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Robotic versus Laparoscopic versus Open Gastrectomy: A Meta-Analysis

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Purpose: To define the role of robotic gastrectomy for the treatment of gastric cancer, the present systematic review with meta-analysis was performed.

Materials and Methods: A comprehensive search up to July 2012 was conducted on PubMed, EMBASE, and the Cochrane Library. All eligible studies comparing robotic gastrectomy versus laparoscopic gastrectomy or open gastrectomy were included.

Results: Included in our meta-analysis were seven studies of 1,967 patients that compared robotic (n=404) with open (n=718) or laparoscopic (n=845) gastrectomy. In the complete analysis, a shorter hospital stay was noted with robotic gastrectomy than with open gastrectomy (weighted mean difference: -2.92, 95% confidence interval: -4.94 to -0.89, P=0.005). Additionally, there was a significant reduction in intraoperative blood loss with robotic gastrectomy compared with laparoscopic gastrectomy (weighted mean difference: -35.53, 95% confidence interval: -66.98 to -4.09, P=0.03). These advantages were at the price of a significantly prolonged operative time for both robotic gastrectomy versus laparoscopic gastrectomy (weighted mean difference: 63.70, 95% confidence interval: 44.22 to 83.17, P<0.00001) and robotic gastrectomy versus open gastrectomy (weighted mean difference: 95.83, 95% confidence interval: 54.48 to 137.18, P<0.00001). Analysis of the number of lymph nodes retrieved and overall complication rates revealed that these outcomes did not differ significantly between the groups.

Conclusions: Robotic gastrectomy for gastric cancer reduces intraoperative blood loss and the postoperative hospital length of stay compared with laparoscopic gastrectomy and open gastrectomy at a cost of a longer operating time. Robotic gastrectomy also provides an oncologically adequate lymphadenectomy. Additional high-quality prospective studies are recommended to better evaluate both short and long-term outcomes.

Key Words: Robotics; Laparoscopy; Gastrectomy; Stomach neoplasms

Introduction

Minimally invasive surgery (MIS) has enjoyed wide acceptance since the first laparoscopic gastrectomy (LG) for cancer was reported in 1994.[1,2] Numerous approaches to this procedure have been developed, and many patients have benefited from their effectiveness. This is particularly salient as recently demonstrated by phase III clinical trials for early gastric cancer.[3-5] However, laparoscopic surgery has certain limitations, such as two-dimensional imaging, restricted range of motion of the instruments, and poor ergonomic positioning of the surgeon. Moreover, indications to treat advanced gastric cancers by MIS still remain to be defined.[3,6,7]

The robotic surgery system was introduced as a solution to minimize the shortcomings of laparoscopy. This emerging method provides undoubted technical advantages over conventional laparoscopy,[8] but its role for gastric cancer is still unclear.[9-14] Since

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robotic gastrectomy (RG) has been reported,[8,15] the application of this new approach is increasing in experienced centers. Yet, to date only a limited number of studies have focused on this new method. Thus, we have performed a meta-analysis of studies that have compared RG with open gastrectomy (OG) and with LG for gastric cancer. In the era of rapid penetration of robotic technology, we specifically aimed to systematically and objectively assess the value of RG for the treatment of gastric cancer.

Materials and Methods

1. Search strategy

Publications were identified by searching the major medical databases, such as PubMed, EMBASE, and the Cochrane Library for all articles published until July 19, 2012. We adopted the MeSH form strategy for PubMed and the Cochrane Library as follows: (stomach cancer or gastric cancer or stomach neoplasm or gastric neoplasm or stomach carcinoma or gastric carcinoma or stomach tumor or gastric tumor or stomach tumour or gastric tumour or stomach neoplasms or gastric neoplasms) and (robot or robotic or robotics). We used the Emtree form strategy for EMBASE as reported: ('stomach cancer' or 'gastric cancer' or 'stomach neoplasm' or 'gastric neoplasm' or 'stomach carcinoma' or 'gastric carcinoma' or 'stomach tumor' or 'gastric tumor' or 'stomach tumour' or 'gastric tumour') and (robot or robotic or robotics).

2. Inclusion and exclusion criteria with quality of literature

Inclusion criteria were: (1) observational studies that compared RG versus OG or LG or both with lymph node dissection for the treatment of gastric cancer; (2) patients with primary gastric adenocarcinoma; and (3) data which included most of the following: operation time, blood loss, number of harvested lymph nodes, hospital stay, and morbidity. Exclusion criteria were: (1) gastrointestinal stromal tumors or benign gastric diseases; and (2) duplicate publication or the publication that did not provide sufficient data for the analyses.

Two of the authors (M.A., Y.Y.C.) evaluated the eligibility of all studies independently collected from the databases based on the selection criteria. The risk of bias in each study was assessed according to the Newcastle-Ottawa Scale for observational studies.[16]

3. Data extraction

Two researchers (M.A., Y.Y.C) extracted data from each study using a structured sheet and entered the data into a database. Another author (J.K.) reviewed this process. The following factors were examined: author, year of publication, source journal, sample size, characteristics of the patients, research design, operative time, blood loss, number of harvested lymph nodes, morbidity, and length of hospital stay.

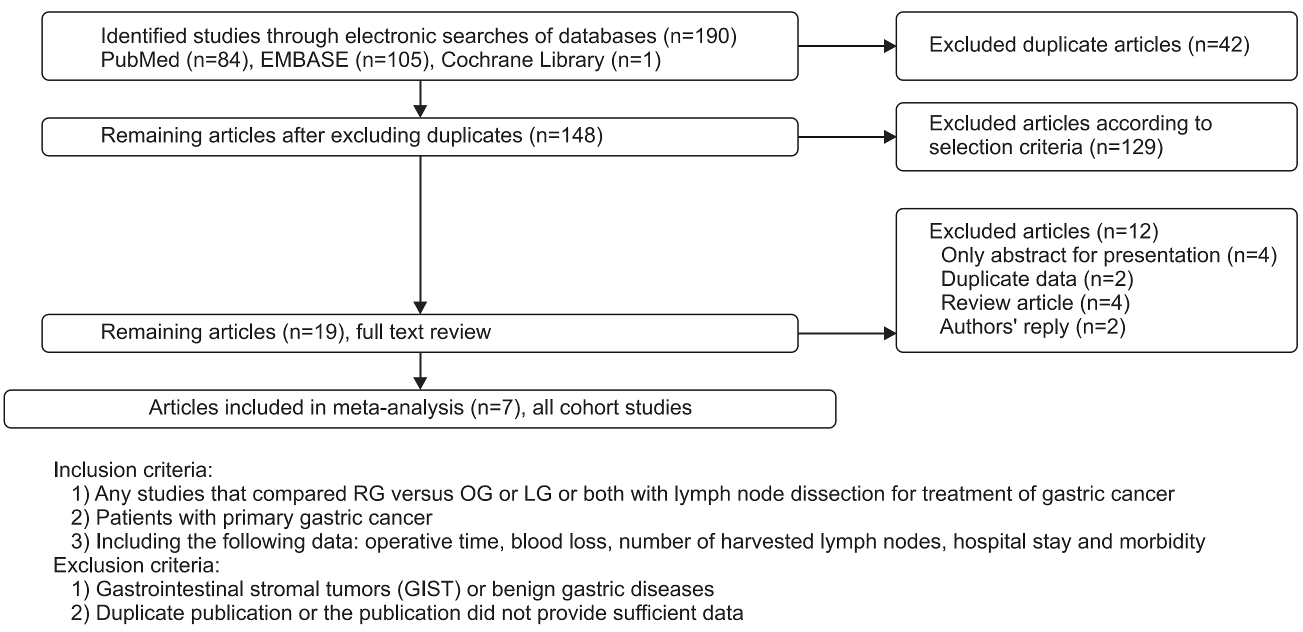


Fig. 1. Flow diagram for identification of selected articles. Seven cohort studies were finally included in the meta-analysis. RG = robotic gastrectomy; OG = open gastrectomy; LG = laparoscopic gastrectomy.

