Surg Endosc (2014) 28:2795–2802
DOI 10.1007/s00464-014-3547-1

A meta-analysis of robotic versus laparoscopic gastrectomy for gastric cancer

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Received: 4 February 2014 / Accepted: 11 April 2014 / Published online: 2 May 2014

Abstract
Background Robot-assisted gastrectomy (RAG) for gastric cancer is still a controversial surgical technique for adequate tumor resection, lymphadenectomy, and postoperative outcome.
Methods A meta-analysis analyzed updated clinical trials that have compared RAG with laparoscopy-assisted gastrectomy (LAG) to evaluate whether RAG is equivalent to LAG.
Results Eight studies were included in the analysis, comprising 1,875 patients. RAG was associated with a longer operative time ($p < 0.05$), lower estimated blood loss ($p < 0.05$), and a longer distal margin ($p < 0.05$). RAG can be performed safely with lower estimated blood loss and a longer distal margin than with LAG. Complications, hospital stay, proximal margin, and harvested lymph nodes for RAG and LAG were similar.
Conclusions RAG is as acceptable as LAG for obtaining safe complications and for performing radical gastrectomy.

Keywords Gastric neoplasm · Robot-assisted gastrectomy · Laparoscopy-assisted gastrectomy

The development of laparoscopy-assisted gastrectomy (LAG) for gastric cancer has been ongoing since it was reported by Kitano et al. [1]. The clinical efficacy of laparoscopic radical gastrectomy has now been recognized. A large number of non-randomized trials, randomized controlled trials (RCTs), and meta-analyses comparing laparoscopic with open surgery have confirmed that minimally invasive laparoscopic surgery has obvious advantages [2–8]. Clinical trials have shown that laparoscopic radical gastrectomy has the same long-term effects as open radical gastrectomy [9].

Application of the Da Vinci robotic surgical system has opened up a new era of minimally invasive surgery, with laparoscopic surgery now elevated to a new stage. The da Vinci robotic surgery system has been widely used, for example, in urinary tract, hepatobiliary, cardiovascular, and gynecological surgery [10–13]. Hashizume et al. [14] reported the first robot-assisted gastrectomy (RAG) in 2002, followed by similar reports from China, Korea, Japan, and Italy, among others. Because of the complex technical requirements and expensive equipment, however, the development of RAG has been slow.

During the last 5 years, only one meta-analysis on this topic has been published. The meta-analysis by Xiong et al. [15] contains only three trials. Adequate tumor resection is related to survival and local recurrence rates, which is very important to evaluate surgical techniques. However, only one trial reports surgical margins in that meta-analysis. That may be unreliable and unpowerful. In the meta-analysis by Xiong et al., the authors perform a quality assessment referring to Newcastle–Ottawa Scale (NOS) [16], which is developed to assess the quality of case–control and cohort studies. The evaluation items are not adequate.

This study systematically analyzed high-quality clinical trials that have compared RAG with LAG. There is evidence that pooling of high-quality non-randomized studies

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Presented at the SAGES 2014 Annual Meeting, April 2–5, 2014, Salt Lake City, Utah.

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is as credible as pooling RCTs when comparing clinical surgical outcomes [17]. The meta-analysis allowed clinical outcomes to be quantified for evaluating the advantages of RAG.

Methods

Literature search

A literature search was performed in Pubmed, Embase, and Web of Science databases for clinical research published before May 2013 that compared RAG with LAG. Article language was limited to English. The search used the following terms: gastric neoplasms, robotic surgery, robot-assisted surgery, minimally invasive laparoscopic gastrectomy, or laparoscopy-assisted gastrectomy. The references of all relevant articles were evaluated to find other related studies.

Study selection

Inclusion criteria: (1) Study compared the outcomes of RAG and LAG; (2) Study reported at least one of the following clinical outcomes: complications, harvested lymph nodes, proximal margin, distal margin, hospital stay, operative time, and estimated blood loss; (3) If the same team published more than one article, the latest or the most detailed data were included. Exclusion criteria: (1) Study included recurrent gastric cancer, gastrointestinal stromal tumors, or benign gastric diseases; (2) Study included emergency operation cases; (3) Impossible to extract effective data from the study's defined clinical outcomes.

