

Comparison of perioperative and short-term outcomes between robotic and conventional laparoscopic surgery for colonic cancer: a systematic review and meta-analysis

Sungwon Lim*, Jin Hee Kim^{1,*}, Se-Jin Baek², Seon-Hahn Kim², Seon Heui Lee³

National Evidence-Based Healthcare Collaborating Agency, Seoul, ¹Department of Nursing, College of Medicine, Chosun University, Gwangju, ²Division of Colorectal Surgery, Department of Surgery, Korea University College of Medicine, Seoul, ³Department of Nursing Science, College of Nursing, Gachon University, Incheon, Korea

Purpose: Reports from several case series have described the feasibility and safety of robotic surgery (RS) for colonic cancer. Experience is still limited in robotic colonic surgery, and a few meta-analysis has been conducted to integrate the results for colon cancer specifically. We conducted a systematic review of the available evidence comparing the surgical safety and efficacy of RS with that of conventional laparoscopic surgery (CLS) for colonic cancer.

Methods: We searched English databases (MEDLINE, Embase, and Cochrane Library), and Korean databases (KoreaMed, KMBase, KISS, RISS, and KisTi). Dichotomous variables were pooled using the risk ratio, and continuous variables were pooled using the mean difference (MD).

Results: The present study found that the RS group had a shorter time to resumption of a regular diet (MD, -0.62 days; 95% CI, -0.97 to -0.28), first passage of flatus (MD, -0.44 days; 95% CI, -0.66 to -0.23) and defecation (MD, -0.62 days; 95% CI, -0.77 to -0.47). Also, RS was associated with a shorter hospital stay (MD, -0.69 days; 95% CI, -1.12 to -0.26), a lower estimated blood loss (MD, -19.49 mL; 95% CI, -27.10 to -11.89) and a longer proximal margin (MD, 2.29 cm; 95% CI, 1.11–3.47). However, RS was associated with a longer surgery time (MD, 51.00 minutes; 95% CI, 39.38–62.62).

Conclusion: We found that the potential benefits of perioperative and short-term outcomes for RS than for CLS. For a more accurate understanding of RS for colonic cancer patients, robust comparative studies and randomized clinical trials are required.

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Key Words: Robotic surgical procedures, Colonic neoplasms

INTRODUCTION

In the last decade, laparoscopic surgery has become popular in many surgical fields due to its advantages compared to the open approach, such as less pain, faster recovery/resumption of daily activities, and better cosmesis [1,2]. However, because laparoscopic surgery is more technically demanding, for reasons including the limited range of instrument motion, relative

loss of dexterity, and inadequate visualization, laparoscopic surgery continues to be stressful for surgeons, and the learning curve is very steep [3,4]. The da Vinci robotic surgical system (Intuitive Surgical, Sunnyvale, CA, USA) has been applied to overcome the ergonomic discomfort of laparoscopic surgery, with advanced technologies including superior 3-dimensional views and an internal articulated EndoWrist[®] that improves dexterity and allows seven degrees of freedom [5,6]. With these

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Corresponding Author: Seon Heui Lee

Department of Nursing Science, College of Nursing, Gachon University,
 191, Hambangmoe-ro, Yeonsu-gu, Incheon 21936, Korea

Tel: +82-32-820-4235, Fax: +82-32-820-4201

E-mail: sunarea87@gachon.ac.kr

*Sungwon Lim and Jin Hee Kim contributed equally to this study as co-first authors.

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advantages, robotic surgery (RS) has been adopted rapidly for advanced surgical procedures in many fields, such as urologic, gynecologic, and cardiac surgery [7-9].

The first robot-assisted colorectal surgery was reported in 2002 [10]. Recently, much of the reported data has been from robotic surgeries for rectal cancer, because robotic technology is of maximal advantage in narrow spaces such as the mediastinum and pelvic cavity, and it is very useful for the pelvic dissection known as total mesorectal excision in rectal cancer surgery [11,12]. On the other hand, the role of robotic surgical systems in colonic surgery is still under debate. Thus, there are a few reports of robot-assisted colonic surgery, and only one meta-analysis of RS for right colon cancer has been reported [13]. Therefore, we conducted a systematic review of the available evidence comparing the surgical safety and efficacy of RS with that of conventional laparoscopic surgery (CLS) for colonic cancer.

METHODS

Search strategy and study selection

We searched Ovid-MEDLINE (1946–2014), Embase (inception–2014), and the Cochrane Library on June 25, 2014. Korean databases (KoreaMed, KMBase, KISS, RISS, and KIST) also were searched. To ensure a highly sensitive search, we designed search strategies that included pertinent MeSH (medical

subject headings), common keywords, and comprehensive combinations of them. Search terms combined patient-related terms (colon neoplasms, colon cancer, colon carcinoma, and colon tumor), operation terms (colectomy) and intervention terms (robotic, computer-assisted surgery, telerobot, remote operation, remote surgery, and da Vinci).

A total of 775 records were identified through the search. After duplicates were removed, 635 studies were imported for the first title and abstract screening. We excluded 584 after examining the titles and abstracts, based on exclusion criteria. A total of 51 articles were obtained to conduct the full-text review. Next, we excluded 46 publications because 9 included nonrelevant patients, 4 included nonrelevant interventions, 2 included nonrelated comparators, 7 were not original papers, 23 were gray literature, and 1 was not in English or Korean. Also, one additional article was found during our hand searches of relevant bibliographies. We considered sample size, publication year, study design, and the number of outcomes of interest, in order to choose high-quality data with a low risk of bias for publications with possible overlap. Ultimately, six publications were selected for the meta-analysis (Fig. 1).

