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Outcomes of laparoscopic repeat liver resection for recurrent liver cancer

A system review and meta-analysis

Yufu Peng, MD, Fei Liu, MD, Yonggang Wei, MD*, Bo Li, MD, PhD*

Abstract

Background: With the improvements of surgical instruments and surgeons' experience, laparoscopic liver resection has been applied for recurrent tumors. However, the value of laparoscopic repeat liver resection (LRLR) is still controversial nowadays, which compelled us to conduct this meta-analysis to provide a comprehensive evidence about the efficacy of LRLR for recurrent liver cancer.

Methods: A computerized search was performed to identify all eligible trials published up to April 2019. This meta-analysis was conducted to estimate the perioperative data and oncological outcomes of LRLR by compared with open repeat liver resection (ORLR) and laparoscopic primary liver resection (LPLR). A fixed or random-effect modal was established to collect the data.

Results: A total of 1232 patients were included in this meta-analysis (LRLR: n=364; ORLR: n=396; LPLR: n=472). LRLR did not increase the operative time compared to ORLR (WMD=15.92 min; 95%CI: −33.53 to 65.37; P=.53). Conversely, LRLR for patients with recurrent tumors was associated with less intraoperative blood loss (WMD=−187.33 mL; 95%CI: −249.62 to −125.02; $P<.00001$), lower transfusion requirement (OR=0.24; 95%CI: 0.06–1.03; P=.05), fewer major complications (OR=0.42; 95%CI: 0.23–0.76; P=.004), and shorter hospital stays (WMD=−2.31; 95%CI: −3.55 to −1.07; P=.0003). In addition, the oncological outcomes were comparable between the two groups. However, as for the safety of LRLR compared with LPLR, although the operative time in LRLR group was longer than LPLR group (WMD=58.63 min; 95%CI: 2.99–114.27; P=.04), the blood loss, transfusion rates, R0 resection, conversion, postoperative complications, and mortality were similar between the two groups.

Conclusions: LRLR for recurrent liver cancer could be safe and feasible in selected patients when performed by experienced surgeons.

Abbreviations: CCC = central cholangiocarcinoma, CLM = colorectal liver metastasis, CI = confidence interval, HCC = hepatocellular carcinoma, LPLR = laparoscopic primary liver resection, LRLR = laparoscopic repeat liver resection, NETLM = neuroendocrine tumor liver metastasis, OR = odds rations, ORLR = open repeat liver resection, WMD = weighted mean difference.

Keywords: laparoscopy, meta-analysis, primary liver resection, recurrent liver cancer, repeat liver resection

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1. Introduction

With the technical and medical innovations, liver resection has now been widely accepted as the optimal treatment for patients with liver tumors.[1] However, patients often develop tumor recurrence after liver resection which is commonly limited in the residual liver.[2,3] As for the intrahepatic recurrent tumor, various therapeutic modalities including repeat liver resection, liver transplantation, radiofrequency ablation, and transarterial chemoembolization could be used to manage it, but repeat liver resection is still performed as the first-line treatment.[4–6]

Laparoscopic liver resection has been rapidly adopted worldwide following the improvements of surgical instruments and surgeons' experience since the First International Consensus Conference on Laparoscopic Liver Surgery Convened in Louisville in 2008.[7] As being a minimally invasive surgery, it was reported with some advantages compared with traditional open liver resection, including less blood loss, fewer complications, shorter hospital stays, and equivalent oncological outcomes.[8–12] However, due to the presence of adhesions and altered anatomy caused by the previous resection, repeat liver resection has more challenges compared to initial resection, thus it was mainly performed by traditional open approach in most centers.[3–6]

Recently, some centers have applied laparoscopy for repeat hepatectomy and evaluated the safety of laparoscopic repeat liver resection (LRLR).[13–23]

Although there were a few systematic reviews that have assessed the outcomes of LRLR versus open repeat liver resection (ORLR),[24,25] some new and high-quality literatures have been published recently.[20,21] In addition, there was little strong evidence about the safety and feasibility of LRLR compared with laparoscopic primary liver resection (LPLR). Thus, this meta-analysis was conducted to review and update the perioperative and survival outcomes of LRLR compared with ORLR and LPLR, which could provide a comprehensive evidence about the efficacy of LRLR for recurrent tumors.

2. Materials and methods

2.1. Literature search strategy

This meta-analysis was conducted following the PRISMA guidelines.[26] Systematic searches of MEDLINE, EMBASE, Cochrane Library, and Web of science were performed to retrieve articles published up to April 2019. The following search terms were used: "laparoscopic or minimally invasive surgery," "repeat liver resection or repeat hepatectomy," "recurrent liver cancer or recurrent liver tumor," "recurrent hepatocellular carcinoma or recurrent HCC or recurrent metastasis tumor." The reference lists of eligible studies were manually searched to identify potential articles.

2.2. Study selection

The inclusion criteria were as follows:

1. observational and/or randomized studies about LRLR for recurrent liver cancer compared with LPLR, or those comparing LRLR versus ORLR for recurrent liver cancer;
2. the perioperative and/or survival outcomes could be used for analysis.

The exclusion criteria were as follows:

1. with insufficiency of data (<30 cases);
2. without clearly reported outcomes of interest.

2.3. Data extraction and quality assessment

Two reviewers (P.Y.F. and L.F.) independently extracted information from each eligible articles, and disagreements were solved by discussion among all authors. The following data were extracted: the first author, publication year, country, study design, number of patients in each group, patient baseline characteristics, surgical outcomes (operative time, blood loss, transfusion requirements, open conversion, R0 resection rates), postoperative outcomes (overall complications, major complications, mortality, postoperative hospital stay), and survival outcomes. Quality of trials was assessed by using the Newcastle-Ottawa Scale (NOS),[27] which included patient selection, comparability of the study groups, and assessment of outcomes. A score of 0 to 9 was allocated to each study according to the parameters above, and studies with a score ≥6 were defined as high quality.