Data extraction

Two reviewers (W.S.S., H.Q.X) independently extracted relevant data. The following data were extracted from each study: first author, year of publication, type of study, study period, selection criteria, age, sex, body mass index, number of participants, operative factors, short-term outcomes, and pathological parameters.

Assessment of methodological quality of included studies

The quality of the non-randomized studies was assessed using the Methodological Index for Non-randomized Studies (MINORS) scale [18]. To meet the needs of our study, we changed the evaluation criterion of MINORS that referred to a meta-analysis of non-randomized and randomized studies [19] as follows: (1) Two of the 12 items were not considered because they are more suitable for assessing long-term outcomes (follow-up period appropriate to the aim of the study; lost to follow-up <5 %); (2) The item "Prospective calculation of the study size" was modified to assess weight given by the actual number of RAG cases. Scoring was assigned as follows: 0 points for <15 LDG cases; 1 point for >15 but <35 cases; and 2 points for ≥35 RAG cases. We assessed the quality of a study by evaluating ten items. Studies with ≥15 points were considered high quality and were included in the meta-analysis.

Statistical analysis

Stata 12.0 software (StatCorp, College Station, TX, USA) was used for statistical analysis. Harvested lymph nodes, proximal margin, distal margin, hospital stay, operative time, and estimated blood loss were compared using weighted mean differences (WMDs). Complications were compared using odds ratios (ORs). Statistical heterogeneity was evaluated using the χ^2 and I^2 statistics. A value of $p < 0.10$ indicated significance. Generally, a fixed-effect model was used. If the test of heterogeneity was statistically significant, a random-effect model was used. Publication bias was evaluated with the Begg's test. A p value of <0.05 was regarded as significant.

Results

Selected studies

Our search strategy initially retrieved 134 potential articles. After screening the title and abstract, 71 reports were excluded. After reading the abstract, 45 reports were excluded because there was no control group or it was a review, editorial, or case report. After reading the full text, four reports were excluded because there was no control group. Six reports were excluded owing to overlapping patients in multiple studies. Eight studies were eligible for the meta-analysis. The selection process is shown in Fig. 1. The characteristics of the included studies can be found in Table 1 [20–27].

Short-term outcomes

Six studies reported data on the adequacy of the hospital stay. Because of significant heterogeneity ($I^2 = 80.6$ %, $p < 0.1$), a random-effect model was used. There was no difference in hospital stay between the RAG and LAG groups (WMD = −1.00, 95 % CI −2.57 to 0.56, $p > 0.05$) (Table 2). All eight studies reported postoperative complications. There was no significant heterogeneity ($I^2 = 0$, $p > 0.1$), and a fixed-effect model was used. The incidence

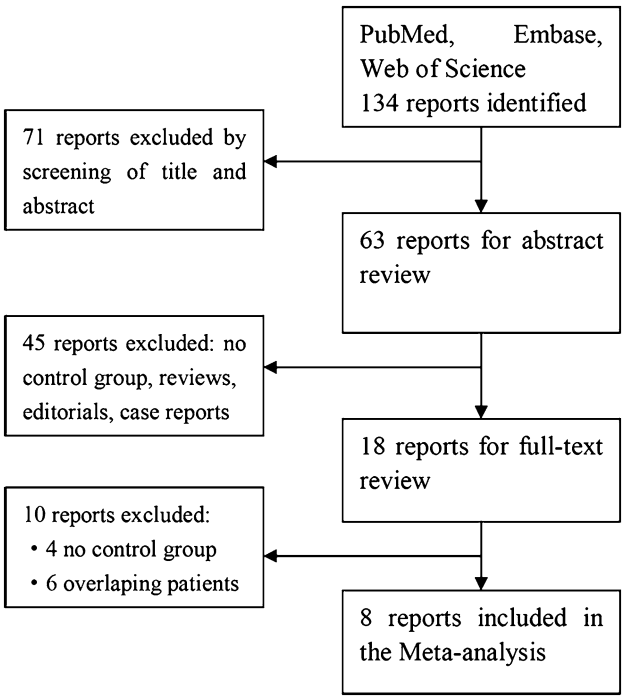

Fig. 1 Identification of eligible studies for the meta-analysis comparing the outcomes of robot-assisted gastrectomy (RAG) with laparoscopy-assisted gastrectomy (LAG)

of postoperative complications was not significantly different in the two groups (OR 0.95, 95 % CI 0.7–1.28, $p > 0.05$) (Fig. 2).

