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Mini-invasive vs open resection of colorectal cancer and liver metastases: A meta-analysis

Shan-Ping Ye, Hua Qiu, Shi-Jun Liao, Jun-Hua Ai, Jun Shi

ORCID number: Shan-Ping Ye (0000-0002-3588-7559); Hua Qiu (0000-0003-0942-0864); Shi-Jun Liao (0000-0002-9496-9458); Jun-Hua Ai (0000-0002-1902-0058); Jun Shi (0000-0002-7333-5448).

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Shan-Ping Ye, Hua Qiu, Shi-Jun Liao, Jun-Hua Ai, Jun Shi, Department of General Surgery, First Affiliated Hospital of Nanchang University, Nanchang 330006, Jiangxi Province, China

Corresponding author: Jun Shi, MD, Chief Doctor, Professor, Department of General Surgery, First Affiliated Hospital of Nanchang University, No. 17, Yongwaizheng Street, Nanchang 330006, Jiangxi Province, China. shijunfy@sina.com

Telephone: +86-791-88694893

Fax: +86-791-88694893

Abstract

BACKGROUND

The safety and feasibility of the simultaneous resection of primary colorectal cancer (CRC) and synchronous colorectal liver metastases (SCRLM) have been demonstrated in some studies. Combined resection is expected to be the optimal strategy for patients with CRC and SCRLM. However, traditional laparotomy is traumatic, and the treatment outcome of minimally invasive surgery (MIS) is still obscure.

AIM

To compare the treatment outcomes of MIS and open surgery (OS) for the simultaneous resection of CRC and SCRLM.

METHODS

A systematic search through December 22, 2018 was conducted in electronic databases (PubMed, EMBASE, Web of Science, and Cochrane Library). All studies comparing the clinical outcomes of MIS and OS for patients with CRC and SCRLM were included by eligibility criteria. The meta-analysis was performed using Review Manager Software. The quality of the pooled study was assessed using the Newcastle-Ottawa scale. The publication bias was evaluated by a funnel plot and the Begg's and Egger's tests. Fixed- and random-effects models were applied according to heterogeneity.

RESULTS

Ten retrospective cohort studies involving 502 patients (216 patients in the MIS group and 286 patients in the OS group) were included in this study. MIS was associated with less intraoperative blood loss [weighted mean difference (WMD) = -130.09, 95% confidence interval (CI): -210.95 to -49.23, $P = 0.002$] and blood transfusion [odds ratio (OR) = 0.53, 95%CI: 0.29 to 0.95, $P = 0.03$], faster recovery of intestinal function (WMD = -0.88 d, 95%CI: -1.58 to -0.19, $P = 0.01$) and diet (WMD = -1.54 d, 95%CI: -2.30 to -0.78, $P < 0.0001$), shorter length of postoperative

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hospital stay (WMD = -4.06 d, 95%CI: -5.95 to -2.18, $P < 0.0001$), and lower rates of surgical complications (OR = 0.60, 95%CI: 0.37 to 0.99, $P = 0.04$). However, the operation time, rates and severity of overall complications, and rates of general complications showed no significant differences between the MIS and OS groups. Moreover, the overall survival and disease-free survival after MIS were equivalent to those after OS.

CONCLUSION

Considering the studies included in this meta-analysis, MIS is a safe and effective alternative technique for the simultaneous resection of CRC and SCRLM. Compared with OS, MIS has less intraoperative blood loss and blood transfusion and quicker postoperative recovery. Furthermore, the two groups show equivalent long-term outcomes.

Key words: Minimally invasive surgical procedures; Laparotomy; Colorectal neoplasms; Synchronous liver metastases; Meta-analysis

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Core tip: For patients with colorectal cancer (CRC) and synchronous colorectal liver metastases (SCRLM), there is no consensus regarding whether minimally invasive surgery (MIS) or open surgery (OS) is more beneficial. We conducted this meta-analysis to compare the treatment outcomes of MIS and OS for the simultaneous resection of CRC and SCRLM. We assessed the two methods in terms of short- and long-term outcomes. Compared with OS, MIS has less intraoperative blood loss and blood transfusion and quicker postoperative recovery. Furthermore, the two groups show equivalent long-term outcomes.

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INTRODUCTION

Colorectal cancer (CRC) remains one of the leading causes of cancer-related deaths worldwide. The incidence and mortality of CRC rank third (10.2%) and second (9.2%), respectively, among all cancers worldwide^[1]. Moreover, according to the latest global cancer report issued by the International Agency for Research on Cancer for 2018 alone, more than 1.8 million patients were newly diagnosed with CRC, and 881000 patients died of CRC^[1]. The liver is the most common organ for metastasis from colorectal neoplasms. Approximately 40% of patients with CRC eventually develop liver metastases, and 15%-20% of CRC patients have synchronous colorectal liver metastases (SCRLM) at the time of initial diagnosis; the metastases are limited to the liver in 70%-80% of these patients, but only a subset of these metastases are resectable^[2-4]. Complete radical resection of primary and metastatic lesions is a potential curative treatment strategy for patients with resectable CRC and SCRLM, which is directly related to the prognosis of these patients^[5,6].

The resection methods for CRC and SCRLM include simultaneous resection and staged resection. Staged resection of the initial tumor and SCRLM was first developed and performed, removing the primary CRC tumor, followed by adjuvant chemotherapy and liver metastasis tumor resection^[7]. Recently, an increasing number of studies have suggested that the simultaneous resection of primary CRC and SCRLM is safe and acceptable and may become an optimal treatment strategy for patients with resectable CRC and SCRLM^[8,9]. Simultaneous resection of CRC and SCRLM was only performed by laparotomy before minimally invasive surgery (MIS) such as laparoscopy or robotics was applied in the treatment of CRC^[10,11]. MIS displayed superior short-term and similar long-term treatment outcomes to conventional open surgery (OS) in some studies^[12,13]. However, most of the studies were case series or reports, and the sample sizes were small^[14,15]. The advantages of

MIS over OS remained unclear, particularly concerning the long-term outcomes. Therefore, this meta-analysis was conducted to compare the short- and long-term outcomes of MIS and OS for the simultaneous resection of primary CRC and SCRLM based on the current available literature. The present study followed the principle of PICOS.