2.4. Statistical analysis

This meta-analysis was performed using Review Manager Version 5.3 (Cochrane Collaboration) and STATA statistical software Version13. Continuous variables were calculated by the use of weighted mean difference (WMD) with 95% confidence interval (CI), and dichotomous variables were assessed by the use of odds rations (OR) with 95%CI. Results were considered statistically significant at P value < .05. Both the Cochran's Q test and the I-square index (I^2) were conducted to assess heterogeneity of the eligible studies. $P > .1$ and $I^2 < 50\%$ were defined low heterogeneity, thus a fixed effect model was selected for statistical analysis. Otherwise, a random effect model was used. Sensitivity analysis was conducted according to the design of case matched and non-case match studies. Risk of publication bias was assessed by using Begg's test and Egger's test.

3. Results

3.1. Study eligibility

According to the search strategy above, a total of 718 studies were identified from the electronic databases. After removing duplicates, screening titles and abstracts, and reading full-text articles, 11 studies were enrolled in this meta-analysis. Of these, 7 studies compared LRLR and ORLR for recurrent tumors, 2 studies assessed the safety and feasibility of LRLR versus LPLR, and 2 studies evaluated the outcomes of LRLR compared with the ORLR and LPLR. Figure 1 illustrated the selection process.

3.2. Study characteristics

A total of 1232 patients were included in this meta-analysis (LRLR: n=364; ORLR: n=396; LPLR: n=472). Indications for liver resection of the 11 studies mainly were HCC (n=582, 47.24%) and colorectal liver metastasis (CLM) (n=578, 46.92%). There were no statistical differences in patients demographics between the groups, and the baseline characteristics of the included studies were showed in Tables 1 and 2.

According to NOS scores, all the studies were assessed as high quality ranged from 7 to 9 points. Study quality assessment results were shownd in Table 3.

3.3. Short-term outcomes of LRLR versus ORLR

The operative time was similar between the LRLR and ORLR groups (WMD=15.92 min; 95%CI: −33.53 to 65.37; P=.53). However, the intraoperative blood loss was significantly less in the LRLR group than that in the ORLR group (WMD=−187.33 mL; 95%CI: −249.62 to −125.02; P<.00001), thus transfusion requirement was relatively more in the ORLR group (OR=0.24; 95%CI: 0.06–1.03; P=.05). In addition, the rate of R0 resection was significantly higher in LRLR group than in ORLR group (OR=2.40; 95%CI: 1.37–4.21; P=.002). The surgical outcomes of LRLR versus ORLR were showed in Figure 2.

The meta-analysis of 7 studies showed the overall complications were comparable between LRLR and ORLR groups (OR= 3.7; 95%CI: 0.11–1.24; P=.11). According to the Clavien-Dindo classification, major complication was defined as Clavien-Dindo grade III and above.[28] The rate of major complications was significantly lower in LRLR group than ORLR group (OR=0.42; 95%CI: 0.23–0.76; P=.004). The pooled data showed that early postoperative mortality (OR=2.14; 95%CI: 0.63–7.28; P=.23) was similar between the two groups, but postoperative hospital stay was shorter in the LRLR group than that in the ORLR group (WMD=−2.31; 95%CI: −3.55 to −1.07; P=.0003). The

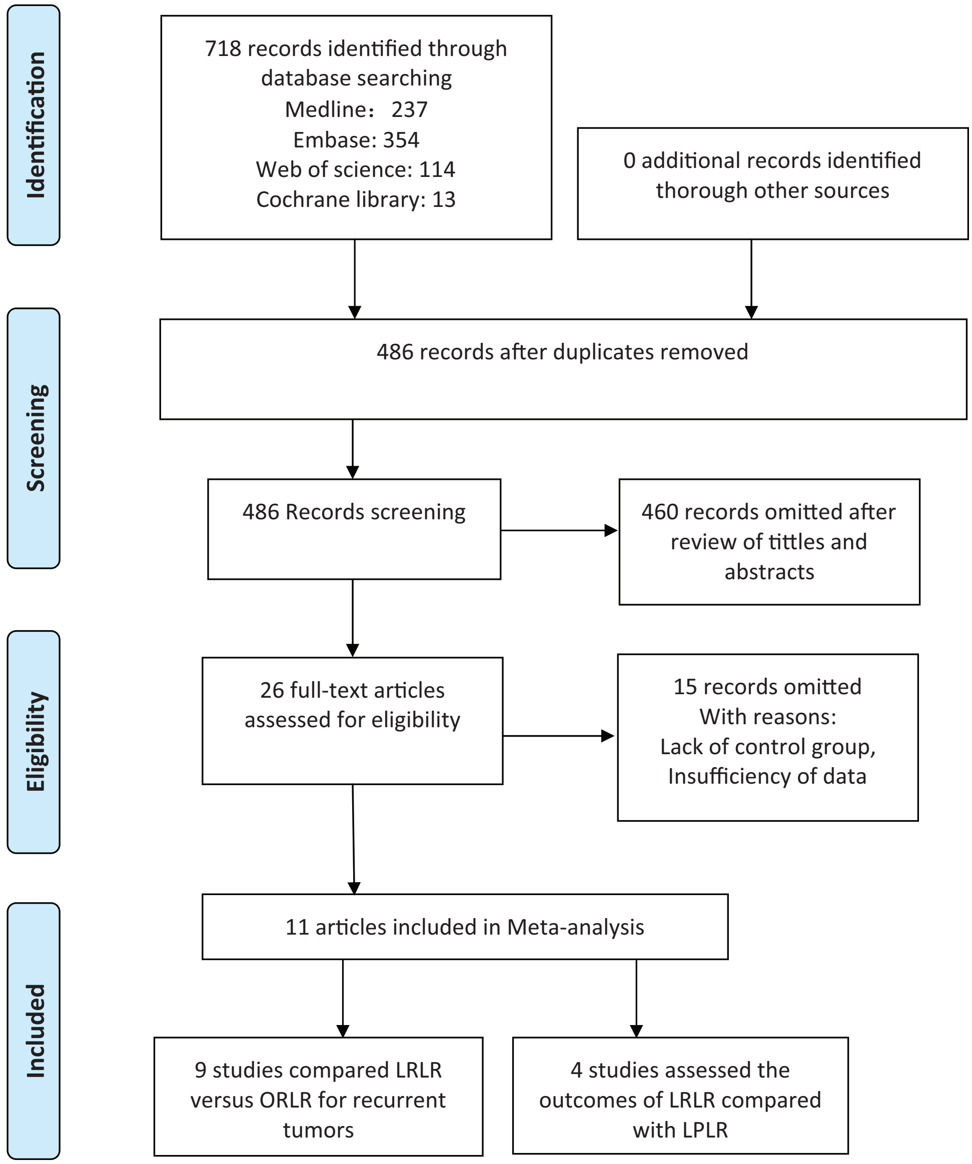

Figure 1. Flow chart illustrating the trials selection process.

postoperative short-term outcomes of LRLR versus ORLR were showed in Figure 3.