Operative factors

Seven studies reported the operative time. Because significant heterogeneity was observed in seven studies ($I^2 = 86.6$ %, $p < 0.1$), a random-effect model was used. Operating time was longer for RAG than for LAG (WMD = 48.46 min, 95 % confidence interval (CI) 29.49–67.43, $p < 0.05$) (Table 2). The data regarding the estimated blood loss (EBL) were reported in six studies. Because of significant heterogeneity ($I^2 = 93.3$ %, $p < 0.1$), a random-effect model was used. RAG was associated with less EBL than LAG (WMD = −38.43 ml, 95 % CI −67.55 to −9.30, $p < 0.05$) (Table 2).

Pathological parameters

Proximal margin was recorded in three studies. There was no significant heterogeneity ($I^2 = 0$, $p > 0.1$), and a fixed-effect model was used. The proximal margin was not significantly different in the RAG and LAG groups (WMD = 0.1 cm, 95 % CI −0.25 to 0.45, $p > 0.05$) (Fig. 3). Distal margin was recorded in three studies. There was no significant heterogeneity ($I^2 = 0$, $p > 0.1$), and a fixed-effect model was used. The distal margin in RAG was longer than that in LAG (WMD = 1.04 cm, 95 % CI 0.46–1.62, $p < 0.05$) (Fig. 4). Harvested lymph nodes were reported in seven studies. Significant heterogeneity was recognized in the studies ($I^2 = 74.1$ %, $p < 0.1$), so a random-effect model was used. Harvested lymph nodes were similar in the two groups (WMD = 1.06, 95 % CI −2.33 to 4.45, $p > 0.05$) (Fig. 5).

Publication bias

Publication bias was evaluated based on postoperative complications using the Begg's test. There was no publication bias in eight studies ($p = 0.386$). Funnel plot analysis of the studies is shown in Fig. 6.

Discussion

Surgeons have accepted the use of laparoscopic techniques, and they are being used more and more frequently. For example, not only gastrectomy that retains gastric function is performed in patients with early gastric cancer, but also special gastrectomy is being performed laparoscopically combined with endoscopy [28]. There are also many reports on laparoscopic surgery for advanced gastric cancer, with no difference in long-term outcomes between laparoscopic and open surgery [29–32]. Although laparoscopic surgery has a number of advantages, there are also deficiencies, such as the surgeon's postural discomfort, performing a reverse operation, and the possibility of tremor. These factors hinder the use of laparoscopy for complex surgery. Robotic surgery is superior to laparoscopic surgery in that it has wristed instruments, tremor filtration, the ability to scale motion, and stereoscopic vision [33, 34]. These characteristics improve a surgeon's dexterity and allow precise lymph node dissection and intracorporeal anastomoses [35].

The results in our analysis indicated that RAG requires a longer operative time (WMD = 48.46 min, $p < 0.05$). On one hand, the most important reason is that robot-assisted gastrectomy requires "setting and docking" time for the robotic arms, which results in a longer operative time [36]. On the other hand, most studies reported the mean operative times for all their robotic cases. Also, they did not consider the learning curve for RAG, which can increase the operative time. In our meta-analysis, three studies reported that the operative time for RAG decreased between the initial RAG and gastrectomies performed after experience had been gained [21, 25, 27]. Woo et al. [24], whose study contained the largest number of robotic cases, found that the mean operative time was reduced from 233