MATERIALS AND METHODS

Search strategy

A systematic search of the Web of Science, Cochrane Library, Embase, and PubMed was performed to identify relevant studies comparing MIS and OS for simultaneous resection of CRC and SCRLM published up to December 22, 2018. The search strategy was performed using the following terms: "colon", "rectal", "rectum", or "colorectal"; "liver metastas*", "hepatic metastas*"; "robot*", "Da Vinci", "laparoscop*", or "minimally invasive"; and "simultaneous", "coinstantaneous", "synchronous", or "combined". The language of the articles was not limited to any language. The references of relevant reviews and meta-analysis were also manually searched for potentially relevant studies. All relevant studies that met the inclusion criterion were reviewed for data extraction. This meta-analysis was prepared in accordance with the Preferred Reporting Items for Systemic Reviews and Meta-Analysis (PRISMA) statement^[16], and the work was reported in line with the Assessing the Methodological Quality of Systematic Reviews (AMSTAR) guidelines^[17].

Study selection

Two authors (Ye SP and Qiu H) independently scanned the titles and abstracts from the studies identified in the electronic search. Relevant papers were further identified through perusing full texts. Disagreements were resolved by discussion and consensus between authors. Studies were included in this meta-analysis according to the following inclusion criteria: (1) They compared the treatment outcomes of MIS with OS for simultaneous resection CRC and SCRLM, and MIS was only limited to laparoscopic or robotic-assisted procedure; (2) The papers were accepted or published, and the full texts were available; and (3) The articles reported on at least three treatment outcomes mentioned below. The exclusion criteria included were as follows: (1) Patients with metachronous colorectal liver metastasis; (2) Hand-assisted laparoscopy; (3) Hepatic diseases, including benign liver lesions or primary liver malignancies through preoperative diagnosis; and (4) Noncomparative studies, duplicate studies, articles presented at meetings, review articles, conference abstracts, guidelines, case reports or series, or letters.

Data extraction and quality assessment

Two researchers (Ye SP and Qiu H) reviewed each article by a structured list and extracted data into a database independently. Disagreements of opinions were settled through discussion between authors. Data with the following items were extracted: (1) Characteristics, including first author, country, publication year, sample size, gender and age of patients, body mass index, study type, primary CRC tumor location and size, size and number of liver metastases; (2) Short-term outcomes, including operation time, intraoperative blood loss, time to intestinal function recovery, time to diet, number of blood transfusions during the operation, length of postoperative hospital stay, type (surgical or general complications) and severity (Clavien-Dindo grade ≥ 3) of postoperative complications (surgical complications including anastomotic leakage, bile leakage, ileus, abdominal abscess, wound infection, and chylous ascites; and general complications including urinary tract infection, pulmonary complications, and pleural effusion); and (3) Long-term outcomes, including overall survival and disease-free survival (DFS). Disagreements in data extraction were resolved by discussion. The time to intestinal function recovery was referred to the time to the first flatus after operation. The type and severity of complications were assessed by the sum number of the relevant complications reported in each study. The Newcastle-Ottawa scale (NOS) was used to evaluate the methodological quality of the studies^[18]. The scale has three parts: Patient selection, comparability, and outcome. Two reviewers (Ai JH and Liao SJ) appraised the quality of studies independently. Disagreements were solved by consensus. The scale changes from 0 to 9 stars, and studies with a score \geq six stars could be deemed as high quality.

Statistical analysis

The software Review Manager, version 5.3, was adopted to analyze the data. The odds ratio (OR) with 95% confidence interval (CI) was utilized to assess the

dichotomous variables. The weighted mean difference (WMD) and 95%CI were analyzed for continuous variables. If continuous variables were presented as medians and ranges in some studies, the mean and standard deviation (SD) of these variables were estimated, as reported by Hozo *et al*^[19]. The hazard ratio (HR) was used to assess the difference in the DFS and overall survival between the groups. If HR was not reported, then HR was estimated from the data of DFS and overall survival extracted from the survival curve in the included papers, as described by Tierney *et al*^[20]. The I^2 statistic was utilized to evaluate the heterogeneity among the studies^[21]. The random-effects model was adopted if I^2 was $> 50\%$; otherwise, the fixed-effects model was utilized. Potential publication bias was determined by a funnel plot and assessed by the Begg's test and Egger's test (STATA software version 12.0 was adopted). A P -value < 0.05 was considered statistically significant.

RESULTS

Search results and study characteristics

In total, 1198 potential articles were initially retrieved from the electronic databases, and 684 potentially relevant articles were obtained for further assessment after eliminating duplicates. Next, 654 articles were excluded by screening the title and abstract. Thirty articles were retrieved for full-text evaluation. Finally, ten comparative cohort studies were included for this meta-analysis^[22-31]. A flow chart of the search strategies that contains reasons for the exclusion of studies is shown in Figure 1. The study by Chen *et al*^[28] was also included although it contained six patients with liver tumors not metastatic from the CRC diagnosed based on the postoperative pathological report because this did not influence the intraoperative procedure, and the study excluded these patients for further analysis of long-term outcomes. The characteristics of each study and study quality evaluated using the NOS are presented in Table 1. The preoperative characteristics of all patients from the two groups are shown in Table 2.

Intraoperative outcomes

All studies reported the operative time and intraoperative blood loss. The operative time showed no significant difference between the two groups (WMD = 34.05 min, 95%CI: 0.65 to 67.46, $P = 0.05$, $I^2 = 84\%$ for heterogeneity, $P < 0.00001$; Figure 2A). However, the intraoperative blood loss was less in the MIS group than in the OS group (WMD = -130.09, 95%CI: -210.95 to -49.23, $P = 0.002$, $I^2 = 91\%$ for heterogeneity, $P < 0.00001$; Figure 2B). Seven studies reported the number of intraoperative blood transfusions in 407 patients^[24-27,29-31]. The number of intraoperative blood transfusions was significantly less in the MIS group than in the OS group (OR = 0.53, 95%CI: 0.29 to 0.95, $P = 0.03$, $I^2 = 0\%$ for heterogeneity, $P = 0.81$; Figure 2C).

Postoperative outcomes

In this meta-analysis, postoperative outcomes included the time to bowel functional recovery, time to start diet, length of postoperative hospital stay, and postoperative complications. Five studies reported the time to bowel functional recovery in 222 patients^[23,24,26,30,31]. The pooled mean time to bowel functional recovery was shorter in the MIS group than in the OS group (WMD = -0.88 d, 95%CI: -1.58 to -0.19, $P = 0.01$, $I^2 = 94\%$ for heterogeneity, $P < 0.00001$; Figure 2D). Four studies provided the time to recovery of diet in 162 patients^[24,26,27,31]. The time to recovery of diet for MIS was significantly shorter than that for OS (WMD = -1.54 d, 95%CI: -2.30 to -0.78, $P < 0.0001$, $I^2 = 88\%$ for heterogeneity, $P < 0.0001$; Figure 2E). All studies reported the length of hospital stay, but only six studies clearly recorded the length of postoperative hospital stay, including 87 patients in the MIS group and 136 patients in the OS group^[22-24,27,29,30]. According to the pooled data from the six studies, the patients in the MIS group were discharged earlier than those in the OS group after operation (WMD = -4.06 d, 95%CI: -5.95 to -2.18, $P < 0.0001$, $I^2 = 69\%$ for heterogeneity, $P = 0.006$; Figure 2F).