4. Statistical analysis

We conducted a meta-analysis with the software Review Manager (RevMan) ver. 5.1 by the Cochrane Collaboration (Nordic Cochrane Center, Copenhagen, Denmark). We calculated the effect sizes by odds ratio (OR) for dichotomous variables and weighted mean differences (WMD) for continuous outcome measures with 95% confidence intervals (CIs). The Higgins I^2 and chi-square tests were used to evaluate the heterogeneity of the results across studies. We considered a P-value of chi-square less than 0.10 with an I^2-value of greater than 50% as indicative of substantial heterogeneity. The inverse variance method with fixed-effects model was applied if no heterogeneity was considered, whereas the random effects model was used in opposite cases. The correction of the zero cell counts was automatically performed by the RevMan program with

Table 1. Selected studies

Author	Country and year	Surgery	Number of patient	Resection extent of surgery (TG/SG)	LN dissection (D1+α or β/D2)	Depth of invasion
Kim et al.[17]	South Korea, 2010	RG	16	0/16	2/14	<T2N1MO
		LG	11	0/11	3/8	
		OG	12	0/12	0/12	
Pugliese et al.[18]	Italy, 2010	RG	18	0/18	0/18	EGC+AGC
		LG	52	0/52	0/52	
Yoon et al.[19]	South Korea, 2012	RG	36	36/0	NA	<T2N1MO
		LG	65	65/0	NA	
Woo et al.[20]	South Korea, 2011	RG	236	62/172	13/105	<T2N1MO
		LG	591	108/481	312/279	
Eom et al.[21]	South Korea, 2012	RG	30	0/30	10/20	EGC
		LG	62	0/62	28/34	
Caruso et al.[22]	Italy, 2011	RG	29	12/17	0/29	EGC+AGC
		OG	120	37/83	0/120	
Huang et al.[23]	Taiwan, 2012	RG	39	7/32	5/34	<T2N1MO
		LG	64	7/57	52/12	
		OG	586	179/407	70/516	

TG = total gastrectomy; SG = subtotal gastrectomy; LN = lymph node; RG = robotic gastrectomy; LG = laparoscopic gastrectomy; OG = open gastrectomy; NA = not available; EGC = early gastric cancer; AGC = advanced gastric cancer.

Table 2. The assessment of the risk of bias in each study using the Newcastle-Ottawa scale

Type of study	Study	Selection (0~4)				Comparability (0~2)		Outcome (0~3)			Total
		REC	SNEC	AE	DO	SC	AF	AO	FU	AFU	
Cohort studies	Kim et al.[17]	*	*	*	*			*		*	6
	Pugliese et al.[18]	*	*	*	*			*	*	*	7
	Yoon et al.[19]	*	*	*	*			*	*	*	7
	Woo et al.[20]	*	*	*	*			*		*	6
	Eom et al.[21]	*	*	*	*			*		*	6
	Caruso et al.[22]	*		*	*			*	*	*	6
	Huang et al.[23]	*		*	*			*		*	5

REC = representativeness of the exposed cohort; SNEC = selection of the non-exposed cohort; AE = ascertainment of exposure; DO = demonstration that outcome of interest was not present at start of study; SC = study controls for age, sex, marital status; AF = study controls for any additional factors; AO = assessment of outcome; FU = follow-up long enough for outcomes to occur; AFU = adequacy of follow-up of cohorts.
*Asterisk means that the study is satisfied the item, and no asterisk means the opposite situation.

exclusion of the outcome from the meta-analysis if there was no event in both arms in one study. We obtained the standard deviation from the article by contacting the authors by e-mail if it was not reported or by extracting the estimated standard deviation from the P-value 「Cochrane Handbook for systematic reviews of interventions version 5.0.2」 if it was not directly available from the authors. The symmetry of Begg's funnel plot was used to evaluate the presence of publication bias in the studies.

Results

From a total of 190 articles seven[17-23] were selected according to our inclusion and exclusion criteria (Fig. 1). All are non-randomized, non-blinded, retrospective cohort studies. The characteristics of the seven selected articles are shown in Table 1.

Next to the intraoperative outcomes, this analysis was directed at the short-term results of RG because long-term outcomes were not sufficiently addressed by the included studies. A total of 1,967 patients affected by gastric cancer were analyzed, including 404 who underwent RG, 718 who underwent OG, and 845 who underwent LG. The risk of bias of included studies is shown in Table 2, whereby two received seven stars, one received five stars, and the remaining received six stars. The mean number of stars for the risk of bias was 6.1. Each meta-analysis was performed twice; with

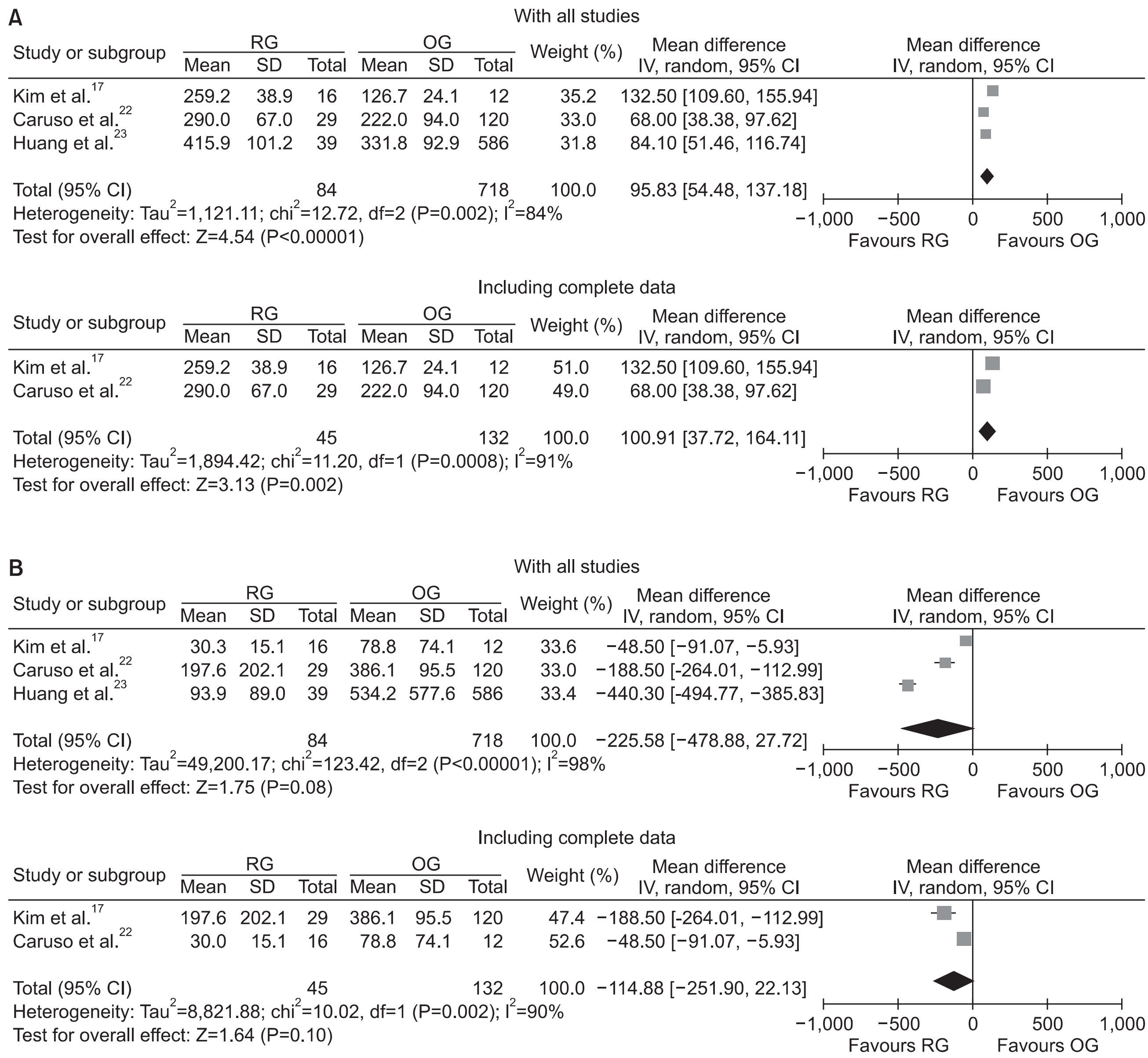


Fig. 2. Forest plots of studies comparing robotic gastrectomy (RG) vs. open gastrectomy (OG) for gastric cancer. (A) Operative time. (B) Blood loss. (C) Number of harvested lymph-nodes. (D) Overall complication rate. (E) Hospital stay. SD = standard deviation; CI = confidence interval; df = degree of freedom.