Table 1 Characteristics of studies included in the meta-analysis

Study	Year	Type of study	Study period	Quality score	Selection Criteria	Group	N	Sex	Age	BMI
Hyun [20]	2013	Retrospective study from a prospective database	2008.6–2010.11	18	cT1N0M0, cT1N1M0, cT2N0M0	RAG	38	25/13	54.2 ± 12.7	23.8 ± 2.6
						LAG	83	55/28	60.3 ± 12.3	23.8 ± 2.9
Kang [21]	2012	Retrospective study from a prospective database	2008.11–2011.3	16	cT1 or T2 and N0 or N1	RAG	100	63/37	53.23 ± 12.06	23.72 ± 3.68
						LAG	282	191/91	58.78 ± 12.40	23.63 ± 3.47
Kim [22]	2010	Retrospective study from a prospective database	2007.12–2008.6	18	Lower than cT2N1M0	RAG	16	10/6	53.8 ± 15.6	21.3 ± 3.4
						LAG	11	10/1	57.9 ± 13.1	25.3 ± 2.5
Yoon [23]	2012	Retrospective study	2009.2–2011.5	17	cT1N0, cT1N1, cT2N0	RAG	36	18/18	53.9 ± 11.7	23.2 ± 2.5
						LAG	65	31/34	56.9 ± 12.3	23.6 ± 3.4
Woo [24]	2011	Retrospective study from a prospective database	2005.7–2009.4	16	cT1N0M0, cT1N1M0, cT2N0M0, cT2N1M0	RAG	236	136/100	54.0 ± 12.7	23.5 ± 3.0
						LAG	591	364/227	58.3 ± 11.6	23.5 ± 3.0
Huang [25]	2012	Retrospective study from a prospective database	2006.1–2012.2	16	Lower than cT2N1M0	RAG	39	19/20	65.1 ± 15.9	24.2 ± 3.7
						LAG	64	43/21	65.6 ± 14.8	24.7 ± 3.3
Pugliese [26]	2010	Retrospective study	2000.6–2009.10	15	Any cTN, M0	RAG	16	–	–	–
						LAG	48			
Uyama [27]	2012	Retrospective study from a prospective database	2009.1–2010.12	16	cT1	RAG	25	14/11	61.6 ± 11.0	22.6 ± 3.1
						LAG	225	156/69	62.6 ± 9.9	22.0 ± 3.1

RAG robot-assisted gastrectomy, *LAG* laparoscopy-assisted gastrectomy

Table 2 Results of meta-analysis of the all outcomes

Outcomes	No. of studies	Heterogeneity		Effect size	95 % CI of effect	*P*
		I^2(%)	*p* Value			
Hospital stay (day)	6	80.6	0.000	WMD = −0.1	−2.57 to 0.56	0.209
Complications	8	0.0	0.571	OR = 0.95	0.7–1.28	0.713
Operative time (min)	7	86.6	0.000	WMD = 48.46	29.49–67.43	0.000
Estimated blood loss	6	93.3	0.000	WMD = −38.43	−67.55 to −9.30	0.01
Proximal margin (cm)	3	0.0	0.950	WMD = 0.1	−0.25 to 0.45	0.564
Distal margin (cm)	3	0.0	0.698	WMD = 1.04	0.46–1.62	0.001
Harvested lymph nodes	7	74.1	0.001	WMD = 1.06	−2.33 to 4.45	0.54

