

Laparoscopic versus open surgery in the treatment of hepatic hemangioma

A meta-analysis

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Abstract

Background: The aim of this study was to systematically evaluate and compare the effectiveness and safety of laparoscopic versus open resection (LR vs OR) in the treatment of hepatic hemangioma.

Methods: We searched PubMed, the Cochrane Library, Web of Science, Medline, EMBASE, and the Chinese Biomedicine Database from January 2000 to April 2020 for studies comparing the outcomes of laparoscopic versus open surgery in hepatic hemangioma treatment.

Results: Based on the preset criteria, 12 randomized clinical trials (RCTs) and 12 observational clinical studies (OCSs) were selected for analysis. Our results showed that laparoscopic surgery was more effective than open surgery in terms of reducing operation time, intraoperative blood loss, postoperative exhaust time, postoperative complications, postoperative bile leak, postoperative intra-abdominal infection, postoperative alanine aminotransferase (ALT) and aspartate aminotransferase (AST) values, postoperative visual analog scale (VAS) scores, and hospitalize length. No significant differences were found between the 2 groups in hepatectomy time, hospitalized cost, intra-abdominal hemorrhage, and the postoperative recurrence of hemangioma.

Conclusion: While similar therapeutic effect was achieved by the compared herein surgical methods, the findings of our analysis revealed that laparoscopic surgery is superior over open surgery in terms of less trauma, faster recovery, less postoperative pain, shorter hospitalize length, and reduced postoperative complications. Therefore, laparoscopic resection of hepatic hemangioma is a safe, effective, and feasible surgical method that is worth considering in clinical applications.

Abbreviations: ALT = alanine aminotransferase, AST = aspartate aminotransferase, CI = confidence interval, LR = laparoscopic resection, MINORS = Methodological Index for Nonrandomized Studies, OCSs = observational clinical studies, OR = open resection, ORs = Odds ratios, RCTs = randomized clinical trials, VAS = visual analog scale, WMDs = weighted mean differences.

Keywords: hepatic hemangioma, laparoscopic surgery, meta-analysis

1. Introduction

Hepatic hemangioma is a common benign tumor of the liver, characterized by a high incidence rate of approximately 0.3% to 0.4% in the Chinese population. Genetic and environmental factors, as well as eating habits, are considered to be associated with this high incidence rate. Most patients have mild symptoms

or no symptoms at all.^[1,2] Although spontaneous rupture of hepatic hemangioma is rare,^[3] liver trauma or liver lesions can cause tumor rupture with severe symptoms such as abdominal hemorrhage and shock, with a mortality rate of approximately 78%.^[4] Advances in molecular biology and pathology have provided a deeper understanding of the underlying mechanisms of hepatic hemangioma recurrence and local invasion. Nevertheless, surgical resection is currently the main treatment of choice for hepatic hemangioma.

Surgical treatment of hepatic hemangioma is mainly performed by laparotomy, which prevents the rapid recovery of patients.^[5] Laparoscopic surgery has many advantages, including the use of small incision sites that facilitate a quick postoperative recovery, as well as an enlarged operational field of vision, fine anatomy and timely hemostasis, and reduced incidence rates of postoperative complications.^[6] However, resection of the hepatic hemangioma by laparoscopy is difficult due to the abundant blood supply and the considerable anatomic specificities of the liver. Improved surgical skills and technological advances have increased the safety and feasibility of laparoscopic hepatectomy and gradually contributed to a change in the concept of hepatic hemangioma treatment from open resection (OR) to laparoscopic resection (LR). However, challenges and problems are still present in hepatic hemangioma surgery such as the interruption of the liver blood flow during an operation. Moreover, laparoscopic hepatectomy has certain disadvantages, including

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All data generated or analyzed during this study are included in this published article [and its supplementary information files].

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difficult effective control of bleeding in case of an emergency during the operation, which has raised concerns regarding its clinical value. Nevertheless, with the recent advances in laparoscopic equipment and the improvement of surgical hemostatic devices, an increasing number of reports on laparoscopic resection of hepatic hemangioma have been published.

Currently, no consensus has been reached regarding the clinical application of laparoscopic hepatectomy. In this paper, we present a meta-analysis of the clinical indicators of 2 surgical methods used for the treatment of hepatic hemangioma. We aimed to explore the safety and effectiveness of laparoscopic hepatectomy to provide novel insights and guidance that would increase the efficacy of the clinical treatment of hepatic hemangioma.

2. Methods

We searched PubMed, the Cochrane Library, Web of Science, Medline, EMBASE, and the Chinese Biomedicine Database from January 2000 to April 2020. Our searches included both MESH words and free terms related to the subject without language restrictions. The following search terms were used: (“hepatic hemangioma” OR “hemangioma of liver” OR “liver hemangioma” OR “hemangioma” OR “cavernous hemangioma” OR “hepatic cavernous hemangioma” OR “cavernous hemangioma of liver” OR “liver cavernous hemangioma”) AND (“laparoscope” OR “laparoscopic resection” OR “laparoscopic excise”) AND (“open surgery” OR “laparotomy” OR “open”) NOT “animals.” Using these keywords, 2 independent researchers searched for titles, medical subject headings, and abstracts. A final decision on article eligibility for inclusion was reached by consensus of the 2 researchers. When no consensus was achieved, a third scientist made the final decision. The results of our search strategy are presented in a flow diagram. All analyses were based on previous published studies; thus, no ethical approval and patient consent are required.

2.1. Inclusion criteria

The following criteria were applied in the selection of studies for inclusion on the current analysis:

- (1) Studies that involved comparisons between groups of patients who had undergone laparoscopic versus open surgery;
- (2) If the same datum had been published more than once, only the latest datum was considered;
- (3) Only studies having at least 1 relevant research result were included;
- (4) Only studies with available full-text access were considered;
- (5) High-quality studies, randomized clinical trials (RCTs) with Jadad score ≥ 4 , or observational clinical studies (OCSs) with a Methodological Index for Nonrandomized Studies (MINORS) score > 12 were deemed to be of high quality.

2.2. Exclusion criteria

The following studies were excluded from the current analysis:

- (1) Studies that did not report a detailed type of surgery;
- (2) Studies that did not perform a comparison between a laparoscopic and an open surgery group, that is, studies that did not have data on the treatment effects or complications, and studies whose results did not include complete or available perioperative and postoperative data;

- (3) Low-quality studies and such with design flaws;
- (4) Studies that were classified as case reports, letters, abstracts, animal studies, comments and reviews, or studies with incomplete data.

