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REVIEW ARTICLE

Clinical efficacy of robot-assisted versus laparoscopic liver resection: a meta analysis☆

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Meta-analysis

Summary To compare the clinical efficacy and safety of robotic-assisted liver resection (RLR) and laparoscopic liver resection (LLR) by the means of meta-analytical techniques. We searched PubMed, Cochrane library, Embase and Web of Science databases, collecting randomized or non-randomized studies about robotic-assisted and laparoscopic liver resections. The searching cutoff date was 2017/6/30, all the data obtained were statistically analyzed using RevMan5.3 software recommended by Cochrane Collaboration. A total of thirteen articles, involving 938 patients were enrolled in meta-analysis. Among them, 435 cases underwent RLR, and 503 cases underwent LLR. Compared with LLR, the RLR had longer operative time [MD = 65.49, 95%CI (42.00, 88.98) P < 0.00001 = more intraoperative blood loss [MD = 69.88, 95%CI (27.11, 112.65) P = 0.001] and a higher cost [MD = 4.24, 95%CI (3.08, 5.39) P < 0.00001 = . There were no significant differences between the two groups in transfusion rate, complication rate, conversion rate, the R1 resection rate and hospital stay. In the subgroup analysis of surgery after 2010, a lower conversion rate was observed in RLR, other clinical outcomes are comparable between RLR and LLR. In the subgroup analysis of minor hepatectomy, RLR is still associated with longer operative time, but there is no difference in other outcomes. In the subgroup analysis of left hemihepatectomy or left lateral hepatectomy, RLR is associated with more blood loss. Although RLR associated with Longer operative time and more intraoperative blood loss, it displays the same safety and effectiveness as LLR for hepatectomies. And the high cost is still a major hindrance for the widely application of robotic surgery.

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1. Introduction

Hepatectomy is one of the most effective therapies for liver tumors. Since the first laparoscopic hepatectomy was reported by Reich et al [1] in 1991, LLR has been widely used for benign and malignant liver diseases. In 2008, a consensus conference about conventional laparoscopic liver resection (LLR) was held in Louisville,[2] which has been reached on indications for LLR: left lateral and minor hepatic resections (benign tumors$\leq$5 cm, malignant tumors$\leq$3 cm) over anteroperipheral segments. But currently, with the improvement of technique, the left lateral resection is recommended as a standard procedure for LLR[3,4] , there is no penalty zone in minimally invasive liver surgery (MILS), all liver segments can be reached by MILS.[5,6]There bas been some studies comparing LLR to open liver resection (OLR) evidencing significant decrease of blood loss, lower complication rate and reduced hospital stay, this two procedures are comparable in terms of safety and pathological outcomes.[7,8]

However, the inherent limitations of laparoscopic instruments such as: limited by a fixed pivot point with only four-degree of freedom and a two-dimensional view, lack of depth perception and lead to hand tremor and surgeon fatigue during the prolonged procedures. These shortcomings remain a major hindrance to its wider application in complex abdominal operations.[9]

The da Vinci Surgical System (Intuitive Surgical, Sunnyvale, California, USA) was introduced in 1990s to overcome the limitations of conventional laparoscopic surgery. This is based on a high resolution three-dimensional image with instruments of seven-degree of freedom, and hand tremor can be filtered through the operating robotic arms. A boom in the number of robotic liver resections being performed because of these theoretical benefits.[9] Although several series of RLR have been published,[10–12] there is little evidence that it provides superior outcome when compared with LLR.[13] Presently, the use of RLR remains relatively new and indications for its application remain controversial.[14] Therefore, we conducted the current meta-analysis to investigate the clinical efficacy and safety of RLR versus LLR.

2. Methods

2.1. Literature search strategy

A comprehensive literature search was performed using PubMed, Cochrane library, Embase and Web of Science databases for those from inception to June 2017 with no limits. The following medical subject heading (MeSh) terms were used: robot, robotic, robotic-assisted, Da Vinci, laparoscopic, laparoscopy or minimally invasive, hepatectomy, hepatic resection, liver resection, liver surgery.

2.2. Study selection criteria

Criteria for inclusion: (1) patients: who are diagnosed with focal liver lesions, include HCC, cholangiocarcinoma, focal nodular hyperplasis (FNH), hemangioma , hepatic adenoma and all kind of metastases; (2) intervention: robotic-assisted liver resection (RLR) versus laparoscopic liver resection (LLR), hand-assisted LLR was also included; (3) type of studies: randomized controlled trial or non-randomized controlled trial; (4) reporting at least one of the following outcomes: operation time, intraoperative blood loss, blood transfusion rate, complications, conversion rate, R1 resection rate and the hospital stays; (5) if dual or multiple studies were reported by the same institution or authors, only keep the trials having better quality or more comprehensive information.

Exclusion criteria (1) reviews, letters, case reports nonhuman studies expert opinions and uncontrolled studies; (2) trials did not clearly report the outcomes of interest attributed to each intervention.

2.3. Data extraction

Two reviewers (R.G. and K.Y.) independently and critically selected the studies according to the criteria described above. Data were independently extracted by two reviewers (R.G. and D.M.), the extracted data included (1) first author, year of publication, study type, patient demographics and disease characteristics; (2) treatment outcomes: operation time, intraoperative blood loss, blood transfusion rate, complications, conversion rate, R1 resection rate and the hospital stays. Discrepancies between the two authors were resolved by mutual discussion or with a third author if necessary.

2.4. Quality assessment and publication bias

A modification of the Newcastle—Ottawa scale[15] was used for non-randomized controlled trials to assess quality, the scale consists of three items describing patient selection, comparability of the RLR groups and LLR groups, and assessment of outcomes of interest. The full score was 9, and studies with NOS$\geq$6 were considered to be of high quality. Potential publication bias was evaluated by funnel plots.

2.5. Statistical methods

Calculation for dichotomous variables was carried out using the odds ratio (OR) and 95% confidence interval (CI) while

continuous variables using mean difference (MD) and their 95% CI. If the studies provided medians and interquartile ranges instead of mean ± SD, medians were convert to means using the method described by Hozo et al.[16] The heterogeneity among the included studies was assessed by the I^2 statistics. $I^2 < 25\%$ was considered as no heterogeneity, $I^2 \geq 25\%$ and $\leq 50\%$ was considered as moderate heterogeneity and $I^2 > 50\%$ was considered as high heterogeneity. If the I^2 was larger than 50%, implying significant statistical heterogeneity between studies, the random effects model was applied; otherwise fixed effect model was applied. $P < 0.05$ was considered statistically significant. The current meta-analysis was performed using RevMan5.3 software recommended by Cochrane Collaboration.