Study eligibility

In accordance with the preferred reporting items for randomized controlled trials (RCTs), systematic reviews and meta-analysis statement, 2 authors (Lim and Kim) independently

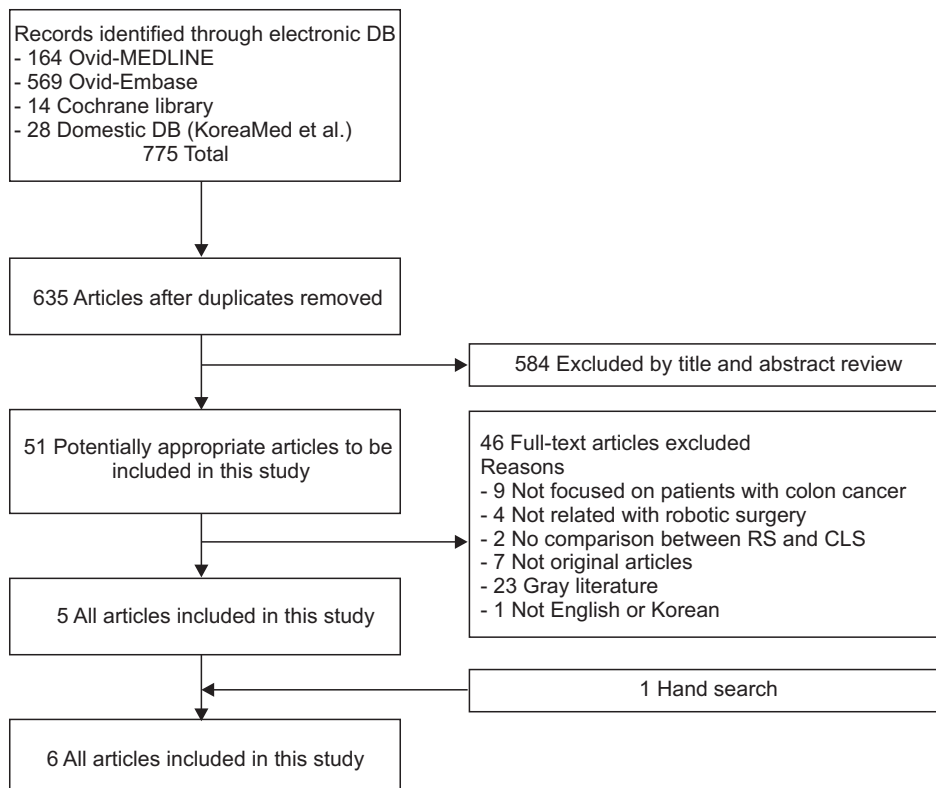


Fig. 1. Flow diagram of the study selection process. RS, robotic surgery; CLS, conventional laparoscopic surgery.

evaluated the titles and abstracts of the references to exclude irrelevant studies, and full-text review was subsequently performed for potentially relevant articles. The inclusion criteria allowed studies of patients with colonic cancer and compared surgical and patient outcomes between RS and CLS. The inclusion criteria were as follows: (1) studies that focused on patients only with colonic cancer; (2) comparative studies of RS and CLS; and (3) studies that reported at least one outcome of interest. Studies were excluded if they were (1) not original articles and (2) preclinical studies and protocols.

Data extraction and quality assessment

Two independent authors (Lim and Kim) performed the data extraction and quality assessment using a data extraction form. Quality assessment also was performed independently by the reviewers using the Cochrane Risk of Bias (RoB) for randomized controlled trials [14] and the Risk of Bias Assessment tool for Nonrandomized Studies (RoBANS 2.0) for nonrandomized comparative studies [15]. RoB is composed of 7 domains and RoBANS 2.0 is composed of 8 domains to assess the methodological quality of studies. Each criterion was evaluated as 'low risk of bias', 'high risk of bias', or 'unclear'. If the study did not mention a certain criterion, we evaluated it as 'unclear'. In each instance of disagreement, the case was discussed with all authors.

Baseline characteristics of the study participants

Age, sex ratio, body mass index, American Society of Anesthesiologists class, clinical stage and pathology, and tumor size were recorded as demographic and clinical characteristics.

Information about interventions

The collected information about RS and CLS included the extent of surgical colonic resection, the anastomosis technique (e.g., extracorporeal or intracorporeal) and the name of the equipment used.

Outcomes for safety

Adverse event and postoperative complication variables included 30-day mortality, conversion to open surgery, ileus, anastomotic leakage, wound rupture, postoperative bleeding, pneumonia, chyloperitoneum, intra-abdominal abscess, acute myocardial infarction, stroke, wound infection, and urinary tract infection.

Outcomes for efficacy

Readmission rate, time to regular diet, time to first flatus, time to first defecation, proximal margin, distal margin, operative time, length of stay, and estimated blood loss (EBL) were assessed.

Table 1. Characteristics of the eligible studies

Study	Year	Country	Study type	Cancer location	No. of patients		Sex, M:F		Age (yr)		BMI (kg/m ²)		Anastomosis technique	
					Total	RS	CLS	RS	CLS	RS	CLS	RS		CLS
Park et al. [18]	2012	Korea	RCT	Right-sided colon	70	35	35	14:21	16:19	62.8 ± 10.5	66.5 ± 11.4	24.4 ± 2.5	23.8 ± 2.7	Intracorporeal and extracorporeal
Shin [19]	2012	Korea	NCS	Right-sided and left sided colon	31	13	18	NR	NR	NR	NR	NR	NR	Extracorporeal
Lim et al. [17]	2013	Korea	RCS	Sigmoid colon	180	34	146	23:11	87:59	59.6 ± 8.4	59.7 ± 11.5	24.8 ± 2.1	23.8 ± 3.8	Extracorporeal
Morpurgo et al. [20]	2013	Italy	NCS	Right-sided colon	96	48	48	27:21	16:32	68 ± 8	74 ± 11	25 ± 3.5	28 ± 4	Intracorporeal
Helvind et al. [21]	2013	Denmark	NCS	All colonic cancer	263	101	162	43:58	69:93	72.2 (39-93)	75.3 (47-96)	24.6 (16.8-36.0)	24.9 (15.2-45.7)	Extracorporeal
de'Angelis et al. [22]	2015	France	NCS	Transverse colon	44	22	22	15:7	15:7	72.18 ± 10.79	71 ± 10.14	24.12 ± 2.64	24.28 ± 2.7	Extracorporeal

Values are presented as mean ± standard deviation or median (range) unless otherwise indicated. RS, robotic surgery; CLS, conventional laparoscopic surgery; BMI, body mass index; RCT, randomized controlled trials; NCS, nonconcurrent cohort study; RCS, retrospective cohort study; NR, no record.