C

With all studies

Study or subgroup	RG Mean	RG SD	RG Total	OG Mean	OG SD	OG Total	Weight (%)	Mean difference IV, fixed, 95% CI
Kim et al.[17]	41.1	10.9	16	43.3	10.4	12	14.8	−2.20 [−10.15, 5.75]
Caruso et al.[22]	28.0	11.2	29	31.7	15.6	120	38.3	−3.70 [−8.64, 1.24]
Huang et al.[23]	32.0	13.7	39	34.0	14.8	586	46.9	−2.00 [−6.46, 2.46]
Total (95% CI)			84			718	100.0	−2.68 [−5.74, 0.38]

Heterogeneity: chi^2=0.27, df=2 (P=0.88); I^2=0%
Test for overall effect: Z=1.72 (P=0.09)

Including complete data

Study or subgroup	RG Mean	RG SD	RG Total	OG Mean	OG SD	OG Total	Weight (%)	Mean difference IV, fixed, 95% CI
Kim et al.[17]	41.1	10.9	16	43.3	10.4	12	27.9	−2.20 [−10.15, 5.75]
Caruso et al.[22]	28.0	11.2	29	31.7	15.6	120	72.1	−3.70 [−8.64, 1.24]
Total (95% CI)			45			132	100.0	−3.28 [−7.48, 0.91]

Heterogeneity: chi^2=0.10, df=1 (P=0.75); I^2=0%
Test for overall effect: Z=1.53 (P=0.13)

D

With all studies

Study or subgroup	RG Events	RG Total	OG Events	OG Total	Weight (%)	Odds ratio IV, fixed, 95% CI
Kim et al.[17]	0	16	2	12	3.6	0.13 [0.01, 2.92]
Caruso et al.[22]	12	29	51	120	52.5	0.96 [0.42, 2.17]
Huang et al.[23]	6	39	86	586	43.9	1.06 [0.43, 2.60]
Total (95% CI)		84		718	100.0	0.93 [0.51, 1.68]
Total events	18		139			

Heterogeneity: chi^2=1.63, df=2 (P=0.44); I^2=0%
Test for overall effect: Z=0.24 (P=0.81)

Including complete data

Study or subgroup	RG Events	RG Total	OG Events	OG Total	Weight (%)	Odds ratio IV, fixed, 95% CI
Kim et al.[17]	0	16	2	12	6.5	0.13 [0.01, 2.92]
Caruso et al.[22]	12	29	51	120	93.5	0.96 [0.42, 2.17]
Total (95% CI)		45		132	100.0	0.84 [0.38, 1.86]
Total events	12		53			

Heterogeneity: chi^2=1.49, df=1 (P=0.22); I^2=33%
Test for overall effect: Z=0.43 (P=0.66)

E

With all studies

Study or subgroup	RG Mean	RG SD	RG Total	OG Mean	OG SD	OG Total	Weight (%)	Mean difference IV, random, 95% CI
Kim et al.[17]	5.1	0.3	16	6.7	1.4	12	49.0	−1.60 [−2.41, −0.79]
Caruso et al.[22]	9.6	2.8	29	13.4	8.5	120	37.0	−3.80 [−5.63, −1.97]
Huang et al.[23]	11.3	14.4	39	16.5	13.6	586	14.0	−5.20 [−9.85, −0.55]
Total (95% CI)			84			718	100.0	−2.92 [−4.94, −0.89]

Heterogeneity: Tau^2=2.01; chi^2=6.47, df=2 (P=0.04); I^2=69%
Test for overall effect: Z=2.82 (P=0.005)

Including complete data

Study or subgroup	RG Mean	RG SD	RG Total	OG Mean	OG SD	OG Total	Weight (%)	Mean difference IV, random, 95% CI
Kim et al.[17]	5.1	0.3	16	6.7	1.4	12	57.3	−1.60 [−2.41, −0.79]
Caruso et al.[22]	9.6	2.8	29	13.4	8.5	120	42.7	−3.80 [−5.63, −1.97]
Total (95% CI)			45			132	100.0	−2.54 [−4.67, −0.41]

Heterogeneity: Tau^2=1.90; chi^2=4.65, df=1 (P=0.03); I^2=78%
Test for overall effect: Z=2.33 (P=0.02)

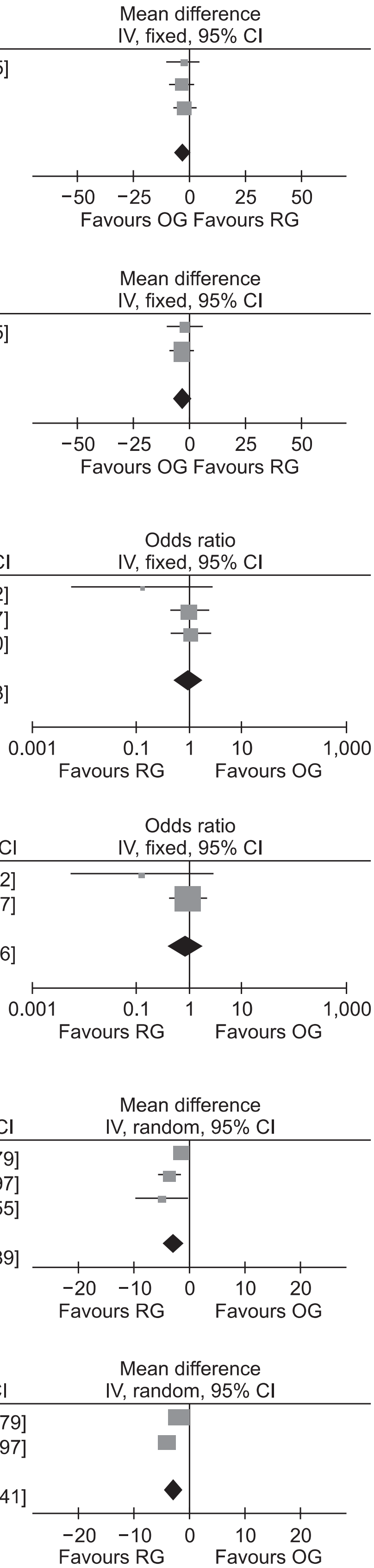


Fig. 2. Continued.

A

With all studies

Study or subgroup	RG Mean	RG SD	RG Total	LG Mean	LG SD	LG Total	Weight (%)	Mean difference IV, random, 95% CI
Kim et al.[17]	259.2	38.90	16	203.9	36.40	11	16.2	55.30 [26.56, 84.04]
Pugliese et al.[18]	344.0	62.00	16	235.0	23.00	48	15.3	109.00 [77.93, 140.07]
Yoon et al.[19]	305.8	115.80	36	210.2	57.70	65	12.1	95.60 [55.26, 135.94]
Woo et al.[20]	219.5	46.80	236	170.7	55.80	591	24.2	48.80 [41.32, 56.28]
Eom et al.[21]	229.1	52.21	30	189.4	52.21	62	18.7	39.70 [16.94, 62.46]
Huang et al.[23]	415.9	101.20	39	362.2	72.80	64	13.4	53.70 [17.27, 90.13]
Total (95% CI)			373			841	100.0	63.70 [44.22, 83.17]

Heterogeneity: $Tau^2=392.63$; $chi^2=19.28$, df=5 (P=0.002); $I^2=74\%$
Test for overall effect: Z=6.41 (P<0.00001)