3.4. Short-term outcomes of LRLR versus LPLR

According to this meta-analysis, the operative time was significant longer in the LRLR group than that in LPLR group (WMD = 58.63 min; 95%CI: 2.99–114.27; P = .04). However, there was no significant difference in the intraoperative blood loss (WMD = 68.36 mL; 95%CI: −193.86 to 330.58; P = .61), transfusion (OR = 0.56; 95%CI: 0.23–1.37; P = .20), R0 resection (OR = 0.85; 95%CI: 0.34–2.12; P = .72), and conversion (OR = 1.08; 95%CI: 0.43–2.68; P = .87) between the LRLR group and LPLR group. Moreover, there were no significant differences in the term of overall complications (OR = 0.79; 95% CI: 0.44–1.43; P = .44), major complications (OR = 0.68; 95% CI: 0.29–1.58; P = .37), early postoperative mortality (OR = 2.42; 95%CI: 0.50–11.62; P = .27), and postoperative hospital stay (WMD = 0.0; 95%CI: −0.24 to 0.24; P = .99). The postoperative short-term outcomes of LRLR versus LPLR were showed in Figures 4 and 5.

3.5. Long-term outcomes

A total of 5 studies reported the survival outcomes, but the data on tumor recurrence were available in only 4 studies. The pooled results suggested that there was no significant difference in the tumor recurrence between the LRLR group and ORLR group (OR = 1.11 95%CI: 0.64–1.92; P = .71).

3.6. Sensitivity analysis

Sensitivity analysis was conducted in outcomes of LRLR versus ORLR and different results were found in transfusion. The results were listed in Table 4.

Due to the limited dataset available, sensitivity analysis was not performed in outcomes of LRLR versus LPLR.

Table 1

Characteristics of included studies comparing LRLR with ORLR.

Study (author, year)	Country	Type	Group	NO.	Age (years)	Gender (M vs F)	Child-Pugh (A vs B)	Previous (L vs O)	Tumor size (cm)	Cirrhosis (n, %)	MLR (n, %)	Conversion (n, %)	Indication (n)
Kanazawa et al, 2013	Japan	RM	LRLR	20	70 (46–83)	15:5	19:1	5:15	1.7 (0.7–3.5)	7 (35.0%)	NP	2 (10.0%)	HCC=20
			ORLR	20	65 (43–74)	19:1	17:3	NP	2.2 (1.3–4.1)	7 (35.0%)	NP	–	HCC=20
Chan et al, 2014	China	RM	LRLR	11	61 (43–81)	8:3	11:0	5:6	2 (1.0–4.5)	8 (72.7%)	0	0	HCC=11
			ORLR	22	62 (43–76)	16:6	NP	NP	2 (1.0–5.0)	NP	NP	–	HCC=22
Zhang et al, 2016	China	P	LRLR	31	54 (37–66)	26:5	NP	0:31	2.5±1.0	NP	0	0	HCC=31
			ORLR	33	59.5 (34–65)	27:6	NP	0:33	3.8±1.1	NP	0	–	HCC=33
Liu et al, 2017	China	PSM	LRLR	30	56.5 (27–79)	23:7	30:0	9:21	2.1 (1.0–5.0)	26 (96.7%)	1 (3.3%)	4 (13.3%)	HCC=30
			ORLR	30	48.5 (28–79)	28:2	27:2	NP	2.45 (1.0–4.3)	26 (86.7%)	3 (10.0%)	–	HCC=30
Hallet et al, 2017	France	PSM	LRLR	27	63.6 (59.0–70.9)	20:7	NP	NP	NP	NP	25 (92.6%)	1 (3.1%)	CLM=27
			ORLR	81	62.8 (57.5–70.3)	50:31	NP	NP	NP	NP	75 (92.6%)	–	CLM=81
Ome et al, 2018	Japan	R	LRLR	33	73 (45–84)	26:7	33:0	12:21	1.8 (0.4–4.5)	13 (39.4%)	NP	0	HCC=16, CLM=15, B=2
			ORLR	37	71 (45–84)	27:10	36:1	3:34	2.4 (0.7–5.5)	10 (27.0%)	NP	–	HCC=16,CCC=1,B=2, CLM=16, others=2
Noda et al, 2018	Japan	R	LRLR	20	68.8±9.7	15:5	19:1	8:12	2.41±1.26	8 (40.0%)	NP	1 (5.0%)	HCC=15,CLM=5
			ORLR	48	67.2±8.4	39:9	44:4	2:46	2.21±1.09	16 (33.3%)	NP	–	HCC=36,CLM=12
van der Poel et al, 2019	7 European counties	PSM	LRLR	105	61±10.7	62:43	NP	39:66	2.8 (1.9–4.4)	NP	49 (46.7%)	11 (10.5%)	CLM=105
			ORLR	105	62±9.6	62:43	NP	36:69	3.0 (2.0–4.0)	NP	49 (46.7%)	–	CLM=105
Goh et al, 2019	Singapore	PSM	LRLR	20	68.5 (67.0–71.75)	18:2	NP	13:7	2 (1.15–2.775)	7 (35.0%)	2 (10.0%)	3 (15.0%)	HCC=20
			ORLR	20	69 (63.0–72.25)	18:2	NP	NP	2.6 (1.5–3.0)	7 (35.0%)	0	–	HCC=20

B=combined HCC and CCC, CCC=central cholangiocarcinoma, CLM=colorectal liver metastasis, F=female, HCC=hepatocellular carcinoma, L=laparoscopic, LRLR=laparoscopic repeat liver resection, M=male, MLR=major liver resection, NP=not reported, O=open, ORLR=open repeat liver resection, P=prospective cohort, PSM=propensity score-matched cohort, R=retrospective cohort, RM=retrospective matched cohort.

Table 2

Characteristics of included studies comparing LRLR with LPLR.