Statistical analysis

We performed all meta-analyses with Review Manager, V. 5.3 (RevMan, Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2014) and used the two-tailed test of significance ($P < 0.05$). Dichotomous variables were pooled using the risk ratio (RR), and continuous variables were pooled using the mean difference (MD). RR and MD were calculated and reported with 95% confidence intervals (CI). The Cochrane Q statistic and I^2 statistic were used to evaluate statistical heterogeneity [16]. A fixed effects model was used for studies with low or moderate statistical heterogeneity ($I^2 < 25$, 25%–50%), and a random effects model was used for studies with high statistical heterogeneity ($I^2 > 50\%$). Meta-analyses of dichotomous variables were conducted using the Mantel-Haenszel method, and those of continuous variables were performed using the inverse variance method.

Ethical consideration

This study was reviewed and approved by the Institutional Review Board at the National Evidence-Based Healthcare Collaborating Agency (NECA); approval number: NECA IRB 14-019.

RESULTS

Study characteristics

Table 1 shows the characteristics of the included studies [17-22]. The six studies included 684 patients: 253 in the RS group and 431 in the CLS group. One study was an RCT, one was a prospective cohort study, and four were historical cohort studies. Of the 6 studies, 3 were conducted in Korea, 1 was conducted in Italy, 1 was conducted in Denmark, and 1 was conducted in France. All studies had been published during the previous 4 years (2012–2015) (Table 1). Importantly, Shin [19] reported perioperative outcomes divided into left-sided and right-sided colon cancer. So, this outcomes were included respectively. The risk of bias in the RCT was high, and the quality of the cohort studies was poor. The detailed information is summarized in Fig. 2.

Safety outcomes

In terms of safety, there were no significant differences in operative outcome between the RS and CLS groups, including complications. The meta-analysis revealed no differences between the two groups in terms of 30-day mortality (RR, 0.26; 95% CI, 0.03–2.13) and conversion to open surgery (RR, 1.06; 95% CI, 0.39–2.87). Also, no significant differences between

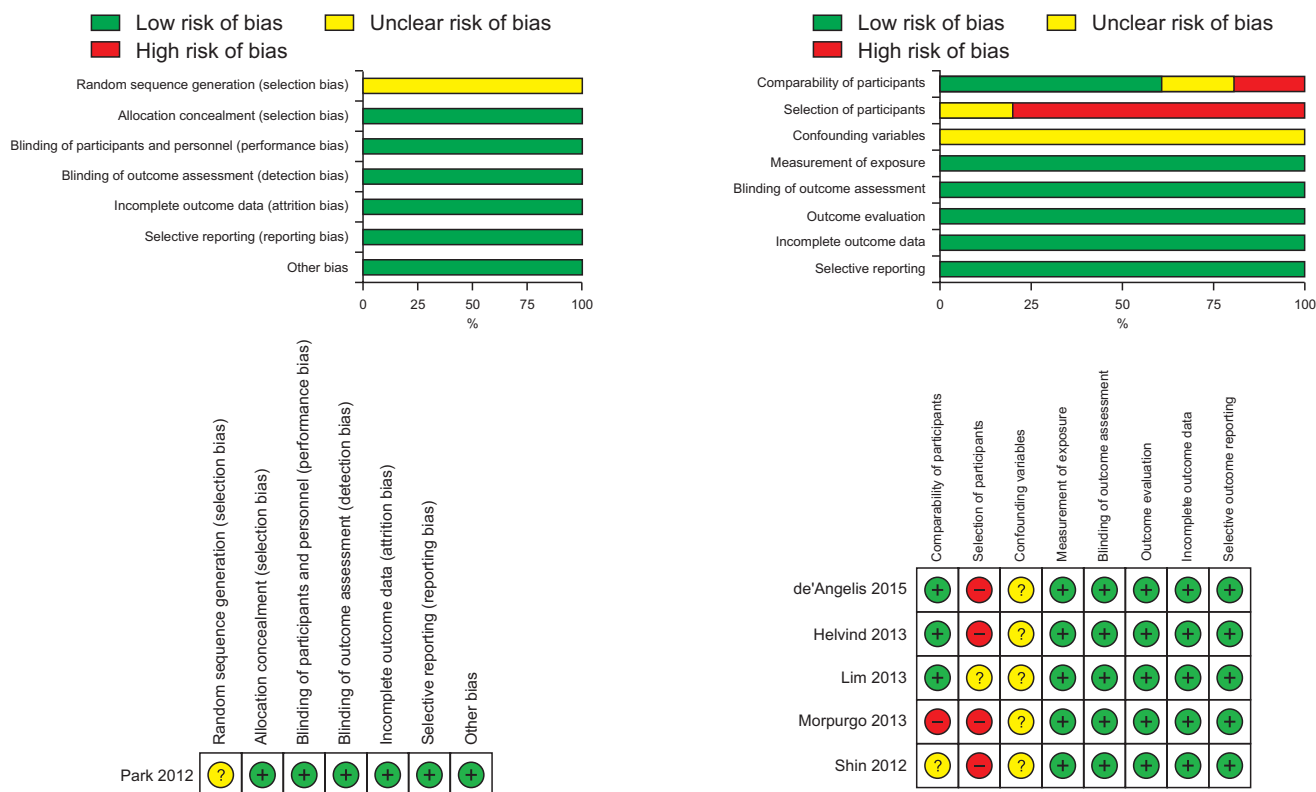


Fig. 2. Quality assessment of included studies. Quality assessment was performed using cochrane risk of bias (RoB) for randomized controlled trials and nonrandomized studies (RoBANS 2.0) for nonrandomized comparative studies. Green, low risk of bias; yellow, unclear; red, high risk of bias.