2.3. Data extraction and definition

The outcome indices included:

- (1) Operation time;
- (2) Intraoperative blood loss;
- (3) Hepatectomy time;
- (4) Postoperative exhaust time (from the end of the operation to the first exhaust);
- (5) Overall postoperative morbidity (defined as any complication occurring within 30 days after an operation);
- (6) Postoperative liver function;
- (7) Postoperative visual analog scale (VAS) score (from 0 for a total absence of pain to 10 for extremely severe experienced pain);
- (8) Postoperative hospitalize length;
- (9) Hospitalized cost;
- (10) Postoperative hemangioma recurrence.

2.4. Quality assessment

The methodological quality of RCTs and OCSs was assessed using the Jadad scoring system and the MINORS, respectively. The quality checklist recommended in the Cochrane Handbook was used for assessment of the risk of bias of the included RCTs. The following parameters were included:

- (1) sequence generation;
- (2) evaluating the aspects of allocation concealment;
- (3) incomplete data outcomes;
- (4) blinding;
- (5) selective reporting bias; and
- (6) other potential sources of bias (Fig. 1).

2.5. Statistical analysis

PRISMA (evidence-based minimum set of items for reporting in systematic reviews and meta-analyses) requires the use of the Review Manager software provided by the Cochrane Collaboration for meta-analysis. Odds ratios (ORs) with corresponding 95% CIs and weighted mean differences (WMDs) with corresponding 95% CIs were employed to analyze categorical and continuous variables, respectively. The heterogeneity between studies was examined by the Mantel-Hansel, Chi-squared, and I^2 tests. In the cases when $I^2 > 50\%$, a random effects model was applied, whereas if $I^2 < 50\%$, a fixed effects model was applied; $P < .05$ was considered to indicate statistically significant differences. The potential publication bias was evaluated by funnel plots.

3. Results

3.1. Characteristics and quality assessment of the included studies

A total number of 12 RCTs and 12 OCSs were included in this meta-analysis. The total number of patients was 1367, 620 of whom were in the LR group and 747 in the OR group. The

	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of participants and personnel (performance bias)	Blinding of outcome assessment (detection bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)	Other bias
Fu KH	+	+	+	+	?	+	?
Gao WB	+	?	+	+	+	+	+
Huang AH	+	+	+	?	+	+	+
Jiang SF	+	+	+	+	+	?	?
Lin JP	+	+	+	?	?	+	?
Liu LJ	+	+	+	?	?	+	+
Liu PY	+	+	?	+	+	+	+
Li YJ	+	+	?	?	+	?	?
Wang ZC	+	+	+	?	+	+	?
Zhang JP	+	+	+	?	+	+	+
Zhang XD	+	+	+	+	+	?	?
Zou Y	+	+	?	+	+	?	+

Figure 1. Risk of bias of RCTs: “+” indicated a “low” risk of bias; “?” indicated an “unclear” risk of bias.

characteristics of the studies that were included in the meta-analysis are presented in Table 1 (RCTs) and Table 2 (OCSs). We calculated the scores of the included studies. The included RCT studies had scores from 5 to 7, indicating that they were of high quality (Table 3). The quality of the included OCSs was assessed

using MINORS; the scores for most of the studies ranged from 19 to 22 out of 24 (Table 4).

4. Meta-analysis result

4.1. Operating time

Twenty-three included studies reported the operation time. Using a Random model ($I^2=69\%$), the results of meta-analysis show that operating time was significantly shorter in LR group (WMD = -13.04; 95% confidence interval [CI], -17.88 to 8.2; $P < .00001$). The result of RCTs and OCS subgroup both reveals that the operating time was significantly shorter in LR group (RCTs [$I^2=59\%$, WMD = -16.6; 95%CI, -22.74 to 10.46; $P < .00001$], OCS [$I^2=72\%$, WMD = -8.89; 95%CI, -16.38 to 1.4; $P = .02$]) (Fig. 2).

4.2. Intraoperative blood loss

Twenty included studies reported the intraoperative blood loss. Using a Random model ($I^2=100\%$), the results of meta-analysis show that blood loss was significantly less in LR group (WMD = -83.09; 95%CI, -117.95 to 48.23; $P < .00001$). The result of RCTs and OCS subgroup both reveals that the blood loss was significantly less in LR group (RCTs [$I^2=99\%$, WMD = -54.29; 95%CI, -89.71 to 18.88; $P = .003$], OCS [$I^2=100\%$, WMD = -110.92; 95%CI, -176.41 to 45.43; $P = .009$]) (Fig. 3).

4.3. Hepatectomy time

Six included studies reported the hepatectomy time. Using a Random model ($I^2=99\%$), there was no significant difference between 2 groups (WMD = 3.35; 95%CI, -10.72 to 17.42; $P = .64$). The result of RCTs and OCS subgroup both reveals no significant difference between 2 groups (RCTs [$I^2=100\%$, WMD = 2.05; 95%CI, -23.15 to 27.24; $P = 0.87$], OCS [$I^2=99\%$, WMD = 4.69; 95%CI, -11.26 to 20.64; $P = .56$]) (Fig. 4).

4.4. Postoperative exhaust time

Five included studies reported the postoperative exhaust time ($I^2=89\%$), using a Random model. The results of meta-analysis show that the postoperative exhaust time was significantly shorter in LR group (WMD = -1.59; 95%CI, -2.26 to 0.93; $P < .00001$) (Fig. 5).

4.5. Postoperative complications

Ten included studies reported the rate of postoperative complications, using a fixed model ($I^2=0\%$). The results of meta-analysis show that the rate of postoperative complications was significantly lower in LR group (OR = 0.14; 95%CI, 0.09–0.23; $P < .00001$). The result of RCTs and OCS subgroup both reveals the rate of postoperative complications was significantly lower in LR group (RCTs [$I^2=0\%$, OR = 0.15; 95%CI, 0.07–0.29; $P < .00001$], OCS [$I^2=0\%$, OR = 0.13; 95%CI, 0.06–0.28; $P < .00001$]) (Fig. 6).

