**REVIEW ARTICLE**

# Comparison of laparoscopic versus open liver resection for lesions located in posterosuperior segments: a meta-analysis of short-term and oncological outcomes

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## Abstract

**Background** The role of laparoscopic liver resection (LLR) for lesions located in posterosuperior (PS) segments remains a matter of development to be further assessed. This systematic review aims to compare the short-term and oncological outcomes between laparoscopic and open liver resection (OLR) in PS lesions.

**Methods** EMBASE, MEDLINE and Cochrane Library were searched from date of inception to June 2019. This meta-analysis was performed using the STATA 12.0 statistical software. Standardized mean differences (SMDs), odds ratios (ORs) and hazard ratios (HRs) were calculated for continuous variables, dichotomous variables and long-term variables, respectively, with 95% confidence intervals (CIs).

**Results** A total of 788 patients from eight studies were identified for the final analysis, with 371 patients in the LLR group and 417 in the OLR group. Although the operation time (SMD 0.22; 95% CI 0.08–0.36; $P = 0.003$) was longer whereas overall complication rate (OR 0.50; 95% CI 0.36–0.70; $P < 0.001$) and postoperative hospital stay (SMD $-0.45$; 95% CI $-0.59$ to $-0.30$; $P = 0.003$) were lower in the LLR group than in the OLR group, no significant differences in blood loss (SMD $-0.14$; 95% CI $-0.28$ to $0.00$; $P = 0.054$), transfusion rate (OR 0.92; 95% CI 0.56–1.54; $P = 0.764$), major complication rate (OR 0.63; 95% CI 0.38–1.05; $P = 0.079$), R0 resection rate (OR 1.04; 95% CI 0.55–1.96; $P = 0.902$), and disease-free survival (DFS) for hepatocellular carcinoma (HCC) (HR 1.43; 95% CI 0.95–2.17), DFS for colorectal liver metastases (HR 1.05; 95% CI 0.61–1.81), overall survival for HCC (HR 1.00; 95% CI 0.43–2.30) were noted between the groups.

**Conclusion** LLR is technically feasible and safe without compromising long-term oncological outcomes for selected patients with lesions in the PS segments of the liver.

Since laparoscopic liver resection (LLR) was described for the first time in 1992 [1], there has been an exponential growth of reported LLRs from a worldwide review that published by Nguyen et al. [2]. Recent series of systematic reviews on LLR demonstrated that the procedure offer improved short-term outcomes and comparable oncological outcomes over open approach [3–5]. Nonetheless,

LLR for posterosuperior segments (segments I, IVa, VII, VIII and superior part of VI) remains the most challenging procedures.

The posterosuperior segments are located in the bottom of the small subphrenic cage and adjacent to left, middle and right hepatic veins. This location makes haptic veins more easily injured during laparoscopic parenchyma division. Besides, the operative fields in the posterosuperior segments were distant from transabdominal trocars and blocked by anterolateral segments with laparoscopic caudal view that make limited visualization [6]. For a long time, open liver resection (OLR) were the standard methods for lesions in the posterosuperior segments.

However, using of intercostal trocars with lateral approach as well as postural changes, several experienced centers have documented the safety and feasibility of LLR

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for posterosuperior segments [6, 7]. Several studies have compared laparoscopic versus open liver resection for posterosuperior segments and have reported their results [8–15]. While there were no consensus between them. Therefore, this study aimed to provide a systematic review and meta-analysis focusing on short-term and oncological outcomes of LLR versus OLR for lesions located in posterosuperior segments.

## Materials and methods

### Search strategy, data sources and eligibility criteria

All retrospective studies reporting on LLR for posterosuperior segments published until June 2019 were identified by searching on PubMed, Embase, and the Cochrane Library database. The search terms used were as follows: ((((segments 7[Title/Abstract] OR VII[Title/Abstract]) OR segment 8[Title/Abstract]) OR VIII[Title/Abstract]) OR posterosuperior[Title/Abstract]) AND ((laparoscopic[Title/Abstract] OR laparoscopy[Title/Abstract]) OR minimally invasive[Title/Abstract]). All titles and abstracts were scanned, and candidate studies were identified. A manual search of the references of selected articles was also performed to identify other potential articles.

Two reviewers (Zheng and Xiang) reviewed the retrieved studies and independently extracted the first author, publication year, subject location, study type, study population characteristics, surgical parameters, postoperative outcomes, survival outcomes, hepatectomy type, number of subjects undergoing each type of operation, and other such data. When divergence occurred, articles were re-examined and a consensus was reached by discussion. The following criteria were used to determine eligibility for inclusion: (1) studies comparing between LLR and OLR for PS segments, (2) studies reporting on the perioperative short-term outcomes with a clear description of the results; (3) clear definition of the position of lesions as 'PS' and (4) use of the most recent and/or the highest quality publication when the same subjects were used in different studies.

