RESEARCH ARTICLE

Meta-analysis of Outcomes Compared between Robotic and Laparoscopic Gastrectomy for Gastric Cancer

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Abstract

This meta-analysis was performed to evaluate and compare the outcomes of robotic gastrectomy (RG) and laparoscopic gastrectomy (LG) for treating gastric cancer. A systematic literature search was carried out using the PubMed database, Web of Knowledge, and the Cochrane Library database to obtain comparative studies assessing the safety and efficiency between RG and LG in May, 2013. Data of interest were analyzed by using of Review Manager version 5.2 software (Cochrane Collaboration). A fixed effects model or random effects model was applied according to heterogeneity. Seven papers reporting results that compared robotic gastrectomy with laparoscopic gastrectomy for gastric cancer were selected for this meta-analysis. Our meta-analysis included 2,235 patients with gastric cancer, of which 1,473 had undergone laparoscopic gastrectomy, and 762 had received robotic gastrectomy. Compared with laparoscopic gastrectomy, robotic gastrectomy was associated with longer operative time but less blood loss. There were no significant difference in terms of hospital stay, total postoperative complication rate, proximal margin, distal margin, numbers of harvested lymph nodes and mortality rate between robotic gastrectomy and laparoscopic gastrectomy. Our meta-analysis showed that robotic gastrectomy is a safe technique for treating gastric cancer that compares favorably with laparoscopic gastrectomy in short term outcomes. However, the long term outcomes between the two techniques need to be further examined.

Keywords: Meta-analysis - robotic - laparoscopic - gastrectomy - gastric cancer

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Introduction

Gastric cancer is rampant in most countries as the fourth most common cancer and the second leading cause of cancer death in the world (Crew and Neugut, 2006). Surgical resection is considered to be the gold standard and potentially curative treatment for patients with gastric cancer (O'Connor, 1999; Wu et al., 2011). Since the first minimally invasive distal gastrectomy for gastric cancer was reported in 1994 (Kitano et al., 1994), it has been widely accepted for the treatment of gastric cancer. Most of studies reported the efficiency and safety of laparoscopic gastrectomy (LG) (Shuang et al., 2011). Compared with open surgery, LG owns the benefits of lower blood loss, less postoperative pain, shorter hospital stay and lower complications (Ohtani et al., 2010; Vinuela et al., 2012). However, conventional laparoscopic surgery has its own drawbacks, such as unstable video camera imaging, loss of dexterity, amplification of physiologic tremors and the limited motion of instruments. Besides, the learning curve of laparoscopic gastrectomy is steep and long, especially in lymph node dissection (Kang et al., 2010). To overcome these limitations, robot-assisted surgery provides potential countermeasures.

The advantages of robotic surgery include a 3D imagine, convenient movements of the robotic arm, no tremor, and ambidextrous capability (Baik et al., 2009; Kim et al., 2010; Buchs et al., 2011). Robotic surgery is now widely performed in the fields of gynecology, urology and general surgery. Robotic gastrectomy (RG) is able to dissect lymph node precisely and offers some benefits over conventional laparoscopic surgery. Studies on robotic gastrectomy have been widely reported (Song et al., 2009; Hur et al., 2010; Lee et al., 2011; Park et al., 2012; Uyama et al., 2012).

Several studies have been compared the safety and efficiency between RG and LG, and described that RG offered some benefits over LG. However, the proof is still weak and the benefits are controversial. We conducted this meta-analysis by comparative studies between RG and LG regarding to intraoperative outcomes and postoperative outcomes.

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Table 1. Baseline Characteristics of Patients in the Included Studies

Study	Country	Design	No. patients LG/ RG	Quality score
Huang KH 2012	China	retrospective	64/39	5
Hyun MH 2013	Korea	retrospective	83/38	5
Kang BH 2012	Korea	retrospective	282/100	5
Kim KM 2011	Korea	retrospective	861/436	5
Pugliese R 2010	Italy	retrospective	48/16	6
Yoon HM 2012	Korea	retrospective	65/36	5
Zhang XL 2012	China	retrospective	70/97	5

LG, indicates laparoscopic gastrectomy; RG, robotic gastrectomy

Materials and Methods

Search Strategy

A systematic literature search was carried out using the PubMed database, Web of Knowledge, and the Cochrane Library database to obtain comparative studies assessing the safety and efficiency between RG and LG in May,2013. The following searching terms were used: ((gastrectomy OR gastric cancer) AND (robot OR Da vinci OR robot*)) AND (laparoscopic OR laparos*). In addition, in an attempt to broaden the search, the related articles as well as the reference lists were also searched manually for all available articles.

