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Single-port versus conventional multi-port laparoscopic surgery in the treatment of colorectal cancer: A systematic review and meta-analysis

Wei Xu[1,a], Jianqin Lai[1], Jin Gong[2,b,*]

[1]Jinan University, Guangzhou, China
[2]The First Affiliated Hospital of Jinan University, Guangzhou, China
[a]travisxy@stu2020.jnu.edu.cn, [b]gongjin153@163.com
[*]Corresponding author

Abstract: *Objective: To compare the clinical efficacy of single-port laparoscopic surgery (SILS) and conventional multi-port laparoscopic surgery (CMLS) in the treatment of colorectal cancer.Methods: A systematic literature search was performed in Pubmed, Embase, Cochrane library, Web of science and ClinicalTrials.gov. Randomized controlled trials (RCTs) studies comparing SILS and CMLS for colorectal cancer (CRC) were enrolled. Quality assessment was performed using the Cochrane Collaboration's risk of bias tool. Meta-analysis was performed using Review Manager 5.4.1.Results: Eight RCTs with a total of 1143 patients were finally included. The results of meta-analysis showed that the incision length of SILS group was shorter than that of CMLS group in radical resection of CRC [P = 0.003, MD = -2.64, 95% CI (-4.39, -0.89)], the tumor size in pathological specimens of SILS group was smaller than that of CMLS group [P = 0.008, MD = 0.12, 95% CI (0.03, 0.22)]; while the operation time, intraoperative blood loss, conversion rate, postoperative first anus exhaust time, postoperative first day rest pain score, hospital stay, incidence of postoperative complications, incidence of reoperation, number of dissected lymph nodes, length of pathological specimens, distance from the distal resection margin of the tumor and distance from the proximal resection margin of the tumor was not statistically different between SILS and CMLS.Conclusion: SILS is feasible and safe in the treatment of colorectal cancer, and may be more advantageous in terms of cosmetic results. Long-term outcomes need to be confirmed by larger RCTs with complete follow-up data.*

Keywords: *Single-port laparoscopic surgery, Conventional multi-port laparoscopic surgery, Meta-analysis, Colorectal cancer*

1. Introduction

The first laparoscopic colectomy was completed in 1991 by Jacobs [1], and laparoscopic surgery has been applied in the field of colorectal surgery for 30 years. Compared with open surgery, laparoscopic colorectal cancer surgery not only has the advantages of small tissue injury, small surgical scar, mild postoperative pain, rapid postoperative recovery and shortened hospital stay [2], but also can ensure the safety of surgery and oncological efficacy [3-5]. At present, laparoscopic surgery has become the preferred surgical method for colorectal cancer [6]. CMLS for colorectal cancer usually requires 3 – 5 puncture holes and an auxiliary incision for specimen extraction, which is more invasive to patients. In order to make laparoscopic colorectal surgery more minimally invasive, Bucher [7] et al and Remzi [8] et al pioneered the successful use of single-port laparoscopy for right hemicolectomy surgery for colonic polyps in 2008. One year later, Bucher [9] et al carried out the first single-port laparoscopic radical surgery for left colon cancer. SILS refers to the placement of laparoscopic instruments into the abdominal cavity through a small abdominal incision for surgical operation, which has the advantages of reducing the incidence of complications related to the puncture hole and auxiliary incision, reducing postoperative pain and making the postoperative incision more beautiful [10]. After more than 10 years of development, SILS has been widely used in the treatment of CRC [11]. However, there is still a lack of high-quality evidence-based medical evidence for the safety and efficacy of SILS in the treatment of CRC compared with CMLS, and some previous meta-analyses included too many retrospective non-randomized studies [12-14], resulting in poor reliability and stability of this result. Therefore, the main purpose of this study is to systematically evaluate the published high-quality RCT of SILS and CMLS in the treatment of CRC to objectively evaluate the safety and efficacy of SILS in CRC surgery.

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2. Materials and methods

2.1 Literature Search

We searched the literature from Pubmed, Embase, Cochrane library, Web of science and ClinicalTrials.gov. Additional supplementation was performed by manually searching the references of relevant studies. The search period was from database establishment to September 1, 2021. The literature search terms were as follows: "SILS, LESS, single port, single trocar, single incision, single site or single access", "laparoscopies, laparoscopy or colorectal", "colon, colon, rectum, rectal or rectal" and "randomized controlled trial, randomized controlled trials, RCT or RCTs". We take PubMed database as an example to show the search strategy (supplemental file 2).

2.2 Literature inclusion and exclusion criteria

Inclusion criteria:(1) Published RCTs comparing SILS with CMLS for CRC; (2) At least one outcome measure is reported in the literature.

Exclusion criteria:(1) One-way study without control group; (2) Literature with insufficient data, no specific data that can be compared. (3) Literatures in which the original text cannot be obtained; (4) Literatures in which the primary outcome measures are not included.

In case of duplicate publications or publications by the same investigator or institution, the most recent publication was selected.

2.3 Data extraction

Two investigators independently screened and evaluated the literatures according to the inclusion and exclusion criteria, and extracted the literature information. Two investigators entered and cross-checked the data by double computer. If there were two different opinions, they were resolved after consultation with the third investigator. The extracted data included: first author, publication year, study type, publication region, Outcomes of interests, and so on.

2.4 Outcomes of interests

Outcomes of interests mainly included: operation time, intraoperative blood loss, total length of surgical incision, conversion rate, number of dissected lymph nodes, tumor size in pathological specimens, length of pathological specimens, tumor and distal resection margin, postoperative first exhaust time, postoperative day 1 resting state pain score, postoperative hospital stay, incidence of postoperative complications and incidence of postoperative anastomotic leakage, incidence of postoperative wound infection, incidence of postoperative intestinal obstruction, incidence of secondary surgery.

2.5 Risk of bias assessment

The included RCT studies were uniformly evaluated for quality using the bias evaluation tool recommended by the Cochrane Collaboration Uniform Workbook [16]. A short summary of the resulting evidence was presented in tabular form using GradePro, a tool provided by the Cochrane Collaboration.

2.6 Statistical Methods

RevMan 5.4.1 statistical software was used for statistical analysis of all included literatures. Measurement data are described by mean difference (MD). If the original data extracted is in the form of median (range), the mean and standard deviation are calculated by the method provided by Hozo et al. [17]. Enumeration data were described using odds ratio (OR). Pooled statistics with 95% confidence intervals (CI) were calculated. Mantel-Haenszel test was used to test the heterogeneity of the included studies, and the corresponding calculation model was selected according to the results of heterogeneity test. The fixed-effect model was used for the studies with good homogeneity ($P > 0.05$, $I^2 \leq 50\%$), and the random-effect model was used for the studies with heterogeneity ($P < 0.05$, $I^2 > 50\%$). The source of heterogeneity was found by analysis and sensitivity analysis. P value<0.05 was considered statistically significant.