Different types of hepatectomies may has different clinical outcomes, major liver resection may take more time and have more blood loss, longer hospital stay is required for patients to recover. Therefore, we performed subgroup analysis to identify the safety and efficacy of RLR versus LLR in minor and major hepatectomies. Unlike conventional laparoscopic liver surgeries, the robotic procedure was applied to clinical for only about two decades, with the accumulation of experience, clinical outcomes may be improved. Take this matter into account, another subgroup analysis was pooled to evaluate the results of RLR versus LLR in surgery performed after 2010.

3. Results

3.1. Characteristics of identified studies

Fig. 1 presents the flowchart of the study screening and selection process. The detailed information of the included studies was summarized in Table 1. Finally, seventeen studies[13,17–32] were selected for full-text review, among these, four redundant studies[21,25,28,31] were from the same medical center, the latest one[13,22,24] with the most comprehensive information was enrolled. A total of thirteen retrospective comparative studies, involving 938 patients were enrolled in meta-analysis. Among them, 435 cases underwent RLR, and 503 cases underwent LLR. The characteristics of these patients are summarized in Table 2. The detailed information of subgroup analysis was summarized in Table 3.

3.2. Quality of the included studies

According to the NOS scale, full-text of all enrolled studies was downloaded and reviewed. The comparability between

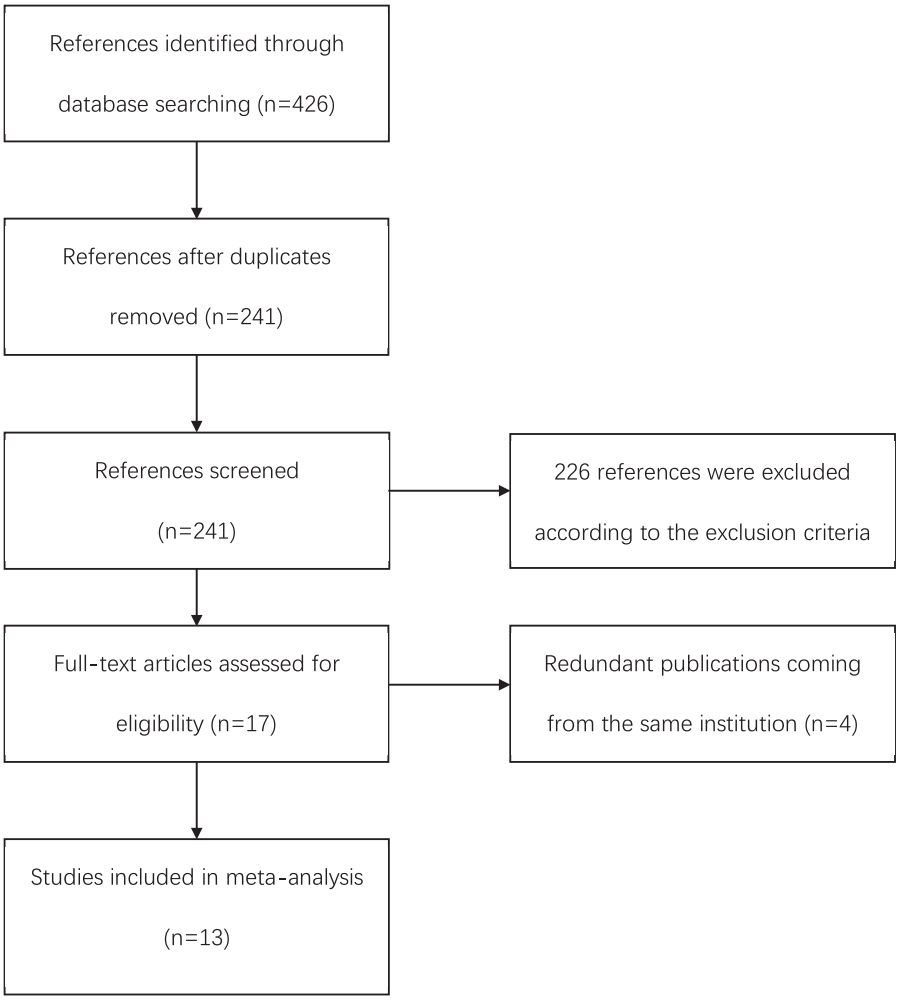

Figure 1 Flowchart of searching strategy for meta-analysis study selection.

Table 1 Characteristics of included studies.

First Author (y)	Country	Study type	Approach	Cases	Age (y)	Sex (M/F)	Tumor size (cm)	Tumor type (malignant/benign)	NOS
Berber (2010)	United States	Retro/	RLR	9	66.6 ± 6.4	7/2	3.2 ± 1.3	9/0	9
		Comparative	LLR	23	66.7 ± 9.6	12/11	2.9 ± 1.3	23/0	
Croner (2016)	Germany	Retro/	RLR	10	64 (45–76)	8/2	4.8 (2.9–10.5)	10/0	8
		Case-control	LLR	19	59 (32–85)	13/6	4.1 (1.8–8.5)	15/4	
Ji (2011)	China	Retro/	RLR	13	53 (39–79)	9/4	6.35 (1.8–12)	8/5	7
		Case-control	LLR	20	NA	NA	NA	NA	
Kim (2016)	Korea	Retro/	RLR	12	54.1 ± 12.2	6/6	2.3 (2.0–3.6)	7/5	8
		Comparative	LLR	31	56.4 ± 11.6	18/13	2.4 (1.7–3.0)	24/7	
Lai (2016)	China (Hong Kong)	Retro/	RLR	100	62.1 ± 10.8	66/29	3.3 ± 1.9	100/0	7
		Comparative	LLR	35	57.9 ± 10.3	26/19	2.7 ± 1.3	35/0	
Lee (2015)	China (Hong Kong)	Retro/	RLR	70	58 (20–82)	46/24	2.5 (0.6–9.0)	54/16	8
		Comparative	LLR	66	58 (25–85)	39/27	2.5 (1.0–12.0)	57/9	
Montalti (2015)	Italy & Belgium	Retro/	RLR	36	62 ± 13	21/15	4.4 ± 3.06	NA	7
		Case-control	LLR	72	56.8 ± 15	39/31	4.95 ± 3.5	NA	
Spampinato (2014)	Italy & Belgium	Retro/	RLR	25	63 (32–80)	13/12	NA	NA	9
		Comparative	LLR	25	62 (33–80)	10/15	NA	NA	
Tranchart (2014)	France & Belgium	Retro/	RLR	28	66.5 (42–84)	13/15	3.5 (0.6–11.5)	13/15	8
		Comparative	LLR	28	66 (41–78)	13/15	4.0 (0.6–13.0)	11/17	
Tsung (2014)	United States	Retro/	RLR	57	58.35 ± 14.6	33/24	3.15 (2.05–5.0)	26/10	7
		Case-control	LLR	114	58.72 ± 15.8	67/47	3.5 (2.0–6.0)	54/18	
Yu (2014)	Korea	Retro/	RLR	13	50.4 ± 12.2	7/6	3.11 ± 1.6	10/3	7
		Comparative	LLR	17	52.5 ± 9.7	9/8	3.48 ± 1.82	5/12	
Wu (2014)	China (Taiwan)	Retro/	RLR	38	60.9 ± 14.9	36/2	6.34 ± 1.7	38/0	7
		Comparative	LLR	41	54.1 ± 14	28/13	2.5 ± 1.6	41/0	
Magistri (2017)	Italy	Retro/	RLR	22	66.56 ± 11.82	15/9	3.40 ± 1.35	22/0	8
		Comparative	LLR	24	60.88 ± 9.85	18/4	2.26 ± 1.13	24/0	