A study included for this meta analysis must meet the following criteria: (1) It was comparative studies between LG and RG with the quantitative outcomes data. (2) If the same institution and/or authors reported more than one study, we enrolled the larger scale number studies or high quality studies. (3) Study was published in English or Chinese. (4) The number of cases was more than 50 in each study. Letter to editorials, comments, meeting papers, review articles and animal experimental studies were excluded.

Data Extraction and quality assessment

Two reviewers extracted the following parameters from each included study independently: first author, year of publication, sample size (RG group and LG group), study design, mean age, body mass index (BMI), intraoperative data (operative time, blood loss) and postoperative data (hospital stay, complication rate) and pathological details (numbers of harvested lymph nodes, distal margin and proximal margin, and hospital mortality rate). Results were verified by reviewers. If discrepancy was present, the authors had a discussion and drew a final decision. The quality of included studies was estimated according to the Newcastle-Ottawa Scale (http://www.ohri.ca/programs/clinical_epidemiology/oxford.asp) and a previously published meta-analysis (Xiong et al., 2012).

Statistical analysis

This meta-analysis was carried out using the Review Manager (RevMan) software, version 5.2. In the included studies, if continuous data described as medians and ranges, using approach reported by Hozo et al. (2005) to calculate means and standard deviations (SD). If continuous data reported only as medians, we excluded this parameter. Continuous variables using weighted mean difference (WMD) and a 95% confidence interval (CI); dichotomous variables was analyzed using odds ratios (OR) and 95% CI. A fixed effect mode or a random effects model mode was applied. Heterogeneity was evaluated by χ^2 and I^2. We considered heterogeneity to be present if the I^2 statistic was >50%, and a random effect model were adopted. However, if I^2 statistic was < 50%, we used a fix effect model. $P < 0.05$ was considered to be significant. Funnel plot was used to evaluate publication of bias.

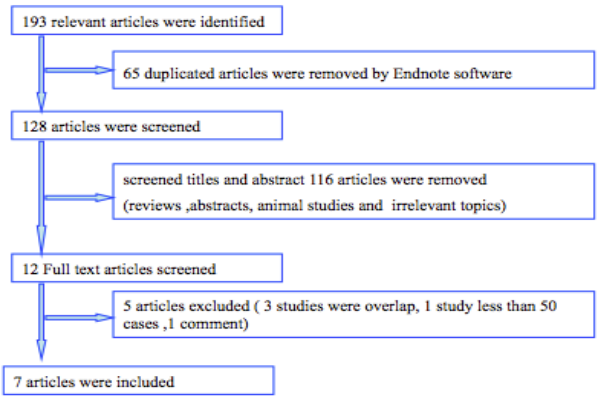

Figure 1. Eligibility Study for Selection

Results

Study Characteristics

A total of 193 potentially relevant articles were identified (Figure 1). By carefully screening titles, abstracts and even full texts, seven retrospective studies (Pugliese et al., 2010; Huang et al., 2012; Kim et al., 2012; Yoon et al., 2012; Kang et al., 2012; Zhang et al., 2012; Hyun et al., 2013) met all inclusion criteria entered in this meta-analysis. In all, our meta-analysis included 2235 patients with gastric cancer, in which 1473 patients had undergone LG, and 762 had undergone RG. Six of the included studies were published in English, and one published in Chinese (Zhang et al., 2012). Four studies were from Korea (Kim et al., 2012; Kang et al., 2012; Yoon et al., 2012; Hyun et al., 2013) and one from Turkey (Pugliese et al., 2010), and two from China (Zhang et al., 2012; Huang et al., 2012). The baseline characteristics and quality assessment of all included studies were listed in Table 1. Six of the included studies mentioned the mean age, sex composition and body mass index (BMI), and one study did not described those variables (Pugliese et al., 2010). In this meta analysis, we found there was no statistical difference in mean sex composition and BMI (Table 2). However, in terms of mean age, we found statistical significance between the two groups (Table 2).