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3. Results

3.1 Basic characteristics of included literatures and bias risk assessment

Table 1: Basic characteristics of included literatures

Study	Registration No.	Area	Patient,n		Age,years		Gender,M/F		BMI,kg/m²		PAS,n	
			S	C	S	C	S	C	S	C	S	C
Bulut2015	NCT01579721	Denmark	20	20	69(50-86)	73(50-84)	12/8	12/8	24(16-32)	24(19-29)	3	7
Huscher2012	NR	Italy	16	16	70±11	70±13	6/10	9/7	NR	NR	NR	NR
Kang 2017	NCT01203969	Korea	31	31	63.2±11.4	62.2±9.4	19/12	16/15	24.0±3.0	24.5±3.0	7	9
Poon2012	NCT01101672	Hong Kong	25	25	67(37-83)	67(57-81)	14/11	18/7	23.2(16.9-28.8)	23.6(16.5-28.2)	7	8
Takemasa2014	NR	Japan	150	150	64.3±11.7	65.6±12.5	75/75	71/79	21.7±3.3	22.4±4.7	31	39
Velthuis2012	NR	Netherlands	50	50	73±13.2	71±11.8	21/29	22/28	25(20-32)	25(20-36)	11	15
Watanabe 2016	UMIN000007220	Japan	100	100	68(61-74)	67(61-74)	56/44	56/44	22.9(20.3-25.2)	23.1(21.1-24.8)	NR	NR
Yoon SL 2020	NCT01480128	Korea	179	180	63.4(34-84)	62.6(28-85)	97/82	99/81	24.3(17.0-32.0)	24.3(18.0-35.0)	36	43

S: SILS; C: CMLS; NR: Not reported; BMI: Body mass index; PAS: Previous abdominal surgery

Table 1: (continue)

Study	ASA score		Tumor location		cTNM stage		Single-port device
	S	M	S	M	S	M	
Bulut2015	1/2/3 (5/12/3)	1/2/3 (4/13/3)	RC	RC	I+II/III (9/11)	I+II/III (4/16)	SILS port (Covidien)
Huscher2012	1/2/3 (4/9/3)	1/2/3 (4/6/6)	RCC/LCC (8/8)	RCC/LCC (6/10)	NR	NR	SILS port (Covidien)
Kang 2017	1/2 (11/20)	1/2(16/15)	RCC/LCC (11/20)	RCC/LCC (14/17)	NR	NR	Octo port (Dalim)/SILS port(Covidien)
Poon2012	1/2/3 (3/19/3)	1/2/3 (3/18/4)	RCC/LCC/RC (8/3/14)	RCC/LCC/RC (9/3/13)	0/I/II/III (4/8/7/6)	0/I/II/III (4/5/4/12)	Tri-port access (Olympus)/Octo port (Dalim)
Takemasa2014	1/2/3(40/83/27)	1/2/3(33/85/32)	RCC/LCC (69/81)	RCC/LCC (69/81)	I/II/III (76/48/26)	I/II/III (65/49/36)	SILS Port (Covidien)/EZ Access (Hakko, Nagano, Japan)
Velthuis2012	1+2/3 (40/10)	1+2/3 (43/7)	RCC	RCC	NR	NR	Tri-port access (Olympus)/SILS Port (Covidien)
Watanabe 2016	1/2 (29/71)	1/2 (22/78)	RCC/LCC/RC (30/54/16)	RCC/LCC/RC (30/54/16)	I/II/III (56/16/28)	I/II/III (54/25/21)	EZ Access (Hakko, Nagano, Japan)
Yoon SL 2020	1/2 (101/78)	1/2 (96/84)	RCC/LCC (62/117)	RCC/LCC (54/126)	NR	NR	Octo port (Dalim)/SILS port (Covidien)

ASA: American Society of Anesthesiologists; RCC: right-sided colon cancer; LCC: left-sided colon cancer; RC: rectal cancer.

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The screening process was performed according to the PRISMA process, as shown in Figure 1. Eight randomized controlled studies [18 – 25] were finally included, including five studies from Eastern countries [20 – 22, 24, 25] and three studies from Western countries [18, 19, 23]. The total number of samples included in this analysis was 1143, including 571 in the SILS group and 572 in the CMLS group. The basic characteristics of the included articles are shown in Table 1. There was no significant difference between the two groups in terms of age, gender, Body mass index (BMI), previous abdominal surgery (PAS), American Society of Anesthesiologists (ASA) score, tumor location, and clinical TNM stage. The results of the quality evaluation of RCT articles are shown in Figure 2. A summary of the evidence analyzed in the GRADE-Pro tool is shown in Figure 3, representing high-quality evidence of outcomes based on the protocol scoring system.

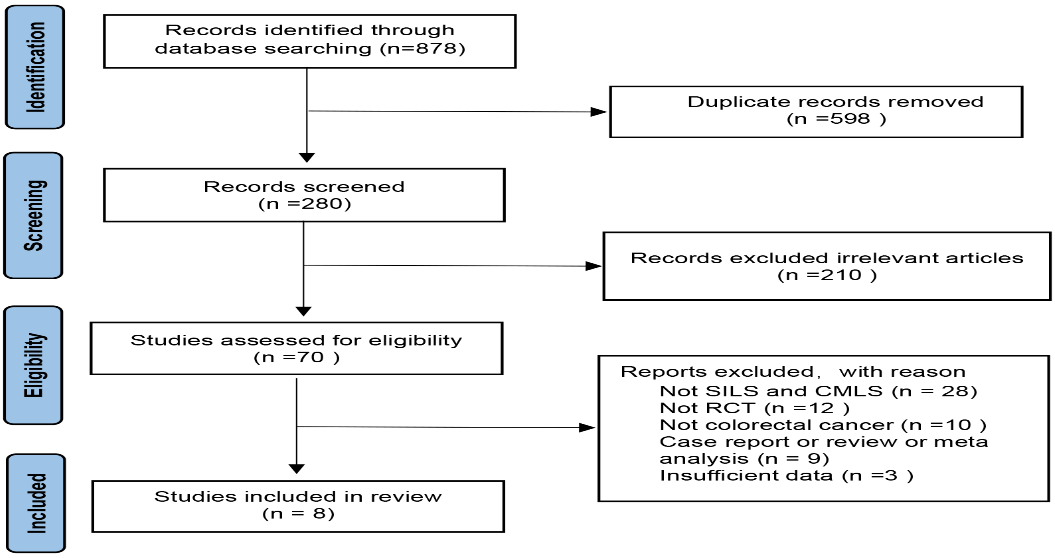
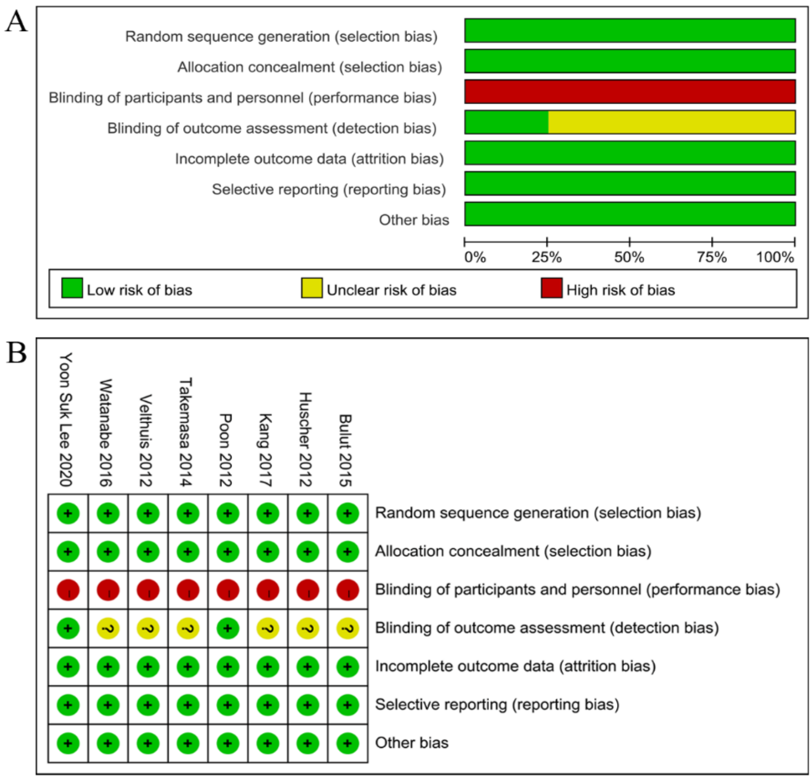