NA: Not available; NOS: Newcastle–Ottawa Scale.

RLR group and LLR group was matched in the following aspects: tumor size, tumor location, tumor type, resection procedure, patient characteristics. Exposure and outcome assessment were confirmed by operation records and record linkage respectively. The NOS score of each included study is listed in Table 1.

3.3. Operative time

All studies reported results regarding operative time,[13,17–20,22–24,26,27,29,30,32] heterogeneity was significant ($P < 0.00001$, $I^2 = 80\%$) among studies, the random effect model was used. According to Fig. 2, the operation time of RLR group was longer than that LLR group, [MD = 65.49, 95%CI (42.00, 88.98) $P < 0.00001$].

3.4. Intraoperative blood loss

Eleven studies[13,17,20,22–24,26,27,29,30,32] reported the intraoperative blood loss, and there was significant heterogeneity among studies ($P = 0.0009$, $I^2 = 67\%$), random effect model was used. According to Fig. 3, more Intraoperative blood loss was observed in the RLR group compared to the LLR one, [MD = 69.88, 95%CI (27.11, 112.65) $P = 0.001$].

3.5. Blood transfusion rate

Eight studies[19,20,22,23,26,27,29,32] reported the blood transfusion rate, there was no significant heterogeneity between these studies ($P = 0.41$, $I^2 = 2\%$), so we use fixed effect mode. Fig. 4 show that there was no significant difference in blood transfusion rate between the RLR group and LLR group. [OR = 0.96, 95%CI (0.47, 1.97), $P = 0.91$].

3.6. Complications

According to the Dindo-Calvien classification criteria for surgical complications,[33] grade 1–2 was minor complication, and grade 3–5 was major. All studies[13,17–20,22–24,26,27,29,30,32] reported the overall incidence of complications, no significant heterogeneity was observed ($P = 0.29$, $I^2 = 16\%$), we use fixed effect model, the results in Fig. 5 showed that there was no statistically significant difference between the two groups [OR = 0.80, 95%CI (0.56, 1.14), $P = 0.21$], eight studies[13,18–20,24,26,27,32] classified the complications, there was no significant heterogeneity ($P = 0.82$, $I^2 = 0\%$), fixed effect model was used. According to Fig. 6, There was no significant difference in major complication rate between the two groups [OR = 1.00, 95%CI (0.49, 2.06), $P = 1.00$].

Table 2 Raw data of the included studies and characteristics of patients.

Studies (year)	Group	Operative time (min)	Intraoperative blood loss (ml)	Hospital stay (d)	Complication (Major complication)	Conversion	Transfusion	R1 resection	Cost
Berber et al	RLR	258.5 ± 27.9	136 ± 61	NA	1(NA)	1	NA	NA	NA
(2010)	LLR	233.6 ± 16.4	155 ± 54	NA	4(NA)	0	NA	NA	NA
Croner et al	RLR	321 ± 92.5	NA	NA	5 (0)	NA	NA	0	8.765EURO
(2016)	LLR	242 ± 99.5	NA	NA	6 (1)	NA	NA	0	3.437EURO
Ji et al	RLR	338 ± 166.9	NA	NA	1 (0)	0	0	0	$12046
(2011)	LLR	130 ± 42.5	NA	NA	2 (0)	2	3	0	$10548
Kim et al	RLR	403.8 ± 139	225 ± 43.35	7.25 ± 1.12	3 (2)	NA	1	0	$8183.3±$3343.2
(2016)	LLR	245.9 ± 100.7	150 ± 93.75	6.75 ± 0.75	6 (3)	NA	1	0	$5190.9±$3148.3
Lai et al	RLR	207.4 ± 77.1	334.6 ± 582.5	7.3 ± 5.3	14(NA)	4	9	4	NA
(2016)	LLR	134.2 ± 41.7	336 ± 498.75	7.1 ± 2.6	7(NA)	2	4	3	NA
Lee et al	RLR	305 ± 130.75	675 ± 624.5	8.5 ± 5	8(NA)	4	3	1	NA
(2015)	LLR	260 ± 77.5	453 ± 401.25	6.75 ± 3.25	3(NA)	8	1	0	NA
Montalti et al	RLR	306 ± 182	415 ± 414	6 ± 2.9	13 (4)	6	NA	4	1906EURO
(2015)	LLR	295 ± 107	437 ± 523	4.9 ± 2.95	16 (5)	7	NA	9	1406EURO
Spampinato et al	RLR	456.2 ± 121	625 ± 450	10.5 ± 4.5	4 (1)	1	1	0	NA
(2014)	LLR	375 ± 105	512.5 ± 287.5	10.2 ± 4.25	9 (3)	1	4	4	NA
Tranchart et al	RLR	236 ± 108.75	562.5 ± 588.6	7 ± 3.5	5 (3)	4	4	NA	NA
(2014)	LLR	197.25 ± 97.5	331.3 ± 322.9	15.5 ± 12.25	6 (3)	2	1	NA	NA
Tsung et al	RLR	253 ± 43.75	200 ± 76.875	4.125 ± 0.625	11 (1)	4	NA	17	NA
(2014)	LLR	198.5 ± 20.625	100 ± 50	4 ± 0.33	29 (1)	10	NA	16	NA
Yu et al	RLR	240.9 ± 68.6	388.5 ± 65	7.8 ± 2.3	0(NA)	0	0	NA	$11475±$2174
(2014)	LLR	291.5 ± 85.1	342.6 ± 84.7	9.5 ± 3	2(NA)	0	0	NA	$6762±$1436
Wu et al	RLR	380 ± 166	325 ± 480	7.9 ± 4.7	3(NA)	2	NA	NA	NA
(2014)	LLR	227 ± 80	173 ± 165	7.2 ± 4.4	4(NA)	5	NA	NA	NA
Magistri	RLR	318 ± 113.5	587.5 ± 432.35	5.1 ± 2.4	15 (2)	0	1	1	NA
(2017)	LLR	211 ± 78.13	464 ± 292.91	6.2 ± 2.57	24 (3)	4	1	1	NA

NA: Not available.