Table 2. Efficacy and safety outcomes

Outcomes	No. of studies	Study size (n)		Heterogeneity		Effect measure	Statistical method	Analysis model	Pooled effect		
		RS	CLS	P-value	I ² (%)				95% CI	P-value	
Safety outcomes											
30-Day mortality	5	239	407	-	-	RR	M-H	FE	0.26 (0.03 to 2.13)	0.210	
Conversion to open surgery	4	166	234	0.150	47	RR	M-H	FE	1.06 (0.39 to 2.87)	0.900	
Ileus	4	190	359	0.260	25	RR	M-H	FE	1.25 (0.48 to 3.30)	0.650	
Anastomotic leakage	4	139	251	0.560	0	RR	M-H	FE	0.64 (0.18 to 2.29)	0.490	
Postoperative bleeding	4	191	364	0.620	0	RR	M-E	FE	0.70 (0.17 to 2.90)	0.620	
Pneumonia	2	81	304	-	-	RR	M-E	FE	3.36 (0.87 to 12.93)	0.080	
Intra-abdominal abscess	4	189	359	0.660	0	RR	M-E	FE	0.54 (0.18 to 1.66)	0.280	
Wound infection	5	238	406	0.870	0	RR	M-E	FE	0.74 (0.35 to 1.54)	0.300	
Efficacy outcomes											
Time to regular diet (day)	3	91	203	0.870	0	MD	IV	FE	-0.62 (-0.97 to -0.28)	<0.001	
Time to first flatus (day)	5	152	269	0.050	55	MD	IV	FE	-0.44 (-0.66 to -0.23)	<0.001	
Time to first defecation (day)	2	82	194	0.070	69	MD	IV	FE	-0.62 (-0.77 to -0.47)	<0.001	
Number of retrieved lymph nodes	4	130	247	0.190	35	MD	IV	FE	-1.86 (-4.13 to 0.42)	0.110	
Proximal margin (cm)	2	69	181	0.250	24	MD	IV	FE	2.29 (1.11 to 3.47)	<0.001	
Distal margin (cm)	2	69	181	0.160	50	MD	IV	FE	0.76 (-0.41 to 1.94)	0.200	
Operative time (min)	5	152	269	0.460	0	MD	IV	FE	51.00 (39.38 to 62.62)	<0.001	
Length of stay (day)	5	152	269	0.090	48	MD	IV	FE	-0.69 (-1.12 to -0.26)	0.002	
Estimated blood loss (mL)	3	82	199	0.620	0	MD	IV	FE	-19.49 (-27.10 to -11.89)	<0.001	

RS, robotic surgery; CLS, conventional laparoscopic surgery; CI, confidence interval; RR, risk ratio; MD, mean difference; M-H, Mantel-Haenszel; IV, inverse variance; FE, fixed effects.

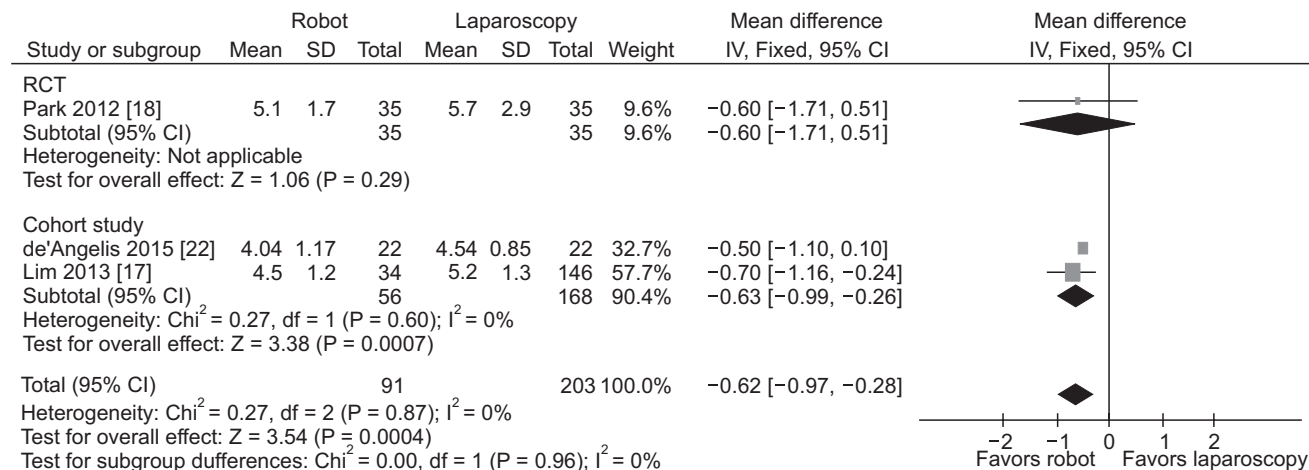
the 2 groups were found in complications such as ileus (RR, 1.25; 95% CI, 0.48–3.30), anastomotic leakage (RR, 0.64; 95% CI, 0.18–2.29), postoperative bleeding (RR, 0.70; 95% CI, 0.17–2.90), pneumonia (RR, 3.36; 95% CI, 0.87–12.93), intra-abdominal abscess (RR, 0.54; 95% CI, 0.18–1.66), and wound infection (RR, 0.74; 95% CI, 0.35–1.54), with a low heterogeneity (Table 2).