Figure 1: Flow diagram of included studies



(A. Risk of bias graph; B. Risk of bias summary)

Figure 2: The results of the quality evaluation of RCT articles

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SILS and CMLS compared to for Colorectal Cancer

Patient or population: patients with Colorectal Cancer
Settings:
Intervention: SILS
Comparison: CMLS

Outcomes	Illustrative comparative risks* (95% CI) Assumed risk CMLS	Corresponding risk SILS	Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)	Comments
Operation time		The mean operation time in the intervention groups was **0.16 higher** (7.09 lower to 7.41 higher)		1143 (8 studies)	⊕⊕⊕⊝ **moderate**[1]	
Blood loss		The mean blood loss in the intervention groups was **9.22 lower** (29.58 lower to 11.14 higher)		1011 (6 studies)	⊕⊕⊕⊝ **moderate**[1]	
Conversion to open surgery	**Study population**		**OR 1.69** (0.73 to 3.89)	961 (5 studies)	⊕⊕⊕⊝ **moderate**[1]	
	17 per 1000	**28 per 1000** (12 to 62)				
	Moderate					
	20 per 1000	**33 per 1000** (15 to 74)				
Incision length		The mean incision length in the intervention groups was **2.64 lower** (4.39 to 0.89 lower)		961 (5 studies)	⊕⊕⊕⊕ **high**	
Tumor size		The mean tumor size in the intervention groups was **0.12 higher** (0.03 to 0.22 higher)		1111 (7 studies)	⊕⊕⊕⊕ **high**	
Lymph nodes		The mean lymph nodes in the intervention groups was **0.62 higher** (0.76 lower to 2.01 higher)		1143 (8 studies)	⊕⊕⊕⊕ **high**	
Specimen length		The mean specimen length in the intervention groups was **0.81 higher** (0.14 lower to 1.76 higher)		472 (4 studies)	⊕⊕⊕⊕ **high**	
Distal margin		The mean distal margin in the intervention groups was **0.35 higher** (0.23 lower to 0.92 higher)		743 (6 studies)	⊕⊕⊕⊝ **moderate**[1]	
Proximal margin		The mean proximal margin in the intervention groups was **0.95 higher** (0.06 lower to 1.97 higher)		671 (4 studies)	⊕⊕⊕⊕ **high**	
Time to first flatus		The mean time to first flatus in the intervention groups was **0 higher** (0.05 lower to 0.05 higher)		621 (3 studies)	⊕⊕⊕⊕ **high**	
OPD1 REST Pain score		The mean opd1 rest pain score in the intervention groups was **1.21 lower** (2.92 lower to 0.51 higher)		709 (3 studies)	⊕⊕⊕⊕ **high**	
Hospitalization time		The mean hospitalization time in the intervention groups was **0 higher** (0.05 lower to 0.04 higher)		1143 (8 studies)	⊕⊕⊕⊝ **moderate**[2]	
Postoperative complications	**Study population**		**OR 0.78** (0.56 to 1.07)	1143 (8 studies)	⊕⊕⊕⊕ **high**	
	178 per 1000	**145 per 1000** (108 to 188)				
	Moderate					
	158 per 1000	**128 per 1000** (95 to 167)				
Anastomotic leakage	**Study population**		**OR 0.72** (0.33 to 1.6)	1031 (6 studies)	⊕⊕⊕⊕ **high**	
	29 per 1000	**21 per 1000** (10 to 46)				
	Moderate					
	50 per 1000	**37 per 1000** (17 to 78)				
Ileus	**Study population**		**OR 0.75** (0.39 to 1.47)	1049 (6 studies)	⊕⊕⊕⊕ **high**	
	38 per 1000	**29 per 1000** (15 to 55)				
	Moderate					
	45 per 1000	**34 per 1000** (18 to 65)				
Wound infection	**Study population**		**OR 1** (0.54 to 1.87)	1143 (8 studies)	⊕⊕⊕⊕ **high**	
	33 per 1000	**33 per 1000** (18 to 60)				
	Moderate					
	31 per 1000	**31 per 1000** (17 to 56)				
Reoperation	**Study population**		**OR 0.64** (0.32 to 1.3)	672 (5 studies)	⊕⊕⊕⊕ **high**	
	60 per 1000	**39 per 1000** (20 to 76)				
	Moderate					
	63 per 1000	**41 per 1000** (21 to 80)				

*The basis for the **assumed risk** (e.g. the median control group risk across studies) is provided in footnotes. The **corresponding risk** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: Confidence interval; **OR:** Odds ratio;

GRADE Working Group grades of evidence
High quality: Further research is very unlikely to change our confidence in the estimate of effect.
Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very low quality: We are very uncertain about the estimate.

[1] Discrepant results across studies
[2] No explanation was provided

Figure 3: GRADE-Pro Levels of Evidence

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3.2 Meta-analysis of intraoperative outcomes

Basic information on the intraoperative outcomes of the included studies is presented in Table 2.