Table 3 Information of subgroup analysis.

Study (year)	Patients select time	Resection type	Group	Major hepatectomies	P Value
Berber et al (2010)	2008.10—2009.9	minor	RLR	0	/
			LLR	0	
Croner et al (2016)	2011—2015	minor	RLR	0	/
			LLR	0	
Ji et al (2011)	2009.4—2009.7	major and minor	RLR	9 (69.2%)	NA
			LLR	NA	
Kim et al (2016)	2007.5—2013.7	minor	RLR	0	/
			LLR	0	
Lai et al (2016)	2009—2015.2	major and minor	RLR	27 (26.4%)	0.002*
			LLR	1 (2.9%)	
Lee et al (2015)	2010.9—2015.1	major and minor	RLR	14 (20%)	0.002*
			LLR	2 (3%)	
Montalti et al (2015)	2008.6—2014.2	minor	RLR	0	/
			LLR	0	
Spampinato et al (2014)	2009.1—2012.12	major	RLR	25 (100%)	/
			LLR	25 (100%)	
Tranchart et al (2014)	2008.1—2013.4	minor	RLR	0	/
			LLR	0	
Tsung et al (2014)	2007.11—2011.12	major and minor	RLR	21 (36.8%)	1
			LLR	42 (36.8%)	
Yu et al (2014)	2007.6—2011.10	major and minor	RLR	3 (23%)	NA
			LLR	11 (64.7%)	
Wu et al (2014)	2012	major and minor	RLR	NA	NA
			LLR	NA	
Magistri (2017)	2012.1—2016.5	major and minor	RLR	NA	NA
			LLR	NA	

NA: Not available.
*Indicates a statistically significant difference ($P < 0.05$).

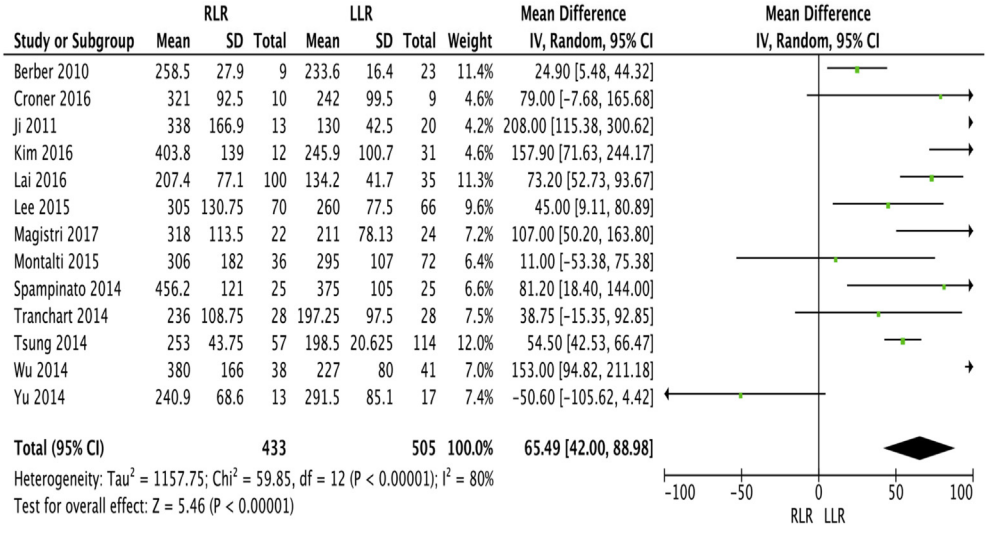

Figure 2 Forest plot of the meta-analysis on operative time.

3.7. Conversion rate

Among the twelve studies included in this meta-analysis, eleven studies[13,17,19,22—24,26,27,29,30,32] reported the conversion rate, no heterogeneity was observed ($P = 0.53$, $I^2 = 0\%$), the fixed effect model was used., according to Fig. 7. There was no significant difference between RLR group and LLR group in conversion rate [OR = 0.75, 95%CI (0.45, 1.25), P = 0.27].

3.8. R1 resection rate

Nine studies[13,18—20,22—24,26,32] reported R1 resection rate, heterogeneity was significant among studies (P = 0.31,

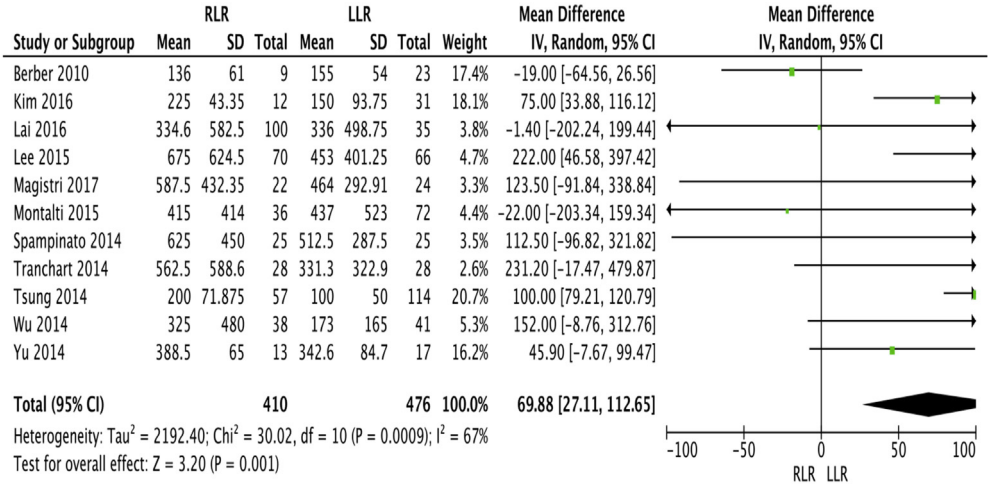

Figure 3 Forest plot of the meta-analysis on intraoperative blood loss.