Including complete data

Study or subgroup	RG Mean	RG SD	RG Total	LG Mean	LG SD	LG Total	Weight (%)	Mean difference IV, random, 95% CI
Kim et al.[17]	259.2	38.90	16	203.9	36.40	11	19.0	55.30 [26.56, 84.04]
Pugliese et al.[18]	344.0	62.00	16	235.0	23.00	48	18.1	109.00 [77.93, 140.07]
Yoon et al.[19]	305.8	115.80	36	210.2	57.70	65	14.6	95.60 [55.26, 135.94]
Woo et al.[20]	219.5	46.80	236	170.7	55.80	591	26.7	48.80 [41.32, 56.28]
Eom et al.[21]	229.1	52.21	30	189.4	52.21	62	21.5	39.70 [16.94, 62.46]
Total (95% CI)			334			777	100.0	65.82 [43.27, 88.37]

Heterogeneity: $Tau^2=480.49$; $chi^2=19.28$, df=4 (P=0.0007); $I^2=79\%$
Test for overall effect: Z=5.72 (P<0.00001)

B

With all studies

Study or subgroup	RG Mean	RG SD	RG Total	LG Mean	LG SD	LG Total	Weight (%)	Mean difference IV, random, 95% CI
Kim et al.[17]	30.3	15.10	16	44.7	37.10	11	25.0	−14.40 [−37.54, 8.74]
Pugliese et al.[18]	90.0	48.00	16	148.0	53.00	48	23.5	−58.00 [−85.89, −30.11]
Woo et al.[20]	91.6	152.60	236	147.9	269.00	591	23.1	−56.30 [−85.44, −27.16]
Eom et al.[21]	152.8	173.46	30	88.3	173.46	62	10.8	64.50 [−11.11, 140.11]
Huang et al.[23]	93.9	89.00	39	163.7	154.70	64	17.5	−69.80 [−116.88, −22.72]
Total (95% CI)			337			77.6	100.0	−35.53 [−66.98, −4.09]

Heterogeneity: $Tau^2=891.12$; $chi^2=16.30$, df=4 (P=0.003); $I^2=75\%$
Test for overall effect: Z=2.21 (P=0.03)

Including complete data

Study or subgroup	RG Mean	RG SD	RG Total	LG Mean	LG SD	LG Total	Weight (%)	Mean difference IV, random, 95% CI
Kim et al.[17]	30.3	15.10	16	44.7	37.10	11	30.0	−14.40 [−37.54, 8.74]
Pugliese et al.[18]	90.0	48.00	16	148.0	53.00	48	28.4	−58.00 [−85.89, −30.11]
Woo et al.[20]	91.6	152.60	236	147.9	269.00	591	28.0	−56.30 [−85.44, −27.16]
Eom et al.[21]	152.8	173.46	30	88.3	173.46	62	13.6	64.50 [−11.11, 140.11]
Total (95% CI)			298			712	100.0	−27.82 [−63.60, 7.95]

Heterogeneity: $Tau^2=969.58$; $chi^2=14.36$, df=3 (P=0.0002); $I^2=79\%$
Test for overall effect: Z=1.52 (P=0.13)

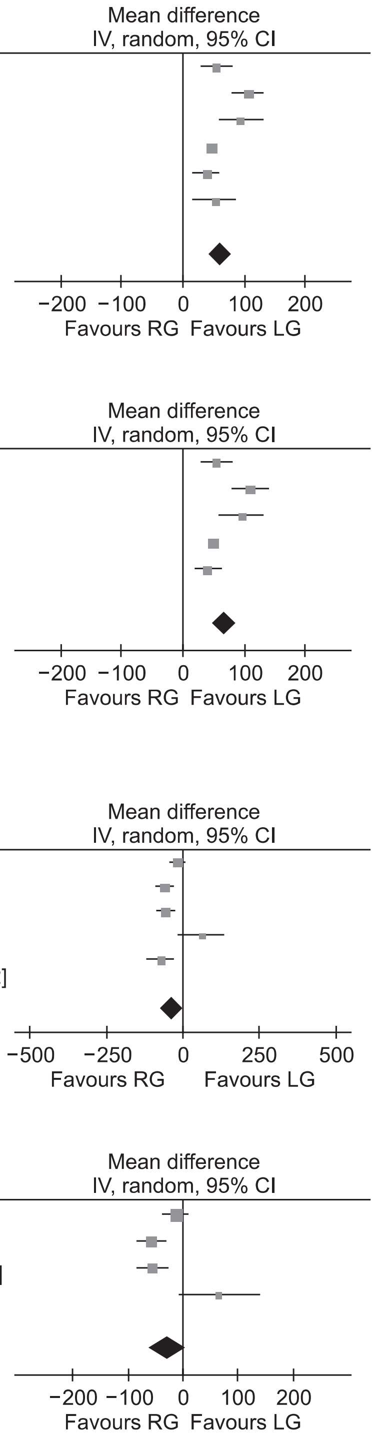


Fig. 3. Forest plots of studies comparing robotic gastrectomy (RG) vs. laparoscopic gastrectomy (LG) for gastric cancer. (A) Operative time. (B) Blood loss. (C) Number of harvested lymph nodes. (D) Overall complication rate. (E) Hospital stay. SD = standard deviation; CI = confidence interval; df = degree of freedom.

all available studies and those including only complete data which was analyzed excluding the study showing results with high risk of bias.[23] The forest plots of each outcome, subdivided in two different groups, are shown in Fig. 2 and 3.

1. Comparing RG with OG

We found that three out of seven selected articles compared RG to OG (Table 1). The operative time, amount of blood loss, number of lymph nodes retrieved, overall complications, and hospital stay

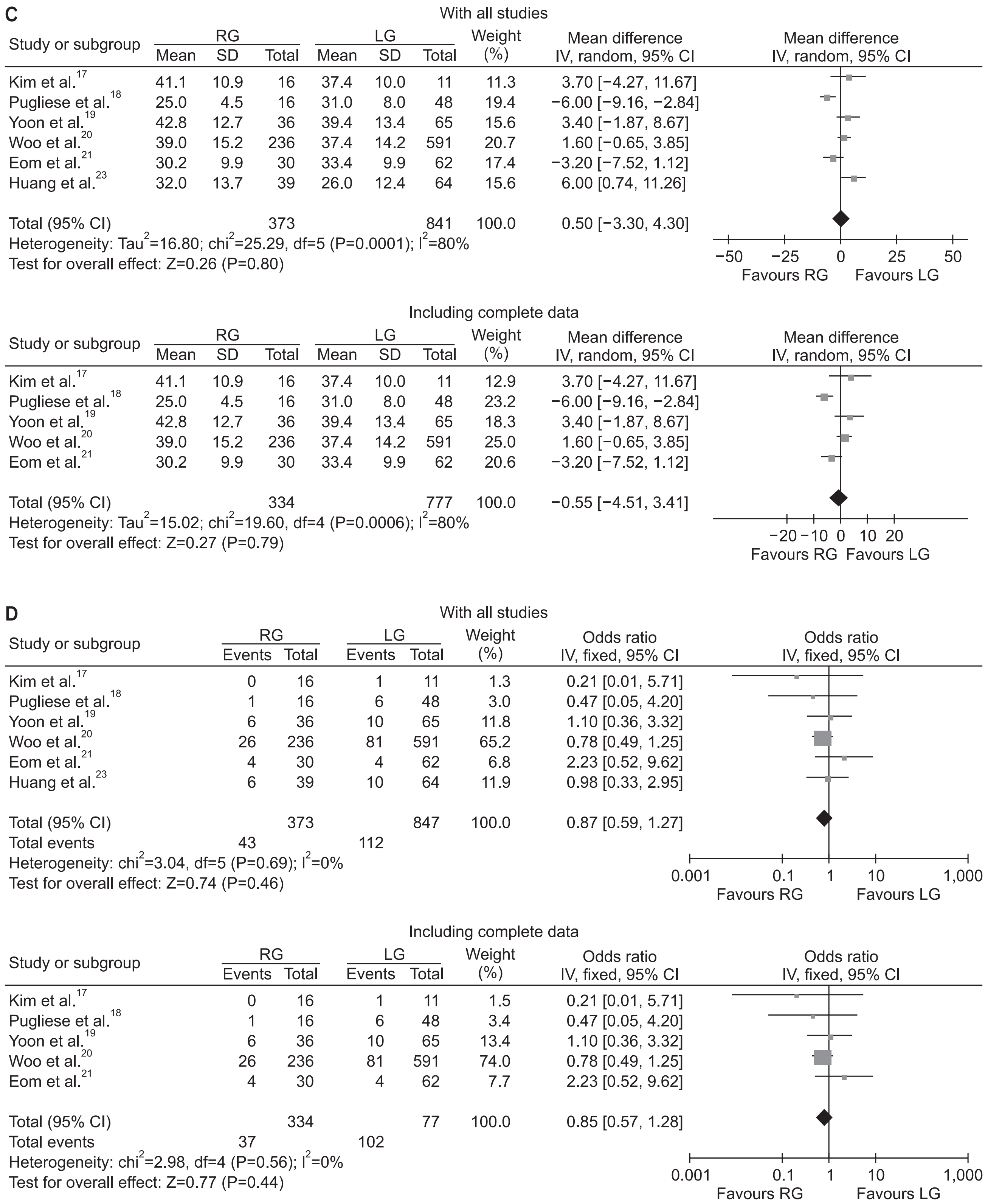
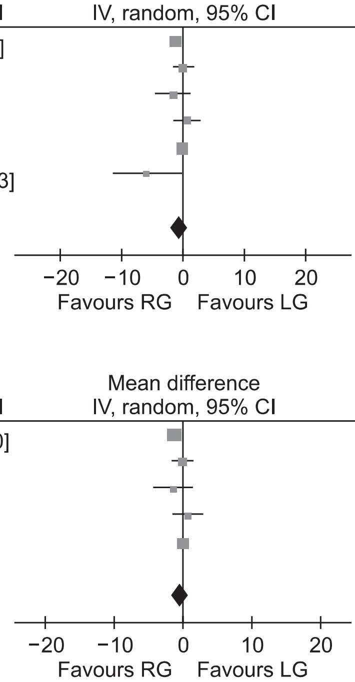