Meta analysis of intraoperative parameters

Operative time and blood loss intraoperative parameters were included for analysis. Six studies which reported of operative time were available for analysis. Pooled analysis of the data showed that the operative time was longer in RG than that of LG, with a high heterogeneity (WMD:-50, 95%CI: -69.93 to -30.07, $P<0.0001$, $I^2=88$) (Table 2).

However, in terms of blood loss, we found RG had

Table 2. Meta Analysis of Outcomes Between Laparoscopic Gastrectomy (LG) and Robotic Gastrectomy (RG)

Outcomes	No. study	No. patients		WMD/OR	95%CI	*P*	I^2
		LG	RG				
Baseline characteristics							
Age	6	1425	746	3.04	-0.02 to 6.11	0.05	86
Gender ratio	6	1425	746	0.86	0.71 to 1.03	0.10	0
BMI	6	1425	746	-0.11	-0.39 to 0.16	0.42	0
Intraoperative outcomes							
Operative time(min)	6	1409	723	-50.00	-69.93 to -30.07	0.00	88
Blood loss(ml)	6	1344	687	46.97	6.12 to 87.83	0.02	98
Postoperative comes							
Hospital stay(d)	5	1326	685	0.50	-0.08 to 1.07	0.09	15
Total complication	7	1473	762	0.88	0.67 to1.17	0.38	0
Anastomosis leakage	6	1425	746	0.92	0.53 to 1.61	0.78	0
Anastomosis stenosis	5	564	310	1.26	0.41to 3.89	0.69	0
Intestinal obstruction	4	1277	672	0.66	0.27to 1.63	0.37	0
Bleeding	4	1296	710	0.70	0.32to1.52	0.37	38
Pathology details							
Harvested lymph nodes	6	1191	662	-1.61	-4.39to 1.17	0.26	85
Proximal margin(cm)	3	218	171	-0.31	-0.80 to 0.18	0.22	0
Distal margin(cm)	3	218	171	0.28	-0.23to0.80	0.28	0
Mortality	3	973	491	0.60	0.16 to 2.26	0.45	0

BMI, body mass index; CI , confidence interval; OR, odds ratio; WMD, weighted mean difference

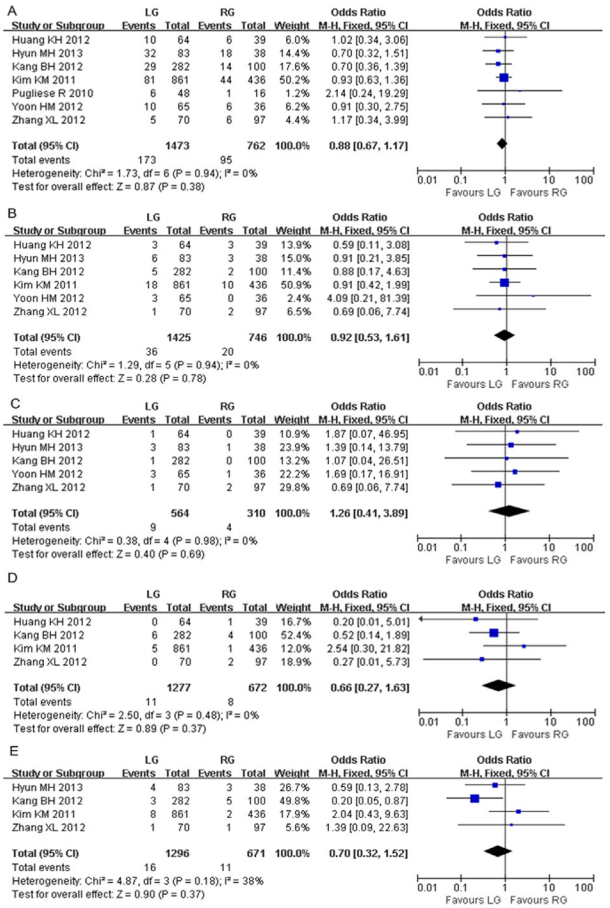

Figure 2. Forest Plot and Meta-analysis of (A) Postoperative Complication, (B) Anastomosis Leakage, (C) Anastomosis Stenosis, (D) Intestinal Obstruction and (E) Bleeding Between Laparoscopic Gastrectomy (LG) and Robotic Gastrectomy (RG). CI, Indicates Confidence Interval; OR, Odds Ratio; M-H, Mantel-Haenszel Method

a benefit of lower blood loss compare to LG, and with a statistical heterogeneity (WMD: 46.97, 95%CI: 6.12 to 87.83, *P*<0.02, I^2=98) (Table 2).