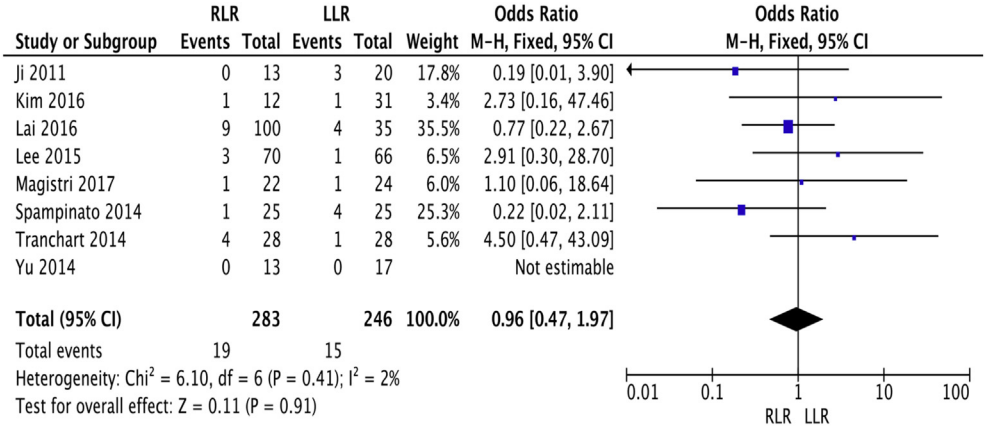

Figure 4 Forest plot of the meta-analysis on transfusion.

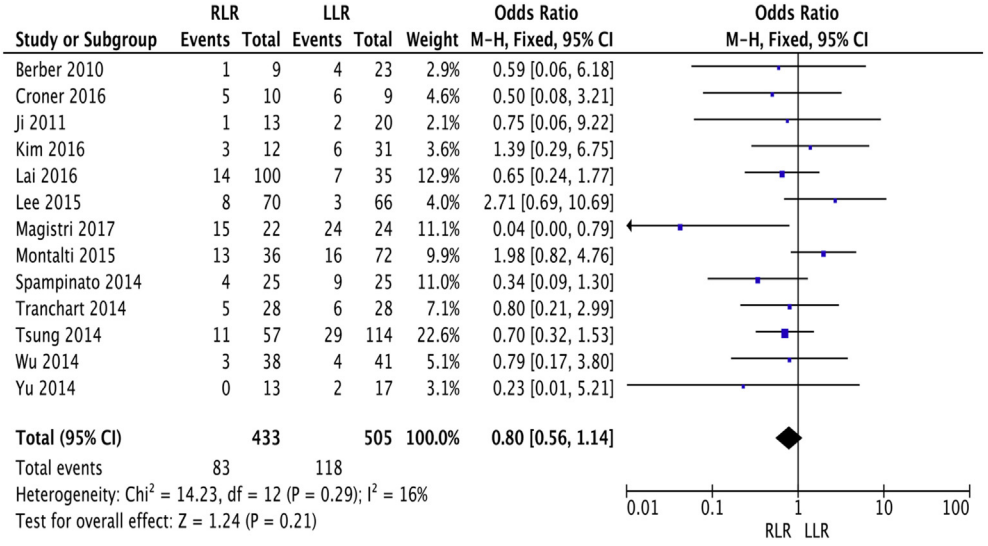

Figure 5 Forest plot of the meta-analysis on complications.

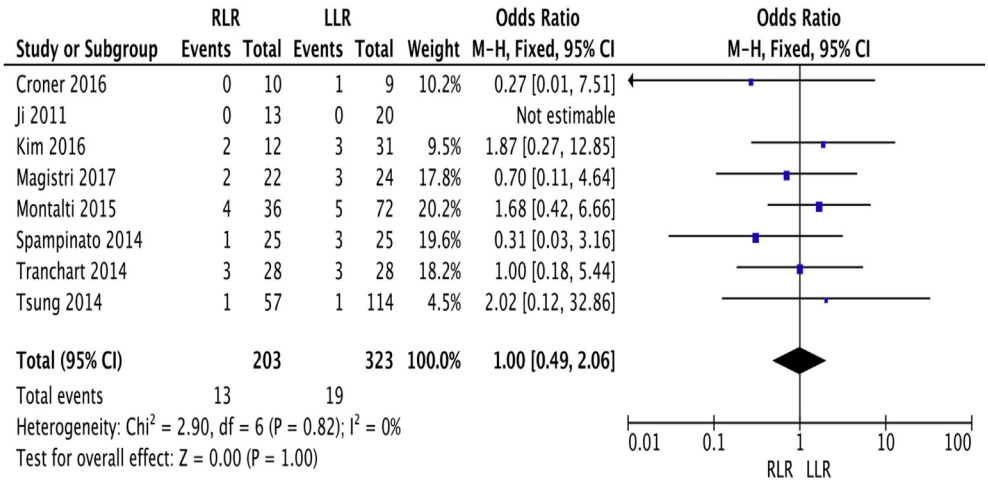

Figure 6 Forest plot of the meta-analysis on major complications.

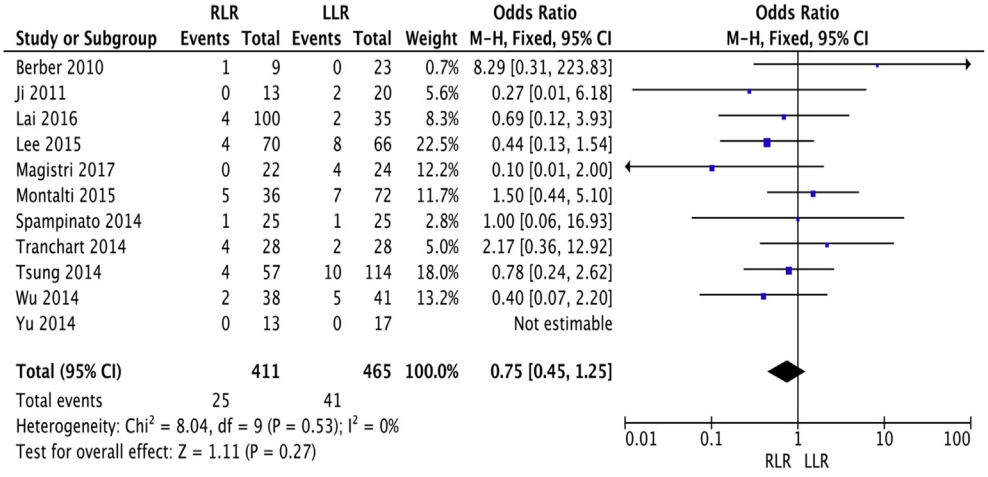

Figure 7 Forest plot of the meta-analysis on conversion.