Fig. 3. Continued.

were analyzed. Detailed information about these outcomes was available in all three selected studies.

The operative time in the robotic group was significantly longer than in the open group (WMD: 95.83, 95% CI: 54.48 to 137.18, $P<0.00001$) in a random effect model ($P=0.002$, I^2: 84%). After exclusion of insufficient data the operative time was still signifi-



With all studies

Study or subgroup	RG Mean	RG SD	RG Total	LG Mean	LG SD	LG Total	Weight (%)	Mean difference IV, random, 95% CI
Kim et al.[17]	5.1	0.30	16	6.5	0.80	11	27.9	−1.40 [−1.90, −0.90]
Pugliese et al.[18]	10.0	3.00	16	10.0	2.60	48	17.3	0.00 [−1.64, 1.64]
Yoon et al.[19]	8.8	3.30	36	10.3	10.80	65	9.4	−1.50 [−4.34, 1.34]
Woo et al.[20]	7.7	17.20	236	7.0	5.70	591	12.7	0.70 [−1.54, 2.94]
Eom et al.[21]	7.9	0.27	30	7.8	0.27	62	29.6	0.10 [−0.02, 0.22]
Huang et al.[23]	11.3	14.40	39	17.2	13.30	64	3.2	−5.90 [−11.47, −0.33]
Total (95% CI)			373			841	100.0	−0.60 [−1.66, 0.45]

Heterogeneity: Tau^2=0.98; chi^2=39.17, df=5 (P<0.00001); I^2=87%
Test for overall effect: Z=1.12 (P=0.26)

Including complete data

Study or subgroup	RG Mean	RG SD	RG Total	LG Mean	LG SD	LG Total	Weight (%)	Mean difference IV, random, 95% CI
Kim et al.[17]	5.1	0.30	16	6.5	0.80	11	29.3	−1.40 [−1.90, −0.90]
Pugliese et al.[18]	10.0	3.00	16	10.0	2.60	48	17.5	0.00 [−1.64, 1.64]
Yoon et al.[19]	8.8	3.30	36	10.3	10.80	65	9.3	−1.50 [−4.34, 1.34]
Woo et al.[20]	7.7	17.20	236	7.0	5.70	591	12.7	0.70 [−1.54, 2.94]
Eom et al.[21]	7.9	0.27	30	7.8	0.27	62	31.2	0.10 [−0.02, 0.22]
Total (95% CI)			334			777	100.0	−0.43 [−1.46, 0.61]

Heterogeneity: Tau^2=0.89; chi^2=34.83, df=4 (P<0.00001); I^2=89%
Test for overall effect: Z=0.81 (P=0.42)

Fig. 3. Continued.

cantly longer in the robotic group (WMD: 100.91, 95% CI: 37.72 to 164.11, P=0.002) in a random effect model (P=0.0008, I^2: 91%). The blood loss was less in RG than OG, but without statistical significance (WMD: −225.58, 95% CI: −478.88 to 27.72, P=0.08) in a random effect model (P<0.0001, I^2: 98%). By considering only complete data, the analysis revealed the same results (WMD: −114.88, 95% CI: −251.90 to 22.13, P=0.10) in a random effect model (P=0.002, I^2: 90%). The number of lymph nodes retrieved was higher in the open group compared with the robotic group, though without a statistically significant difference (WMD: −2.68, 95% CI: −5.74 to 0.38, P=0.09) in a fixed effect model (P=0.88, I^2: 0%). The same non-significant outcomes in favor of OG (WMD: −3.28, 95% CI: −7.48 to 0.91, P=0.13) were noted when including only complete data in a fixed effect model (P=0.75, I^2: 0%). The overall complication rate between the two comparative surgical approaches did not show any significant difference (OR: 0.93, 95% CI: 0.51 to 1.68, P=0.81) in a fixed effect model (P=0.44, I^2: 0%). Additionally, when considering only valid data, the robotic and open groups did not differ significantly in regards to morbidity (OR: 0.84, 95% CI: 0.38 to 1.86, P=0.66) in a fixed effect model (P=0.22, I^2: 33%). However, the hospital length of stay for the robotic group was significantly shorter than for the open group (WMD: −2.92, 95% CI: −4.94 to −0.89, P=0.005) in a random effect model (P=0.04, I^2: 69%). Analysis of data extracted only from the articles including complete data 17,22 also revealed an outcome with a significant difference in favor of the robotic group (WMD: −2.54, 95% CI: −4.67 to −0.41, P=0.02) in a random effect model (P=0.03, I^2: 78%). Fig. 4 shows the symmetry of the funnel plots in each outcome. Estimation of publication bias by funnel plot was difficult as there were only three publications which compared RG to OG. However, publication bias was suspected among the overall complications.

2. Comparing RG to LG

We found that six out of the seven selected articles compared RG to LG (Table 1). The operative time, amount of blood loss, number of lymph nodes retrieved, overall complications, and hospital length of stay were examined. All six articles reported their respective data regarding these particular parameters; however, one report[19] compared the amount of blood loss by the change in the hemoglobin level, and this parameter was excluded from this specific analysis. We found that the operative time for RG was significantly longer than for LG (WMD: 63.70, 95% CI: 44.22 to 83.17, P<0.00001) in a random effect model (P=0.002, I^2: 74%). The results were the same when considering only complete articles, with similar statistical significance (WMD: 65.82, 95% CI: 43.27 to 88.37, P<0.00001) in a random effect model (P=0.0007, I^2: 79%). The amount of blood loss was also significantly less for RG than for LG (WMD: −35.53, 95% CI: −66.98 to −4.09, P=0.03) in a