4.6. Postoperative biliary fistula

Six included studies reported the rate of postoperative bile leak, fixed model was applied ($I^2=0\%$). The results of meta-analysis

Table 1**The characteristics of all the included RCTs.**

Author	Year	Type	Group	N	Gender (M/F)	Age (yr)	Size (cm)	Tumor location (Couinaud segmentation) (case)
Huang et al ^[7]	2018	RCT	LR	30	17/13	51.07 ± 3.92	5.13 ± 1.24	II + III (7), IV + V (13), VI + VII (10)
			OR	30	16/14	50.79 ± 4.05	5.28 ± 1.17	II + III (5), IV + V (14), VI + VII (11)
Zhang et al ^[8]	2018	RCT	LR	30	17/13	41.7 ± 3.8	4.75 ± 1.39	II + III (7), IV (13), V (10), VI (10)
			OR	30	16/14	42.6 ± 4.0	4.83 ± 1.15	II + III (6), IV (8), V (8), VI (8)
Li et al ^[9]	2018	RCT	LR	9	3/6	55.7 ± 2.8	—	—
			OR	9	4/5	53.8 ± 3.5	—	—
Wang et al ^[10]	2017	RCT	LR	30	6/24	41.67 ± 2.48	11.51 ± 0.29	II + III (6), III + IV (6), V (8), VI + VII (5), VIII (5)
			OR	30	7/23	41.13 ± 2.46	11.24 ± 0.42	II + III (6), III + IV (6), V (8), VI + VII (5), VIII (5)
Liu et al ^[11]	2016	RCT	LR	29	13/16	42.5 ± 1.45	7.35 ± 2.74	II (12), VII (11), VIII (6)
			OR	29	17/12	43.2 ± 2.36	7.58 ± 2.28	II (10), VII (14), VIII (5)
Fu et al ^[12]	2016	RCT	LR	37	21/16	48.3 ± 12.2	5.68 ± 0.71	I (3), IV (7), VII (11), VIII (10), IV + VIII (4), VII + VIII (2)
			OR	37	19/18	47.1 ± 11.3	5.53 ± 0.82	I (4), IV (7), VII (9), VIII (6), IV + VIII (5), VII + VIII (6)
Zhang et al ^[13]	2016	RCT	LR	12	7/5	56 (41–60)	5.32 ± 1.75	VII (12)
			OR	12	8/4	54 (43–59)	5.55 ± 1.99	VII (12)
Liu et al ^[14]	2016	RCT	LR	29	11/18	37.45 ± 3.94	7.26 ± 1.02	II + III (5), IV (8), V + VIII (8), VI + VII (8)
			OR	27	11/16	37.46 ± 3.54	5.68 ± 0.57	II + III (6), IV (7), V + VIII (7), VI + VII (7)
Lin et al ^[15]	2016	RCT	LR	28	12/16	49.4 ± 8.5	5.03 ± 1.11	V (6), VI (13), V + VI (9)
			OR	28	13/15	49.1 ± 8.1	5.18 ± 1.04	V (8), VI (12), V + VI (8)
Jiang et al ^[16]	2016	RCT	LR	25	6/19	47.62 ± 7.13	9.58 ± 2.43	—
			OR	25	5/20	47.61 ± 7.36	9.67 ± 2.31	—
Zou et al ^[17]	2013	RCT	LR	15	5/10	38.1 ± 1.2	5.12 ± 0.56	V + VI (6), VII + VIII (9)
			OR	15	5/10	41.1 ± 1.4	6.12 ± 0.56	V + VI (8), VII + VIII (7)
Gao et al ^[18]	2012	RCT	LR	20	6/14	37–43.5	5.2 ± 0.6	II + III (4), V + VI (7), VII + VIII (9)
			OR	28	8/20	37.5–48	6.1 ± 0.6	II + III (7), V + VI (12), VII + VIII (9)

LR = laparoscopic resection, OR = open resection, RCTs = randomized clinical trials.

Table 2**The characteristics of all the included OCSs.**

Author	Year	Type	Group	N	Gender (M/F)	Age (yr)	Size (cm)	Tumor location (Couinaud segmentation) (case)
Fan et al ^[19]	2018	OCS	LR	20	7/13	47.8 ± 8.2	13.2 ± 2.9	II + III (5), IV (4), V + VIII (3), VI + VII (8)
			OR	42	7/35	45.2 ± 6.1	14.9 ± 5.3	II + III (13), IV (4), V + VIII (12), VI + VII (13)
Ji et al ^[20]	2018	OCS	LR	32	14/18	43.5 (27–65)	6.26 ± 1.54	III (5), II + III (10), II + III + IV (8), V + VI (6), VII + VIII (3)
			OR	35	15/20	47.7 (19–67)	6.15 ± 1.73	II + III (3), II + III + IV (9), VI + VII (7), VII + VIII (7), VI + VII + VIII (6), V + VI + VII + VIII (3)
Cheng et al ^[21]	2018	OCS	LR	7	2/5	48.4 ± 10.8	5.49 ± 1.46	II (2), III (3), II + III (2)
			OR	7	1/6	42.43 ± 8.4	5.53 ± 2.01	II (3), III (3), II + III (1)
Chen et al ^[22]	2018	OCS	LR	46	17/29	53.8 ± 7.1	5.7 ± 1.4	II + III (35), IV (11)
			OR	61	21/40	55.1 ± 10.5	6.1 ± 1.7	II + III (41), IV (20)
Qian et al ^[23]	2017	OCS	LR	50	28/22	45.26 ± 8.36	7.26 ± 1.18	II (14), III (8), V + VI (12), VII + VIII (16)
			OR	50	29/21	45.32 ± 8.42	7.28 ± 1.19	II (11), III (13), V + VI (14), VII + VIII (12)
Liu ^[24]	2017	OCS	LR	23	14/9	42.54 ± 0.58	7.26 ± 1.02	II + III + IV (11), V + VI + VII + VIII (12)
			OR	23	13/10	45.74 ± 1.04	5.68 ± 0.57	II + III + IV (9), V + VI + VII + VIII (14)
Fang et al ^[25]	2017	OCS	LR	26	16/10	45.8 ± 4.7	4.9 ± 1.1	II + III (2), IV (9), V–VIII (16)
			OR	20	11/9	42.4 ± 5.4	5.1 ± 0.9	II + III (1), IV (7), V–VIII (12)
Zhang et al ^[26]	2016	OCS	LR	23	12/11	40.29 ± 3.31	6.35 ± 2.58	II (4), III + IV + V (9), VI + VII (4), VIII (6)
			OR	23	13/10	40.23 ± 3.24	6.18 ± 2.29	II (5), III + IV + V (10), VI + VII (4), VIII (4)
Li et al ^[27]	2016	OCS	LR	35	21/14	41.8 ± 7.6	6.5 ± 1.3	II + III (7), IV (5), V (6), VI + VII (9), VIII (8)
			OR	35	19/16	42.5 ± 6.9	6.2 ± 1.5	II + III (8), IV (6), V (7), VI + VII (8), VIII (6)
Yu and Yu ^[28]	2015	OCS	LR	31	15/16	48.6 ± 12.2	—	—
			OR	100	35/65	48.4 ± 9.5	—	—
Fan and Zhou ^[29]	2012	OCS	LR	19	7/12	37–59	7.03 ± 2.86	II (8), III (6), II + III (5)
			OR	27	10/17	36–60	7.27 ± 2.99	II (11), III (9), II + III (7)
Hu et al ^[30]	2008	OCS	LR	14	4/10	37.5 ± 7.8	5.2 ± 0.6	II (4), III (6), II + III (4)
			OR	24	7/17	40.4 ± 8.3	6.1 ± 0.6	II (7), III (12), II + III (5)