Study (author, year)	Country	Type	Group	NO.	Age (years)	Gender (M vs F)	Child-Pugh (A vs B)	Tumor number	Tumor size (cm)	Cirrhosis (n, %)	MLR (n, %)	Conversion (n, %)	Indication (n)
Shelat et al, 2014	UK	RM	LRLR	20	–	–	NP	NP	2.8 (1.0–8.0)	NP	6 (30%)	3 (15.0%)	CLM = 13, NETLM = 4, HCC = 2, others = 1
			LPLR	19	57.5 (23–79)	8:11	NP	NP	2.5 (0.9–7.5)	NP	2 (11%)	0	CLM = 12, NETLM = 4, HCC = 2, others = 1
Nomi et al, 2016	France	R	LRLR	47	62 (34–81)	31:16	NP	2 (1–20)	2.5 (1.0–8.0)	NP	20 (42.6%)	0	CLM = 47
			LPLR	141	63 (26–89)	90:51	NP	1 (1–8)	2.8 (0.5–17)	NP	65 (46.1%)	6 (4.3%)	CLM = 141
Ome et al, 2018	Japan	R	LRLR	33	73 (45–84)	26:7	33:0	1 (1–3)	1.8 (0.4–4.5)	13 (39.4%)	NP	0	HCC = 16, CLM = 15, B = 2
			LPLR	127	69 (39–87)	86:41	121:6	1 (1–5)	2.2 (0.5–11.0)	48 (37.8%)	NP	1 (0.8%)	HCC = 73,CCC = 1,B = 6, CLM = 40,others = 7
Goh et al, 2019	Singapore	PSM	LRLR	20	68.5 (67.0–72.5)	18:2	NP	1 (5%)	2 (1.1–2.85)	13 (65.0%)	2 (10.0%)	3 (15.0%)	HCC = 20
			LPLR	185	63 (57.0–70.0)	18:2	NP	26 (14.1%)	2.8 (2.0–4.2)	93 (50.3%)	20 (10.8%)	27 (14.6%)	HCC = 185

B = combined HCC and CCC, CCC = central cholangiocarcinoma, CLM = colorectal liver metastasis, F = female, HCC = hepatocellular carcinoma, LPLR = laparoscopic primary liver resection, LRLR = laparoscopic repeat liver resection, M = male, MLR = major liver resection, NETLM = neuroendocrine tumor liver metastasis, NP = not reported, PSM = propensity score-matched cohort, R = retrospective cohort, RM = retrospective matched cohort.

3.7. Publication bias

Funnel plot and Begg's test and Egger's test on major complications were used to assess the publication bias. The results showed no evidence of publication bias in studies compared LRLR with ORLR (Begg's test: $P=1.000$; Egger's test: $P=.394$), and there was no publication bias in studies compared LRLR with LPLR (Begg's test: $P=1.000$; Egger's test: $P=.203$) (Fig. 6).

4. Discussion

Repeat liver resection for recurrent tumors is challenging due to the presence of adhesions and altered anatomy caused by the previous resection, which was mainly performed via open approach in most centers.[4–6,29] Recently, with the improvements of surgical instruments and surgeons' experience, some centers have applied laparoscopy for repeat liver resection and assessed the safety and feasibility of LRLR for recurrent liver tumors.[13–23] However, there is still lake of comprehensive evidence about the efficacy of LRLR versus ORLR and LPLR, which compelled us to conduct this meta-analysis. According to this analysis, LRLR had superior short-term outcomes and similar oncological features compared with ORLR, and it did not increase postoperative morbidity and mortality compared to LPLR.

Based on the present study, the operative time was not significantly different between LRLR and ORLR groups, but it was longer in LRLR group than LPLR group. Adhesions were commonly existed after liver resection, mainly between the abdominal wall at the original incision and the resection portion of the liver. Therefore, extra operative time was spent on adhesiolysis, particularly for the densely or vascular-rich adhesions around the hepatic hilum.[24,30] In the present study, our results indicated that the intraoperative blood loss was less in the LRLR group than the ORLR group and it was similar between the LRLR and LPLR groups. These could be associated with the following possible reasons. First, with the imagine magnification of surgical field in laparoscopy, meticulous manipulation was performed to deal with the intrahepatic vasculatures and the adhesions around vessels. Second, the raised intra-abdominal pressure produced by pneumoperitoneum during the LRLR procedures could decrease the bleeding from the cut surface. Moreover, the pneumoperitoneum tensing up adhesions could enable more meticulous adhesiolysis, which also contributed to reduce the blood loss. Finally, the minimally invasive of the abdominal wall could cause less bleeding in the LRLR and LPLR groups.[8,9,11,12,24,25] With respect to the intraoperative conversion, although Liu et al,[17] van der Poel et al[21] and Noda et al[19] reported some patients with the severe

Table 3

Assessing the quality of the nonrandomized studies using the Newcastle-Ottawa Scale.

	Selection					Outcomes			
Study	Representativeness of exposed cohort	Selection of non-exposed cohort	Exposure	Outcome of interest not present at start	Comparability	Assessment of outcome	Follow-up	Adequacy of follow-up	NOS score
Kanazawa et al	Yes	Same	Surgical records	Yes	No restrictions, matched	Record linkage	Unclear	Unclear	7
Chan et al	Yes	Same	Surgical records	Yes	No restrictions, matched	Record linkage	3 years	Complete	7
Zhang et al	Yes	Same	Surgical records	Yes	Recurrent HCC after open surgery, not matched	Record linkage	1.5 years	Complete	7
Liu et al	Yes	Same	Surgical records	Yes	No restrictions, PSM	Record linkage	5 years	Complete	9
Hallet et al	Yes	Same	Surgical records	Yes	No restrictions, PSM	Record linkage	5 years	Unclear	8
Ome et al	Yes	Same	Surgical records	Yes	No restrictions, not matched	Record linkage	Unclear	Unclear	8
Noda et al	Yes	Same	Surgical records	Yes	No restrictions, not matched	Record linkage	Unclear	Unclear	8
van der Poel et al	Yes	Same	Surgical records	Yes	No restrictions, PSM	Record linkage	Unclear	Unclear	9
Goh et al	Yes	Same	Surgical records	Yes	No restrictions, PSM	Record linkage	6 years	Unclear	8
Shelat et al	Yes	Same	Surgical records	Yes	No restriction, matched	Record linkage	Unclear	Unclear	7
Nomi et al	Yes	Same	Surgical records	Yes	No restriction, not matched	Record linkage	5 years	Complete	8

NOS = Newcastle-Ottawa Scale, PSM = propensity score-matched cohort.