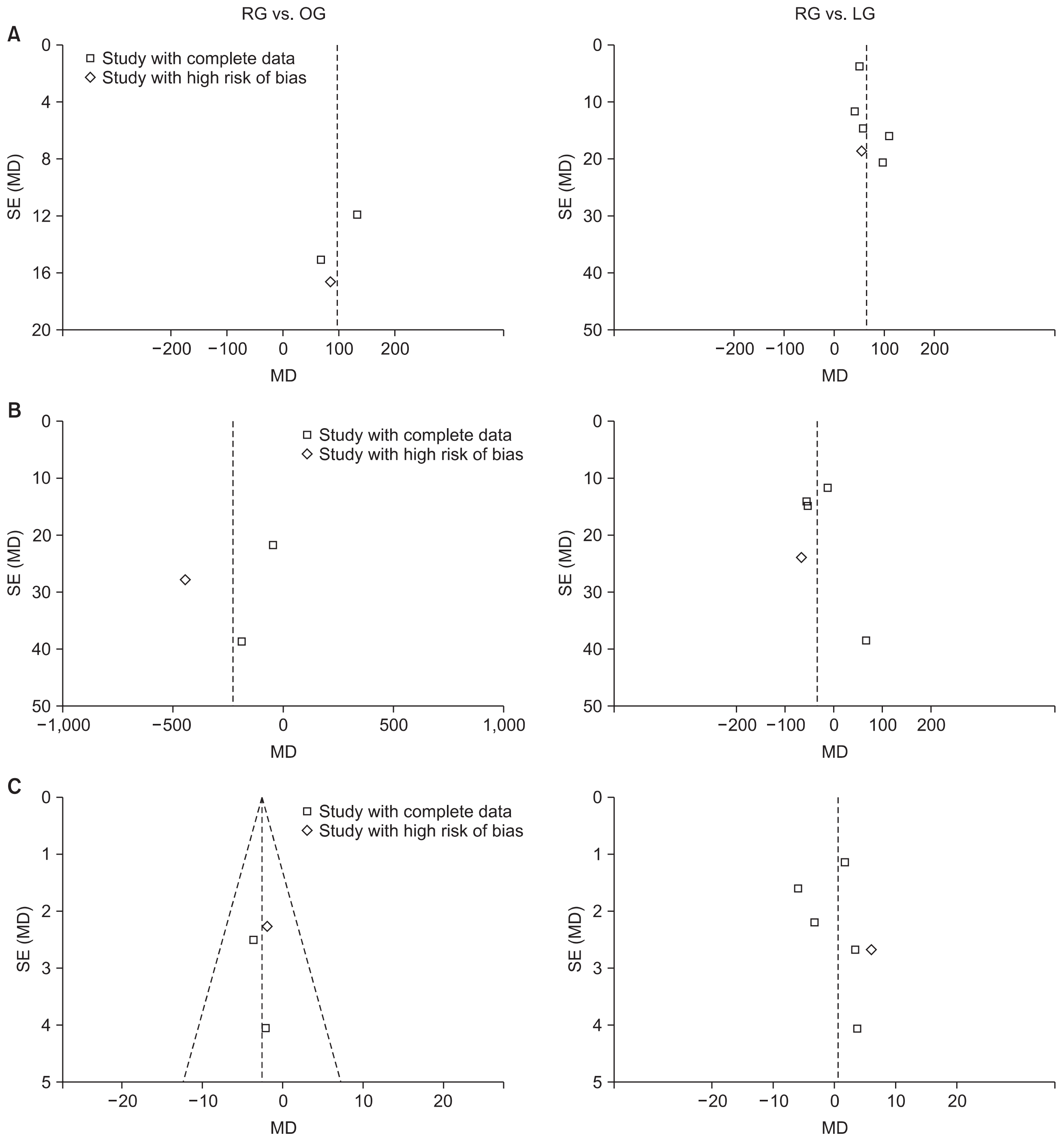


Fig. 4. Begg's funnel plots for identifying publication bias for five perioperative outcomes regarding robotic vs. open and laparoscopic gastrectomy. (A) Operative time. (B) Blood loss. (C) Number of harvested lymph nodes. (D) Overall complication rate. (E) Hospital stay. RG = robotic gastrectomy; OG = open gastrectomy; LG = laparoscopic gastrectomy; SE = standard error; MD = mean difference; OR = odds ratio.

random effect model (P=0.003, I^2: 75%). By including only valid data, analysis of the pooled data revealed that the estimated blood loss was not significantly less for RG than for LG (WMD: −27.82, 95% CI: −63.60 to 7.95, P=0.13) in a random effect model (P=0.002, I^2: 79%). Likewise, our analysis of the number of lymph nodes retrieved demonstrated no significant difference between RG and LG (WMD: 0.50, 95% CI: −3.30 to 4.30, P=0.80) in a random effect model (P=0.0001, I^2: 80%). Analysis of this variable by considering only valid articles also revealed that there was no significant difference in the number of lymph nodes retrieved (WMD: 0.54, 95% CI: −4.51 to 3.42, P=0.79) in a random effect model (P=0.0006, I^2: 80%). The overall complication rate of each surgical approach was

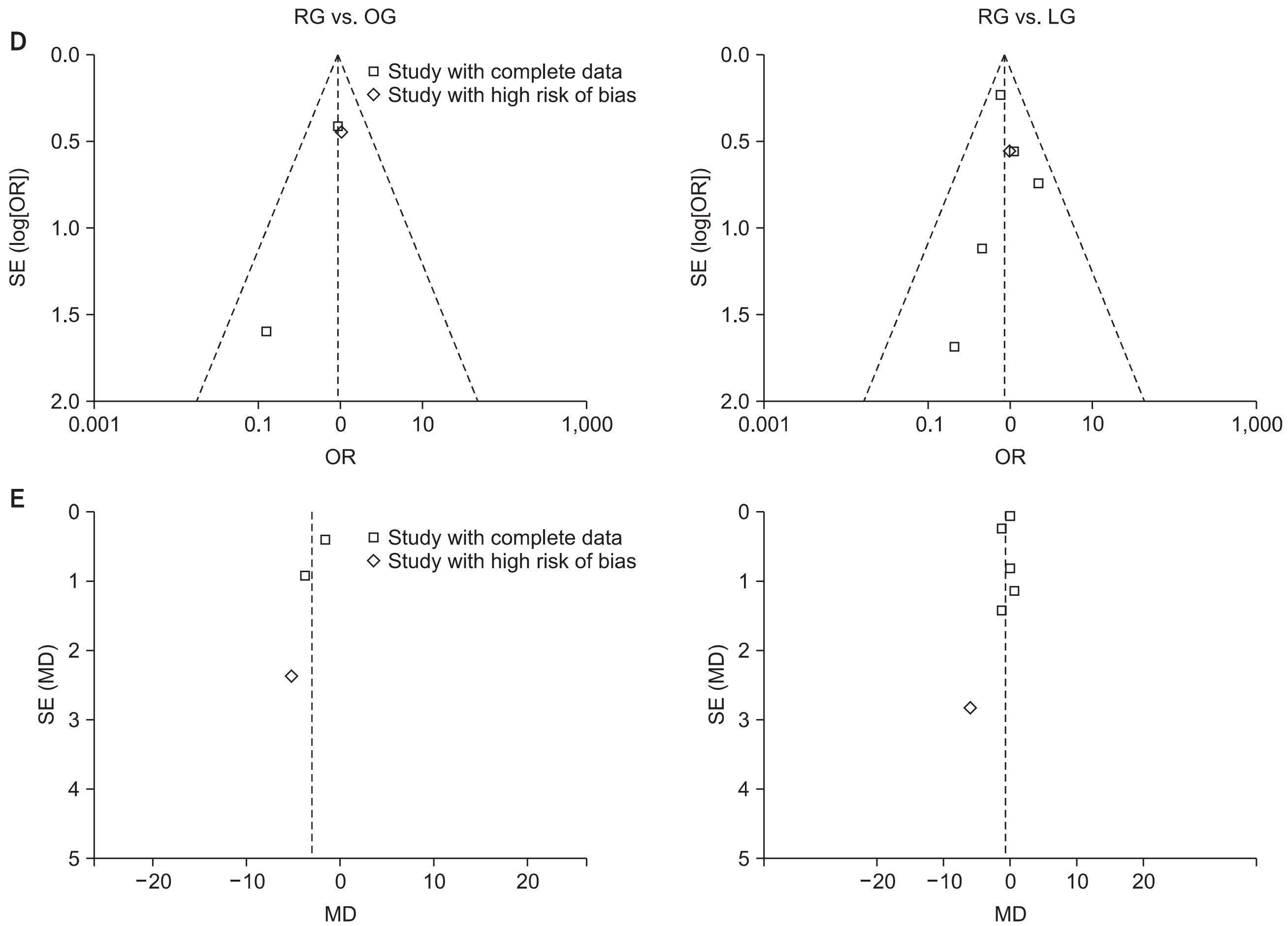


Fig. 4. Continued.