LR = laparoscopic resection, OCSs = observational clinical studies, OR = open resection.

Table 3**Jadad scale system for RCTs.**

Refs	Randomization	Concealment of allocation	Double blinding	Withdrawals and drop out	Total score
Huang et al ^[7]	2	2	1	1	6
Zhang et al ^[8]	2	2	1	0	6
Li et al ^[9]	2	2	1	0	5
Wang et al ^[10]	2	2	0	0	4
Liu et al ^[11]	2	2	1	1	6
Fu et al ^[12]	2	2	1	0	5
Zhang et al ^[13]	2	2	1	0	5
Liu et al ^[14]	2	2	1	0	5
Lin et al ^[15]	2	2	1	1	6
Jiang et al ^[16]	2	2	0	0	4
Zou et al ^[17]	2	2	1	0	5
Gao et al ^[18]	2	2	0	0	4

The quality of the RCT studies was evaluated using the Jadad scale. The system was used to assess randomization, concealment of allocation, blinding, and withdrawals in the study. Each item was given a score of 0–2 and 7 score in total. If the total score was ≥ 4 , the RCT was of high quality.

show that the rate of postoperative bile leak was significantly lower in LR group (OR=0.43; 95%CI, 0.19–0.97; $P=.04$) (Fig. 7).

4.7. Postoperative intra-abdominal hemorrhage

Five studies reported the rate of postoperative intra-abdominal hemorrhage, using a fixed model ($I^2=0\%$). The meta-analysis indicated that there was no significant difference between 2 groups (OR=0.4; 95%CI, 0.15–1.09; $P=.07$) (Fig. 8).

4.8. Postoperative intra-abdominal infection

Six included studies reported the rate of postoperative intra-abdominal infection, using a fixed model ($I^2=0\%$). The results of meta-analysis show that the rate of postoperative intra-abdominal infection was significantly lower in LR group (OR=0.37; 95%CI, 0.16–0.87; $P=.02$) (Fig. 9).

4.9. Postoperative liver function

Four included studies reported the postoperative liver function. The results of meta-analysis show that the values of alanine

aminotransferase (ALT) (WMD=−131.47; 95%CI, −195.52 to 67.42; $P<.0001$) and aspartate aminotransferase (AST) (WMD=−81.12; 95%CI, −134.98 to 27.27; $P=.003$) were significantly lower in LR group. There was no significant difference between 2 groups in the values of ALB (WMD=0.54; 95%CI, −0.15 to 1.23; $P=.13$) and TBil (WMD=2.89; 95%CI, −0.76 to 6.53; $P=.12$) values (Figs. 10–13).

4.10. Postoperative VAS score

Four included studies reported the postoperative VAS score, using a fixed model ($I^2=0\%$). The results of meta-analysis show that the postoperative VAS score was significantly lower in LR group (WMD=−2.89; 95%CI, −3.19 to 2.58; $P<.00001$) (Fig. 14).

4.11. Postoperative hospitalize length

Seventeen included studies reported the postoperative hospitalize length. Using a Random model ($I^2=87\%$), the results of meta-analysis show that postoperative hospitalize length was significantly shorter in LR group (WMD=−3.68; 95%CI, −4.32 to 3.04; $P<.00001$). The result of RCTs and OCS subgroup both

Table 4**Quality assessment for OCSs using MINORS.**

Refs	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)	(9)	(10)	(11)	(12)	Total score
Fan et al ^[19]	2	2	0	2	2	2	2	2	2	2	0	2	20
Ji et al ^[20]	2	2	0	2	2	2	2	2	2	2	0	2	20
Cheng et al ^[21]	2	2	2	2	2	2	2	2	2	2	0	2	22
Chen et al ^[22]	2	2	0	2	2	2	2	2	2	2	0	2	20
Qian et al ^[23]	2	2	0	2	2	2	2	2	2	2	0	2	20
Liu ^[24]	2	2	1	2	2	2	2	2	2	2	0	2	21
Fang et al ^[25]	2	2	0	2	2	2	2	2	2	1	0	2	19
Zhang et al ^[26]	2	2	0	2	2	2	2	2	2	2	0	2	20
Li et al ^[27]	2	2	0	2	2	2	2	2	2	2	0	2	20
Yu and Yu ^[28]	2	2	0	2	2	2	2	2	2	2	0	2	20
Fan and Zhou ^[29]	2	2	2	2	2	2	2	2	2	2	0	2	22
Hu et al ^[30]	2	2	0	2	2	2	2	2	2	2	0	2	20

MINORS criteria include the following items: (1): A stated aim of the study; (2): Inclusion of consecutive patients; (3): Prospective collection of data; (4): Endpoint appropriate to the study aim; (5): Unbiased evaluation of endpoints; (6): Follow-up period appropriate to the major endpoint; (7): Loss to follow-up not exceeding 5%; (8): A control group having the gold standard intervention; (9): Contemporary groups; (10): Baseline equivalence of groups; (11): Prospective calculation of the sample size; (12): Statistical analyses adapted to the study design. Items are scored as follows: 0 (not reported); 1 (reported but inadequate); or 2 (reported and adequate). The ideal global score for comparative studies is 24.