OR odds ratio, *WMD* weighted mean difference

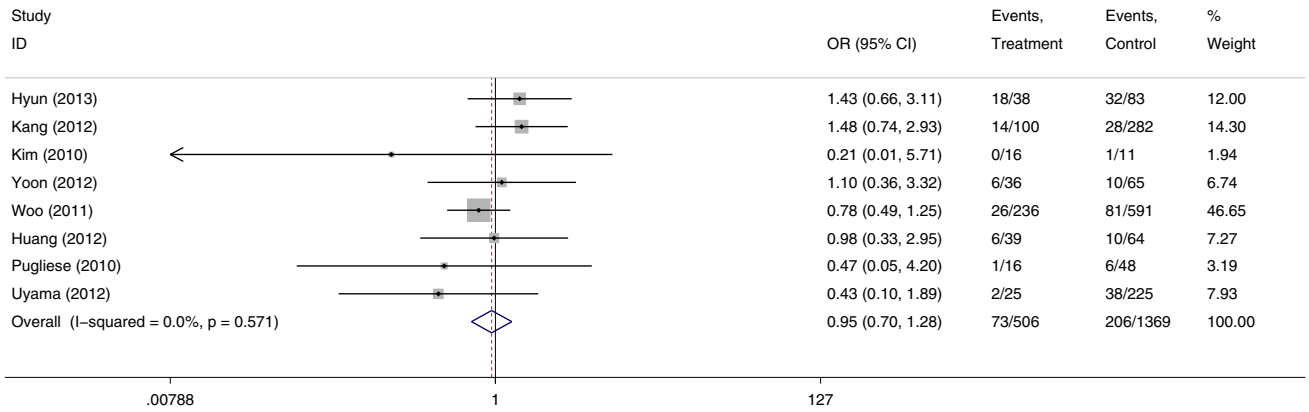

Fig. 2 Meta-analysis of complication rates by robot-assisted gastrectomy (RAG) and laparoscopy-assisted gastrectomy (LDG) shows no difference between the two techniques. Odds ratios (ORs) are shown with 95 % confidence interval (CI)

to 219 min when compared with the previous 100 cases in their study [37]. Therefore, with the development of the Da Vinci robotic surgery system, more experience, and a shortened learning curve, the operative time is mostly often shortened. The meta-analysis indicated that there was less blood loss in the RAG group than in the LAG group (WMD = -38.43 ml, $p < 0.05$). With tremor filtration and stereoscopic vision supplied by the robotic system, a surgeon not only can precisely dissect primary gastric carcinoma and lymph nodes but he or she can also reduce blood loss during the surgery.

According to the studies included in the meta-analysis, six studies performed anastomoses extracorporeally and intracorporeally. Two studies performed anastomoses only intracorporeally. Intracorporeal anastomosis has potential benefits over extracorporeal anastomosis during minimally invasive surgery [38]. Intracorporeal anastomosis is technically difficult and requires a longer time to complete. Robotic systems improve a surgeon's dexterity and are favored for performing intracorporeal anastomoses [35]. Also, with recent technical advancements and stapling devices, robotic is easier than laparoscopic intracorporeal anastomoses. Intracorporeal anastomosis performed with robotic technology is also much faster and simpler than with laparoscopic intracorporeal anastomoses. Therefore, more intracorporeal anastomoses can be accomplished with the robotic system.

Surgical margins are related to survival and local recurrence rates. As a pathological parameter, the proximal margin was similar for RAG and LAG ($p > 0.05$). Moreover, the distal margin was longer in the RAG group ($p < 0.05$). Meta-analysis of seven studies revealed that the number of harvested lymph nodes did not differ significantly between RAG and LAG. From Fig. 5, the mean number of harvested lymph nodes of RAG varies from 25 to 44; the mean number of harvested lymph nodes of LAG varies from 26 to 43. Therefore, the resections of the stomach and lymph nodes appear to be D2 resections. Among these studies, six were reported from eastern countries. One study was reported from Italy. Figure 5 shows that the RAG group had more lymph nodes removed than the LAG groups in every one of the eastern studies. Curative resection for gastric cancer requires adequate extent of lymphadenectomy. RAG has the advantages of dexterity and accuracy over LAG because of a tremor filter, three-dimensional imaging, and an internal articulated EndoWrist with 7° of freedom. These features contribute to precise dissection and lymphadenectomy. With adequate margins and harvested lymph nodes, RAG meets the criteria for performing radical gastrectomy.