All but one study^[26] clearly reported the rate of overall postoperative complications, ranging from 7.1% to 34.8% in the MIS group and from 0% to 50% in the OS group, without a significant difference between the two groups (OR = 0.78, 95%CI: 0.51 to 1.18, $P = 0.24$, $I^2 = 0\%$ for heterogeneity, $P = 0.89$; Figure 3A). The severity (Clavien-Dindo grade ≥ 3) of complications was reported in five studies^[24,25,27,28,31], and the number of severe complications was not significantly different in the two groups (OR = 0.75, 95%CI: 0.42 to 1.34, $P = 0.33$, $I^2 = 31\%$ for heterogeneity, $P = 0.21$; Figure 3B). Different types (surgical or general complications) of postoperative complications were compared for further analysis. The surgical complications were reported in nine studies^[22-25,27-31], and the pooled data identified that the rate of surgical complications in

Table 1 Characteristics of the included studies

Author-year	Country	Study type	Gender (M/F)		BMI (kg/m ²) ²		Age (yr) ²		Quali tysco re ³
			MIS	OS	MIS	OS	MIS	OS	
Chen-2011	China	Retrospective	18/5	14/4	NR	NR	55 ± 10	53 ± 9	8
Chen-2019	China	Retrospective	10/6	9/13	23.8 ± 3.7	23.3 ± 4.1	66.0 ± 10.4	64.8 ± 13.0	7
Gorgun-2017	America	Retrospective	6/8	16/13	25.1 ± 0.8	27.5 ± 1.2	56.3 ± 3.3	57.7 ± 2.5	7
Hu-2012	China	Matched-pair	10/3	9/4	21.5 ± 7.8	22.2 ± 8.4	54.0 ± 10.0	53.0 ± 11.0	8
Ivanecz-2017	Slovenia	Matched-pair	6/4	6/4	26.9 (23.6-32.1)	24.0 (23.1-25.5)	62.2 ± 7.9	65.4 ± 8.1	9
Lin-2015	China	Matched-pair	5/2	21/15	21.9 ± 2.2	21.2 ± 1.6	59.6 ± 3.4	57.4 ± 10.4	7
Ma-2018	China	Matched-pair	9/3	8/4	23.0 (19.3-26.7)	21.6 (75.5-24.9)	3/9 ¹	1/11 ¹	8
Ratti-2016	Italy	Matched-pair	14/11	27/23	NR	NR	60 (37-80)	62 (35-81)	8
Takasu-2014	Japan	Matched-pair	3/4	3/4	NR	NR	74.0 ± 12.0	62.0 ± 4.0	7
Tranchart-2016	France	Matched-pair	42/47	40/49	24.0 ± 3.6	24.7 ± 2.5	66.6 ± 10.8	65.0 ± 9.4	7

¹Dichotomous variables, >60/≤60 years;²The data are expressed as the mean ± SD or medians (range);³According to the Newcastle-Ottawa scale classification. BMI: Body mass index; F: Female; M: Male; MIS: Minimally invasive surgery; OS: Open surgery; NR: Not reported.

the MIS group was significantly reduced compared with the OS group (OR = 0.60, 95%CI: 0.37 to 0.99, $P = 0.04$; $I^2 = 0\%$ for heterogeneity, $P = 0.50$; **Figure 3C**). The general complications between the groups retrieved from eight papers^[22-25,27,28,30,31] showed no significant difference (OR = 1.23, 95%CI: 0.73 to 2.07, $P = 0.44$, $I^2 = 0\%$ for heterogeneity, $P = 0.84$; **Figure 3D**).

Long-term outcomes

The HR was used to assess the differences in the long-term outcomes (DFS and overall survival) between the groups. The HR was estimated from the survival data that were extracted from the survival curve reported in the studies. All studies provided the Kaplan-Meier curves of overall survival, whereas the 95%CI could not be calculated in half of the studies. Another five studies^[23-25,29,31] showed that HR was not significantly different between the groups (HR = 1.15, 95%CI: 0.53 to 2.50, $P = 0.73$, $I^2 = 0\%$ for heterogeneity, $P = 0.94$; **Figure 4A**). Seven studies reported DFS curves, but the 95%CI could not be calculated in one study because it only provided the median follow-up time without a range^[23-25,27,28,31]. Thus, synthetic analysis of the DFS data in the other six studies was conducted. The HR of DFS was not significantly different (HR = 1.00, 95%CI: 0.67 to 1.50, $P = 1.00$, $I^2 = 0\%$ for heterogeneity, $P = 0.48$; **Figure 4B**).

Publication bias

As shown in **Figure 5**, the possible publication bias of the number of intraoperative blood transfusions and overall complications between the groups was assessed by the funnel plot, Egger's test, and Begg's test. The funnel plot of the number of intraoperative blood transfusion was symmetrically distributed, and none of the studies included was outside the 95%CI (**Figure 5A**). No significant publication bias was detected from statistical tests based on the number of intraoperative blood transfusions (Begg's test $P = 1.000$; Egger's test $P = 0.897$). The funnel plot of the overall complications showed a symmetric distribution of all studies, and all were inside the 95%CI (**Figure 5B**). The pooled analysis suggested that there was no significant publication bias in the overall complications (Begg's test $P = 0.283$; Egger's test $P = 0.127$).

DISCUSSION

In past decades, the resection timing of primary CRC and SCRLM has been controversial. Some scholars hold the opinion that staged resection can reduce the rate of operative complications and make the occult micrometastases become perceptible^[32,33]. However, some authors believe that simultaneous resection can reduce the burden of tumors, as well as reduce the economic and psychological burden of patients, leading to patients undergoing one operative procedure instead of two^[34]. Recently, with the advances in the strategy of perioperative management and overall critical care, the operation strategy for resectable patients has been questioned.