$I^2 = 42\%$), random effect model was used. According to Fig. 8, no statistically significant difference was found between the two groups [OR = 1.03, 95%CI (0.41, 2.55), P = 0.95].

3.9. Hospital stay

Ten studies[13,20,22–24,26,27,29,30,32] reported the hospital stay, heterogeneity among studies was significant (P = 0.0008, $I^2 = 68\%$), random effect model was used. According to Fig. 9, no significant difference between RLR and LLR in hospital stay [MD = 0.12, 95%CI (−0.52, 0.77), P = 0.71].

3.10. Cost

Among the twelve studies enrolled in the current meta-analysis, only five studies[18–20,24,29] reported the cost, and two of them[20,29] provided MD ±SD, heterogeneity was not significant (P = 0.19, $I^2 = 42\%$), fixed effect model was used. As consequences showed in Fig. 10, the RLR group was associated with a significantly higher cost than LLR group [MD = 4.24, 95%CI (3.08, 5.39), P < 0.00001].

3.11. Comparison in surgeries performed after 2010

As the improvement in performance over time, the rates of complication and operatives decrease and stabilize, therefore, in the subgroup analysis, four studies[18,23,30,32] were included. These studies were selected not according to the publish date but the patients chosen cut off date, details in Table 3. Cost, transfusion rate and major complications could not be assessed because of the insufficient data, outcomes shows RLR is associated with lower incidence of conversion rate [OR = 0.34, 95%CI (0.13, 0.87), P = 0.02] (Fig. 11), no significant change was found in the subgroup analysis in the remaining results between RLR and LLR.

3.12. Comparison in minor and major hepatectomy

Several included studies reported there were significant more major hepatectomies in RLR (P < 0.05), details in Table 3. This may lead to longer operative time and more blood loss. In this subgroup analysis, resection extent ≤3

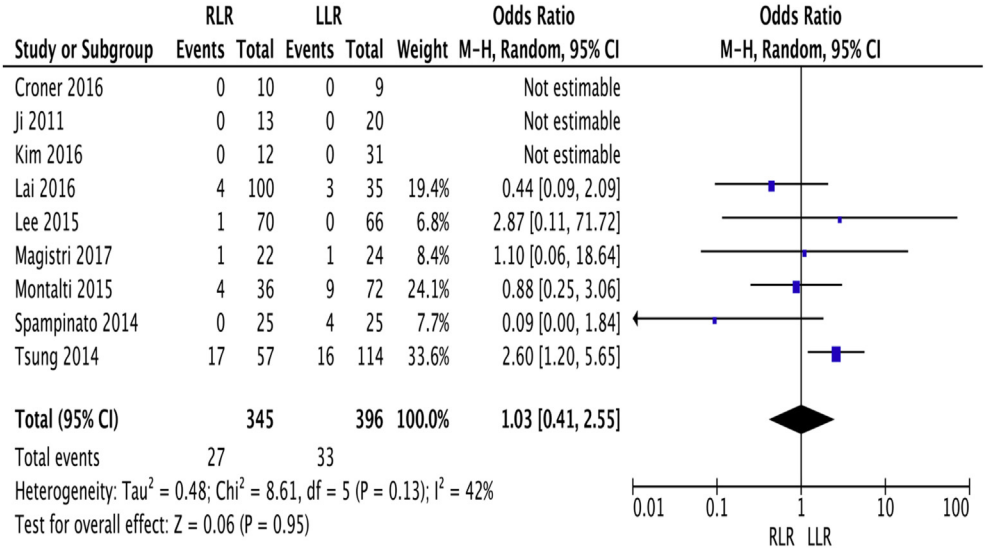

Figure 8 Forest plot of the meta-analysis on R1 resection.

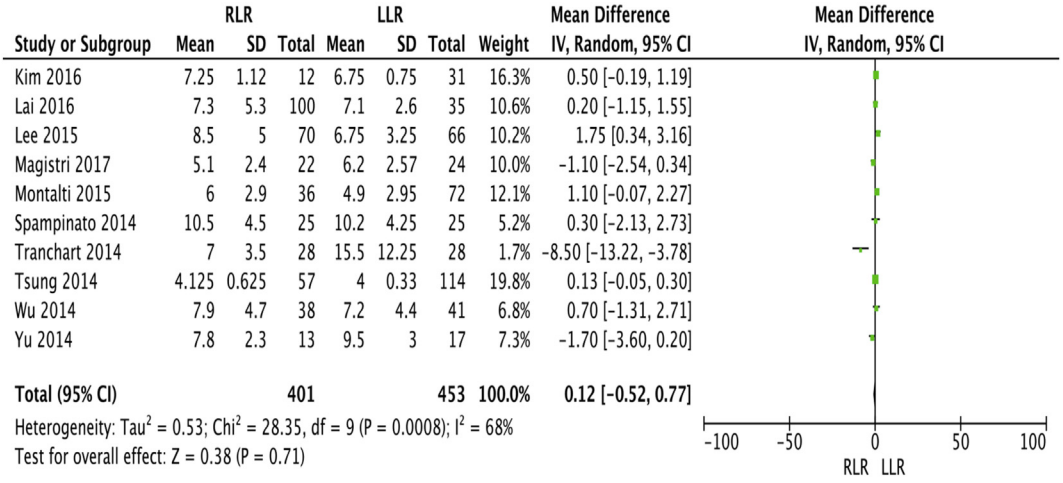

Figure 9 Forest plot of the meta-analysis on hospital stay.

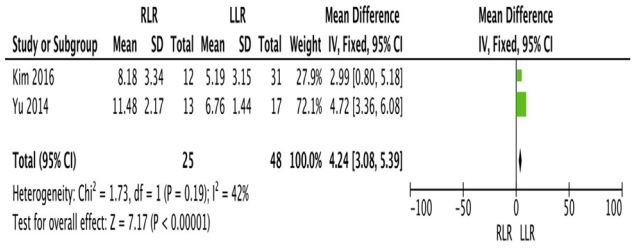

Figure 10 Forest plot of the meta-analysis on cost.