not different between the groups (OR: 0.87, 95% CI: 0.59 to 1.27, P=0.46) in a fixed effect model (P=0.69, I^2: 0%). Inclusion of only the articles that matched our quality assessment did not change the final results, as even in this analysis there was no significant difference in the overall complication rate (OR: 0.85, 95% CI: 0.57 to 1.28, P=0.44) in a fixed effect model (P=0.56, I^2: 0%). Likewise, the duration of hospital stay was not significantly different between the RG and LG groups (WMD: −0.60, 95% CI: −1.66 to 0.45, P=0.26) in a random effect model (P<0.00001, I^2: 87%). Similar results were observed when considering properly sufficient data (WMD: −0.43, 95% CI: −1.46 to 0.61, P=0.42) in a random effect model (P<0.00001, I^2: 89%). Fig. 4 shows the symmetry of the funnel plot for each outcome. Asymmetry was suspected for the amount of blood loss, the overall complications, and the hospital length of stay.

Discussion

The aim of this meta-analysis was to compare RG to OG and LG by means of a thorough evaluation of the available data. Most studies demonstrated similar advantages to RG, including a reduced intraoperative blood loss and shorter hospital stay compared with OG and less intraoperative blood loss compared with LG. These results suggest that robotic surgery can be especially useful for selected patients affected by gastric cancer with severe anemia, as some authors have already published.[20] This is important as transfusion-related problems and risk of gastric cancer recurrence could be reduced.[24-26]

Lymph node dissection is a fundamental part of a radical gastrectomy. In this meta-analysis the overall number of lymph nodes retrieved was high, which is explained by many studies with D2 lymphadenectomies.[27] Evaluation of the pooled data revealed that the number of lymph nodes dissected with RG was less than with OG but greater than with LG, though these differences were not significant. A possible explanation for the high number of lymph nodes retrieved with OG might be that comparative groups of two[22,23] of the three pooled studies were heavily unbalanced by centers highly skilled with OG. Moreover, most patients enrolled in these two open groups were affected by advanced gastric cancer. Therefore, since a more extended lymphadenectomy is recommended for advanced stages,[28,29] one might expect the number of lymph nodes retrieved to be higher than in early stages, which are more common in the robotic group. Nonetheless, even in comparison with the open approach, RG guarantees the removal of at least 15 lymph nodes which still allows for proper staging and prognostication. This is important because it favors greater rates of survival.[30,31] All told, these results demonstrate that RG can be safely performed with adequate oncological principles compared to either OG or LG. RG could also be used for D2 lymphadenectomies, although it was not possible to analyze whether D2 lymphadenectomies were validated by any approach.

These positive results derive from some technical and evidence-based aspects to robotic surgery, such as superior 3-dimensional visualization, more degree of freedom of the wristed-tip instrument, and tremor-filtered control of the four robotic arms.[8,13] These emerging tools may improve a surgeon's dexterity when fine manipulation of tissues in a close, fixed operating field is required, or when hand-sewn sutures and knot-tying are a necessity. The robotic technique provides an easier lymph node dissection, a reduced inflammatory response, less manipulation of the tissues, and a quicker bowel recovery which are reflected by a reduced intraoperative blood loss, a shorter hospital stay, and an easier lymphadenectomy compared with other approaches.[17]

Some limitations were present in our meta-analysis. The quality assessment of all seven selected articles is shown in Table 2. One work had a score of <6 points,[23] whereas the remaining studies all had a valuation of ≥ 6 points.[17-22] Our purpose was to obtain a good quality meta-analysis, but the pooled studies were limited in number. Thus, we decided to compare all selected variables both considering all seven reports as well as excluding only the work that did not match our quality assessment.[23] This decision was aimed at reducing potential bias and to assess for any differences in the results between the two specific groups. According to this strategy, the only difference considering the complete data was regarding the estimated blood loss, which was less in RG vs. LG, though without statistical significance (Fig. 3B).

Another limitation is that significant heterogeneity was recognized in some characteristics of the selected articles. Most of the pooled studies included patients who underwent both subtotal gastrectomy and total gastrectomy without distinction. Furthermore, surgeons performed both robotic gastrectomies and robotic-assisted gastrectomies. The stage of gastric cancer was also not the same for all of the enrolled patients. For instance, inclusion of patients was specifically limited to early gastric cancer in one study,[21] three reports considered patients with both early and advanced gastric cancer,[18,22,23] and three articles[17,19,20] included patients with a preoperative clinical stage Ia or Ib disease. With the exception of one report,[19] the intended extent of lymph node dissection was, however, defined for the RG, LG, and OG groups in all studies (namely D1+β or D2) (Table 1). Finally, the majority of the studies were from Asian populations and accounted for 1,748 of the patients,[17,19-21,23] whereas the remaining two reports were European, consisting of 219 patients.[18,22] This is relevant as gastric cancer is less common in Western countries where it is diagnosed at later stages since screening in Europe is not routine.[32] Additionally, Asian surgeons have been the first to embrace the new robotic system, and to date they continue to perform many robotic gastrectomies in experienced centers. Therefore, it is difficult to generalize the findings of this meta-analysis to worldwide populations of patients with gastric cancer.

To date, only one Chinese meta-analysis comparing RG vs. LG has been published.[33] The authors selected three studies from an initial collection of 52 articles up to December 2011 according to specific criteria. This resulted in a comparison of 268 patients undergoing RG vs. 650 undergoing LG. This Chinese meta-analysis did have some limitations which are acknowledged by the authors, including a limited number of published studies, small sample size, and short duration of follow-up. Indeed, each of these weaknesses is also present in our work, though ours differs in some aspects. First, the aim of our meta-analysis was to compare RG with both OG and LG, for this aspect it can be considered the first one. Second, we collected all 190 articles present in the literature up to July 2012 using an accurate research strategy. We contacted each author if some data of interest were lacking, whereas if data were unavailable, we noted this as incomplete in the database. Finally, we decided to perform a strategic double comparison in order to minimize possible bias since we realized that not all of the seven selected articles had enough quality level data and since the number of patients overall was relatively small.

Nevertheless, our meta-analysis still has some important shortcomings. The pooled studies are all retrospective and obviously limited. The number of patients entered is relatively small and sometimes comparative groups are unbalanced, which may gloss over true differences among some variables. Moreover, some characteristics are not mentioned in all of the pooled studies, such as type of surgical reconstruction, stage of the tumor, short and long-term outcomes, and follow-up period. For instance, in two of the articles,[22,23] the groups do not have the same period of recruitment. Additionally, in another of the two studies, the patients were drawn from the same database;[19,21] although, in one report, only patients who underwent subtotal gastrectomy were enrolled, while in the other report, only those who had received a total gastrectomy were considered. A final important deficiency in our work is the complete lack of information regarding costs, which could represent a real and incontrovertible problem. So far, only one article is present in the literature 21 that has reported some information regarding this aspect. Even if in the near future some other authors do focus on this topic it will remain very difficult to evaluate the cost of the robotic approach and compare it to that of more traditional methods. This is relevant as more than one insurance system is often present in each country and because insurance systems differ between countries. Furthermore, the price of the instruments and the devices is also not equivalent worldwide. Since each type of uniformity cannot be guaranteed, it is likely that the tools generally recognized for the assessment of costs will not be provided.

Many high quality prospective studies must be performed in order to assess the safety and efficacy of RG for the treatment of gastric cancer in the near future. In addition to the outcomes reported in this article, future studies should be directed at more detailed oncologic findings, survival, and costs. Currently, a multicenter prospective analysis regarding the advantage of RG vs. LG (NCT01309256) is in process in Korea, representing a good effort to assess the validity of RG.