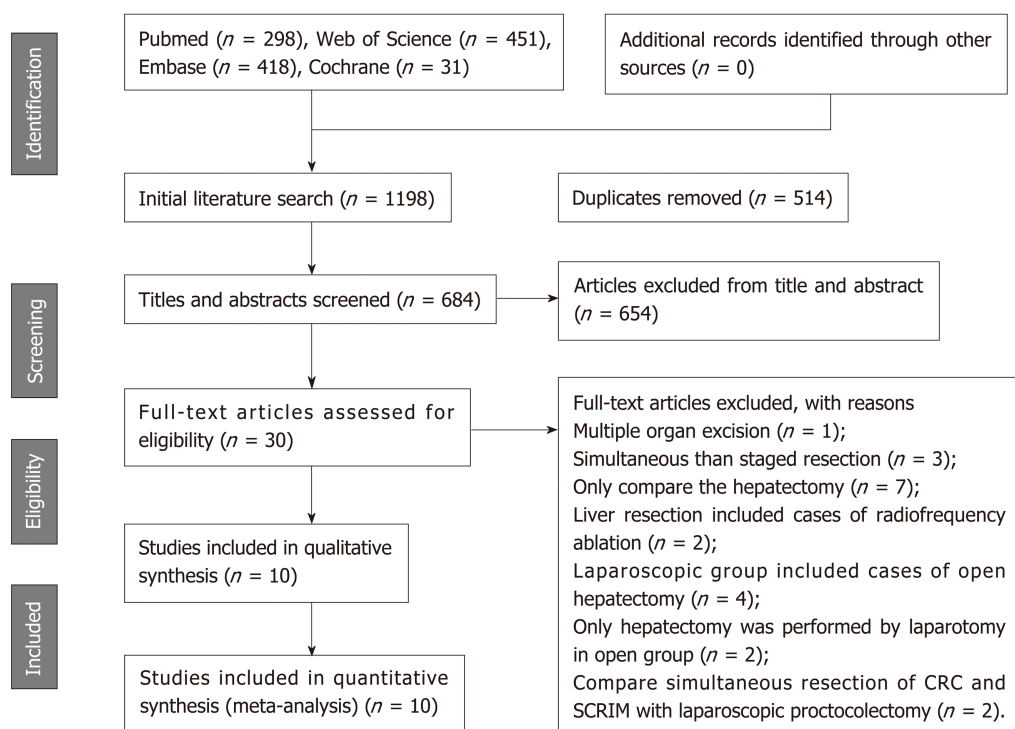


Figure 1 Flow chart of the study search strategies. CRC: Colorectal cancer; SCRLM: Synchronous colorectal liver metastases.

An increasing number of authors support that the optimal operation timing is gradually changing from staged resection to simultaneous resection^[35,36].

Traditionally, simultaneous resection of primary CRC and SCRLM is usually performed by laparotomy. Conventional laparotomy always requires a long abdominal incision for adequate exposure of the operative field, causing severe pain and incision complications^[29]. Laparotomy is also associated with serious physical and psychological operative trauma to the patients. With the improvements in surgical technique and apparatus, MIS showed great advantages in some surgeries such as proctocolectomy or hepatectomy^[11,13]. Furthermore, reports regarding the safety and efficacy of combined resection of CRC and SCRLM have been increased. However, most were case series or reports limited by a small sample size^[14,15]. Our meta-analysis of ten comparative studies with 502 patients provided a large body of information and identified the advantages of MIS over OS in simultaneous resection of CRC and SCRLM.

The pooled results revealed that the operative time was similar between the groups. The operation time depended on the characteristics of primary tumors and liver metastases, severe degree of abdominal adhesion and obesity, and experience of the surgical teams^[37,38]. These might also be the sources of heterogeneity ($P < 0.00001$, $I^2 = 84\%$). The intraoperative blood loss was critical to evaluate the quality of surgery. The most significant finding in this meta-analysis was the reduction of blood loss in MIS *vs* OS ($P = 0.002$). Moreover, the number of intraoperative blood transfusions was also less in the MIS group than in the OS group ($P = 0.03$). Less blood loss indicated a lower blood transfusion rate. Studies have reported that perioperative blood transfusion might lead to poor survival, and transfused patients had more postoperative complications^[39-41]. High heterogeneity ($P < 0.00001$, $I^2 = 91\%$) among groups was observed in this regard that was likely to be related to the methods used to estimate the blood loss and diverse experience of the surgical teams.

Postoperative recovery was also analyzed in the present meta-analysis. Interestingly, the time to both intestinal function recovery and start of the diet in patients accepting MIS was shorter than that in patients undergoing OS ($P = 0.01$, $P < 0.0001$). The cause was that the MIS technique shortened the intestinal exposure time and reduced intestinal irritation. Furthermore, another target to assess the postoperative recovery was the length of postoperative hospital stay. As expected, the length of postoperative hospital stay was shorter in the MIS group than in the OS group ($P = 0.01$). Different surgical teams had different postoperative management concepts, which might interpret the high heterogeneity in the above indexes of postoperative recovery.