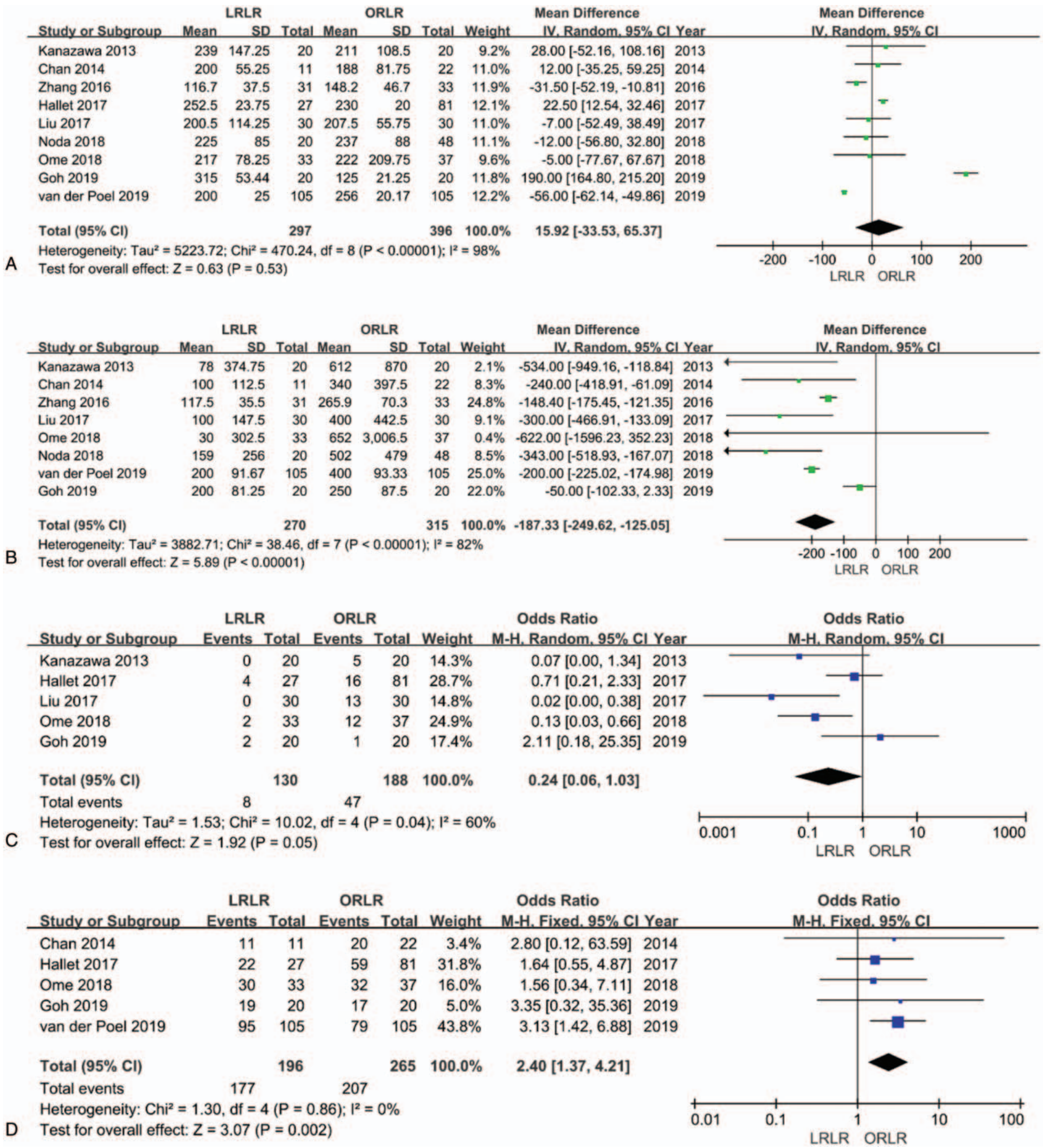

Figure 2. Forest plots comparing intraoperative outcomes between LRLR group and ORLR group: (A) operative time, (B) blood loss, (C) transfusion requirement rate, (D) R0 resection rate. LRLR = laparoscopic repeat liver resection, ORLR = open repeat liver resection.

intra-abdominal adhesions were converted to open surgery, the pooled data suggested that the conversion rate was comparable between the LRLR and LPLR groups. These results indicated LRLR was safe during procedures, but it is noticeable that these LRLRs enrolled in this study were mainly performed by experienced surgeons.

This present study showed that the postoperative major complications were significantly less in the LRLR group than that in the ORLR group, which were comparable between the LRLR and LPLR groups. These results were consist with previous published studies, which reported laparoscopic hepatectomy had the advantages of reducing the major complications.[8,21,31] During the repeat liver resection procedures, the intra-abdominal heavy adhesions could increase the rates of postoperative complications, especially for some adhesions around hepatic hilum or/and intestine involving the adhesions. However, the imagine magnification of surgical field in laparoscopy help surgeons differentiate the adhesions around important tissue or organs, and the tension on adhesions caused by pneumoperitoneum could facilitate more meticulous adhesiolysis. As a