The selected studies were more carefully screened to ensure the comparison of short-outcomes of each group including operation time, blood loss, transfusion rate, complication rate, major complication rate, R0 resection rate, postoperative stay. The Ethics Committees of the Second Affiliated Hospital of Guangzhou University of Chinese Medicine and Jiangning Hospital of Nanjing approved this study.

## Statistical analysis

This meta-analysis was performed using the STATA statistical software (version 12.0, Stata Corporation, College Station, TX, USA). Standardized mean differences (SMDs) and odds ratios (ORs) with 95% confidence intervals (CIs) were calculated for continuous variables and dichotomous variables, respectively. For comparison of OS and DFS, the hazard ratios (HRs) with a 95% CI were used. Results were considered significant at a $P$ value of $< 0.05$.

Heterogeneity was examined using the $Q$ test and was quantified with the $I^2$ index [16]. A $P$ value of $< 0.10$ rather than the conventional $P$ value of $< 0.05$ was considered for assessing the presence of heterogeneity [17] because of the low power of the test [18]. A random effects model was used when significant heterogeneity was observed, while a fixed effects model was used when there was no heterogeneity [19].

Publication bias was examined using Begg's funnel plots. The degree of asymmetry in the funnel plots was evaluated using Egger's test [20]. The presence of publication bias was confirmed when Funnel plots were obviously asymmetric and the $P$ value in Egger's test was $< 0.05$.

## Results

### Search results

The flow chart of the study selection is illustrated in Fig. 1. According to the predetermined search strategy, a total of 975 articles were identified. After reviewing the titles and abstracts, 35 articles were retrieved for full-text evaluation. Finally, eight studies published between 2015 and 2019 were eligible for inclusion [8–15], and all of them were retrospective cohort studies. 4 studies were retrospective case-matched studies [9, 10, 13, 14]. Four studies were performed in Asia [8, 11, 12, 14], three from Europe [9, 10, 15], and one from USA [13] (Table 1).

### Baseline characteristics of the included studies

The eight studies included a total of 788 patients (laparoscopic liver resection = 371, open liver resection = 417). With respect to study quality, the NOS scores of the included studies varied between 7 and 8, indicating that all of them were of good quality (Table 1).

The tumor size, indications for surgery, operative types in the two groups are summarized in Table 2. Indications for resection were malignant disease in 335 of 371 patients (90.3%) in the LLR group and 405 of 417 patients (97.1%)