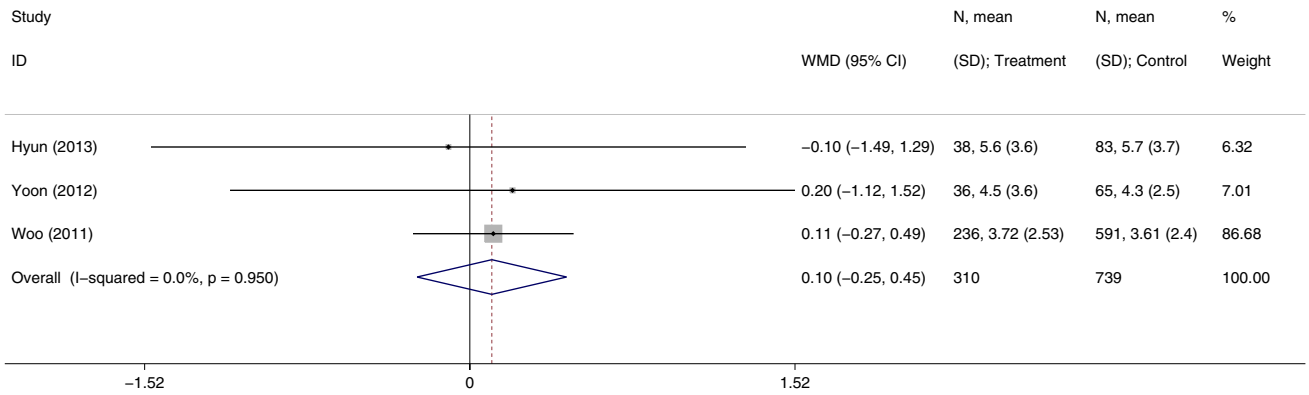

Fig. 3 Meta-analysis of proximal margin shows no difference between robot-assisted gastrectomy (RAG) and laparoscopy-assisted gastrectomy (LDG). Weighted mean differences (WMDs) are shown with 95 % confidence interval (CI)

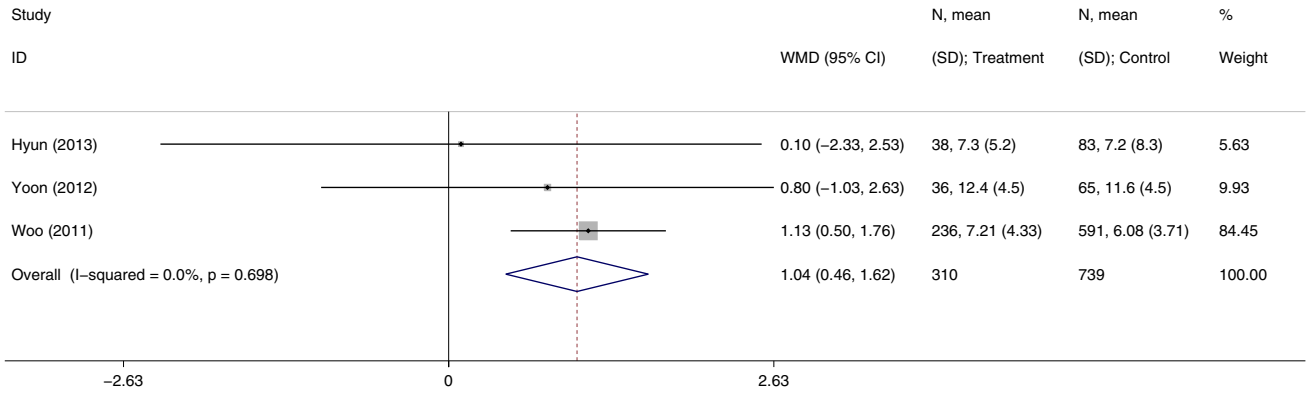

Fig. 4 Meta-analysis of the distal margin shows that robot-assisted gastrectomy (RAG) was associated with a longer distal margin. Weighted mean differences (WMDs) are shown with 95 % confidence interval (CI)