Table 2 Short- and long-term outcomes of the included studies

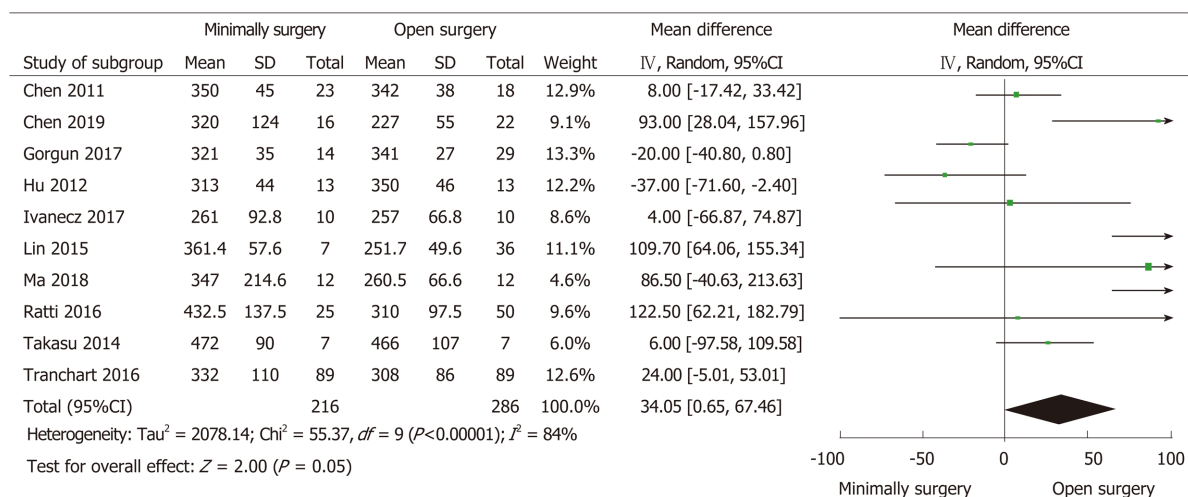
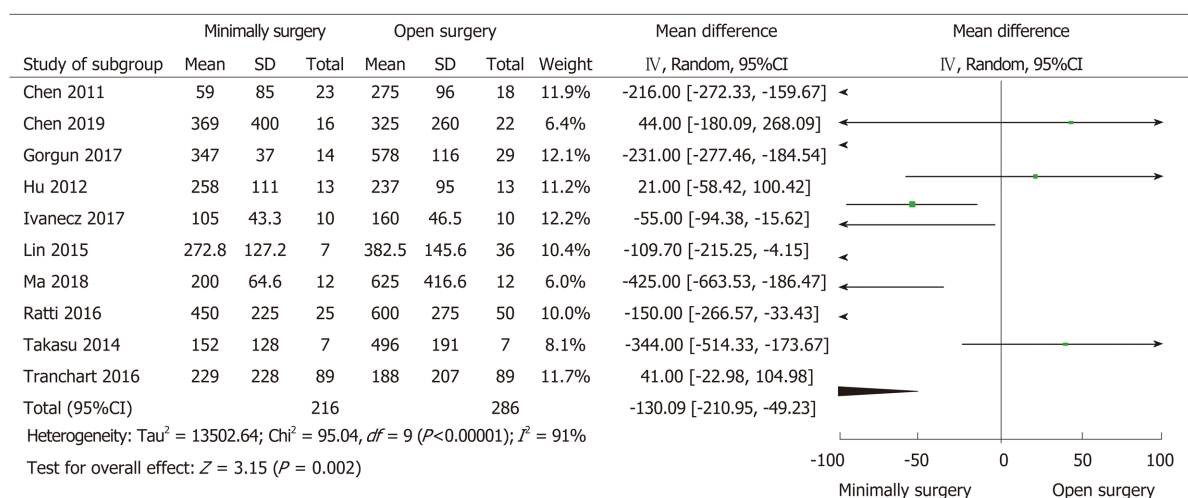
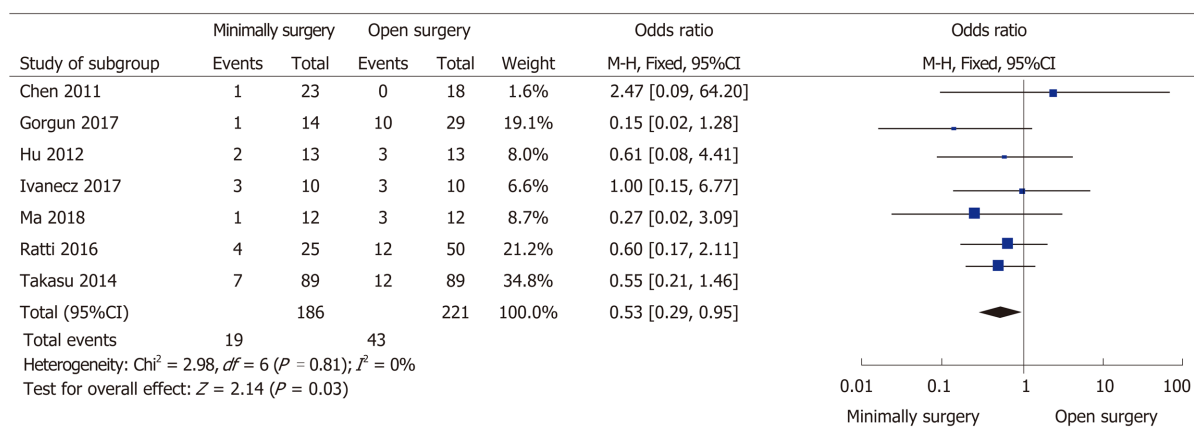
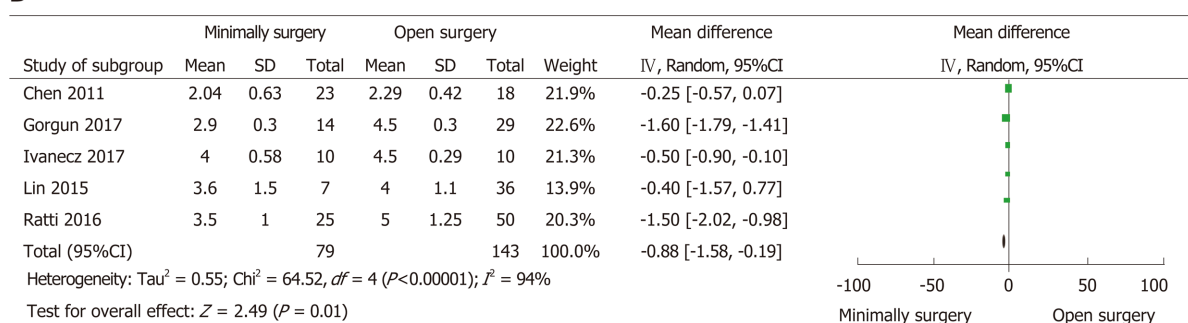
Author-year	Size of CRC (cm)	TD of CRC W+M/P+O	ID of CRC T1-T2/T3-T4	CRC (C/R)	ASAs 1-2/3-4	CEA level	Number of SCRLM	SCRLM (U/B)	Size of SCRLM (cm)
Chen2011-MIS	2.5 ± 0.9	16/7	NR	3/4	NR	38.9 ± 3.5	NR	NR	5.5 ± 1.2
Chen2011-OS	2.3 ± 1.0	14/4	NR	3/4	NR	38.7 ± 3.3	NR	NR	5.6 ± 1.4
Chen2019-MIS	4.0 ± 2.0	NR	2/14	NR	1.9 (1-3)	929 ± 1936	NR	NR	5.5 ± 4.2
Chen2019-OS	5.0 ± 3.0	NR	2/20	NR	2.0 (1-3)	247 ± 728	NR	NR	4.7 ± 3.7
Gorgun2017-MIS	3.7 ± 0.7	NR	2/12	6/8	0/14	36.9 ± 30.4	1.6 ± 0.3	12/2	2.4 ± 0.7
Gorgun2017-OS	3.7 ± 0.5	NR	7/22	14/15	6/23	14.3 ± 4.9	2.1 ± 0.2	19/10	2.7 ± 0.2
Hu2012-MIS	NR	NR	NR	7/6	NR	NR	NR	NR	3.2 ± 1.0
Hu2012-OS	NR	NR	NR	7/6	NR	NR	NR	NR	3.5 ± 0.9
Ivanecz2017-MIS	NR	10/0	1/9	4/6	8/2	7.7 ± 7.7	1 (1-2)	9/1	2.0 ± 1.2
Ivanecz2017-OS	NR	9/1	1/9	6/4	7/3	15.2 ± 12.5	1 (1-2)	9/1	2.9 ± 1.5
Lin2015-MIS	5.3 ± 1.1	4/3	0/7	3/4	6/1	7/2 ¹	1.9 ± 0.9	7/0	3.3 ± 1.8
Lin2015-OS	5.7 ± 1.9	19/17	2/34	19/17	31/5	27/9 ¹	2.1 ± 1.0	26/10	4.2 ± 2.2
Ma2018-MIS	NR	10/2	1/11	7/5	12/0	7/5 ²	1.0 (1-4)	10/2	2.8 (0.5-10.0)
Ma2018-OS	NR	9/3	0/12	7/5	12/0	11/1 ²	2.5 (1-7)	7/5	2.5 (1.2-6.5)
Ratti2016-MIS	NR	21/5	NR	13/12	20/5	35.6 (2-299)	2 (1-6)	13/12	2.9 (0.5-11)
Ratti2016-OS	NR	40/10	NR	27/23	44/6	41.6 (3.1-612)	2 (1-7)	27/23	3.4 (0.9-12)
Takasu2014-MIS	4 ± 2	7/0	2/5	3/4	NR	NR	1.4 ± 0.8	5/2	1.9 ± 0.9
Takasu2014-OS	5 ± 0	7/0	1/6	3/4	NR	NR	1.5 ± 1.1	3/4	2.9 ± 1.1
Tranchart2016-MIS	NR	72/17	12/77	48/41	64/25	61 ± 75	1.4 ± 0.6	81/8	2.9 ± 1.9
Tranchart2016-OS	NR	63/26	10/79	51/38	56/33	31 ± 76	1.5 ± 0.7	78/11	2.8 ± 2.0