**Fig. 1** Flow chart illustrating the literature search results
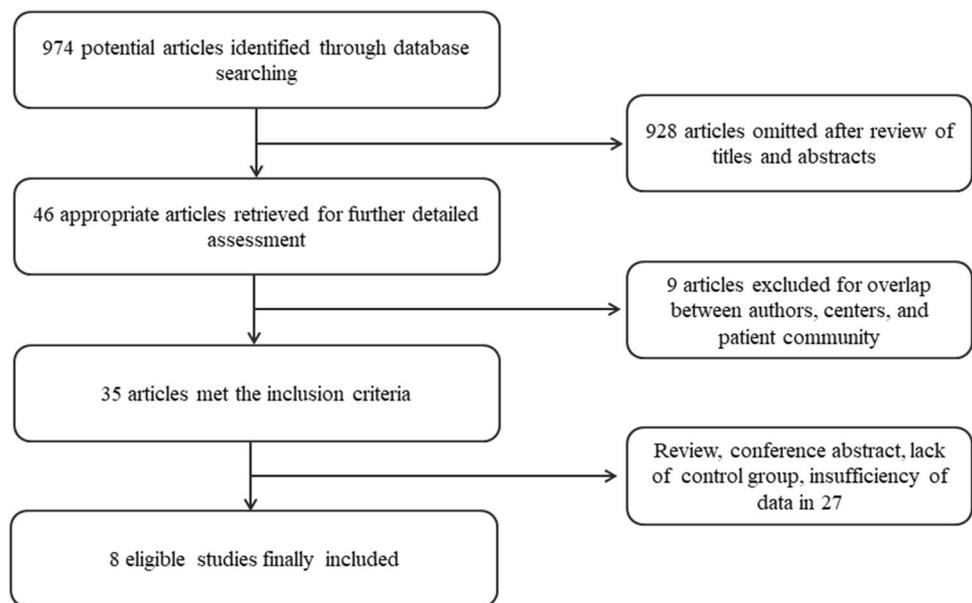


**Table 1** Summary table of characteristics of studies comparing outcomes of LLR versus OLR

| Author | Year | Country | Study type | Patient no. | Patient age | Sex (M/F) | NOS score |
|---|---|---|---|---|---|---|---|
| Xiao | 2015 | China | Retrospective | 41/86 | $52.07 \pm 11.62/50.28 \pm 11.89$ | L:34/7 O:77/9 | 7 |
| Scuderi | 2017 | Seven European Countries | Retrospective matched | 86/86 | 63.9(34–83)/64 (27–80) | L:54/32 O:50/36 | 8 |
| D'Hondt | 2017 | Belgium and Canadian | Retrospective matched | 35/35 | 64 (21–84)/64 (49–84) | L:18/17 O:23/12 | 7 |
| Guro | 2018 | Korea | Retrospective | 46/58 | 62 (48–80)/66 (39–83) | L:35/11 O:47/11 | 7 |
| Li | 2018 | China | Retrospective | 52/29 | $48.96 \pm 11.48/54.62 \pm 8.764$ | L:17/35 O:9/20 | 7 |
| Okun | 2018 | USA | Retrospective matched | 29/29 | 54 (29–78)/54 (33–70) | L:14/15 O:15/14 | 8 |
| Morikawa | 2019 | Japan | Retrospective matched | 20/20 | 65 (43–84)/63.5(15–84) | L:14/6 O:14/6 | 8 |
| Aghayan | 2019 | Norway | Retrospective | 62/74 | $66 \pm 10/67 \pm 9$ | L:48/26 O:31/31 | 7 |

in the open group. Seven studies illustrated the laparoscopic procedures specifically which intercostal trocars were used in three studies [9, 11, 13], two studies [10, 14] reported LLR performed by postural changes and two Chinese centers [8, 12] reported their experience by changing trocar place and raise up the PS segments. Besides, more complications were seen in OLR than in LLR. Five studies [8, 9, 11–13] reported the long-term outcomes for hepatocellular carcinoma (HCC) or colorectal liver metastases (CRLM).

## Postoperative outcomes

The meta-analysis of eight studies showed a longer operative time in the LLR group (SMD, 0.22; 95% CI 0.08–0.36; $P = 0.003$; $I^2$, 52.8%) (Fig. 2A).

In consideration of the intraoperative blood loss, there was a less tendency towards LLR although a non-significant difference was observed (SMD −0.14; 95% CI −0.28 to 0.000 mL; $P = 0.054$; $I^2 = 69.0\%$) (Fig. 2B).

**Table 2** Data on tumor size, indication for surgery, type of resection, complications, and survival from included studies (LLR/OLR)

| Author | Tumor size | Indication for surgery | Procedures performed | Laparoscopic methods | Complications | Survival |
|---|---|---|---|---|---|---|
| Xiao | 4.22 ± 2.05 cm/4.30 ± 1.49 cm | HCC41/86 | AR Segmentectomy 17/36 Sectionectomy 11/20 Lobe resection 6/11 NAR 7/19 | Ports lateral to the lesion in a fan shape. another trocar port was made near the umbilic | 7/32 | LLR 1-years DFS 87.8% 3-years DFS 70.7% 1-years OS 95.1% 3-years OS 78% OLR 1-years DFS 82.6% 3-years DFS 68.6% 1-years OS 89.5% 3-years OS 76.7% |
| Scuderi | Not reported after matched | CRLM 49/52 HCC 19/17 NCRLM 9/9 CCC 2/2 Benign 7/6 | Wedge resection57/55 Segmentectomy 28/28 Bisegmentectomy 1/3 | Intercostal trocars | 12/24 | 3-years DFS for HCC 30% VS 37% 3-years DFS for CRLM 36% VS 36% |
| D'Hondt | 24 (8–86) mm/20 (0–40) mm | 21 CRLM, 8 HCC, 5 other malignancies, 1 adenoma/35 CRLM | AR Segmentectomy17/17 Bisegmentectomy 4/4 Trisegmentectomy 2/2 NAR 5/5 Posterior sectionectomy7/7 | Left lateral position; semiprone position | 9/11 | Not reported |
| Guro | 2.8(1.3–6.9) cm/4.7 (1.0–22.0) cm | HCC 46/58 | AR 17/41 NAR 29/17 | Intercostal trocars | 8/20 | 3-years DFS for HCC 15.4% VS 12.1% 3-years DFS for CRLM 90.2% VS 81.2% |
| Li | 6.44 ± 3.11 cm/6.47 ± 3.13 cm | HCC23/22 Hemangioma23/6 Metastasis 2/1 Other4/0 | Not reported | Ports lateral to the lesion in a fan shape. another trocar port was made near the umbilic | 6/4 | 4-years DFS for HCC 72.7%VS 40.9% 4-years OS for HCC 78.3% VS 47.8% |
| Okun | 1(1–5) cm/1 (1–4)cm | CRLM29/29 | Major resection 4/3 Minor resection 25/26 | Intercostal trocars | 6/12 | LLR 1-years DFS 49.9% 2-years DFS 39.5% Medial DFS 10.6 months 1-years OS 100% 2-years OS 94.1% OLR 1-years DFS 53.8% 2-years DFS 41.4% Medial DFS 13.4 months 1-years OS 100% 2-years OS 95% |
| Morikawa | 23 (10–75) mm/21 (10–65) mm | Liver metastasis 13/12 HCC5/8 Benign tumors1/0 Cholangiocellular carcinoma 1/0 | Not reported | Left, semi-lateral side in a reverse Trendelenburg position | 4/8 | Not specified |
| Aghayan | 23 (14–35) mm/22 (15–34) mm | CRLM 62/74 | Not reported | Not reported | 16/23 | Not reported |