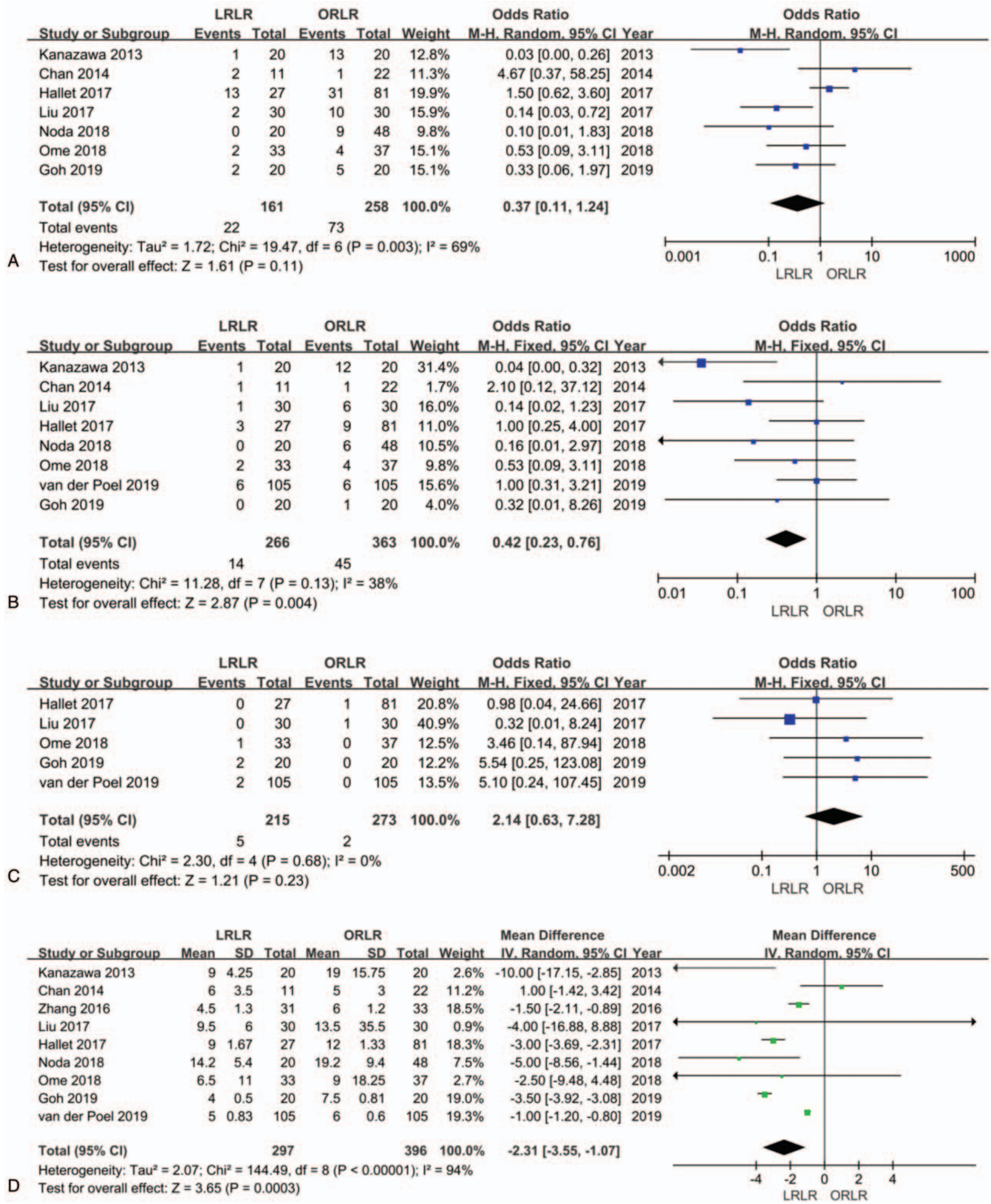

Figure 3. Forest plots comparing postoperative outcomes between LRLR group and ORLR group: (A) overall complications, (B) major complications, (C) early postoperative mortality, (D) hospital stay. LRLR = laparoscopic repeat liver resection, ORLR = open repeat liver resection.

result, meticulous manipulation was performed to reduce some major complications, such as biliary leakage, biliary stricture, massive hemorrhage, intestinal fistula, and liver failure.[8,11,12,21] In addition, as our previous published study, minimally invasive of abdominal collateral circulation in laparoscopic hepatectomy could decrease the occurrence of ascites.[31] Furthermore, with decreased postoperative pain and early postoperative rehabilitation, laparoscopy could reduce pulmonary complications, including respiratory infection, pleural effusion, and respiratory insufficiency.[32] Notably, our analysis suggested LRLR group