Meta analysis of Postoperative Parameters

According to hospital stay, we noted that RG showed a shorter hospital stay than LG, although there was no statistical difference (WMD: 0.50, 95%CI: -0.08 to 1.07, *P*=0.09, I^2=98) (Table 2). All of the included studies present the total postoperative complication rate. Analysis of this index revealed no significant difference between the two techniques (OR: 0.88, 95%CI: 0.67 to1.17, *P*=0.38, I^2=0) (Table 2, Figure 2A). In all, there were 173 cases adverse effect in 1473 patients who underwent LG (the complication rate accounting for 11.74%), and 95 cases adverse effect in 762 who underwent RG (the complication rate accounting for 12.46%).

In terms of anastomosis leakage, pooled analysis of the data revealed that there was no significant difference between the two groups. In all, 36 cases occurred in 1425 patients who underwent LG and 20 in 746 patients who underwent RG. The incidence was 2.52% and 2.68% respectively. The two groups showed a similar rate (OR: 0.92, 95% CI: 0. 0.53 to 1.61, *P*=0.78, I^2=0) (Table 2, Figure 2B).

According to anastomosis stennosis, 9 cases of anastomosis stennosis occurred in 564 patients in LG group, and 4 cases in 310 patients in RG group, difference had no statistical significance (OR: 1.26,95%CI: 0.41 to 3.89, *P*=0.69, I^2=0) (Table 2, Figure 2C).

In regarding to the intestinal obstruction rate, the two groups showed no statistical difference (OR: 0.66, 95%CI: 0.27to 1.63, *P*=0.37, I^2=0) (Table 2, Figure 2D). In regarding to bleeding, we noted no difference between the two groups (OR: 0.70, 95%CI: 0.32 to 1.52, *P*=0.37, I^2=0) (Table 2 , Figure 2E).

Meta analysis of pathology details

In terms of the proximal margin, distal margin, harvested lymph nodes, the two groups showed no significant difference (Table 2). In terms of mortality rate, there was also no statistical difference (OR: 0.60, 95% CI: 0.16 to 2.26, *P*=0.45, I^2=0) (Table 2) .

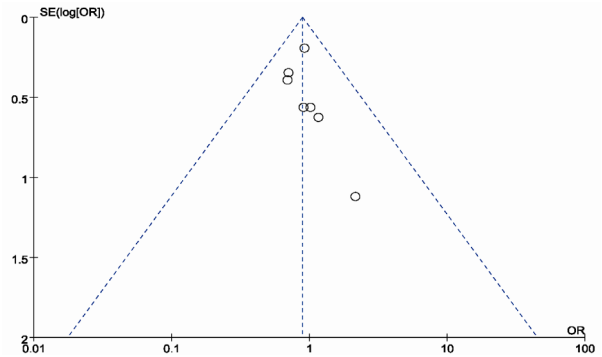

Figure 3. Funnel Plot of Illustrating Postoperative Complication Rate Between Laparocopic Gastrectomy and Robotic Gastrectomy OR, Odds Ratio; SE, Standard Error

Publication of bias

Funnel plot of analysis of the total postoperative complication rate showed no apparently publication of bias. All included studies were inside the 95%CI and symmetrical around the vertical (Figure 3).

Discussion

This meta-analysis included seven studies with a total of 1473 patients who had underwent LG and 762 patients underwent RG. Six studies were published recently (years of publication between 2012 and 2013), one was published in 2010. In addition, one study was reported in Chinese (Zhang et al., 2012). The up-to-date studies might better reflect the current evidence of research. Those included studies were retrospective articles, and none was randomized controlled trials, and thus there may exist publication of bias. However, funnel plots of total postoperative complication rate revealed no obvious publication of bias. Our meta- analysis demonstrated that the blood loss was lower in RG than that in LG, but operative time was longer in RG. There were no significant difference in terms of hospital stay, total complication rate, proximal margin, distal margin, harvested lymph nodes and mortality rate.