¹Dichotomous variables, >5/≤5 ng/mL;²Dichotomous variables, ≥5/<5 ng/mL. B: Bilobar; C: Colon; CRC: Colorectal cancer; ID: Invasion depth; M: Moderate; MIS: Minimally invasive surgery; O: Other; OS: Open surgery; P: Poor; R: Rectal; SCRLM: Synchronous colorectal liver metastases; TD: Tumor differentiation; U: Unilobar; W: Well; NR: Not reported.

Another issue of concern for MIS is the postoperative complications; all studies reported postoperative complications, but the number of complications reported in one article^[26] was too obscure for further analysis. No significant difference was found in the rate ($P = 0.24$) or severity (Clavien-Dindo grade ≥ 3 , $P = 0.33$) of overall postoperative complications. Our meta-analysis also analyzed the type of postoperative complications. The general complications were not different between the groups, but the surgical complications were fewer in the MIS group than in the OS group. Thus, our results suggested that MIS is a safe and effective technique.

A key factor in evaluating the quality of surgery is the long-term oncological outcomes. Nine studies provided overall survival curves, and seven studies reported DFS curves. However, the 95%CI of HR could not be calculated in some studies according to the data extracted from the studies. Finally, further analysis for overall survival and DFS could only be conducted in six and five studies, respectively. The pooled data showed that the HR of DFS and overall survival was similar in the two groups.

Several limitations should be considered in this meta-analysis such as the heterogeneity. First, the surgeries were performed by different surgical teams with different experience and skills, as well as different perioperative management. Second, although these studies were focused on CRC and SCRLM, the involved types of surgeries were different because of different tumor locations. Third, these were all retrospective studies with a small size, without RCTs available. Finally, the number of

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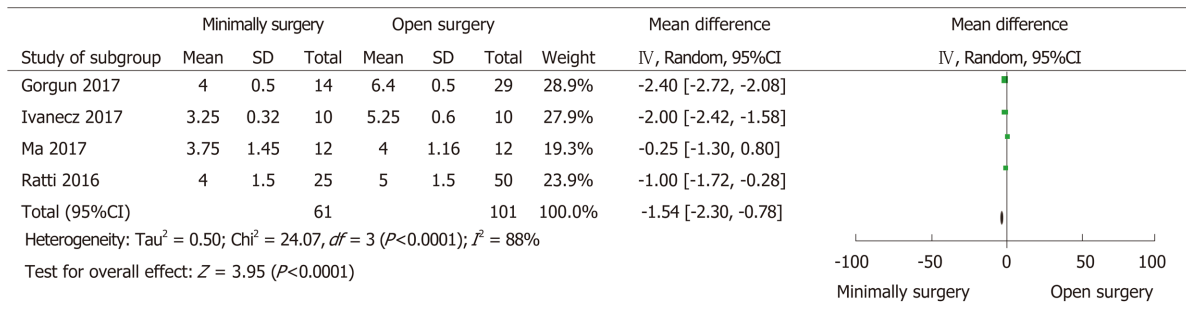
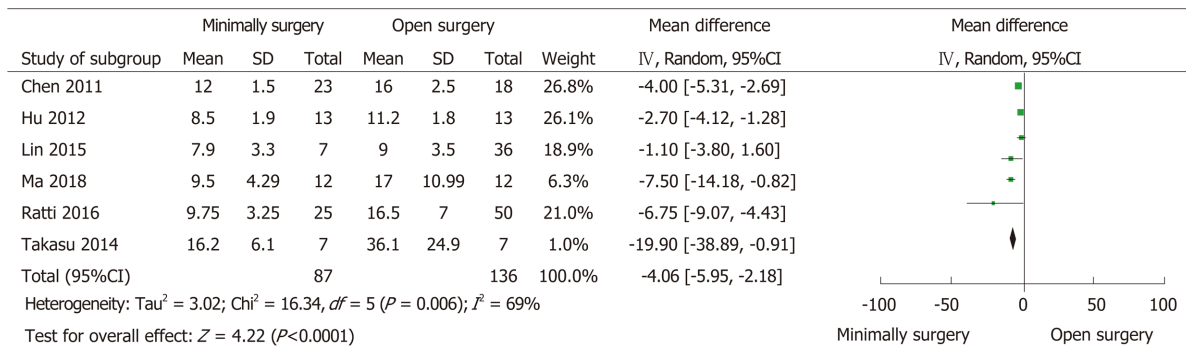
E**F**

Figure 2 Forest plots of the meta-analysis for intraoperative outcomes. A: The operative time was compared between the minimally invasive surgery (MIS) and open surgery (OS) groups; B: Intraoperative estimated blood loss was compared between the MIS and OS groups; C: Number of intraoperative blood transfusions was compared between the MIS and OS groups; D: Time to bowel functional recovery was compared between the MIS and OS groups; E: Time to start diet was compared between the MIS and OS groups; F: Length of postoperative hospital stay was compared between the MIS and OS groups. MIS: Minimally invasive surgery; OS: Open surgery; CI: Confidence interval; SD: Standard deviation.

studies included in our meta-analysis was not large enough because studies focused on MIS and OS for the simultaneous resection of CRC and SCRLM were limited in the electronic databases. Based on the above limitations, caution must be taken in analyzing the results pooled from the ten studies.