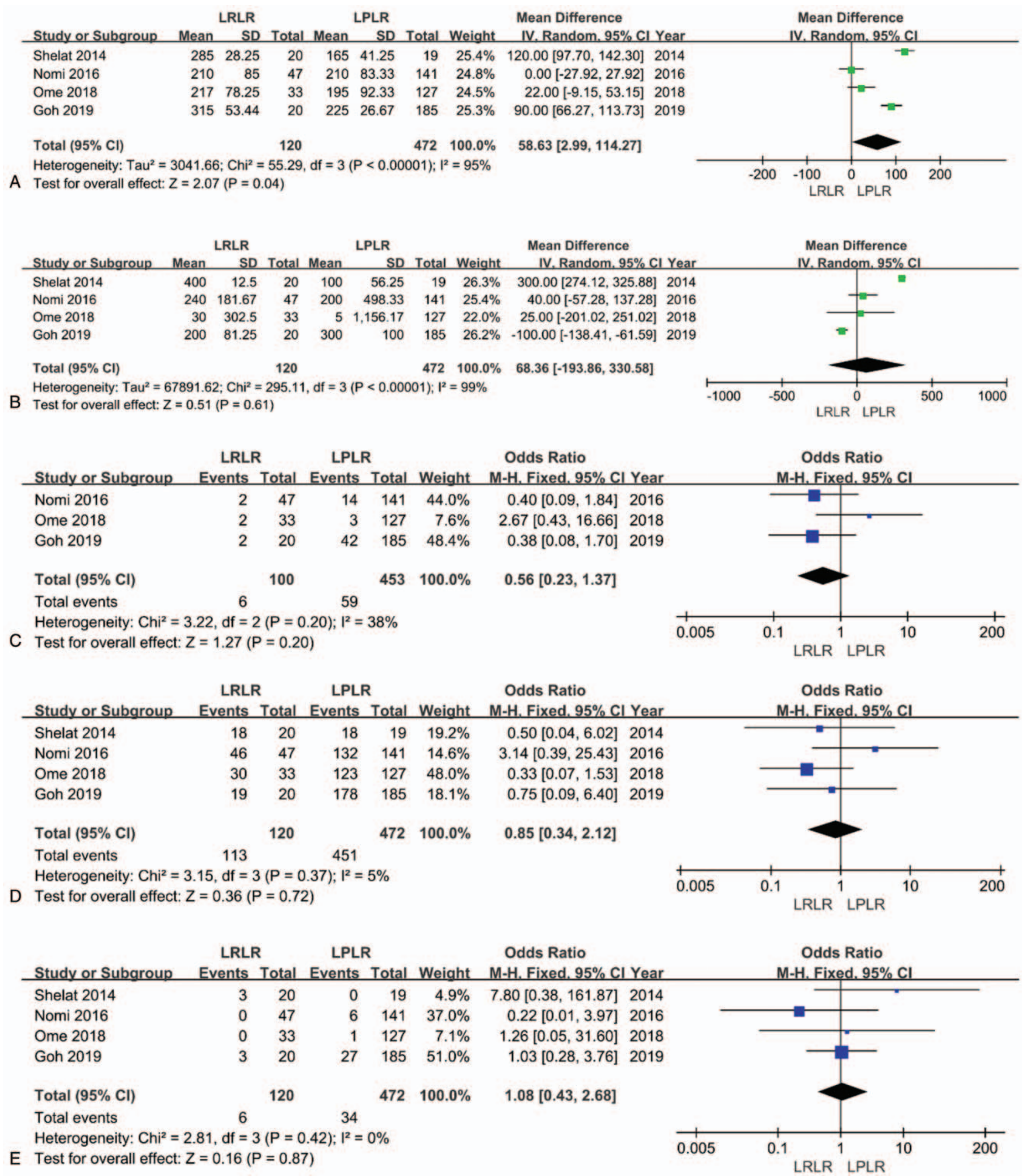

Figure 4. Forest plots comparing intraoperative outcomes between LRLR group and LPLR group: (A) operative time, (B) blood loss, (C) transfusion requirement rate, (D) R0 resection rate, (E) conversion rate. LPLR = laparoscopic primary liver resection, LRLR = laparoscopic repeat liver resection.

had shorter postoperative hospital stay compared with ORLR group, which was in compliance with other literature' reports.[8,11,12,24,25] Because of the less postoperative pain, early mobilization, and the early recovery of gastrointestinal function, the postoperative hospital stay in LRLR group was significantly shorter than ORLR group.[33,34]

It has now been widely accepted that laparoscopic hepatectomy could assure the tumor-free resection margin as the open approach.[9,11,35] Unexpectedly, the results of the present meta-analysis found that the rate of R0 resection was higher in LRLR group than ORLR group. It was in compliance with the trial reported by van der Poel et al which has the weight of 43.8% in

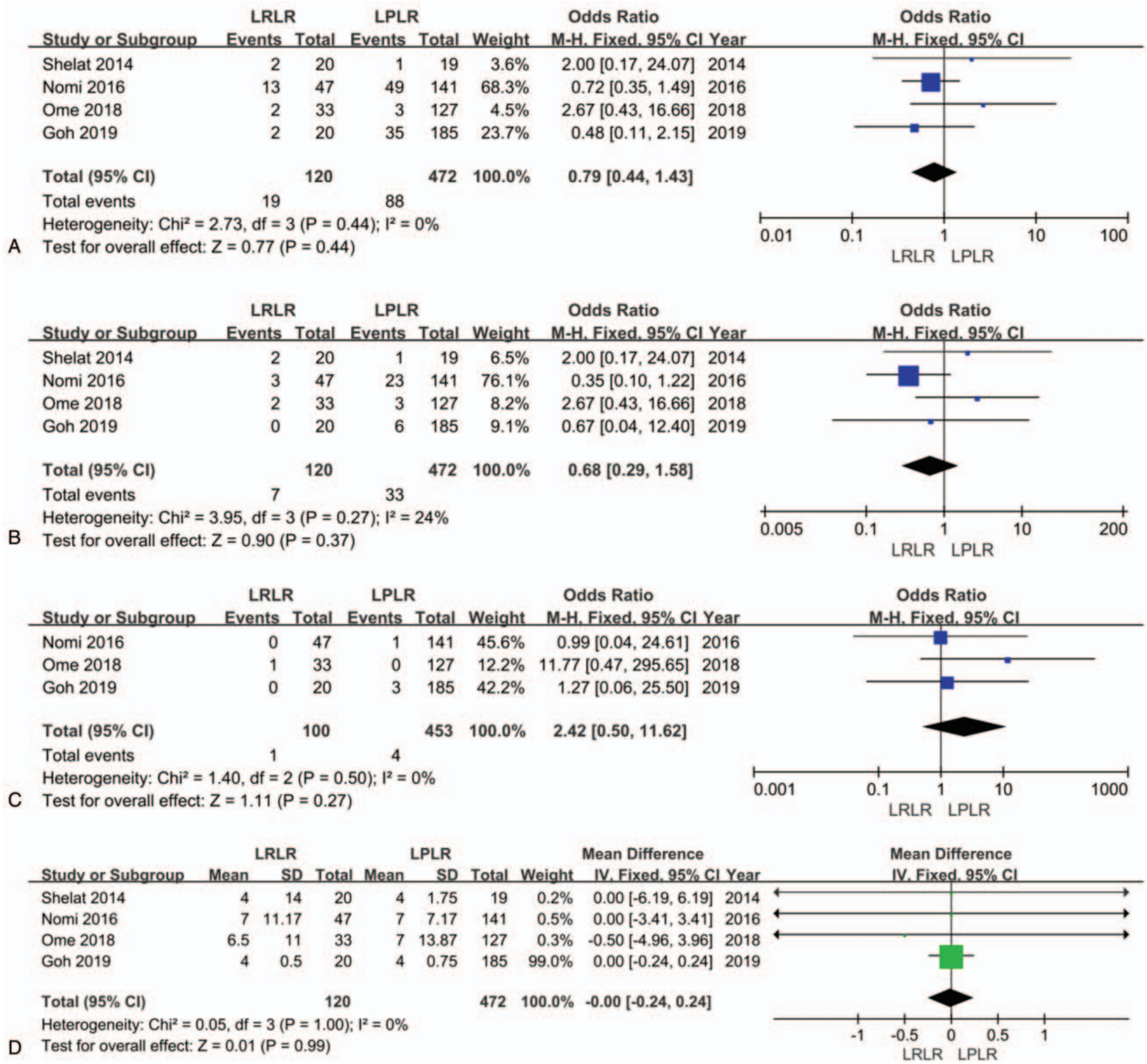

Figure 5. Forest plots comparing postoperative outcomes between LRLR group and LPLR group: (A) overall complications, (B) major complications, (C) early postoperative mortality, (D) hospital stay. LPLR = laparoscopic primary liver resection, LRLR = laparoscopic repeat liver resection.

this meta-analysis. As van der Poel et al[21] reported, the lacking of information such as the use of intraoperative ultrasonography and the exact location of the lesions could cause potential bias, thus the results about the R0 resection should be approached with cautions. Nevertheless, there was a main concern that the lake of palpation could sometimes confuse surgeons' judgement on resection margin, but laparoscopic ultrasonography or ICG fluorescence imaging can be used to compensate it. In our center, laparoscopic ultrasonography was routinely performed to confirm the positions of tumors, prevent the omissions of small tumors and guide the transection line, so that the negative resection margin could be secured. There are increasing evidences to indicate that the laparoscopic liver resection was associated with similar oncologic outcomes compared to open approach.[8,10,11] Our results also showed that the tumor recurrence rate was comparable between LRLR group and ORLR group.