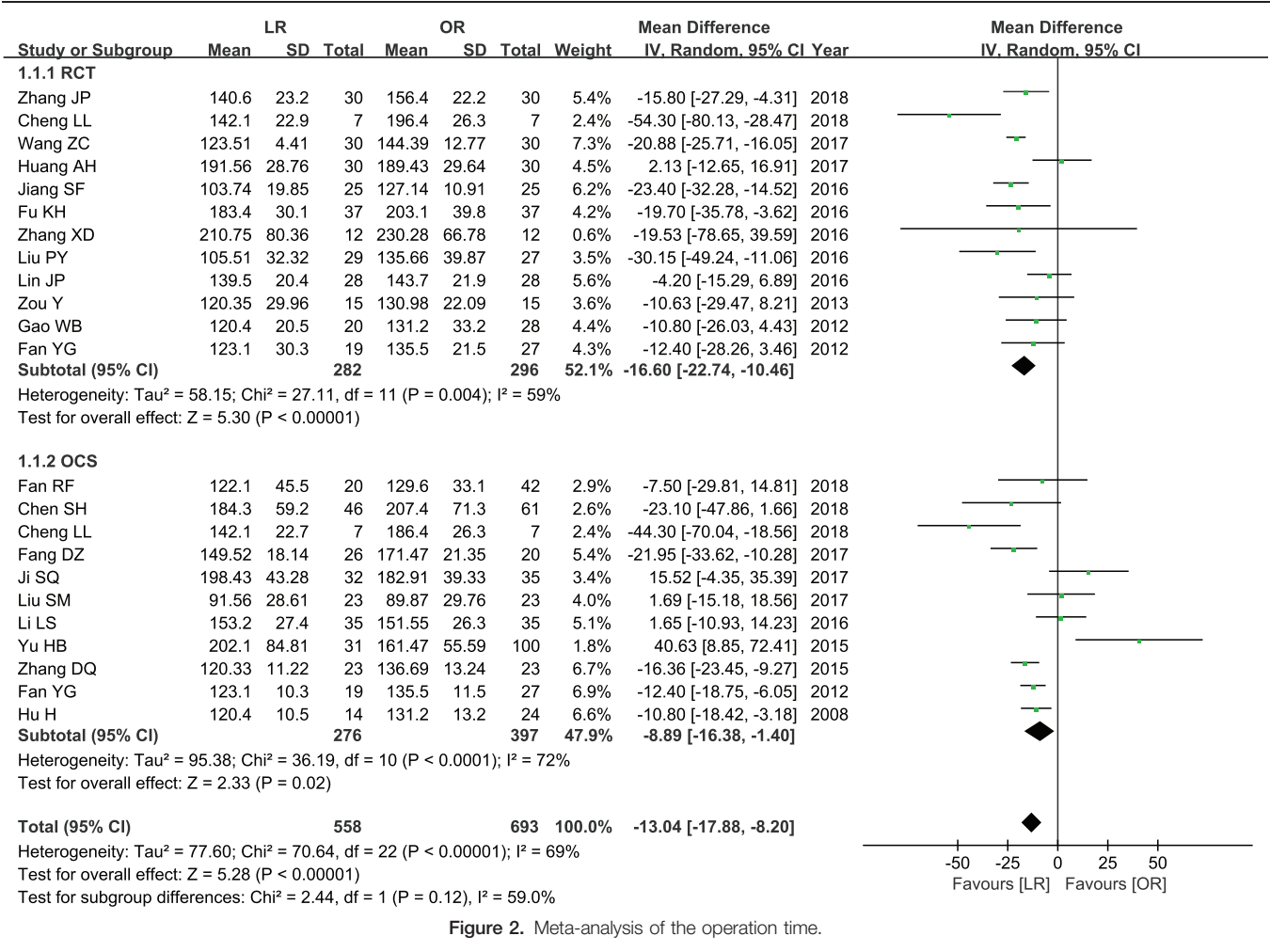


Figure 2. Meta-analysis of the operation time.

reveals that postoperative hospitalize length was significantly shorter in LR (RCTs [$I^2=87\%$, $WMD=-3.28$; 95%CI, -4.2 to 2.36 ; $P<.00001$], OCS [$I^2=87\%$, $WMD=-4.02$; 95%CI, -4.93 to 3.11 ; $P<.00001$]) (Fig. 15).

4.12. Hospitalized cost

Six included studies reported the hospitalized cost, using a Random model ($I^2=61\%$). The results of meta-analysis show that there was no significant difference between 2 groups ($WMD=-0.03$; 95%CI, -0.24 to 0.17 ; $P=.76$) (Fig. 16).

4.13. Postoperative hemangioma recurrence

Five included studies reported the rate of postoperative hemangioma recurrence, fixed model was applied ($I^2=0\%$). The results of meta-analysis show that there was no significant difference between 2 groups ($OR=0.83$; 95%CI, $0.35-1.94$; $P=.67$) (Fig. 17).

4.14. Publication bias

The publication bias of the studies used in the present meta-analysis was evaluated by funnel plots. Figure 18 shows that there

is no obvious asymmetry in the funnel plots, indicating a low probability of publication bias.

5. Discussion

Hepatic hemangioma is usually unintentionally discovered during physical or imaging examination for diagnosis of other diseases. Symptoms such as epigastric discomfort are often experienced when the tumor diameter reaches 4cm or more. Resection is clinically recognized as an effective way of treatment in cases of present clinical symptoms and a gradual increase of hemangioma or its rapid growth, established on the basis of clinical monitoring findings.^[5] However, problems associated with open hepatectomy include high postoperative complications, long postoperative recovery time, and high recurrence rates. After the appearance and along with the increasing application of laparoscopic equipment, laparoscopic hepatectomy has been widely employed in the treatment of liver hemangioma. Clinically, the feasibility of laparoscopic resection of hepatic hemangioma is still disputable. Because of the abundant blood supply within the liver, some scholars consider that the control of the bleeding during laparoscopic operations on patients with hepatic hemangioma is difficult. This may increase the amount of