Efficacy outcomes

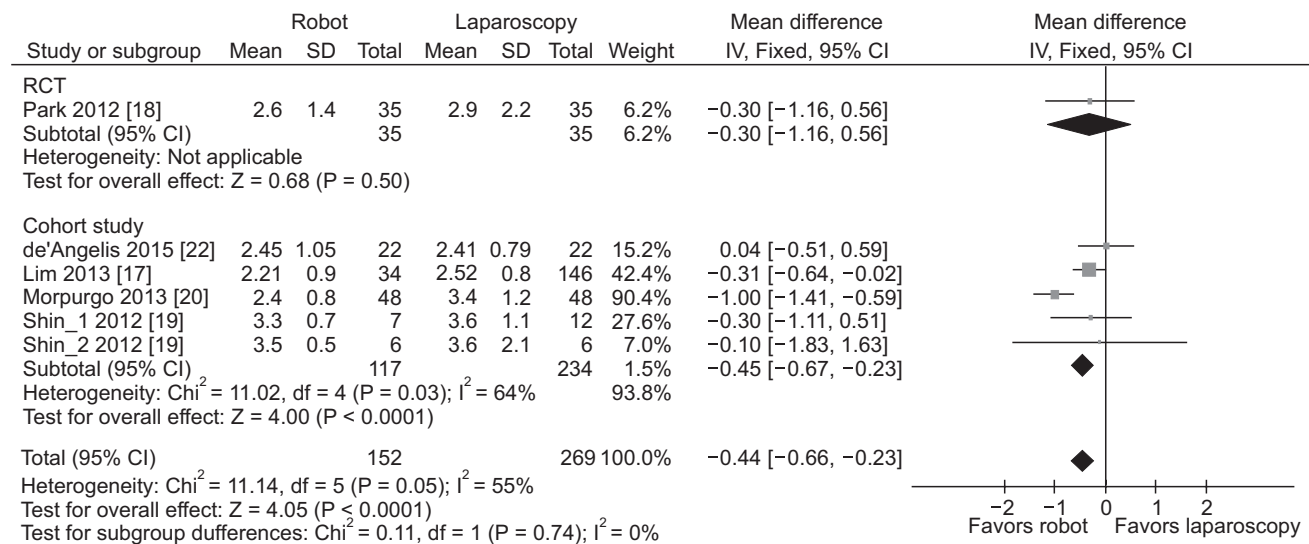
Time to regular diet (days)

Three studies [17,18,22] analyzed the time to regular diet. The pooled estimates using a fixed effects model revealed that the time was significantly shorter for RS than for CLS (MD, -0.62 days; 95% CI, -0.97 to -0.28), with no heterogeneity between

A



B



C

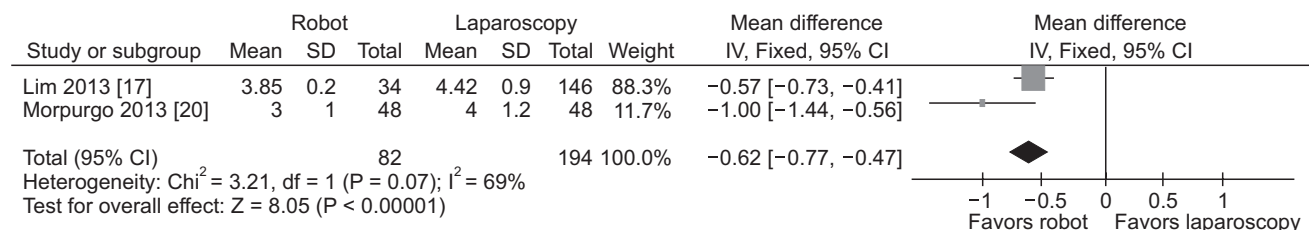
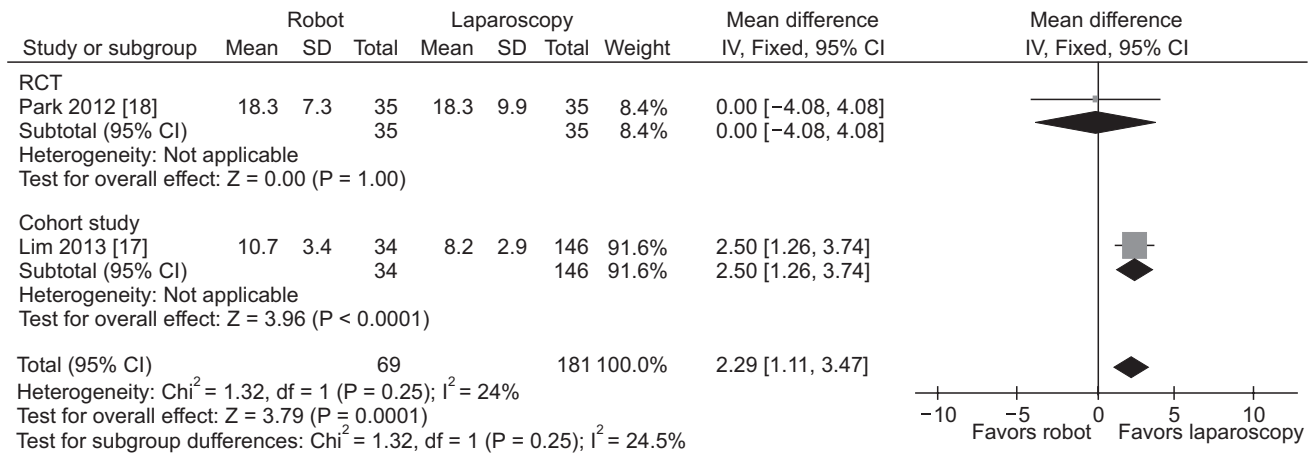
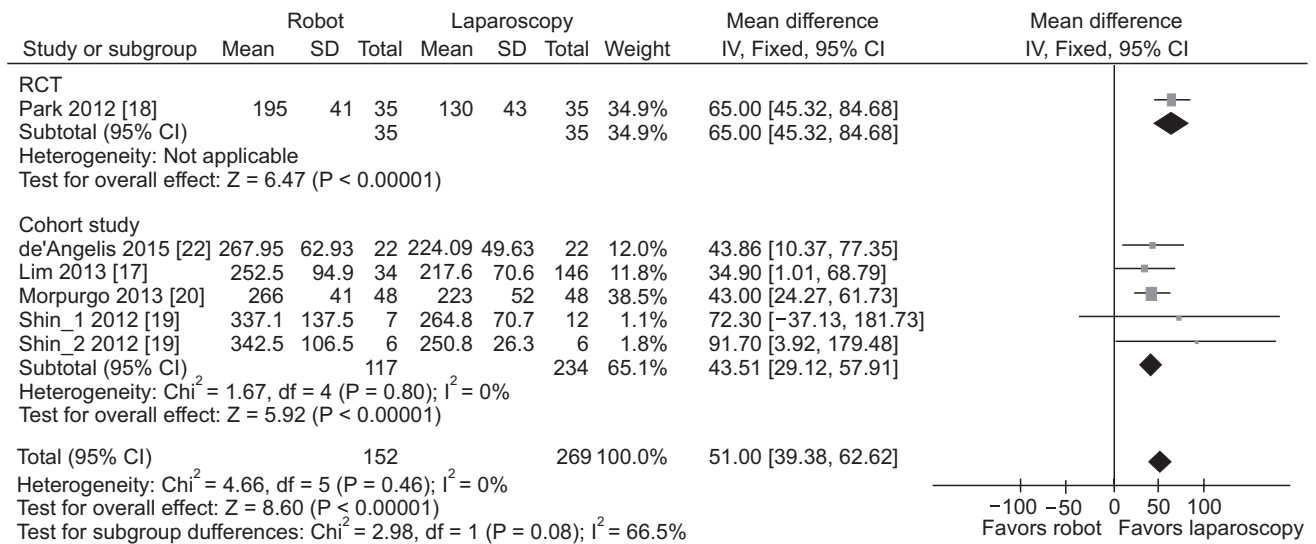