*HCC* hepatocellular carcinoma, *CRLM* colorectal liver metastases, *NCRLM* non-colorectal liver metastases, *CCC* central cholangiocarcinoma, *AR* anatomical resection, *NAR* non-anatomical resection, *DFS* disease-free survival, *OS* overall survival

Despite of more blood loss in OLR group, the meta-analysis of 7 studies [8, 10–15] showed no significant difference in the blood transfusion rate between the LLR
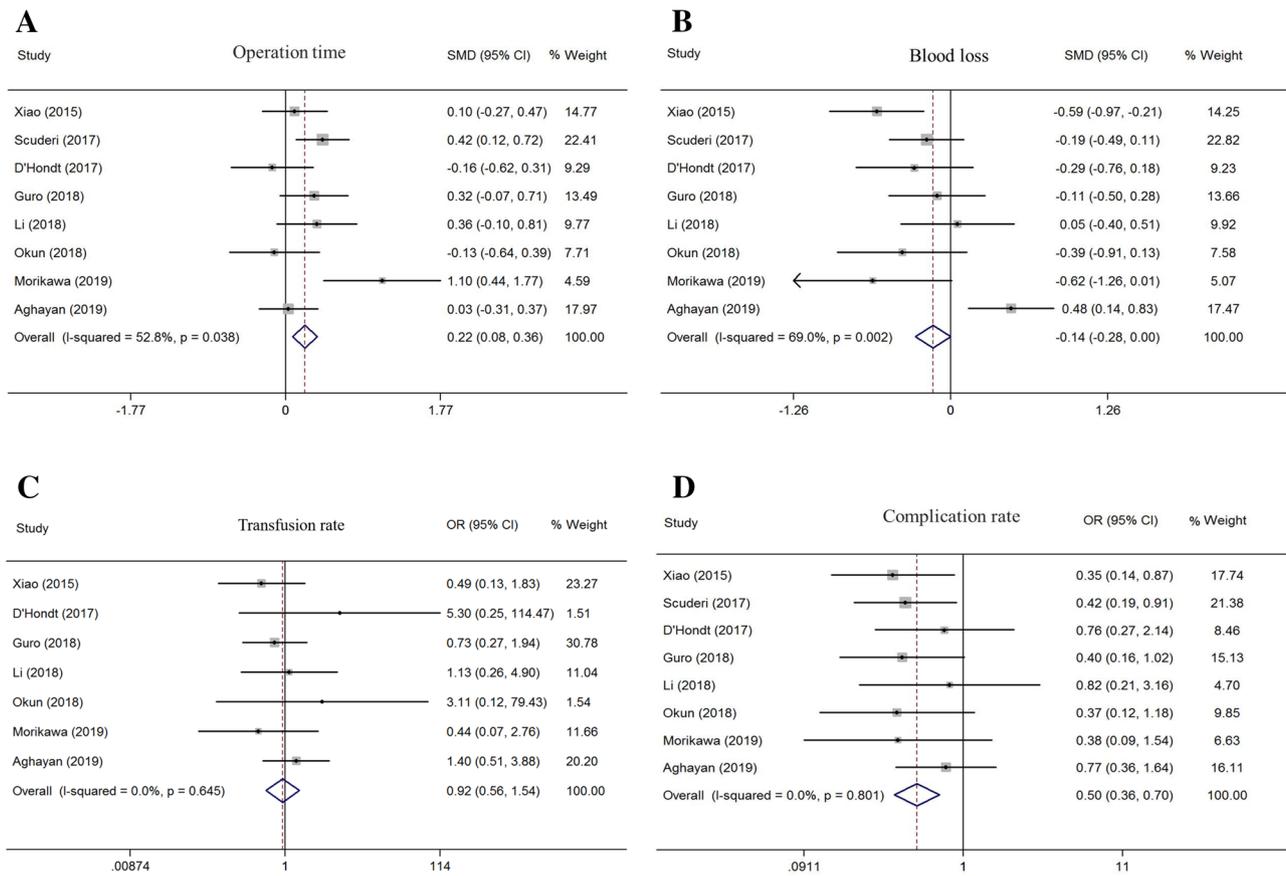
**A**