In conclusion, MIS was proven to be a safe and effective technique in the treatment of patients with CRC and SCRLM. Compared with OS, MIS has less blood loss and blood transfusion, a quicker postoperative recovery, and equivalent long-term outcomes. Further randomized controlled trials are needed to further confirm these advantages.

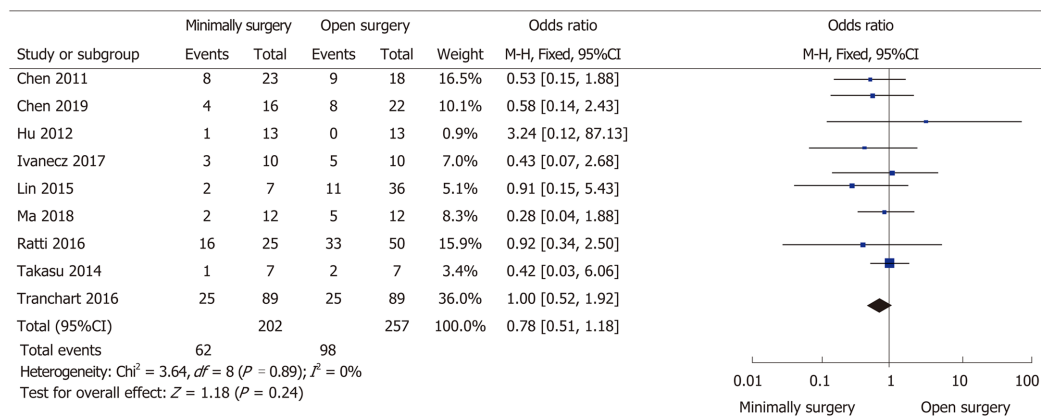
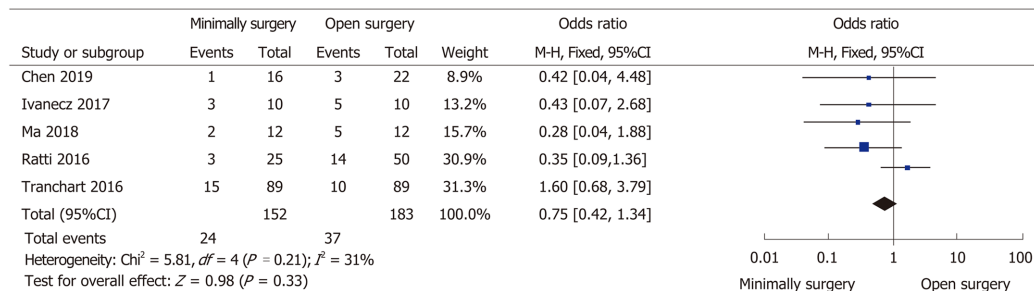
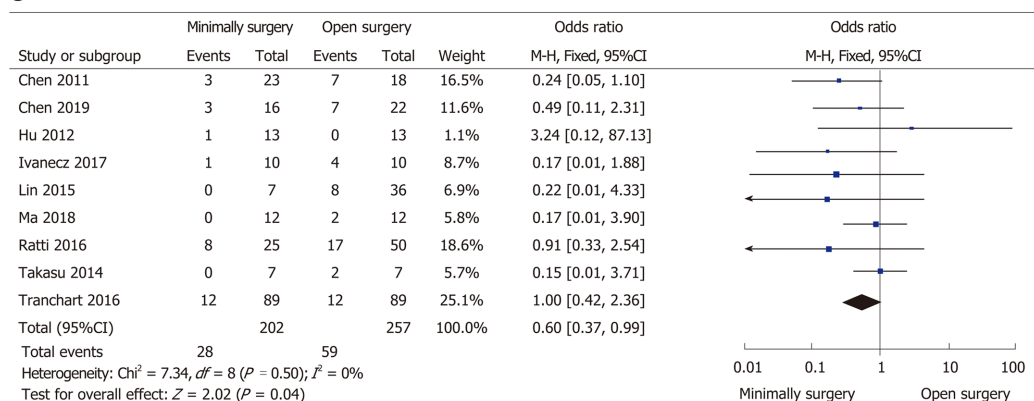
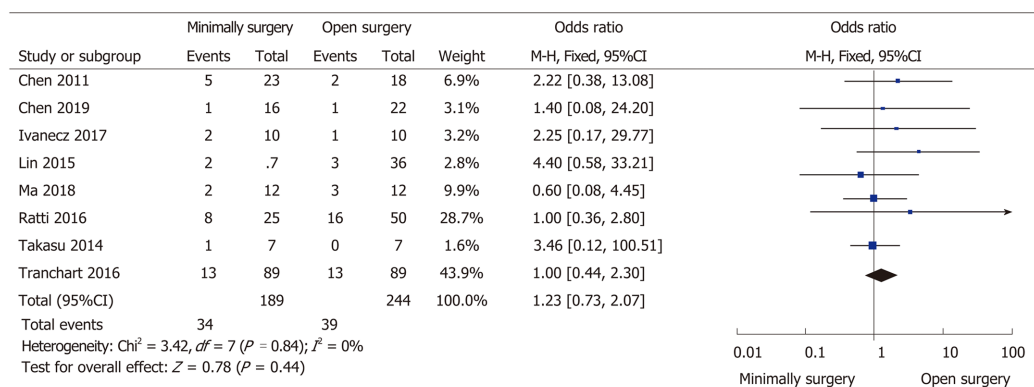
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Figure 3 Forest plots of the meta-analysis for complications. A: Overall complications were compared between the minimally invasive surgery (MIS) and open surgery (OS) groups; B: Severe (Clavien–Dindo grade ≥ 3) complications were compared between the MIS and OS groups; C: Surgical complications were compared between the MIS and OS groups; D: General complications were compared between the MIS and OS groups. MIS: Minimally invasive surgery; OS: Open surgery; CI: Confidence interval.