Fig. 3. Forest plot and meta-analysis of time to regular diet (A); time to first flatus (B); time to first defecation (C); number of proximal margin (D); operative time (E); length of stay (F); and estimated blood loss (G). SD, standard deviation; CI, confidence interval; RCT, randomized controlled trial.

D



E



F

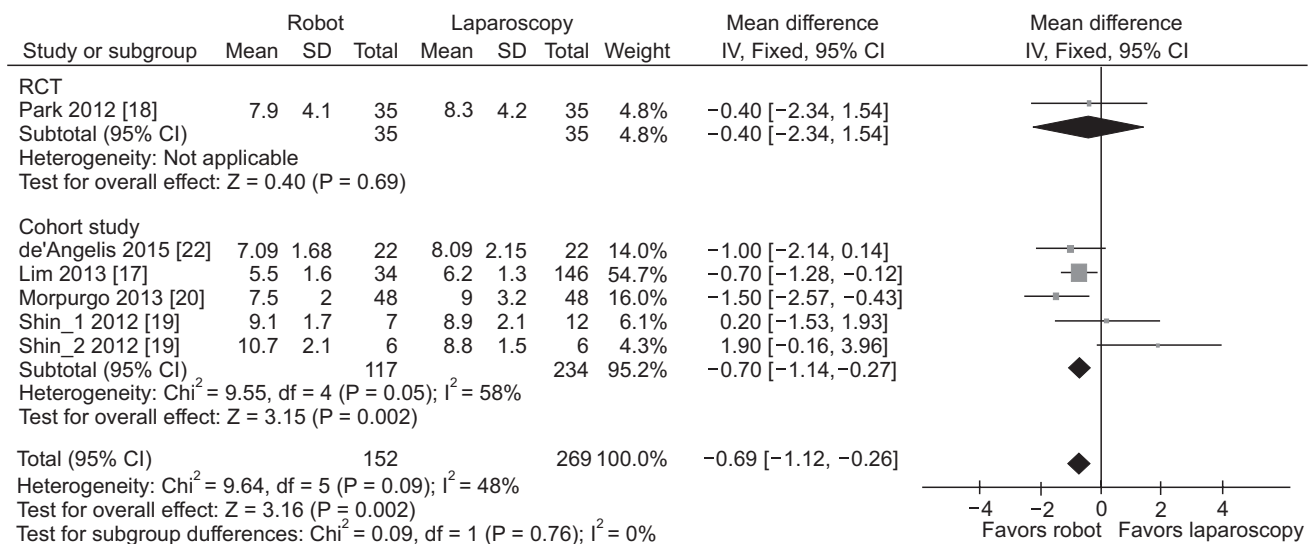


Fig. 3. Continued.

G

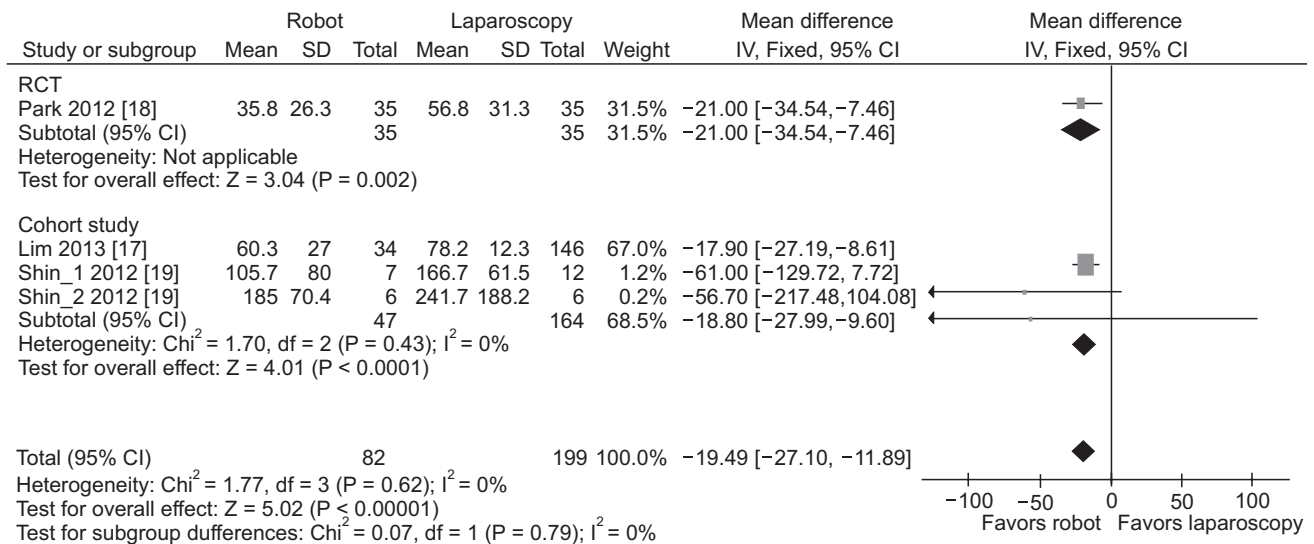


Fig. 3. Continued.

the studies ($P = 0.870$, $I^2 = 0\%$) (Table 2, Fig. 3A).