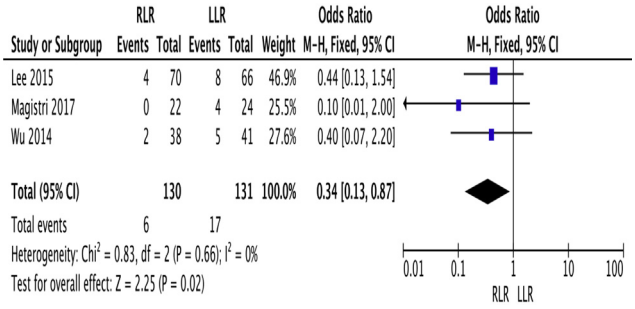

Figure 11 Forest plot of the subgroup analysis (surgery performed after 2010) on conversion.

segments were considered "minor hepatectomy",[34] five studies[17,18,20,24,27] were included. Outcomes demonstrated RLR is still associated with longer operative time [MD = 50.29, 95%CI (10.52, 90.05), P = 0.01] (Fig. 12), there was no sufficient data to assess the cost and transfusion rate, remaining outcomes had no difference between the two groups. Unfortunately, only one study[26] reported outcomes of major hepatectomies, others are mixed hepatectomies (both major and minor), it was not possible to do a meta-analysis. The reported outcomes were comparable in this study of RLR versus LLR.

Only one study[26] reported the outcomes of major hepatectomy, descriptive analysis was performed. No

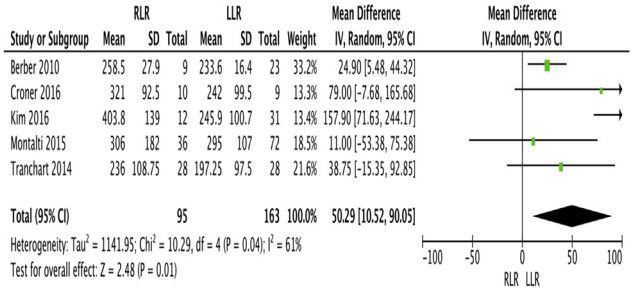

Figure 12 Forest plot of the subgroup analysis (minor hepatectomy) on operative time.

difference was noted in blood loss, operative time, conversion rate and complication rate.

3.13. Comparison in surgeries performed on different locations

The different locations of tumor can influence the performance of RLR and LLR, so in this subgroup analysis, left hemihepatectomy or left lateral hepatectomy, right hemihepatectomy and posterosuperior liver resection were conducted.

However, there is no study focus on right hemihepatectomy, only one study[24] focus on posterosuperior liver resection and could not perform meta-analysis. In this study, RLR and LLR displayed no significant differences in intraoperative blood loss, operative time, hospital stay, R0 negative margin rate and complication. But patients in RLR undergoing longer inflow occlusion time.

As for left hemihepatectomy or left lateral hepatectomy, 3 studies[20,23,29] were included in this analysis. RLR is associated with more blood loss [MD = 74.30, 95%CI (22.80, 125.80) P = 0.005], Fig. 13. There was no sufficient data to assess cost, conversion rate, major complication rate and transfusion rate, remaining outcomes had no difference between the two groups.

3.14. Publication bias

Funnel plot was used to evaluate publication bias of the included studies. Fig. 14 and Fig. 15 illustrate a symmetrical funnel plot of the included studies, suggesting no obvious publication bias exit in the current meta-analysis.

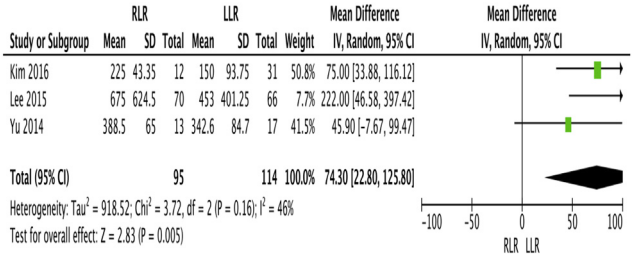

Figure 13 Forest plot of the subgroup analysis (different locations) on intraoperative blood loss.

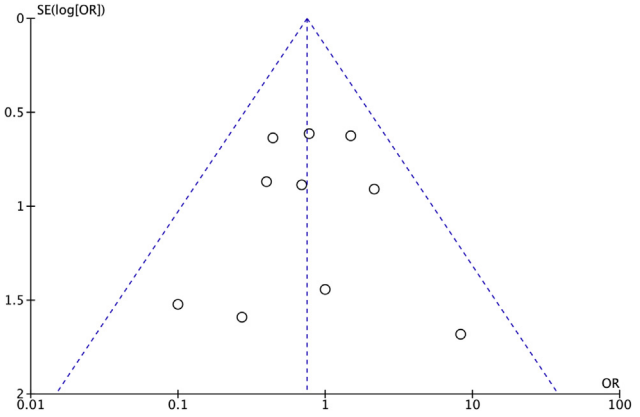

Figure 14 Funnel plot for conversion of the included studies.

3.15. Sensitive analysis

Although subgroup analysis was performed, the outcomes of operative time and intraoperative blood loss is still associated with high heterogeneity. In the current sensitive analysis, large sample size was take into account, seven studies[13,22–24,26,27,30] with ≥25 patients in each group were included. Outcomes showed similar results as the original analysis, heterogeneity was reduced.

4. Discussion

The application of minimally invasive approaches has transformed the surgical landscape over the past 20 years, this techniques has been increasing adopted in subspecialties including urology,[35] colorectal surgery,[36] thoracic surgery[37] and gynecology,[38] but laparoscopic liver surgery lags behind. Several meta-analyses[39–41] have shown that Laparoscopic liver resection was associated with faster recovery, less postoperative pain and shorter hospital stay when compared with open liver resection. LLR is considered a safe option for the treatment of HCC and metastases as well as tumors of benign conditions. Some variants of LLR approaches such as hand-assisted, single port techniques have been described, to date, conventional laparoscopic

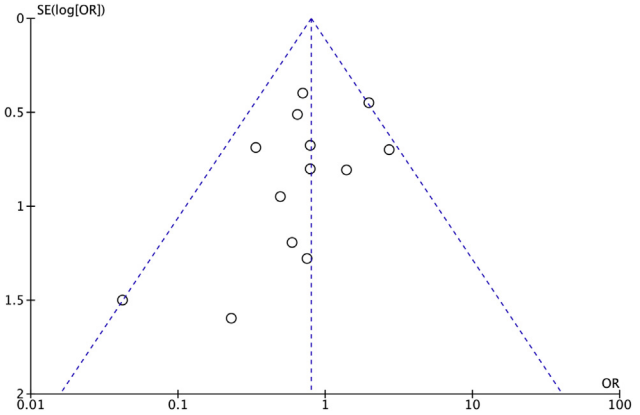

Figure 15 Funnel plot for complications of the included studies.