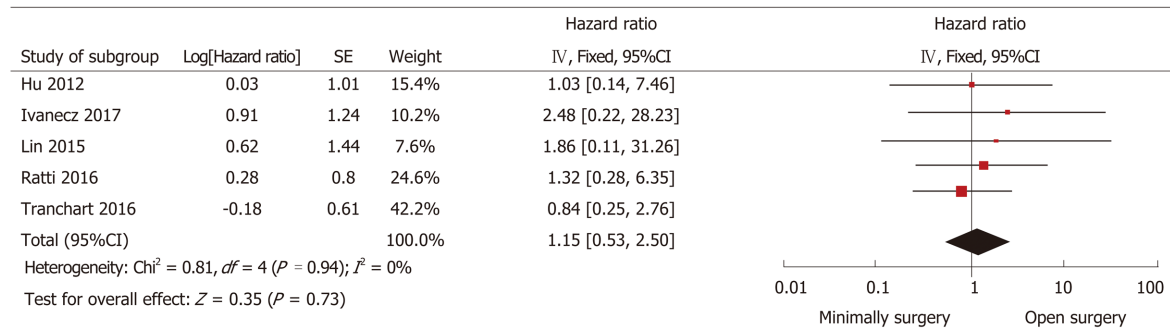
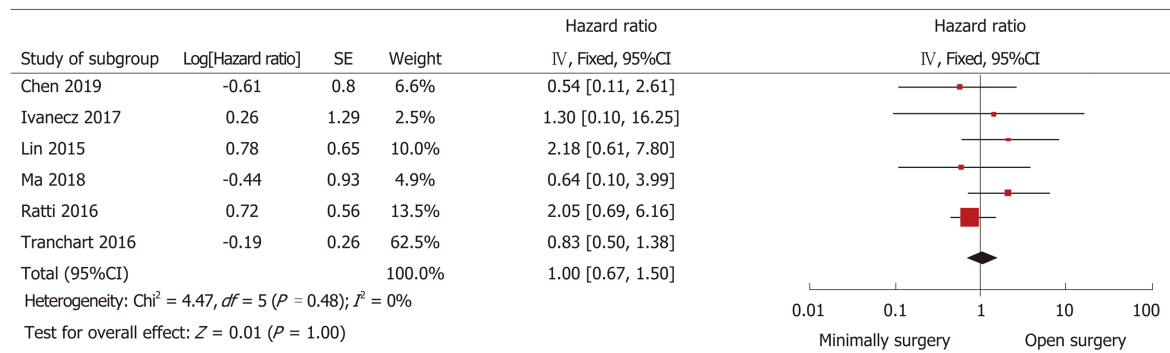
A**B**

Figure 4 Forest plots of the meta-analysis for long-term outcomes. A: The overall survival was compared between the minimally invasive surgery (MIS) and open surgery (OS) groups; B: Disease-free survival was compared between the MIS and OS groups. MIS: Minimally invasive surgery; OS: Open surgery; CI: Confidence interval; SE: Standard error.

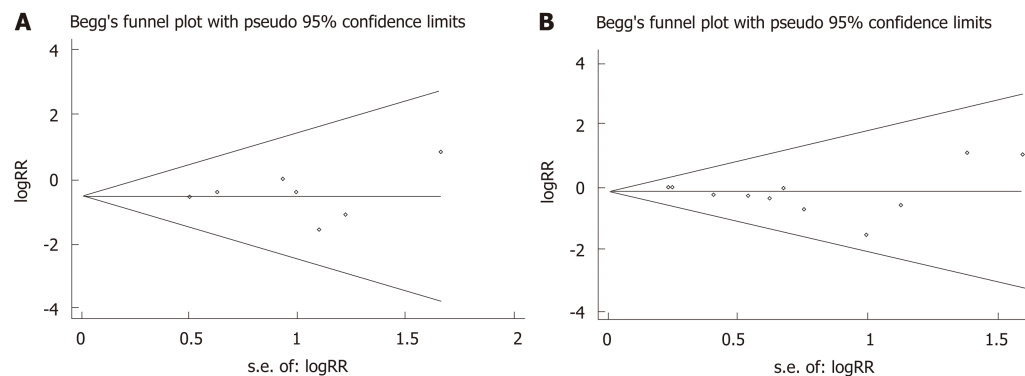


Figure 5 Funnel plots of the number of intraoperative blood transfusions and postoperative complications in patients between the minimally invasive surgery and open surgery groups. A: Intraoperative blood transfusions; B: Postoperative complications. RR: Relative risk.

ARTICLE HIGHLIGHTS

Research background

Colorectal cancer (CRC) is a common cause of cancer-related deaths, especially in cases with liver metastases. Simultaneous surgical resection of primary colorectal tumors and synchronous colorectal liver metastases (SCRLM) is an effective strategy to improve the overall survival rate. Application of minimally invasive surgery (MIS) is increasing, but the true benefits of MIS remain unclear.

Research motivation

We hope to offer guidance on the clinical care of MIS in CRC and SCRLM.

Research objectives

To help identify which optimal surgery method is suitable for patients with CRC and SCRLM.

Research methods

A systematic search was conducted in PubMed, EMBASE, Web of Science, and Cochrane Library databases for studies concerning minimally invasive and open surgery (OS) for the simultaneous resection of CRC and SCRLM. We followed the PRISMA agreement. The meta-analysis was performed using Review Manager Software, and the quality was assessed using the Newcastle-Ottawa scale.

Research results

Two hundred and sixteen patients in the mini-invasive group and 286 patients in the open group were included in this study. Intraoperative blood loss ($P = 0.002$) and blood transfusion ($P = 0.03$) were less, the recovery of intestinal function ($P = 0.01$) and diet ($P < 0.0001$) was faster, the length of postoperative hospital stay ($P < 0.0001$) was shorter, and the number of surgical complications was lower ($P = 0.04$) in the MIS group. However, the operation time, rates and severity of overall morbidity, as well as the rates of general morbidity showed no significant difference between the minimally invasive and OS groups. Moreover, the overall survival and disease-free survival after MIS were similar to those after OS.

Research conclusions

The current meta-analysis showed that MIS is an optimal strategy for the simultaneous resection of CRC and SCRLM.

Research perspectives

The results of the current meta-analysis may help researchers to develop guidelines about surgical methods in CRC and SCRLM more perfectly.

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