sealed opaque envelopes	no	yes	yes	unclear

RAF has only been used a few times. Therefore, it is necessary to study this surgical method further.

All sorts of studies have been published about robot-assisted abdominal surgery including cholecystectomy [29], adrenalectomy [30], fundoplication [12–15, 31], and colonic resection [32]. They all have reported that operating time was prolonged. In our study, the prolonged fundoplication time, as indicated by meta-analysis, may be due to the unadapted length of ports in obese patients, inefficient placement of ports, camera motion interrupting the operative procedure, and the unadapted optical system with an absence of a large general view of the operative field, which prevents a safe continuous dissection and necessitates slow manipulation. Also, the technology used by different doctors was not always exactly the same.

The heterogeneity of the data for the time needed for hiatal dissection, the time from incision to completion of sutures, and total operation time may be caused by a lack of familiarity with the technology. The heterogeneity of the data for the length of the hospital stay could be due to different standards for discharge at different hospitals. Every study [11–15] reported that RAF increased total cost compared with CLF, but the results showed that there was no significant difference between the two groups. The heterogeneity of the data of total cost could be caused by different commodity prices. Higher operation cost can be due to the greater expense and consumption of operating room resources such as space and the availability of skilled technical staff, and expensive semi-disposable instruments, which can only be used for a pre-defined number of procedures.

Fig. 2. Surgical complications (person). RNF = Robotic-assisted Nissen fundoplication; LNF = laparoscopic Nissen fundoplication; M-H = Mantel-Haenszel.

Fig. 3. Fundoplication time (minute). IV = Inverse variance.

Fig. 4. Hiatal dissection time (minute). Abbreviations explained in legends to figures 2 and 3.

Fig. 5. Time from incision to suture (minute). Abbreviations explained in legends to figures 2 and 3.

Present trials display an evaluation of the clinical drawbacks of RAF. According to our study, the only disadvantage of RAF is that it prolonged fundoplication time. In the future, the present difficulties should be overcome, and RAF will offer significant advantages in

terms of intraoperative maneuverability and handling. Under these circumstances, complex surgical procedures will be performed easily and accurately. With the development of new instruments, better positioning, a more suitable length of trocars, an independent optical com-

Fig. 6. Total operation time (minute). Abbreviations explained in legends to figures 2 and 3.

Fig. 7. Hospital stay (day). Abbreviations explained in legends to figures 2 and 3.

Fig. 8. Total cost (Euro). Abbreviations explained in legends to figures 2 and 3.

mand system, a wider field of vision, specially adapted tools for digestive surgery, tactile sensitivity, and force feedback [33], the operation times will most likely be decreased, and also, the operation costs may decrease with a reduction in the price of materials. As familiarity with

the surgery and advances in technology related to the surgery increases, surgical complications will also be reduced.

Postoperative 24-hour pH values, postoperative self-rated change in reflux symptoms, and quality of life

should be important, but they all must be independently reported and evaluated. Only Morino et al. [12] reported that postoperative 24-hour pH values were normalized in all patients, and that there were no significant differences between the 2 groups. Only Draaisma et al. [13] reported postoperative self-rated change in reflux symptoms, and that quality of life improved equally in both groups.

Our review has several limitations. First, the quality of primary studies determines the quality of such reviews, and the studies included in this systematic review had shortcomings in their methodology. Two [12, 15] of the 5 studies included offered adequate descriptions of the randomization process, whereas the other 3 studies [11, 13, 14] failed to describe the method of allocation satisfactorily. Moreover, allocation concealment was specified only in 2 studies [12, 15], and blinding of the outcome assessor was used in only 1 study [11]. This points to possible selection bias and performance bias. In addition, between individual studies, median follow-up and follow-up sequences varied significantly. This incomplete report on follow-up sequences might produce a performance bias. Intention to treat was not used in any trial. Second, because of a shortage of data included in this systematic review, there may be a lack of statistical significance, an

appearance of partial bias, and clinical heterogeneity which may distort our results. Third, a lack of standard commodity prices could result in clinical heterogeneity in terms of price. In addition, the primary emphasis of our review was to provide a short-term outcome to elucidate the value of robotic assistance. Therefore, further trials that focus on long-term outcomes are needed to find potential advantages or disadvantages.

Conclusions

Our study has demonstrated that RAF is safe and effective for treating GERD, but it prolongs the fundoplication time. However, RAF should be the future trend for treatment of GERD. The studies included in this review are limited; therefore, well-designed, large-scale, high-quality RCTs (following the CONSORT criteria) are needed.

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