**B**



**C**



**D**



**Fig. 2** Forest plots: **A** operation time, **B** blood loss, **C** transfusion rate, and **D** complication rate. *SMDs* standardized mean differences, *OR* odds ratio
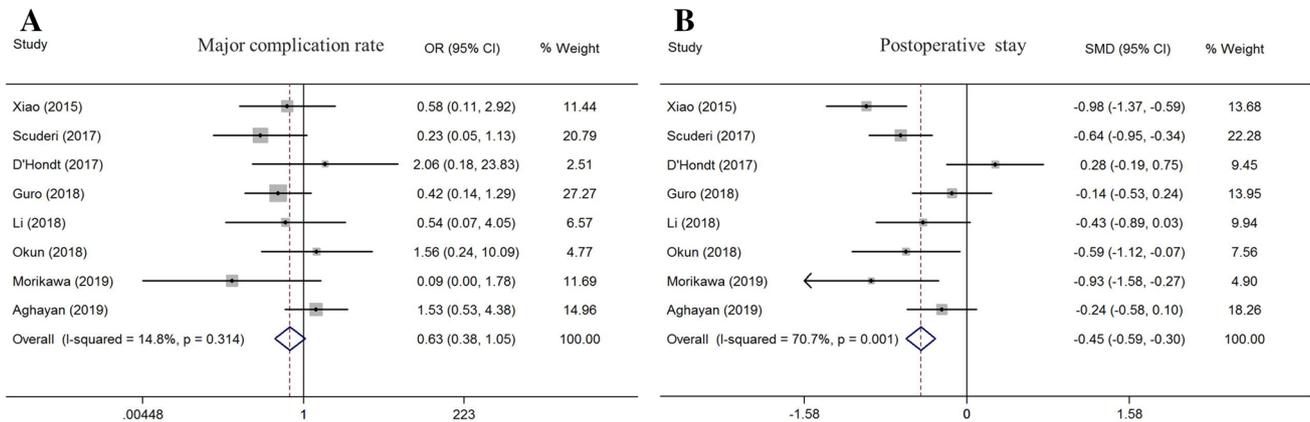
**A**



**B**



**Fig. 3** Forest plots: **A** major complication rate, **B** postoperative stay. *SMDs* standardized mean differences, *OR* odds ratio

and OLR groups (OR 0.92; 95% CI 0.56–1.54; $P = 0.764$; $I^2 = 0.0\%$) (Fig. 2C).