Table 2: Basic information of intraoperative outcomes

Study	Operation time (min)		Blood loss(ml)		Conversion,n		Additional port		Incision length(cm)	
	S	C	S	C	S	C	S	C	S	C
Bulut2015	290.8±89.3	268.5±74.0	91.5±75.0	212.5±162.5	2	1	2	0	5.75±2.5	13.3±3.1
Huscher2012	147±61	129±46	200	NR	0	0	1	0	NR	NR
Kang 2017	134.9±48.3	130.9±34.2	30±125	20±61.25	6	0	NR	0	5.3±4.2	6.5±1.3
Poon2012	156±36	144.5±36.5	63.75±36.25	117.5±72.5	0	0	0	0	NR	NR
Takemasa2014	172±33	173±35	32±26	37±27	2	5	12	0	3.0±0.7	3.1±1.0
Velthuis2012	97±22	112±38.75	NR	NR	0	0	2	0	NR	NR
Watanabe 2016	156±37	162±36	21.4±74.6	8.8±19.3	1	2	9	0	4.4±2.5	6.8±1.3
Yoon SL 2020	175.4±72	164.3±59.83	66.3±133.33	49.9±83.33	3	0	25	0	4.6±3.42	7.2±1.95

3.2.1 Operation time

A total of 8 RCTs comparing the operation time of SILS and CMLS for colorectal cancer were included in this meta-analysis, with a total sample size of 1143. The heterogeneity test showed little heterogeneity among the studies ($P = 0.09$, $I^2 = 43\%$), so the fixed-effect model was used. Meta-analysis showed that there was no statistical difference in operation time between SILS and CMLS groups [P = 0.97, MD = 0.16, 95% CI (-7.09, 7.41)]. (Figure 4A).

3.2.2 Operative blood loss

Six RCTs compared the difference in operative blood loss between SILS and CMLS with a total sample size of 1011. The pooled data showed that the heterogeneity between the two groups was high ($P < 0.0001$, $I^2 = 81\%$), and the random-effects model was used. Meta-analysis showed that there was no statistical difference between the two groups [(P = 0.37, MD = -9.22, 95% CI (-29.58, 11.14)]. (Figure 4B)

3.2.3 Conversion to open surgery

Conversion to open surgery was reported in 5 studies with a total sample size of 961. Heterogeneity analysis showed: $P = 0.13$, $I^2 = 44\%$, using a fixed-effect model. Meta-analysis showed that there was no statistical difference in conversion to open surgery between SILS and CMLS [P = 0.22, OR = 1.69, 95% CI (0.73, 3.89)]. (Figure 4C). However, 9.4% (51/540) of SILS procedures required the insertion of one or more additional ports, as shown Table 2.

3.2.4 Total length of surgical incision

Five RCT studies reported surgical incision length, with a total sample size of 961. Heterogeneity test results: $P < 0.00001$, $I^2 = 98\%$, suggesting high heterogeneity among studies, so the random-effects model was used. Meta-analysis results: The surgical incision length in SILS group was shorter than that in CMLS group, and the difference had statistical significance [P = 0.003, MD = -2.64, 95% CI (-4.39, -0.89)]. (Figure 4D).

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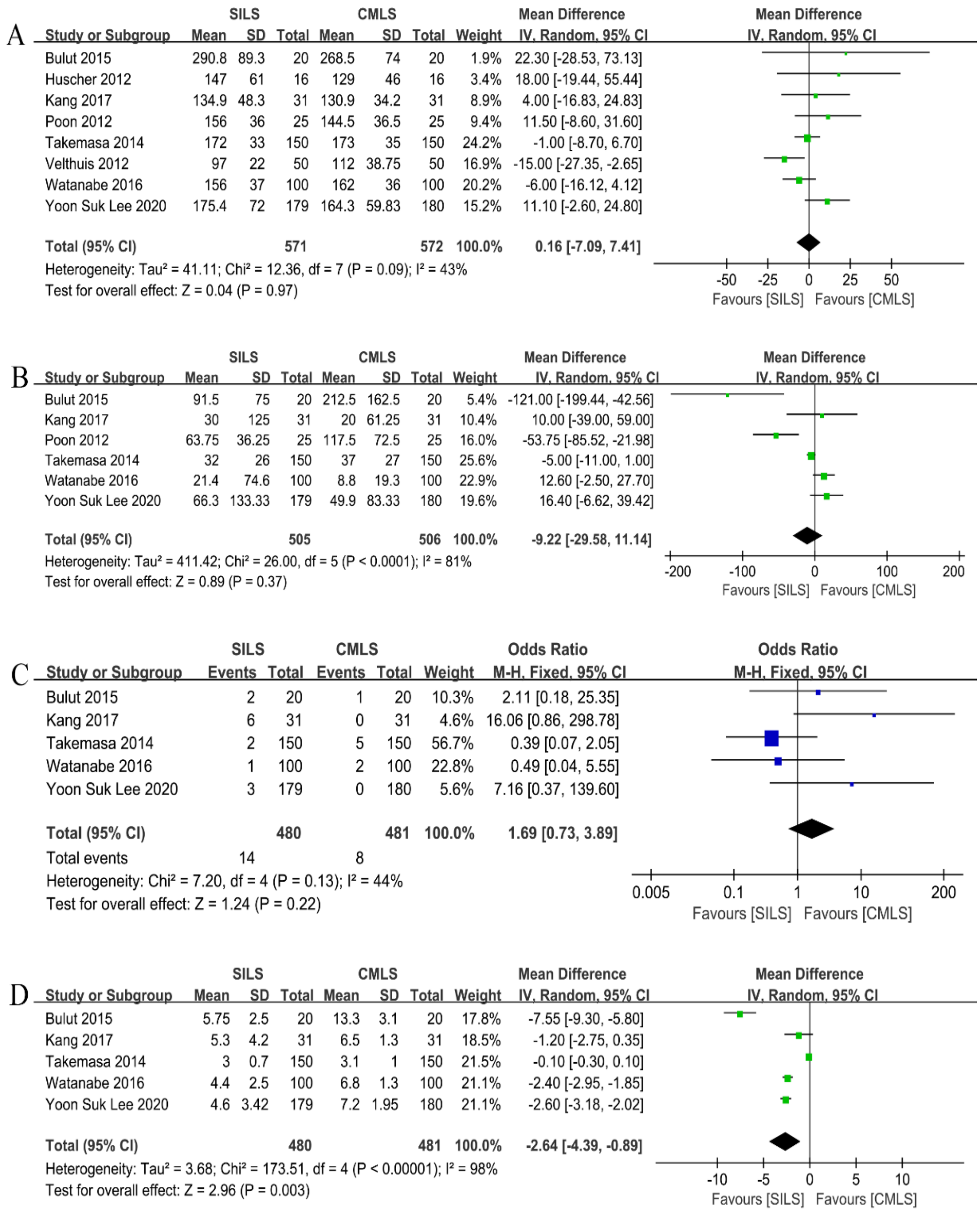

(A: Operation time; B: Operative blood loss; C: Incidence rate of conversion to open surgery; D: Surgical incision length)

Figure 4: Meta-analysis results of intraoperative outcomes

3.3 Meta-analysis of pathological outcomes

Basic information on the pathological outcomes of the included studies is presented in Table 3.