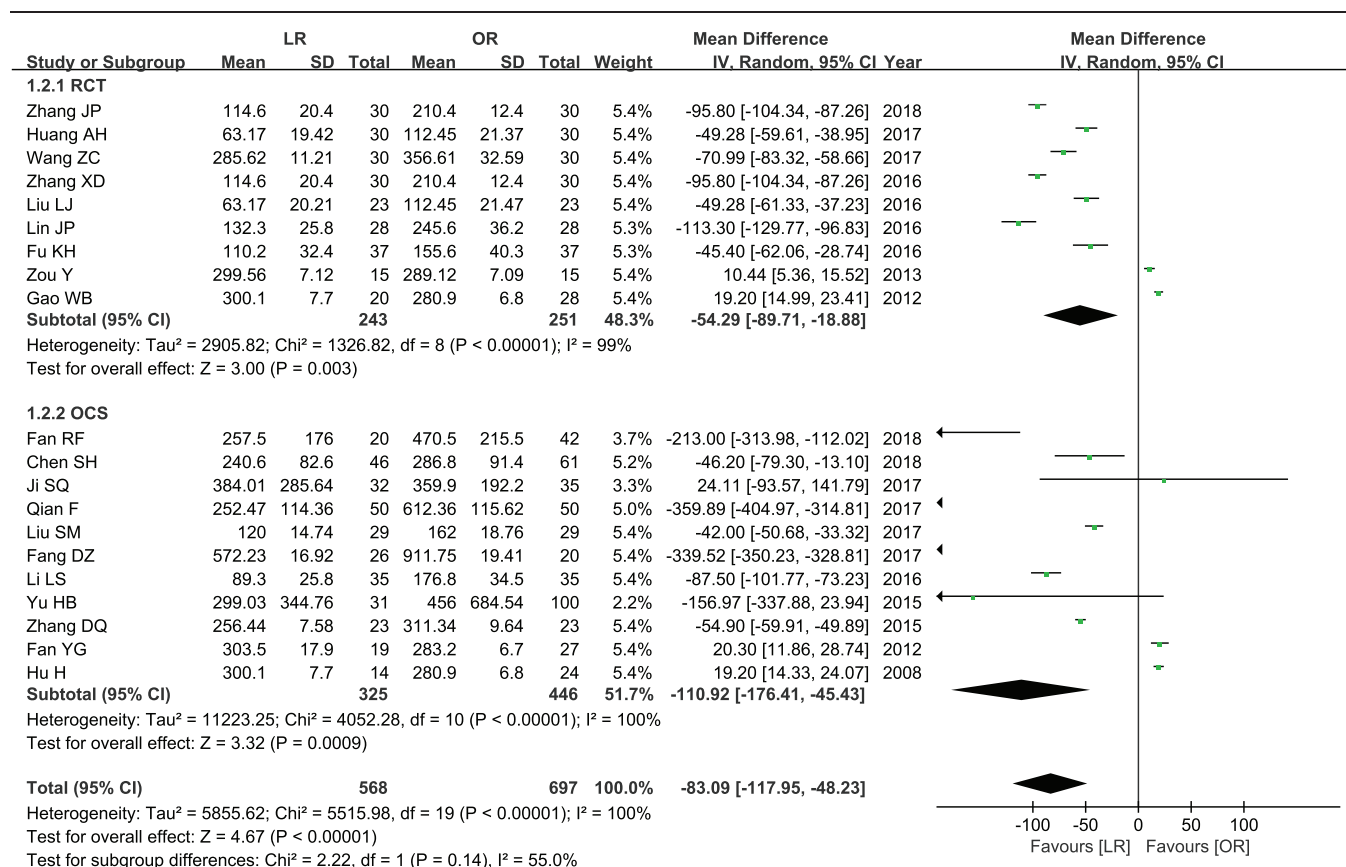


Figure 3. Meta-analysis of the intraoperative blood loss.

bleeding and prolong the operation time.^[31] Hence, in this meta-analysis, we compared the operation time, liver resection time, and intraoperative bleeding between laparoscopic with open operation. We found no significant difference in the liver

resection time between the 2 groups, but the laparoscopic operation time was significantly lower than that of the open operation time. The reduction in the operation time was largely due to the shorter abdominal cavity closing time. In addition, our

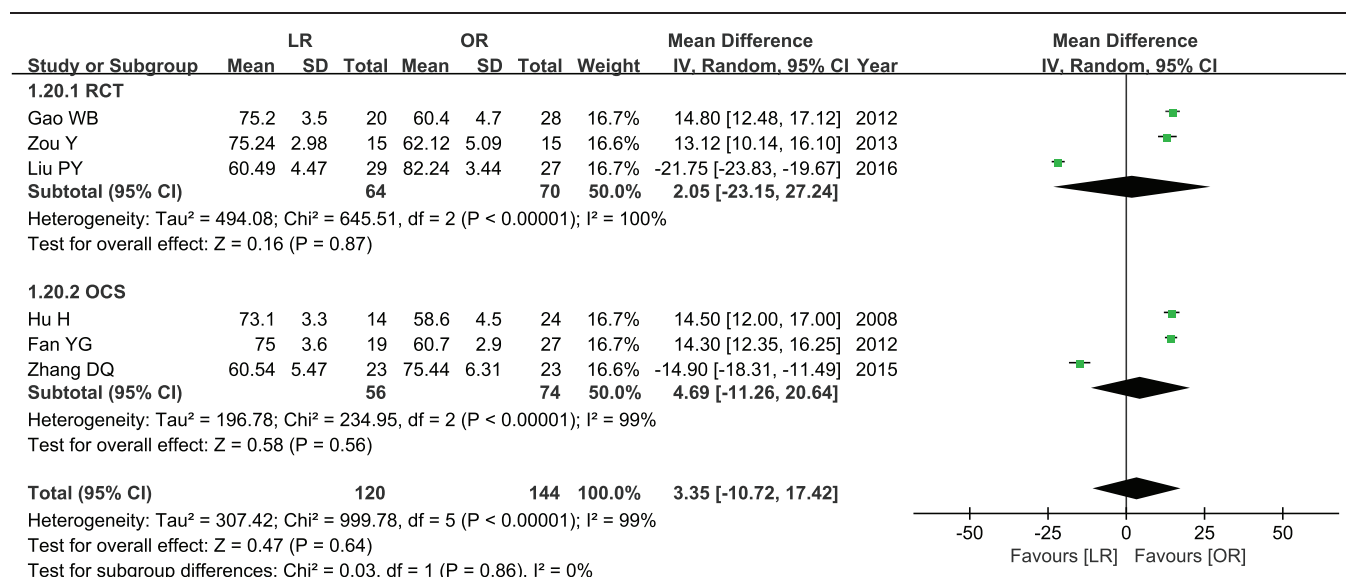


Figure 4. Meta-analysis of the hepatectomy time.