There were a total of 68 complications in LLR group and 134 in OLR. LLR was associated with significantly less overall complications compared to OLR (OR 0.60, 95% CI 0.46–0.77; $P < 0.0001$; $I^2 = 0\%$) (Fig. 2D). However as for major complication of Clavien–Dindo classification ≥ 3 grade, there was a less tendency towards LH although a non-significant difference was observed (OR 0.63, 95% CI 0.38–1.05; $P = 0.079$; $I^2 = 14.8\%$) (Fig. 3A).
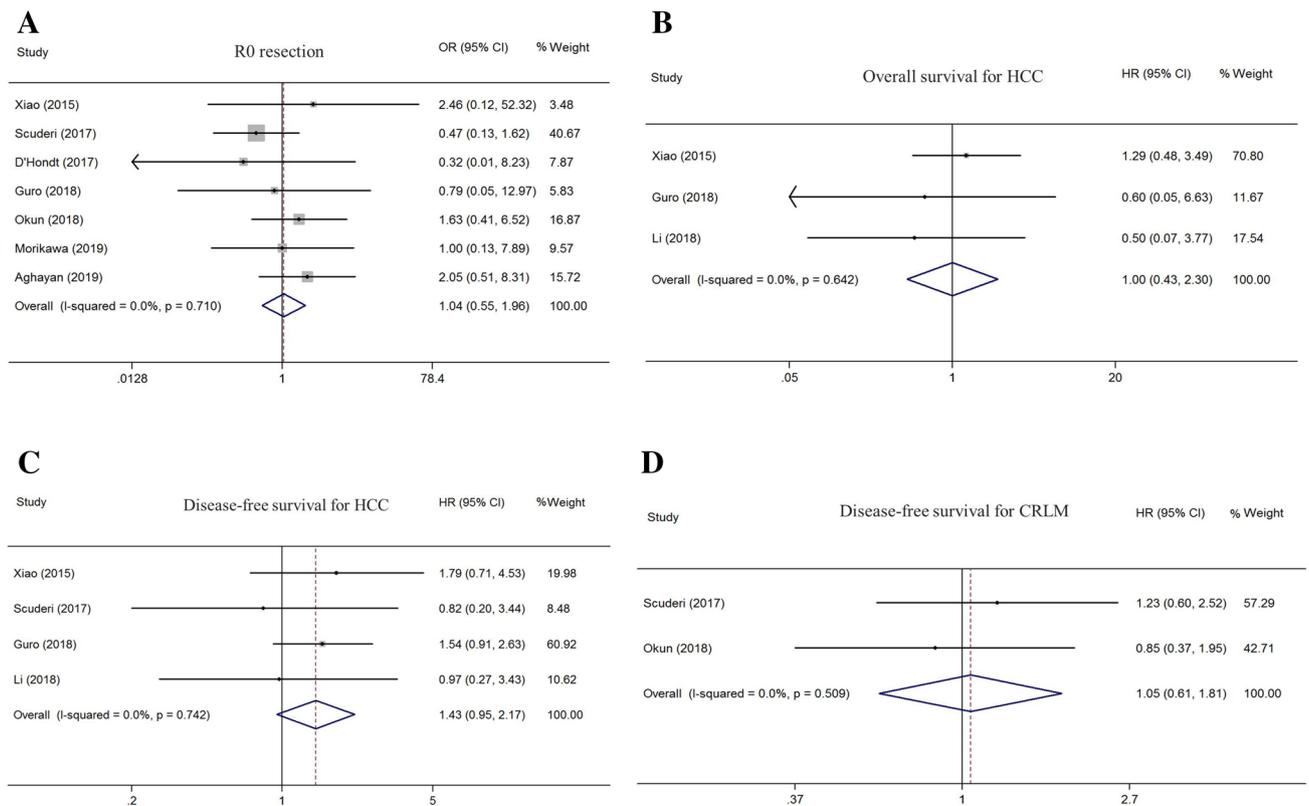
**Fig. 4** Forest plots: **A** R0 resection, **B** overall survival for HCC, **C** disease-free survival for HCC, **D** disease-free survival for CRLM. *OR* odds ratio, *HR* hazard ratio, *HCC* hepatocellular carcinoma, *CRLM* colorectal liver metastases

With regard to postoperative hospital stay, the meta-analysis indicated that LLR was characterized by a reduced postoperative stay in comparison with OLR group (SMD −0.54, 95% CI −0.59 to −0.30; $P = 0.003$; $I^2 = 70.7\%$) (Fig. 3B).

## Oncologic outcomes

To investigate the oncologic outcomes between the LLR and OLR, we extracted data on the R0 resection rate from the included studies. Data on the R0 resection were available in seven studies [8–11, 13–15]. Meta-analysis of the pooled data showed that the R0 resection rate showed no significantly difference (OR 1.04; 95% CI 0.15–1.96; $I^2 = 0.0\%$; $P = 0.902$) (Fig. 4A).

Three of the 8 studies [8, 11, 12] described the long-term overall survival (OS) outcomes for HCC, four [8, 9, 11, 12] described the disease-free survival (DFS) for HCC and two [9, 13] described the DFS for CRLM. For overall survival (OS), no clear evidence of a benefit of LLR on time to survival was identified (HR 1.00, 95% CI 0.43–2.30) (Fig. 4B). With regard to DFS, the pooling data showed no significant difference between the two groups in HCC (HR 1.43, 95% CI 0.95–2.17) (Fig. 4C) and in CRLM (HR 1.05, 95% CI 0.61–1.81, Fig. 3B) (Fig. 4D).