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Table 3: Basic information of pathological outcomes

Study	Tumor size (cm)		Lymph nodes n		Specimen length (cm)		Distal margin (cm)		Proximal margin (cm)	
	S	C	S	C	S	C	S	C	S	C
Bulut2015	3.25±1.5	4.38±2.75	16.25±7.25	19.5±6.5	22±6	19.75±2.75	3.625±1.75	3.125±1.38	NR	NR
Huscher2012	NR	NR	18±6	16±5	24±9	24±10	8±7	6±4	NR	NR
Kang 2017	5.3±2.0	4.5±2.9	23.7±14.4	20.1±8.9	NR	NR	8.1±5.2	9.3±7.3	10.3±5.8	9.3±7.5
Poon2012	3.5±1.5	4±1.5	16.75±5.75	21.25±8.75	NR	NR	7.5±3.25	7.25±2.75	11.75±5.75	9±2.5
Takemasa2014	3.2±1.4	3.3±1.4	22.2±5.6	22.4±6.0	22.3±5.1	21.6±4.4	NR	NR	NR	NR
Velthuis2012	4.81±1.6	4.64±1.8	14.0±4.5	12.5±6.0	26.13±6.9	25.89±8.9	NR	NR	NR	NR
Watanabe 2016	2.65±0.37	2.5±0.37	24±3	22±3.17	NR	NR	9.9±5.3	9.2±5.4	10.8±4.8	10.2±4.5
Yoon SL 2020	3.7±1.5	3.5±1.58	25.6±12.83	23.9±9.33	NR	NR	9.0±4.58	8.9±5.17	12.5±10.5	12.3±17

3.3.1 Tumor size

Seven RCT studies reported tumor size in pathological specimens, with a total sample size of 1111 cases. Heterogeneity test results: P = 0.18, I^2 = 33%, using the fixed-effect model. Meta-analysis showed that the tumor volume in the pathological specimens of the SILS group was smaller than that of the CMLS group, and the difference was statistically significant, [P = 0.008, MD = 0.12, 95% CI (0.03, 0.22)]. (Figure 5A).

3.3.2 Number of lymph nodes

A total of 8 RCTs reported the number of lymph nodes obtained by surgery, with a total sample of 1143. The heterogeneity test showed that there was no significant heterogeneity among the studies (P = 0.005, I^2 = 66%), and the random-effects model was suitable for use. Meta-analysis showed that there was no significant difference in the number of lymph nodes obtained between SILS and CMLS [P = 0.38, MD = 0.62, 95% CI (-0.76, 2.01)], as shown in Figure 5B.

3.3.3 Length of pathological specimens

Four literatures compared the length of resected pathological specimens in the SILS CMLS group, with a total sample size of 572 cases. There was no significant heterogeneity among the studies (P = 0.76, I^2 = 0%). Therefore, the fixed-effect model analysis was used. The meta-analysis results showed that there was no significant difference between the two groups [P = 0.09, MD = 0.81, 95% CI (-0.14, 1.76)]. (Figure 5C).

3.3.4 Distal resection margin of tumor

A total of 6 RCTs reported distal tumor resection margin in the SILS CMLS group, with a total of 743 patients. The heterogeneity test results showed that there was no heterogeneity among the studies (P = 0.83, I^2 = 0%), so the fixed-effect model analysis was used. The meta-analysis results showed that there was no significant difference between the two groups [P = 0.24, MD = 0.35, 95% CI (-0.23, 0.92)], as shown in Figure 5D.

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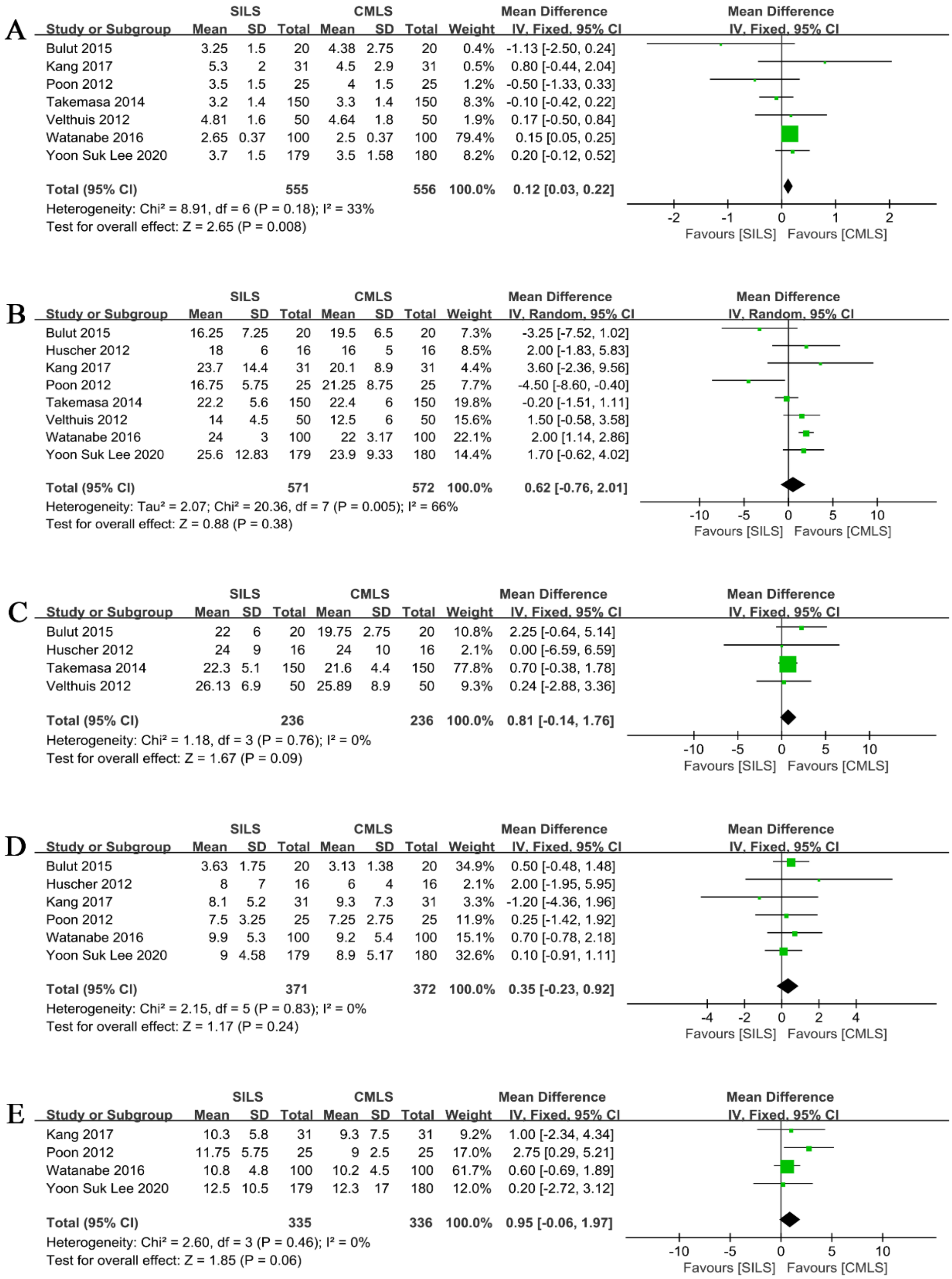
3.3.5 Proximal resection margin of tumor

A total of 4 RCTs comparing SILS and CMLS in terms of tumor resection margin were included in this systematic review, with a sample size of 671. Heterogeneity test results: P = 0.46, I^2 = 0%, fixed effect model analysis should be used, meta-analysis results showed that there was no significant difference between the two groups [P = 0.06, MD = 0.95, 95% CI (-0.06, 1.97)].(Figure 5E).