There are some limitations in our studies. First, although most of the included trials were conducted with case-matched,[13,14,16,17,20–22] in the absence of RCTs examining LRLR versus ORLR for recurrent tumors, selection bias regarding the selection of surgical approach was unavoidable. Second, some of the studies were not provided the important basic statistics, such as the surgical approach of previous hepatectomy and the grade of adhesions. Last but not least, none of the enrolled studies performed subgroup analysis about outcomes of major LRLR for recurrent tumors compared with ORLR and LPLR. However, major laparoscopic liver resection could associate with a relatively high risk of huge intraoperative bleeding, conversion, and liver failure, especially for patients with a history of hepatectomy. Further large sample size, well designed trials should be conducted to validate our results.

Table 4

Sensitivity analysis about the outcomes of LRLR versus ORLR.

Variables	Pooled estimates	95%CI	P	I^2 (%)
Operative time	WMD 15.92	[−33.53, 65.37]	.53	98
Studies with RM	WMD 31.86	[−34.73, 98.45]	.35	99
Studies without RM	WMD −26.63	[−44.81, −8.44]	.004	0
blood loss	WMD −187.33	[−249.62,−125.05]	<.00001	82
Studies with RM	WMD −200.03	[−308.85, −91.20]	.0003	87
Studies without RM	WMD −237.13	[−415.82, −58.45]	.009	64
Transfusion	OR 0.24	[0.06, 1.03]	.05	60
Studies with RM	OR 0.27	[0.04, 1.90]	.19	66
Studies without RM	OR 0.13	[0.03, 0.66]	.01	–
R0 resection	OR 2.40	[1.37, 4.21]	.002	0
Studies with RM	OR 2.56	[1.40, 4.69]	.002	0
Studies without RM	OR 1.56	[0.34, 7.11]	.56	–
Overall complications	OR 0.37	[0.11, 1.24]	.11	69
Studies with RM	OR 0.40	[0.08, 1.94]	.26	78
Studies without RM	OR 0.34	[0.07, 1.54]	.16	1
Major complications	OR 0.42	[0.23, 0.76]	.004	38
Studies with RM	OR 0.44	[0.23, 0.84]	.01	53
Studies without RM	OR 0.34	[0.08, 1.47]	.15	0
Mortality	OR 2.14	[0.63, 7.28]	.23	0
Studies with RM	OR 1.95	[0.51, 7.39]	.33	0
Studies without RM	OR 3.46	[0.14, 87.94]	.45	–
Postoperative stay	WMD −2.31	[−3.55, −1.07]	.0003	94
Studies with RM	WMD −2.26	[−3.91, −0.61]	.007	96
Studies without RM	WMD −2.54	[−4.93, −0.15]	.04	45

LRLR = laparoscopic repeat liver resection, OR = odds rations, ORLR = open repeat liver resection, RM = retrospective matched cohort, WMD = weighted mean difference.

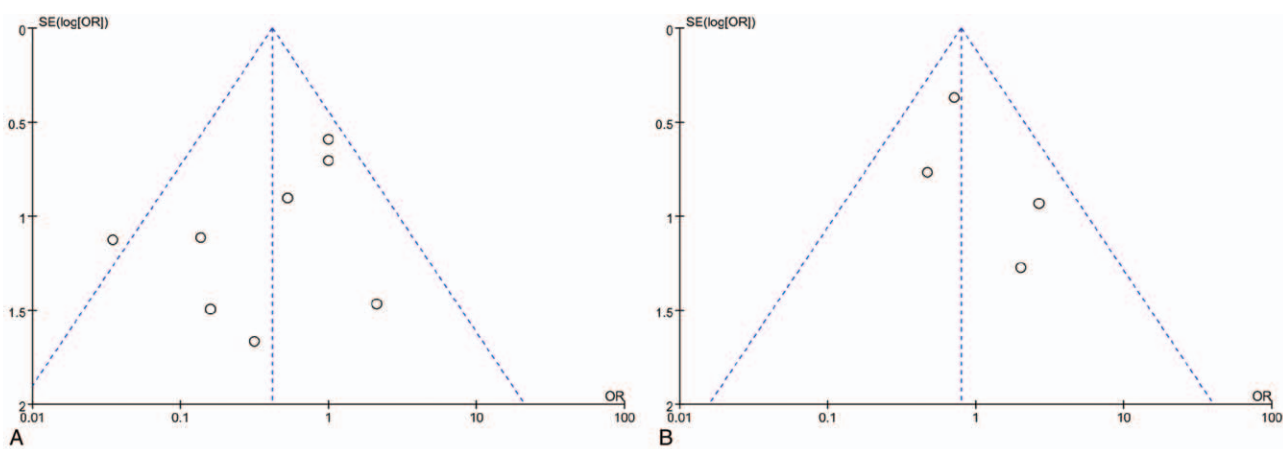

Figure 6. Funnel plot of the major complications in the included studies: (A) LRLR versus ORLR, (B) LRLR versus LPLR. LPLR = laparoscopic primary liver resection, LRLR = laparoscopic repeat liver resection, ORLR = open repeat liver resection, SE = standard error.

In conclusion, our meta-analysis indicted that LRLR had superior short-term outcomes and similar oncological features compared with ORLR. Additionally, it did not increase postoperative morbidity and mortality compared to LPLR. Therefore, LRLR for recurrent liver cancer could be safe and feasible in selected patients when performed by experienced surgeons.

Author contributions

Conception of the work (L.B., and W.Y.G.) Analyzed the data (P. Y.F. and L.F.) Wrote the paper (P.Y.F., and L.F.) Revised the paper (P.Y.F. and L.F.)

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