## Publication bias

For data on postoperative complications, funnel plots showed no evidence of obvious asymmetry (Fig. 5). Additionally, Begg's test and Egger's test showed no evidence of publication bias (Begg's test: $P = 1.000$; Egger's test: $P = 0.652$).

## Discussion

This meta-analysis compared the intraoperative, postoperative, and prognostic outcomes between LLR and OLR in PS segments. We found that the operation time was longer, whereas the complication rates and postoperative hospital stay were significantly shorter in the LLR group than in the OLR group. No difference was observed in blood loss, transfusion rate, major complication rate, R0 resection rate, DFS, and OS between groups. The study revealed that LLR could be considered for lesions located in the PS segments, provided the surgeon has accumulated sufficient experience in performing laparoscopic procedures.

Historically, due to the caudal view and interference caused by the anteroinferior segments, major hepatectomies

**Fig. 5** Funnel plot of the complication rate in the included studies showing no publication bias. *OR* odds ratio, *SE* standard error



Begg's funnel plot with pseudo 95% confidence limits
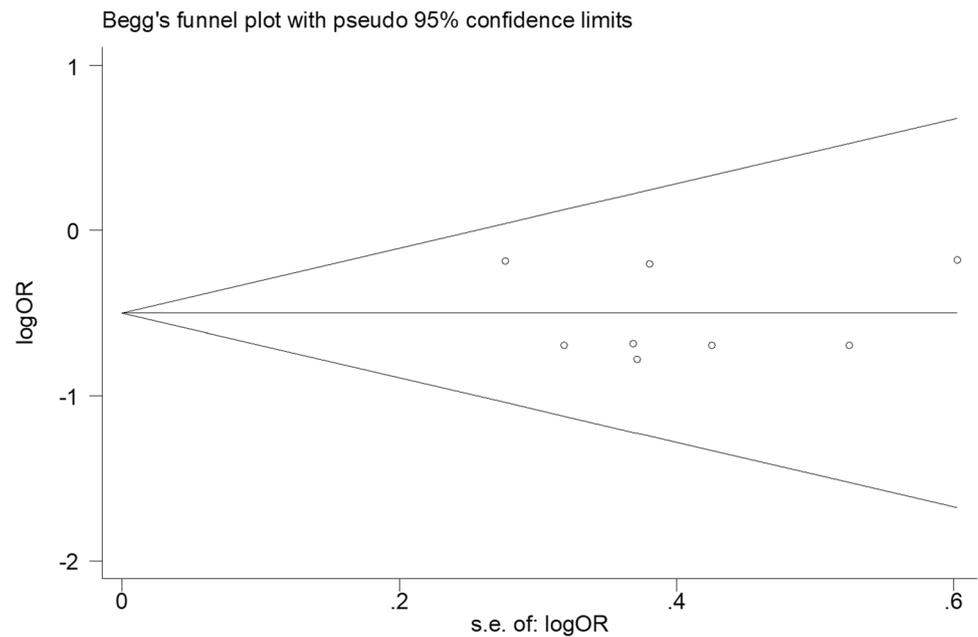
(right posterior sectionectomy or right hemihepatectomy) were more frequently used when laparoscopic approach was performed for lesions located in PS segments [21]. However, in liver surgery for CRLM, a shift from major hepatectomy toward a parenchymal-sparing approach is observed. The use of a parenchymal-sparing approach has been associated with decreased mortality and offer a comparable survival compared to major hepatectomies [22]. Additionally, parenchymal-sparing approach also is the alternative method for HCC patients with insufficient future liver remnant. Cho et al. [23] reported that compared to laparoscopic major hepatectomies (right posterior sectionectomy or right hemihepatectomy), laparoscopic minor hepatectomies (segmentectomy or tumorectomy) demonstrated no statistical difference in operation time and blood loss for lesions located in VII or VIII.

When to compare the technical differences of OLR and LLR, Ogiso et al. [24] illustrated that the view and access of OLR is ventral approach with parenchymal division in the craniocaudal direction, as compared with caudal approach with parenchymal division in the anteroposterior direction in LLR. With regard to short- and long-term outcomes, previous reports have demonstrated that LLR has yielded improved short-term outcomes, specifically shorter hospital stay, lesser blood loss and blood transfusion, and overall complications. Furthermore, the long-term survival rate in LLR is noninferior to OLR and even better [25–27]. However, that is not always the case for LLR in PS segments. Three classification system [28–30] which established to assess the difficulty of various LLR procedures defined posterosuperior segmentectomy as the one of most difficult resection types consistently. Compared with those less complicated laparoscopic resection types, LLR in PS segments

demonstrated increased blood loss, operation time and complications [28, 29].