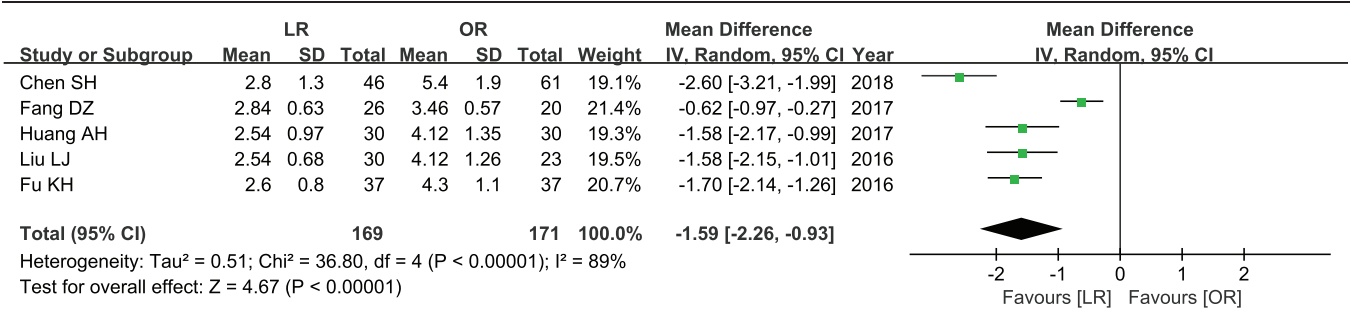


Figure 5. Meta-analysis of the postoperative exhaust time.

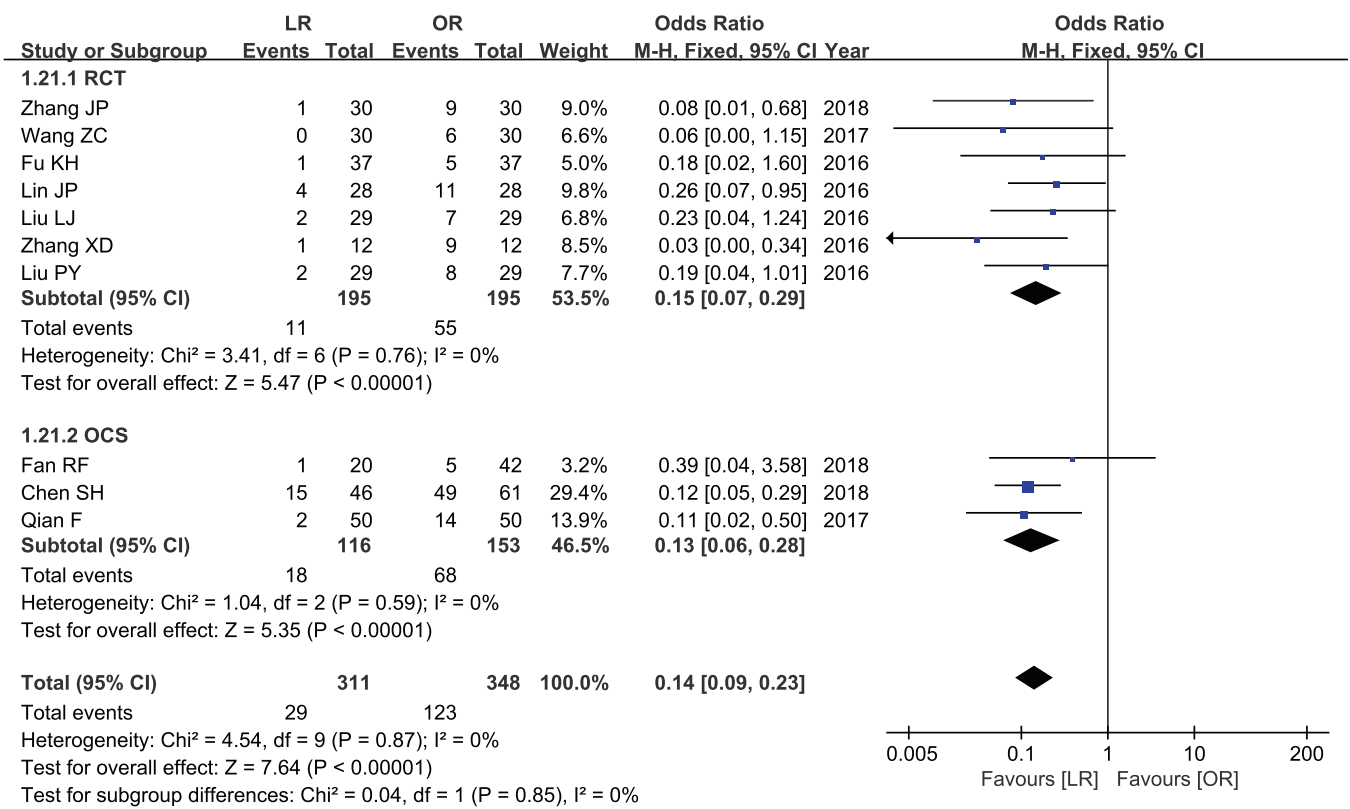


Figure 6. Meta-analysis of the postoperative complications.

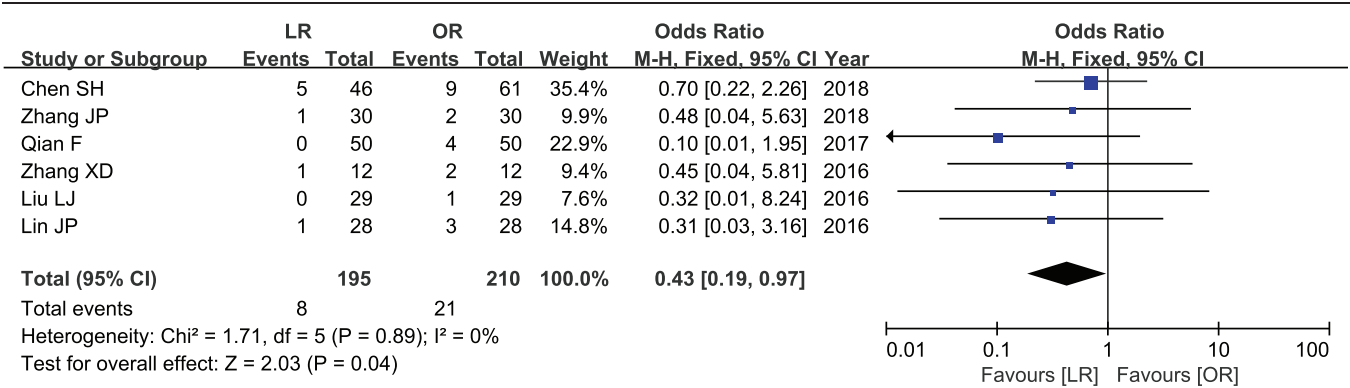


Figure 7. Meta-analysis of the postoperative biliary fistula.