(A: Tumor size; B Number of dissected lymph nodes; C: Pathological specimen length; D:Distal resection margin of tumor ; E:Proximal resection margin)

Figure 5: Meta-analysis results of pathological outcomes

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3.4 Meta-analysis of postoperative outcomes

Basic information on the postoperative outcomes of the included studies is presented in Table 4.

Table 4 Basic information of postoperative outcomes

Study	Time to first flatus (days)		Pain score		Hospitalization time (days)		Complications,n		Anastomotic leakage，n		Ileus，n		Wound infection，n		Reoperation，n	
	S	C	S	C	S	C	S	C	S	C	S	C	S	C	S	C
Bulut2015	NR	NR	0.25	0.95	17±12	12.5±6.5	7	8	4	4	0	1	2	0	2	2
Huscher2012	NR	NR	NR	NR	6±3	7±2	3	5	0	1	NR	NR	1	2	0	1
Kang 2017	1.9±1.0	1.9±0.8	3.6	3.9	6.8±1.9	6.5±1.4	6	4	0	0	NR	NR	0	1	0	0
Poon2012	NR	NR	0.25±0.25	3±1.5	5.5±2.0	5.25±1.25	1	3	NR	NR	0	1	1	2	NR	NR
Takemasa2014	NR	NR	4.2±2.7	5.1±3.3	8.2±2.7	8.7±3.3	18	25	2	2	6	8	5	4	4	8
Velthuis2012	NR	NR	NR	NR	6±9.75	6±25.25	17	17	1	3	5	3	4	3	4	6
Watanabe 2016	1±0.17	1±0.17	NR	NR	6±0.17	6±0.17	12	15	2	4	1	1	0	3	3	3
Yoon SL 2020	2.5±1	2.5±1	3.17±0.13	3.19±0.14	7.0±3.17	7.4±5.5	19	25	2	1	3	6	6	4	NR	NR

3.4.1 Postoperative initial anus exhaust time

A total of 3 literatures compared the postoperative initial exhaust time, with a total of 621 cases. There was no heterogeneity among the studies (P = 1.00, I^2 = 0%), so fixed-effect model analysis was used. Meta-analysis showed that there was no significant difference in postoperative initial exhaust time between SILS group and CMLS group [MD = 0.00, 95% CI (– 0.05, 0.05), P = 1.00], as shown in Figure 6A.

3.4.2 Pain score at rest on the first day after surgery

A total of 3 RCTs comparing the pain score on the first day after surgery between the SILS and CMLS groups were included in this systematic review, with a sample size of 709. The heterogeneity test results showed that there was a strong heterogeneity among the studies (P < 0.00001, I^2 = 98%). The fixed-effect model should be used for analysis. The meta-analysis results showed that there was no significant difference between the two groups [P = 0.17, MD = -1.21, 95% CI (-2.92, 0.51)], as shown in Figure 6B.

3.4.3 Hospital stay

A total of 8 literatures reported the hospital stays of patients, with a total sample size of 1143 cases. There was no heterogeneity among the studies (P = 0.43, I^2 = 0%), so the fixed-effect model was used for analysis. The meta-analysis results showed that there was no statistically significant difference in the hospital stays between the SILS group and CMLS group [P = 0.93, MD = -0.00, 95% CI (-0.05, 0.04)]. (Figure 6C).

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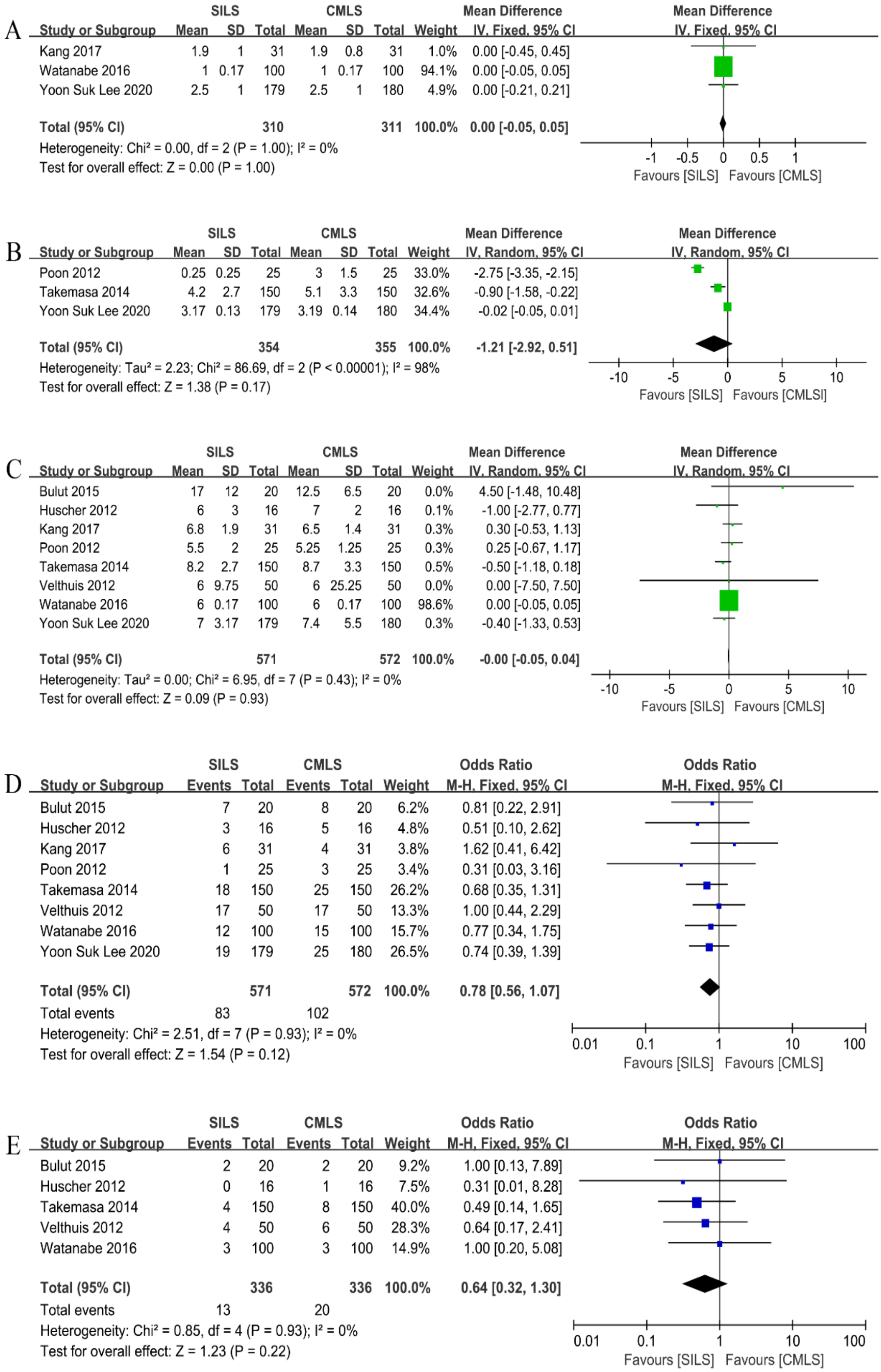