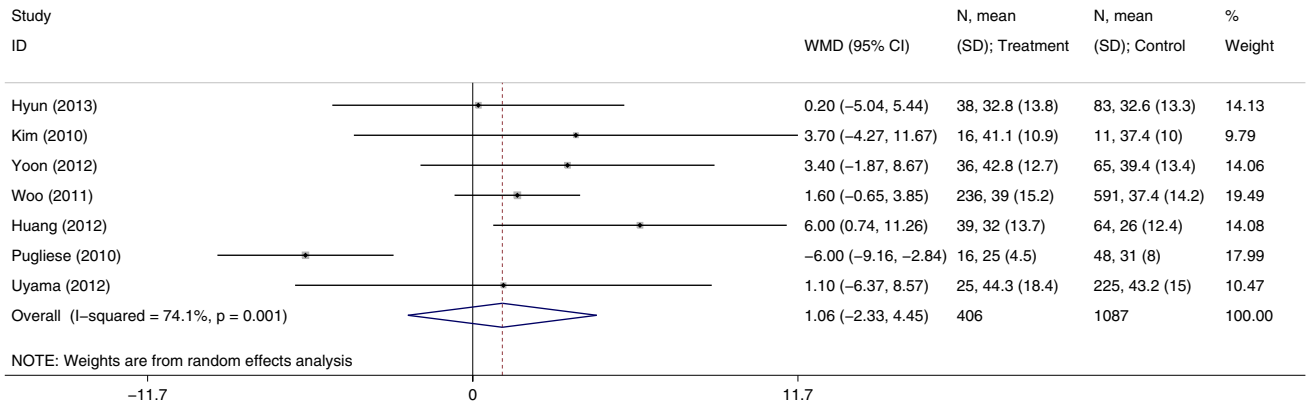

Fig. 5 Meta-analysis of harvested lymph nodes by robot-assisted gastrectomy (RAG) and laparoscopy-assisted gastrectomy (LDG) shows no difference between the two techniques. Weighted mean differences (WMDs) are shown with 95 % confidence interval (CI)

Many studies have reported that minimally invasive laparoscopy surgery has reduced the hospital stay [2–8]. Two studies that compared open gastrectomy (OG) with laparoscopic gastrectomy [22, 25] are included in this meta-analysis. Both studies showed that the hospital stay in the OG group was longer than that in the LAG and RAG groups. As observed in the meta-analysis, hospital stay was not significantly different in the RAG and LAG groups ($p > 0.05$). Postoperative recovery time was also similar in the RAG and LAG groups. The postoperative complication

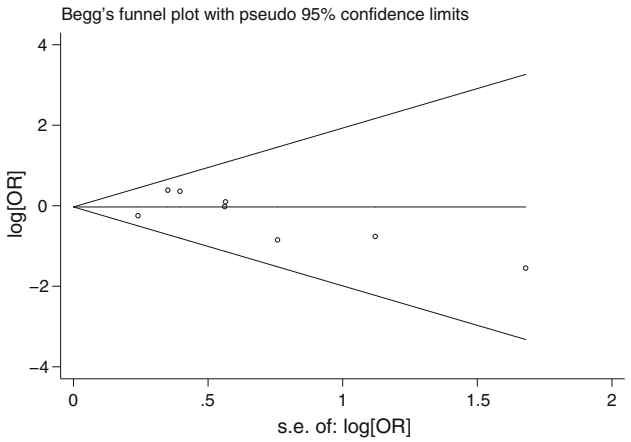

Fig. 6 Funnel plot depicts the distribution of odds ratios comparing complications for the eight studies included in the meta-analysis. It shows that there is no publication bias

rate is an important indicator of the short-term outcome, which with RAG is acceptable according to our finding of similar complication rates for the two groups ($p > 0.05$). Based on these results, we deduced that RAG is safe and acceptable.

In general, the Da Vinci robotic system overcomes the technical limitations of laparoscopy. This study demonstrated that RAG is as acceptable as LAG for obtaining safe complications and for performing radical gastrectomy. With acceptable complications and radical resection, RAG is a promising approach that improves on LAG. Because of the lack of long-term studies, it is too early to draw final conclusions. Long-term clinical outcomes should be evaluated.

Acknowledgments Supported by the National Nature Science Foundation of China, Nos. 81272698.

Disclosures Wei-song Shen, Hong-qing Xi, Lin Chen, and Bo Wei have no conflicts of interest or financial ties to disclose.

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