In conclusion, our meta-analysis is the most accurate and updated work present in the literature and it can be considered as the starting point for subsequent investigations. Our study demonstrates that RG for gastric cancer is a promising new surgical technique that reduces blood loss and postoperative hospital stays compared with LG and OG, though at the price of longer operating times. RG also allows for an oncologically correct lymphadenectomy for gastric cancer treatment.

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References

1. Kitano S, Shiraishi N. Minimally invasive surgery for gastric tumors. Surg Clin North Am 2005;85:151-164.
2. Kitano S, Iso Y, Moriyama M, Sugimachi K. Laparoscopy-assisted Billroth I gastrectomy. Surg Laparosc Endosc 1994;4:146-148.
3. Kim HH, Hyung WJ, Cho GS, Kim MC, Han SU, Kim W, et al. Morbidity and mortality of laparoscopic gastrectomy versus open gastrectomy for gastric cancer: an interim report--a phase III multicenter, prospective, randomized Trial (KLASS Trial). Ann Surg 2010;251:417-420.
4. Kim YW, Baik YH, Yun YH, Nam BH, Kim DH, Choi IJ, et al. Improved quality of life outcomes after laparoscopy-assisted distal gastrectomy for early gastric cancer: results of a prospective randomized clinical trial. Ann Surg 2008;248:721-727.
5. Katai H, Sasako M, Fukuda H, Nakamura K, Hiki N, Saka M, et al; JCOG Gastric Cancer Surgical Study Group. Safety and feasibility of laparoscopy-assisted distal gastrectomy with suprapancreatic nodal dissection for clinical stage I gastric cancer: a multicenter phase II trial (JCOG 0703). Gastric Cancer 2010;13:238-244.
6. Wei HB, Wei B, Qi CL, Chen TF, Huang Y, Zheng ZH, et al. Laparoscopic versus open gastrectomy with D2 lymph node dissection for gastric cancer: a meta-analysis. Surg Laparosc Endosc Percutan Tech 2011;21:383-390.
7. Park do J, Han SU, Hyung WJ, Kim MC, Kim W, Ryu SY, et al; Korean Laparoscopic Gastrointestinal Surgery Study (KLASS) Group. Long-term outcomes after laparoscopy-assisted gastrectomy for advanced gastric cancer: a large-scale multicenter retrospective study. Surg Endosc 2012;26:1548-1553.
8. Giulianotti PC, Coratti A, Angelini M, Sbrana F, Cecconi S, Balestracci T, et al. Robotics in general surgery: personal experience in a large community hospital. Arch Surg 2003;138:777-784.
9. Hyung WJ. Robotic surgery in gastrointestinal surgery. Korean J Gastroenterol 2007;50:256-259.
10. Gutt CN, Oniu T, Mehrabi A, Kashfi A, Schemmer P, Büchler MW. Robot-assisted abdominal surgery. Br J Surg 2004;91:1390-1397.
11. Baek SJ, Lee DW, Park SS, Kim SH. Current status of robot-assisted gastric surgery. World J Gastrointest Oncol 2011;3:137-143.
12. Wall J, Marescaux J. Robotic gastrectomy is safe and feasible, but real benefits remain elusive. Arch Surg 2011;146:1092.
13. Lanfranco AR, Castellanos AE, Desai JP, Meyers WC. Robotic surgery: a current perspective. Ann Surg 2004;239:14-21.
14. Buchs NC, Bucher P, Pugin F, Morel P. Robot-assisted gastrec-

tomy for cancer. Minerva Gastroenterol Dietol 2011;57:33-42.
15. Hashizume M, Sugimachi K. Robot-assisted gastric surgery. Surg Clin North Am 2003;83:1429-1444.
16. Wells GA, Shea B, O'Connell D, Peterson J, Welch V, Losos M, et al. The Newcastle-Ottawa Scale (NOS) for assessing the quality of non-randomized studies in meta-analyses. Available from: http://www.ohri.ca/programs/clinical_epidemiology/oxford.asp/ Accessed 18 June, 2007.
17. Kim MC, Heo GU, Jung GJ. Robotic gastrectomy for gastric cancer: surgical techniques and clinical merits. Surg Endosc 2010;24:610-615.
18. Pugliese R, Maggioni D, Sansonna F, Costanzi A, Ferrari GC, Di Lernia S, et al. Subtotal gastrectomy with D2 dissection by minimally invasive surgery for distal adenocarcinoma of the stomach: results and 5-year survival. Surg Endosc 2010;24:2594-2602.
19. Yoon HM, Kim YW, Lee JH, Ryu KW, Eom BW, Park JY, et al. Robot-assisted total gastrectomy is comparable with laparoscopically assisted total gastrectomy for early gastric cancer. Surg Endosc 2012;26:1377-1381.
20. Woo Y, Hyung WJ, Pak KH, Inaba K, Obama K, Choi SH, et al. Robotic gastrectomy as an oncologically sound alternative to laparoscopic resections for the treatment of early-stage gastric cancers. Arch Surg 2011;146:1086-1092.
21. Eom BW, Yoon HM, Ryu KW, Lee JH, Cho SJ, Lee JY, et al. Comparison of surgical performance and short-term clinical outcomes between laparoscopic and robotic surgery in distal gastric cancer. Eur J Surg Oncol 2012;38:57-63.
22. Caruso S, Patriti A, Marrelli D, Ceccarelli G, Ceribelli C, Roviello F, et al. Open vs robot-assisted laparoscopic gastric resection with D2 lymph node dissection for adenocarcinoma: a case-control study. Int J Med Robot 2011;7:452-458.
23. Huang KH, Lan YT, Fang WL, Chen JH, Lo SS, Hsieh MC, et al. Initial experience of robotic gastrectomy and comparison with open and laparoscopic gastrectomy for gastric cancer. J Gastrointest Surg 2012;16:1303-1310.
24. Schreiber GB, Busch MP, Kleinman SH, Korelitz JJ. The risk of transfusion-transmitted viral infections. The Retrovirus Epidemiology Donor Study. N Engl J Med 1996;334:1685-1690.
25. Hyung WJ, Noh SH, Shin DW, Huh J, Huh BJ, Choi SH, et al. Adverse effects of perioperative transfusion on patients with stage III and IV gastric cancer. Ann Surg Oncol 2002;9:5-12.
26. Maeta M, Shimizu N, Oka A, Kondo A, Yamashiro H, Tsujitani S, et al. Perioperative allogeneic blood transfusion exacerbates surgical stress-induced postoperative immunosuppression and has a negative effect on prognosis in patients with gastric cancer. J Surg Oncol 1994;55:149-153.
27. Siewert JR, Böttcher K, Roder JD, Busch R, Hermanek P, Meyer HJ. Prognostic relevance of systematic lymph node dissection in gastric carcinoma. German Gastric Carcinoma Study Group. Br J Surg 1993;80:1015-1018.
28. Huang CM, Lin JX, Zheng CH, Li P, Xie JW, Wang JB. Impact of the number of dissected lymph nodes on survival for gastric cancer after distal subtotal gastrectomy. Gastroenterol Res Pract 2011;2011:476014.
29. Marubini E, Bozzetti F, Miceli R, Bonfanti G, Gennari L; Gastrointestinal Tumor Study Group. Lymphadenectomy in gastric cancer: prognostic role and therapeutic implications. Eur J Surg Oncol 2002;28:406-412.
30. Lee HK, Yang HK, Kim WH, Lee KU, Choe KJ, Kim JP. Influence of the number of lymph nodes examined on staging of gastric cancer. Br J Surg 2001;88:1408-1412.
31. Kwon SJ. Evaluation of the 7th UICC TNM staging system of gastric cancer. J Gastric Cancer 2011;11:78-85.
32. Dicken BJ, Bigam DL, Cass C, Mackey JR, Joy AA, Hamilton SM. Gastric adenocarcinoma: review and considerations for future directions. Ann Surg 2005;241:27-39.
33. Xiong B, Ma L, Zhang C. Robotic versus laparoscopic gastrectomy for gastric cancer: a meta-analysis of short outcomes. Surg Oncol 2012;21:274-280.