(A: Postoperative initial anus exhaust time; B: Pain score at rest on the first day after surgery; C Hospital stay; D:Total postoperative complications; E:Incidence of reoperation)

Figure 6: Meta-analysis results of postoperative outcomes

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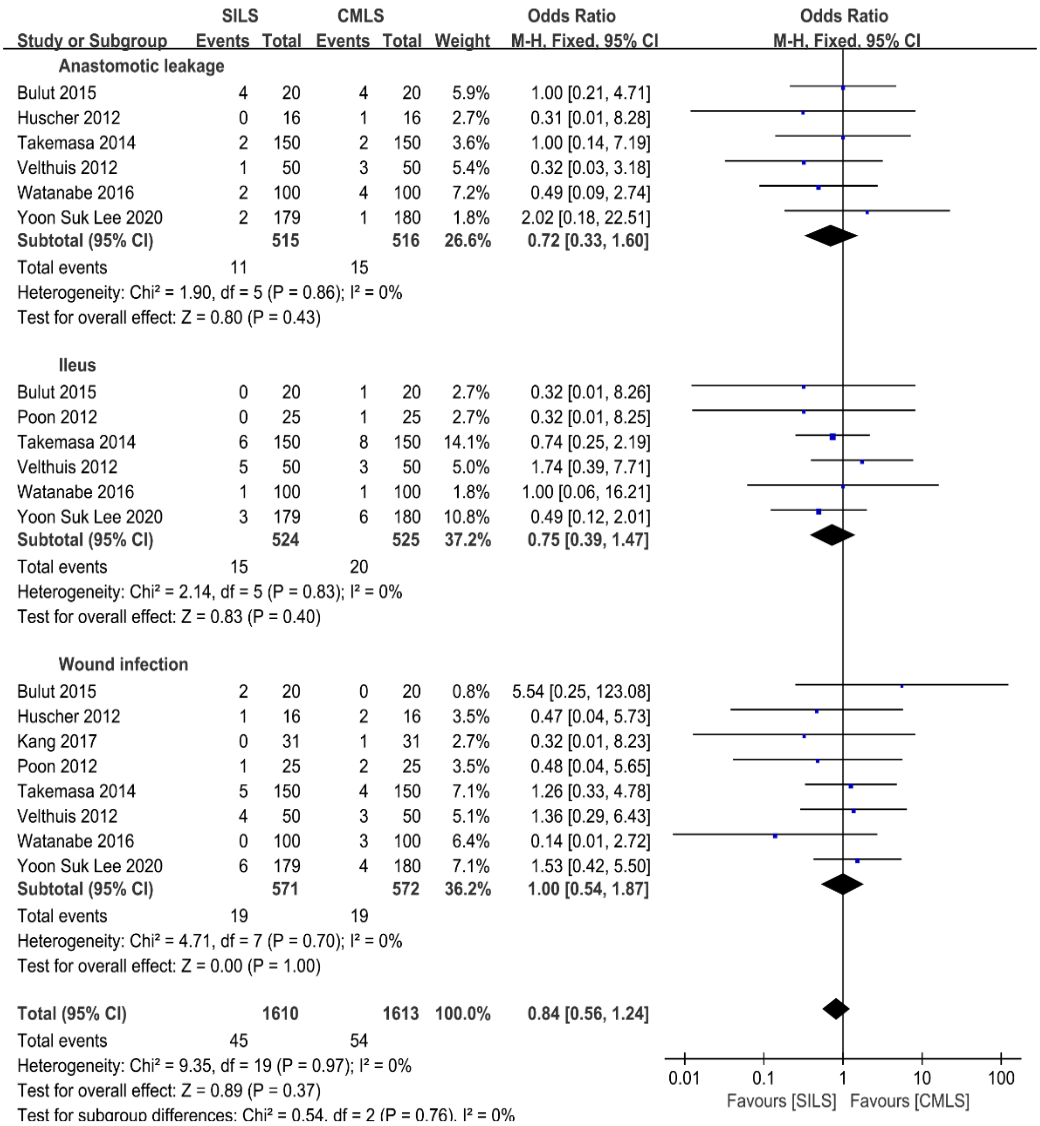

Figure 7: Results of subgroup analysis of postoperative complications

3.4.4 Postoperative complications

A total of 8 literatures reported the incidence rate of total postoperative complications, with a total sample size of 1143 cases. The heterogeneity test showed that there was no heterogeneity in each experimental study (P = 0.93, I^2 = 0%). The fixed-effect model analysis was used. The meta-analysis results showed that there was no significant difference in the incidence rate of total postoperative complications between the SILS CMLS groups [P = 0.12, OR = 0.78, 95% CI (0.56, 1.07)], as shown in Figure 6D. Six of these studies reported anastomotic leakage, six studies reported ileus, and eight studies reported wound infection. The results of analysis showed that there was no statistical difference in anastomotic leakage [P = 0.43, OR = 0.72, 95% CI (0.33, 1.60)], intestinal obstruction [P = 0.40, OR = 0.75, 95% CI (0.39, 1.47)] and incision infection [P = 1.00, OR = 1.00, 95% CI (0.54, 1.87)] between SILS CMLS group, and there was no significant heterogeneity among the studies (I^2 = 0%), as shown in Figure 7.

3.4.5 Reoperation

A total of 5 RCTs comparing the incidence of reoperation between SILS and CMLS groups were included in this systematic review, with a sample size of 672. The heterogeneity test results showed that there was no heterogeneity among the studies (P < 0.93, I^2 = 0%). The fixed-effect model analysis should be used. The meta-analysis results showed that there was no significant difference between the two groups [P = 0.22, OR = 0.64, 95% CI (0.32, 1.30)], as shown in Figure 6E.

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3.5 Sensitivity analysis

Because of the high heterogeneity in blood loss, incision length, and pain score at rest on the first day after surgery, sensitivity analysis was performed by removing the included individual studies one by one, and the results showed no significant difference, and the heterogeneity was still high, suggesting that the results were more stable.

3.6 Reporting biases

Since the number of included literatures was less than 10, no further reporting bias analysis was conducted.