Time to first flatus (days)

Five studies [17-20,22] analyzed the time to first flatus. The pooled estimates using a fixed effects model revealed that the time was significantly shorter for RS than for CLS (MD, -0.44 days; 95% CI, -0.66 to -0.23), with no heterogeneity among the studies ($P = 0.050$, $I^2 = 55\%$) (Table 2, Fig. 3B).

Time to first defecation (days)

Two studies [17,20] analyzed the time to first defecation. The pooled estimates using a fixed effects model revealed that the time was significantly shorter for RS than for CLS (MD, -0.62 days; 95% CI, -0.77 to -0.47), with heterogeneity between the studies ($P = 0.070$, $I^2 = 69\%$) (Table 2, Fig. 3C).

Proximal margin (cm)

Two studies [17,18] reported the proximal margin. Significantly longer proximal margins were observed in patients undergoing RS than in those undergoing CLS (MD, 2.29 cm; 95% CI, 1.11-3.47), with no heterogeneity ($P = 0.250$, $I^2 = 24\%$) (Table 2, Fig. 3D).

Operative time (min)

The operating time was reported in five studies [17-20,22] comparing RS and CLS. The pooled estimates using a fixed effects model revealed a significantly longer operating time for RS than for CLS (MD, 51.00 minutes; 95% CI, 39.38-62.62), with no heterogeneity ($P = 0.460$, $I^2 = 0\%$) (Table 2, Fig. 3E).

Length of stay (days)

The length of stay was reported in five studies [17-20,22] comparing RS and CLS. The pooled estimates using a fixed effects model revealed a significantly shorter length of stay RS than for CLS (MD, -0.69 days; 95% CI, -1.12 to -0.26), with a low heterogeneity ($P = 0.090$, $I^2 = 48\%$) (Table 2, Fig. 3F).

Estimated blood loss (mL)

The EBL was reported in 3 studies [17-19] comparing RS and CLS. The pooled estimates using a fixed effects model revealed a significantly lower blood loss for RS than for CLS (MD, -19.49 mL; 95% CI, -27.10 to -11.89), with no heterogeneity ($P = 0.620$, $I^2 = 0\%$) (Table 2, Fig. 3G).

Finally, no significant differences were found between the 2 groups in the number of retrieved lymph nodes (MD, -1.86; 95% CI, -4.13 to 0.42) or the distal margins (MD, 0.76 cm; 95% CI, -0.41 to 1.94) (Table 2).

Publication bias

Publication bias was tested using the funnel plot analysis of the studies on the overall postoperative outcomes after RS compared to those after CLS. The funnel plot representing potential publication bias among the studies was fairly symmetric (Fig. 4)

DISCUSSION

Our study showed that robot-assisted colectomy was feasible and safe compared with CLS in terms of intraoperative and postoperative complications and the rate of open conversion.