As a matter of course, in terms of operation time, it was significantly longer in RG than in LG. and with a high heterogeneity. The difference might come from time of preparing for robotic surgery. Previously studies reported that mean robotic set-up time of robotic surgery was 62.9±24.6 min (Jimenez-Rodriguez et al., 2013). With experience gained, Ironman's P et al. reported that the set up time was reduced rapidly and did not have a significant increase on operating room time (Iranmanesh et al., 2013). And Huang KH et al. showed that the median docking time was reduced by 30 min after 25 cases of learning curve (Huang et al., 2012). Another reason may be from the difference of surgeons' experience. The operation time was inevitably influenced by the surgeon's learning curve. Previous studies reported that the average of operation time was significant longer in the initial RG group than that in the experienced RG group (Kang et al., 2012; Huang et al., 2012). As experience gained, the operative time will be strikingly reduced.

Pooling data of included studies, we found that the blood loss was significant lower in RG than in LG. The reason may be that use of robotic equipments can benefit of surgeons with a broader perspective view to better control the bleeding of small blood vessels. A lower blood loss may reduce the chance of need blood transfusion. Previous study demonstrated that blood transfusion was associated with long-term survival in patients with resectable gastric cancer, and the relation was negatively impact (Kamei et al., 2009). And most studies demonstrated that perioperative blood transfusion increased cancer recurrence (Hyung et al., 2002; Linder et al., 2013). The intraoperative blood loss was lower in RG, which might improve the long term survival of patients who underwent RG.

In regarding to hospital stay, it seemed to be favor to RG, although no statistical difference was found between the two groups (P=0.09). Huang KH et al. described that the median hospital stay was 7d in RG while it was 11d in LG, and there was a significant difference between the two techniques (Huang et al., 2012). More studies should contribute to this issue for final results.

Anastomotic leakage, anastomotic stenosis, postoperative bleeding, intestinal obstruction etc. are the common complications related to gastrectomy (Etoh et al., 2010). Analysis of the pooled data found that total complication rate was similar in RG and LG. Pooled analysis of the data revealed that the two groups did not showed significant difference in terms of anastomotic leakage, anastomotic stenosis, postoperative bleeding, and intestinal obstruction (Figure 2). These results indicated that RG was safe and effective as LG.

As observed in this meta analysis, there were no significant difference in proximal margin, distal margin and harvested lymph nodes between RG and LG. It is no doubt that extended lymph node dissection is the standard of treatment for gastric cancer with a high risk of node metastasis (Hoshi, 2012). However, it is difficult to perform lymph node dissection during LG for those used to performing open gastrectomy (Huang et al., 2012). Previous studies reported that robot-assisted lymph node dissection was feasibility of a precision and bloodless (Uyama et al., 2012). In all, our data revealed that robotic assisted lymph nodes harvested was safe and could achieve an adequate lymph nodes harvested comparable to LG.

Several limitations of our meta-analysis need to be taken into account. First, although our meta-analysis included a large scale of patients, all included studies were retrospective, and none were randomized controlled trials. However, their methodologies were similar in terms of sex composition and BMI but not age. Second, this meta analysis did not analyze the cost between the two techniques due to insufficient data, it is no doubt that the cost in RG is higher than in LG (Eom et al., 2012). The cost in robotic surgery is significant higher than that of laparoscopic surgery for treating rectal cancer (Baek et al., 2012). Third, the follow-up time was relatively short, only one reported 5-years follow up. It showed that the overall 3-year survival was not significantly different between the two groups (Pugliese et al., 2010). The postoperative quality of life and recurrence rate were not well elucidated. Therefore, long-term oncological outcomes should be

further investigated. Finally, we found that there was significant heterogeneity in terms of operating time, blood loss and harvested lymph nodes. Those parameters can influence by surgeon's experience. And most of the studies did not describe whether the surgeons were proficient in RG or LG.

In conclusion, our meta-analysis showed that RG is a safe technique in treatment of gastric cancer that compared favorably with LG in short term outcomes. The advantage of RG was a lower blood loss compared with LG. However, the operative time was longer in RG than that of LG. The long term outcomes between the two techniques need to be further observed.

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