4. Discussion

The emergence of single-port laparoscopic surgery is a common product of medical technical innovation and increased awareness of minimally invasive surgery for patients. Single-port laparoscopic surgery is developed from traditional laparoscopic surgery. Its early application was mainly in ovarian, fallopian tube, uterine, appendiceal, and gallbladder surgery [26－28], after which it gradually transitioned to the field of colorectal surgery. Because single-port laparoscopic surgery for CRC can complete the operation by only making a 3-4 cm surgical incision in the abdomen, it has significant advantages in reducing postoperative pain, improving cosmetic results, accelerating postoperative rehabilitation, etc., and a number of studies [29-31] have shown that there is no significant difference in the long-term oncological efficacy between single-port laparoscopic CRC resection and traditional laparoscopic surgery, it is favored by patients and surgeons. However, some surgeons also raise objections. They believe that the difficulty of single-port laparoscopic surgery for CRC, device conflict, lack of countertraction and linear perspective make the learning curve of this technique [32]. In addition, there are not many study results with higher level of evidence-based medicine evidence [33], which is not conducive to technical promotion. Whether SILS is superior to CMLS in the treatment of CRC remains unclear, and its safety and efficacy need to be confirmed, therefore, we performed this systematic review.

In this study, we included a total of 8 RCT studies with low risk bias, with a total of 1143 patients. The meta-analysis results showed that in the radical resection of CRC, the incision length of SILS group was shorter than that of CMLS group, and the tumor size in the pathological specimens of SILS group was smaller than that of CMLS group; while the observation indicators such as operation time, intraoperative blood loss, conversion rate, postoperative first anus exhaust time, postoperative first day resting state pain score, hospital stay, incidence rate of postoperative complications, incidence rate of the reoperation, number of lymph node dissection, length of pathological specimens, distance from the tumor to the distal resection margin and distance from the tumor to the proximal resection margin were not statistically significant.

Operation time, intraoperative blood loss, conversion rate, incidence of postoperative complications and incidence of reoperation are important indicators to measure the safety of SILS in the treatment of CRC. There was no significant difference between the SILS and CMLS groups in terms of operative time consumption, which was consistent with the results of a previous meta-analysis of three retrospective studies with higher comprehensive quality [12, 34, 35].Generally, surgeons believe that many challenges in single-port laparoscopic surgery include: loss of operating triangle, parallel coaxial effect, shared fulcrum, chopstick effect, etc., all of which increase the difficulty of surgery and thus prolong the operation time. However, there is only one skin incision throughout single-port laparoscopic surgery, which greatly reduces the time for laparotomy and abdominal closure, and the surgeon can shorten the operation time by improving surgical proficiency, programming the surgical steps, using flexible instruments [36, 37], and adjustable lenses [38, 39].In addition, the factors affecting the operation time also include the patient's body size, whether the surgeon passes the learning curve, tumor location and size, etc. These factors are easy to bias the results and are the reason for the heterogeneity of the results of meta-analysis of operation time, so further study and demonstration are needed. In terms of intraoperative blood loss, the single-port laparoscopic group did not show the advantage of less blood

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loss, which may be due to more intraoperative free tissue and greater internal injury of the incision, resulting in more blood loss, but the total blood loss was basically within 100 ml, indicating the safety of the operation. Heterogeneity may arise from differences in coagulation, vascular fragility in different populations, e.g., patients with advanced age and obesity are more likely to bleed. There was no significant difference between the two groups in terms of conversion to open surgery. 9.4% (51/540) of SILS operations required the addition of an operating hole. When SILS encountered operational difficulties, it was only necessary to convert to SILS + 1 [40-42] operation in most cases, and the operational difficulty could be greatly reduced. In addition, compared with CMLS, SILS did not increase the incidence of complications and reoperation including anastomotic leakage, postoperative ileus, and wound infection. The above results are strong evidence for the safety of SILS in the treatment of CRC.

The key to evaluating the short-term efficacy of CRC surgery lies in oncological efficacy. The indicators include resection of sufficient length of intestinal segment, complete resection of corresponding mesentery, dissection of a certain number of lymph nodes and sufficient range of lymph node dissection. Only by achieving radical resection of the tumor, can patients benefit. At the same time, postoperative cosmetology and recovery can not be ignored. In terms of tumor radicality, there was no significant difference in the number of dissected lymph nodes between the SILS and CMLS group, and the number of dissected lymph nodes was greater than 12, meeting the minimum requirements for radical surgery, which is of great significance for the prognosis of patients and subsequent treatment. There was heterogeneity in the number of dissected lymph nodes among the studies, which may be caused by the difference in the operation level of surgeons. In addition, SILS is not inferior to CMLS in terms of surgical specimen length and tumor resection margin, preliminarily suggesting that single-port laparoscopic colorectal cancer surgery can achieve a tumor resection range comparable to traditional laparoscopic CRC surgery in experienced laparoscopic surgery centers. While this study suggests that SILS for CRC has a smaller surgical incision and better cosmetic outcome, its heterogeneity is high. The results of sensitivity analysis showed that the results of meta-analysis were basically reliable, but the results of this study suggested that the tumor volume in the pathological specimens of the SILS group was smaller than that of the CMLS group, so we should consider that the tumor size is the most important factor affecting the incision length. Most patients who underwent single-port laparoscopic CRC surgery were screened, so there was a bias in judging the cosmetic effect by the length of the incision alone, and some scholars recommended the use of a questionnaire for cosmetic scoring to assess the cosmetic effect[43].There was no difference in the resting state pain score on postoperative d1 between the two groups. However, due to different postoperative analgesic regimens and drug doses between the cases, it was difficult to perform quantitative evaluation and there was great heterogeneity. Therefore, there was also a certain degree of bias. Further study is needed to more comprehensively elaborate. Theoretically, SILS has less trauma to patients, earlier recovery of exhaust and shorter hospital stay. However, the results of this study showed that there was no significant difference in the first exhaust time and hospital stay after SILS CMLS. The reason may be that the increased difficulty of SILS operation makes the recovery of intestinal function slow due to large intra-abdominal trauma and indwelling analgesic pump. The length of hospital stay will be affected by the differences in the criteria for discharge from various medical institutions, as well as by the patient's age, nutritional status, underlying diseases and other factors. The above results demonstrated the short-term efficacy of SILS in the treatment of CRC.

Compared with previous systematic reviews on SILS and CMLS in the treatment of CRC [13, 14], the greatest feature of this study is that the 8 included articles were all high-quality RCT studies, from different countries and regions of the East and West, with some representativeness, of which 5 were registered for clinical trials, so the results had high reliability. The limitations of this study are mainly the lack of long-term follow-up results in the included literature, including local tumor recurrence or distant metastasis rate, survival rate, etc., which cannot evaluate the long-term efficacy of SILS in the treatment of CRC.

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5. Conclusion

In conclusion, this study has preliminarily demonstrated that the choice of SILS for appropriate CRC patients for surgical treatment in experienced medical centers is feasible and safe, has similar surgical efficacy to CMLS, and may be more advantageous in terms of cosmetic outcome. At present, no study has shown that SILS can replace CMLS surgery, and more large-scale RCTs with complete follow-up data are needed in the future to reveal the clinical and prognostic effects of SILS.

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