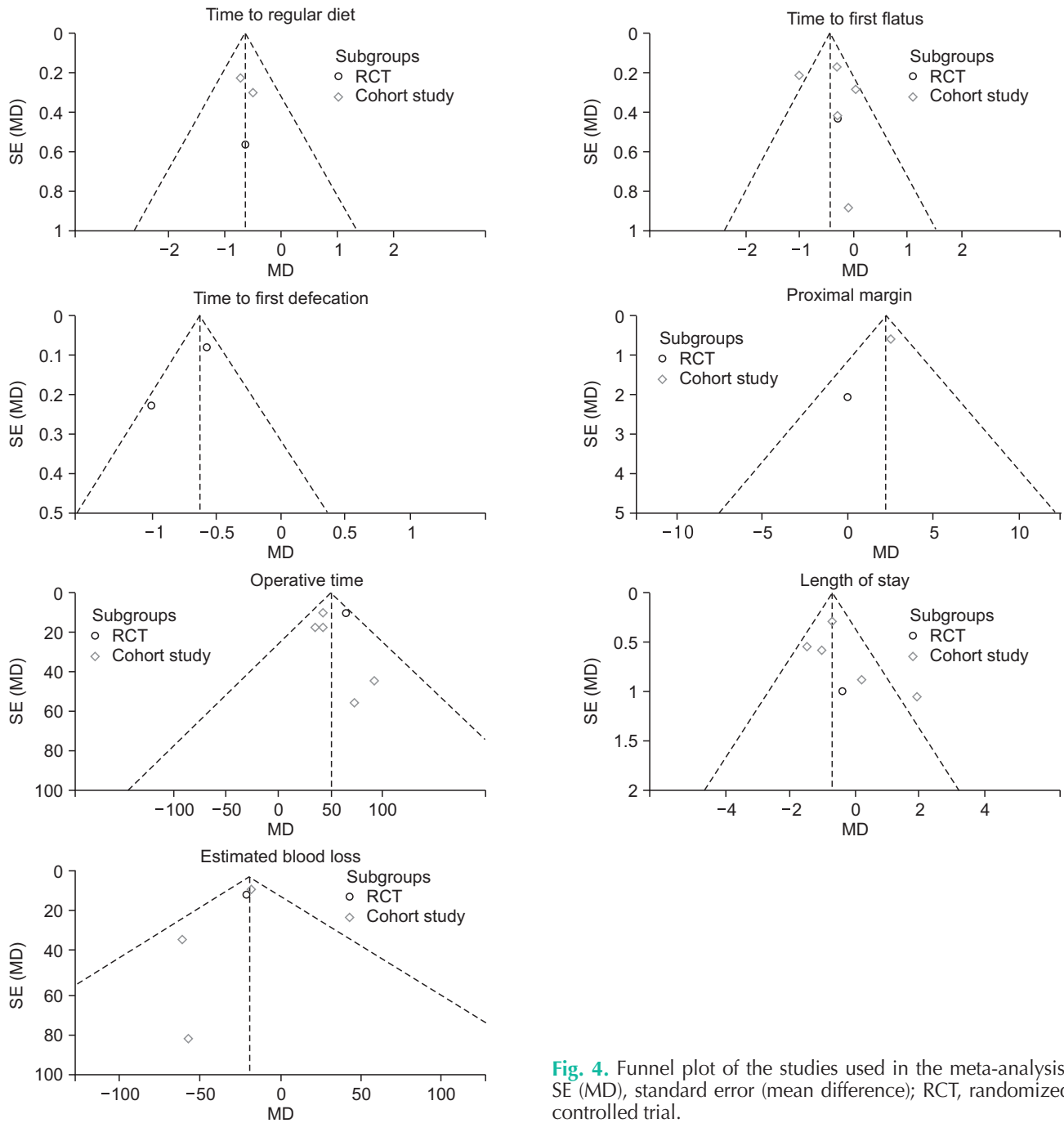


Fig. 4. Funnel plot of the studies used in the meta-analysis. SE (MD), standard error (mean difference); RCT, randomized controlled trial.

In addition, the times to diet resumption, recovery of bowel function, and postoperative hospital release were shorter in the RS group than in the CLS group. In the RS group, the EBL was lower and the proximal margin of the specimen was longer, but the operative time was significantly longer than in the CLS group. These results are similar to those of other published studies and the previous meta-analysis for rectal cancer [12,23-25].

To date, most of the published data for robotic colorectal surgery have described rectal cancer surgery, because the

advantages of robotic technology are maximized in narrow spaces such as the pelvic cavity, and robotic systems have been adopted more rapidly for rectal surgery than for colonic surgery [11,26]. Most of the studies comparing robotic rectal surgery with conventional laparoscopic rectal surgery have reported good results for RS in terms of safety outcomes, and comparable or better results in terms of efficacy outcomes, except for operation time. The current study demonstrated that the advantages of robotic systems shown in rectal surgery also hold true in colonic surgery. To date, there has been only one

systematic review comparing robotic and laparoscopic surgeries for right colectomy, which was reported by Xu et al. [13]. Otherwise, our study is the first systematic review including whole colonic surgery from the right colon to the sigmoid colon.

In fact, colonic surgery can be divided largely into right-sided colectomy and left-sided colectomy, and the 2 types of surgery are very different. There are differences between the 2 groups in most fields of anatomy, tumor characteristics, methods of dissection and anastomosis, and these can affect the incidence of complications and the prognosis. Therefore, the advantages of robotic systems may differ in right-sided colectomy and left-sided colectomy generally. In conventional laparoscopic right-sided colectomy, extracorporeal stapled anastomosis is commonly performed through minilaparotomy. Robotic technology in right-sided colectomy facilitates intracorporeal hand-sewn anastomosis, and can reduce the incision size for specimen extraction, shift the incision site to a Pfannenstiel incision, cause less pain, less incisional hernia and allow better cosmesis [20,27,28]. On the other hand, the advantages of robotic left-side colectomy can be expected to be similar to those of robotic rectal surgery, such as nerve preservation during inferior mesenteric artery dissection, and easy mobilization of the splenic flexure [29].

Because the expected advantages of robotic technology differ among surgery types, the fact that this study included whole colectomy may be a limitation. Nevertheless, it may be an important and significant finding of this study that the advantage of robotic rectal surgery can be applied equally for colonic surgery. In our study, robotic colectomy was not only feasible, but also safe compared with CLS. However, the operative time was significantly longer in the RS group, as reported in other studies, because additional time may be necessary for robot set-up, docking, and the learning curve [30].

A very interesting observation in our study was that there was no difference in the conversion rates of robotic and laparoscopic colectomy. Xu et al. [13] reported similar results. In previous reports of rectal surgery, however, the conversion rate usually was lower in the RS group than in the CLS group [23-25], because the robotic system may help to overcome the anatomical difficulty of the narrow pelvis; this point has been important in justifying the use of robotic rectal surgery. On the contrary, the level of difficulty of colectomy is easy compared with proctectomy, so this advantage of RS may not appear significant for colectomy, although there are some merits of RS for intracorporeal suture or splenic flexure mobilization. Thus, there might not be a significant difference in the conversion rates of the two procedures. This has been the weak point in the justification of the very high cost of RS compared with laparoscopic surgery for colectomy, unlike for rectal surgery, and remains a controversial topic. As our study also demonstrated, however, there are many advantages of RS, such as lower

blood loss, earlier recovery of bowel function, shorter hospital stays, and longer proximal margins of the specimens, and future studies should be performed to evaluate more potential advantages of robotics.

Despite our findings, this study has several limitations. First, there were limitations in the meta-analysis because of the lack of primary studies comparing RS and CLS for patients with colonic cancer. There is a need for additional high-quality primary studies, and when a sufficient number of primary studies become available for analysis, another systematic review and meta-analysis should be conducted and compared with this study. Second, in the present study, three out of 6 studies were conducted among Koreans living in South Korea. The regional concentration of a study population commonly influences the generalizability and makes it difficult to interpret the results in the context of other countries. Finally, the comparability of the studies included in the meta-analysis was weak due to differences in baseline attributes between patients who underwent RS and CLS in the cohorts. In 2 of the 6 studies, patients who received RS were younger than those who received CLS, and the tumor sizes differed between patients who had received RS and CLS.

Prospective, protocolled long-term follow-up studies that report the oncologic results of both CLS and RS are needed to evaluate the safety and efficacy of RS. Moreover, this technique for patients with colonic cancer is still in its infancy, and thus, the technique must be reassessed once the learning curve has been overcome.

In conclusion, the present study found the times to resumption of a regular diet, first passage of flatus and defecation were shorter for RS than for CLS. Also, RS was associated with a shorter hospital stay, lower EBL and longer proximal margin than CLS. However, RS was associated with a longer surgery time. For a more accurate understanding of RS for colonic cancer patients, robust comparative studies and randomized clinical trials including a sizeable number of subjects that take into account future actions are required.

CONFLICTS OF INTEREST

No potential conflict of interest relevant to this article was reported.

ACKNOWLEDGEMENTS

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