In this present meta-analysis, the mean operative time was significantly longer in the LLR than in the OLR group. The result confirmed the technical challenge of laparoscopic procedure for lesions in PS segments. However, when to compare the postoperative complications and the postoperative stay, the LLR demonstrated overwhelming benefits than OLR, which indicated that LLR have the advantage of reducing surgical invasiveness.

One of the main concerns about the application of LLR in the PS segment is the inability to guarantee an adequate resection margin. Indeed, LLR for tumors close to both the hepatic hilum and major hepatic veins is technically challenging because it may be difficult to obtain adequate surgical margins, even in open liver resection. However, our results demonstrated that there was no difference in the positive surgical margin rate between the two groups. Additionally, remarkably, the two groups had the same survival outcomes. A possible explanation for this finding is that intraoperative ultrasound was routine used no matter in LLR or OLR group by all included studies which aid to observe the tumor location and its relationship with adjacent vascular structures, hence allowing a safe surgical margin.

Malignancies, particularly CRLM and HCC, are reportedly the most common indications for LLR and OLR. Therefore, oncologic efficiency is of a paramount importance in these procedures. Previous meta-analyses have demonstrated that LLRs are equivalent even superior to open surgeries in terms of long-term survival for malignancy cases as aforementioned [25, 26]. Our meta-analysis confirms that these results also are established for lesions for PS segments, as

there were no differences between the 2 groups regarding the long-term survival in both CRLM and HCC cases. However, it must be noted that only few studies that reported on the long-term outcomes were identified in this meta-analysis. Thus, larger studies, possibly randomized controlled trials, would be ideal to verify these findings.

In the era of LLR, the most frequently used approach is the standard caudal approach, which offers improved exposure around the right adrenal gland and the vena cava and greatly facilitates identification of the Glissonian pedicle at the hilar plate [6]. However, with interference caused by the anteroinferior segments as aforementioned, LLR in PS segments is difficult with the caudal approach. Therefore, various modified approaches were put forward to overcome the technically challenging limitations of LLR in PS segments. In Xiao's study [8], trocars were placed in a fan shape around the lesion, especially the trocar for laparoscope was placed at upper right of the umbilicus that reduced the distance to the PS segments; In the meantime, a sterile glove perfused with saline was placed under the right liver lobe to raise up the PS segments; The 'cranial approach' was used which parenchymal transection from the head side to the foot side with hepatic veins exposed from the head side. Another current widely used approach is the 'lateral approach' which direct to the PS lesions by inserting the intercostal ports [6]. The lateral approach provided a direct view and short access to the operative field around the dome and in the deep parenchyma. In consideration of the safety of intercostal ports, there are no significant difference in pulmonary complications and overall complications with and without intercostal ports placement [6, 31, 32]. In Okuda's study [32], a caudodorsal approach was used to identify and divide the Glisson branch of S7 by intraoperative ultrasonography, and the lateral approach was used to transect the parenchyma by placing intercostal trocars. Morise et al. [33] reported a caudal approach with postural changes without intercostal trocars. Specifically, the left lateral position is used for posterior sectionectomy and the semi-prone position is used for S7 segmentectomy and partial resections of S7 and deep S6. In contrast to the above modified approaches that via laparoscope, Cloyd et al. [34] applied thoracoscopic transdiaphragmatic approach in resection of S7, S8. However, the thoracoscopic approach is only indicated for patients with small tumors located in the dome of the liver and away from the hepatic veins cause no any inflow control of the liver can be performed.

The present meta-analysis has some limitations. First, only eight studies were included and all were retrospective cohort studies, limiting the ability to obtain a comprehensive result. Second, there was a certain degree of statistical heterogeneity in two parameters (blood loss and hospital stay). Hence, it is imperative to highlight that the findings of this article should be interpreted with caution. Third, this study included a highly diverse collection of procedures, including anatomical and non-anatomical hepatectomies, performed for various indications, including HCC, CRLM, benign diseases, and other tumors.

In conclusion, LLR for lesions located in PS segments represents a high technical challenge in contrast to OLR. Although the longer operation time with LLR for PS lesions than with OLR are indicative of the greater difficulty of LLR for PS lesions. The lower complication rates and shorter postoperative hospital stay between these groups suggest that LLR have the advantage of reducing surgical invasiveness. Therefore, we consider that LLR for lesions located in PS segments is technically feasible and safe without jeopardizing the oncological integrity. Further studies preferably in the form of randomized controlled trials or well-matched case–control studies with a larger number size are required to corroborate these findings.

## Compliance with ethical standards

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