approach can fulfill major and complex hepatectomy like tumors located in posterosuperior liver segments (Segments IVa, VII, VIII).[42]

In the past few years, robotic-assisted liver resection: a new minimally invasive approach for liver surgery emerged. Theoretical advantages of robotic technology include improved flexibility, visual magnification and precision as well as decrease tremor.[43]And for experienced surgeons who are only familiar with open approach, the learning curve for robotic-assisted surgery may be less steep compared with conventional laparoscopic surgery.[44—46] The first reported robotic-assisted liver resection came form Italy in 2003 [47], after this study, case reports and single institution series of robotic liver resections were published, showing the feasibility of robotic approach in major and minor hepatectomies. Despite the inspiring outcomes demonstrated by these studies, no one has provided conclusive results in favor of one of two approaches, outcomes comparing the efficacy of RLR versus LLR is still limited. Our objective of the current meta-analysis was to evaluate the clinical efficacy and safety of this two techniques, and provide more convincing evidence for clinical practice.

Compared with previous published meta-analysis,[48,49] more studies of high quality were included and more patients underwent minimally invasive liver resections were involved. Overlapping studies published by the same center or author were excluded, so that our results may be more convinced. We also performed subgroup analysis to evaluate the outcomes about latest surgeries (surgery after 2010), minor and major hepatectomy and surgeries performed on different locations.

The results of meta-analysis suggested that RLR was associated longer operative time compared with LLR. This can be explained by the large proportion of major hepatectomies in RLR group. In practice, the additional time required for docking and undocking the robotic system. Furthermore, the robotic surgery is a relative new approach, surgeons need more experience and practice. In the subgroup analysis of surgery performed after 2010, no significant differences were found between RLR and LLR in operative time.

To our knowledge, bleeding can be controlled more easily and freely in robotic surgery due to the seven degrees of freedom afforded by the EndoWrist and the three-dimensional optics. However, these advantages do not embody in the present study. On the one hand, more major hepatectomies may prolonged operative time and associated with more blood loss. On the other hand, robotic system does not provide an ultrasonic dissector, which is the most popular device for parenchyma transection in laparoscopic hepatectomies. During the robotic surgery, the parenchyma transection should be conducted using either harmonic scapel or bipolar forceps,[20] and more blood loss was induced. In the recent years, new instruments like CUSA (Cavitron Ultrasonic Surgical Aspirator, CUSA) was employed in robotic system, blood loss may be improved. Our subgroup analysis may prove this, the two approaches are comparable about blood loss in minor hepatectomy group and surgeries after 2010 group, which suggested that with the improvement of the robotic system and instruments, robotic-assisted liver resection have a trend to achieve a reduction of blood loss.

We also found a high frequency use of intermittent inflow occlusion (Pringles manoeuver) in RLR, which is seldom performed in LLR. This procedure could cause ischemia/reperfusion injury during the operating. When operation performed on a cirrhotic liver, the injury may increase,[50] due to the insufficient information of included studies, we could not assess the long-term outcomes on patients using Pringles manoeuver. Future studies should compare both frequency and time about using this approach and the impact on patients, especially on patients with liver cirrhosis.

Another difference we found was the cost, the total medical cost was significantly higher in RLR group. The robotic instrumentation is general adds $500 per case[17] to the laparoscopic equipment cost, and the equipment purchase and annual service fees are an additional financial burden od robotic procedures. Packiam et al[25] indicated that the total surgical supply (laparoscopic and robotic instruments, staples, clips, miscellaneous) costs were not significant different between the RLR and LLR ($5130 versus $4408, $p = 0.401$), and the costs of instruments composed 79% and 84% of the total supply costs for every robotic and laparoscopic surgery respectively. Among these supplies, the costs of clips were significantly different between the two approaches, but they only account limited proportion of the total costs in RLR and LLR respectively ($16, < 1% versus $65, 1.5%). While the indirect costs like fees for robotic system purchase and maintenance added, the total costs of RLR and LLR were significant different ($6653 versus $4408, $p = 0.021$). This shortcoming is still the main limitation hindered the movement of robotic surgery. In spite of the higher cost, there need more operating room to put the robotic panel.

The comparable outcomes in complications, transfusion and conversion rate suggested that the difficulties faced in performing minimally invasive liver resections. Our subgroup analysis demonstrated RLR is associated with lower conversion rate in the recent surgeries, which may result from the accumulations of surgical experiences, robotic surgery could be more safety and convenient, especially in dealing with blood control and the anatomy of adhesions. Although longer operative was observed in RLR, no statistical different was observed in hospital stay, R1 resection rate, hospital stay, which demonstrated the two approaches is comparable in safety and effectiveness.

There are several limitations that should be considered in the current meta-analysis. First, there have no prospective randomized controlled trials comparing the two approaches, our meta-analysis is based on retrospect research, only four of them are case—control studies. Second, most of the included studies were investigated the clinical outcomes in all kind of liver diseases about RLR and LLR, so we could not acquire enough information to evaluate the long-term prognosis. Third, some outcomes such as operative time and intraoperative blood loss were associated with high heterogeneity, this may duo to different type of liver resection and the location of tumors, although subgroup and sensitive analyses were performed, the results are still highly heterogeneous. And the language of included studies were limited to English only, four studies were excluded because of reported by the same institution, therefore a substantial amount of patients were

not involved in the meta-analysis. In the future, more comparative trials are needed to be performed in order to truly evaluate the advantages of robotic hepatectomies.

5. Conclusions

Our meta-analysis demonstrated that robotic-assisted liver resection is associated with longer operative time, more intraoperative blood loss and higher cost compared with laparoscopic liver resection. There was no difference in the transfusion rate, complication rate, conversion rate, the R1 resection rate and hospital stay between the two approaches. RLR seems to be as safety and effective as LLR for liver resections. As for minor liver resection and left hemihepatectomy or left lateral hepatectomy, LLR may be a preferred treatment option for patients underwent minimally invasive hepatectomies. Further studies should investigate the long-term oncologic outcomes about the two procedures and focus on the outcomes about major and posterosuperior hepatectomy.

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