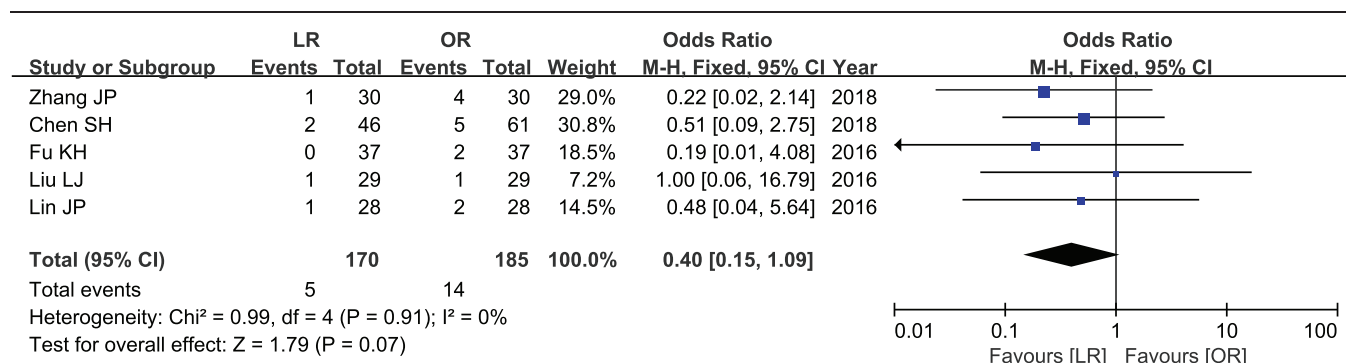


Figure 8. Meta-analysis of the postoperative intra-abdominal hemorrhage.

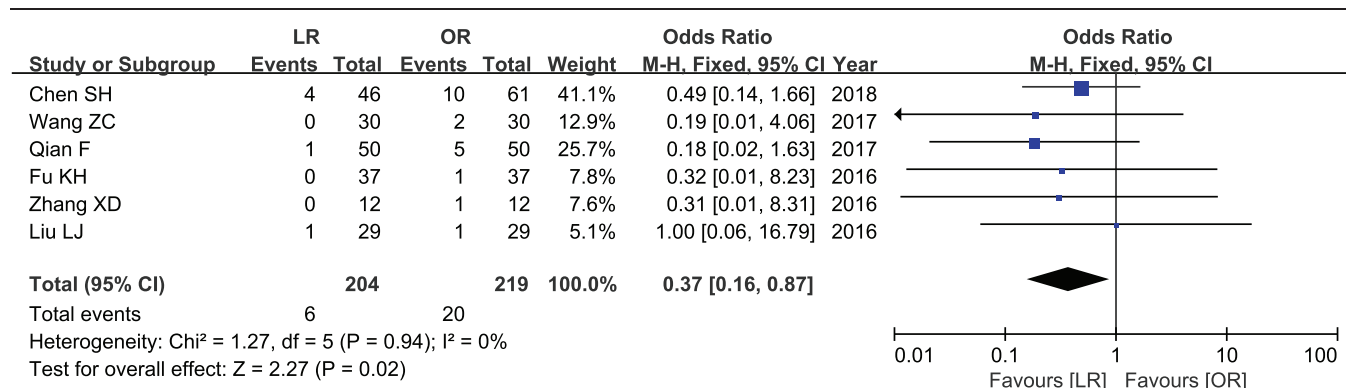


Figure 9. Meta-analysis of the postoperative intra-abdominal infection.

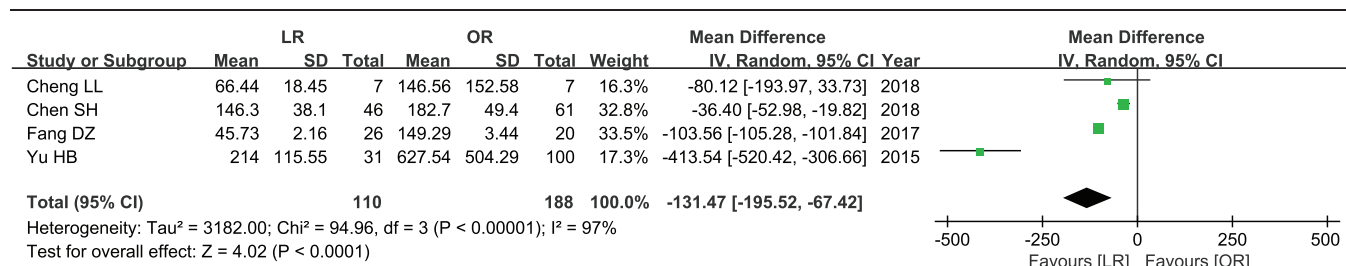


Figure 10. Meta-analysis of the postoperative ALT values.

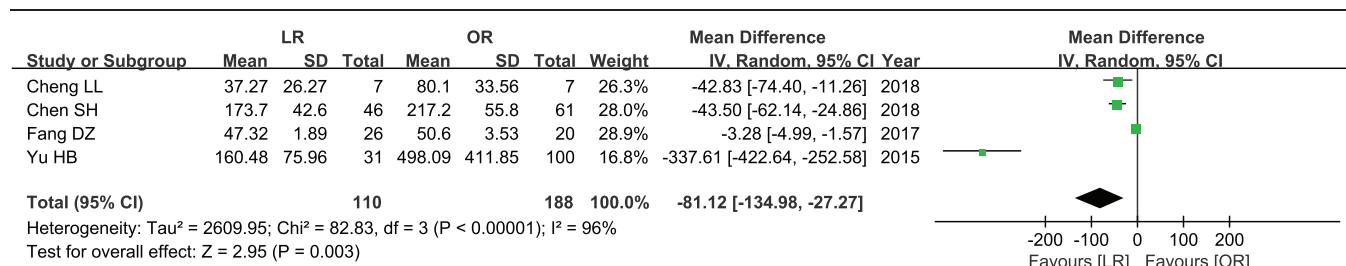


Figure 11. Meta-analysis of the postoperative AST values.

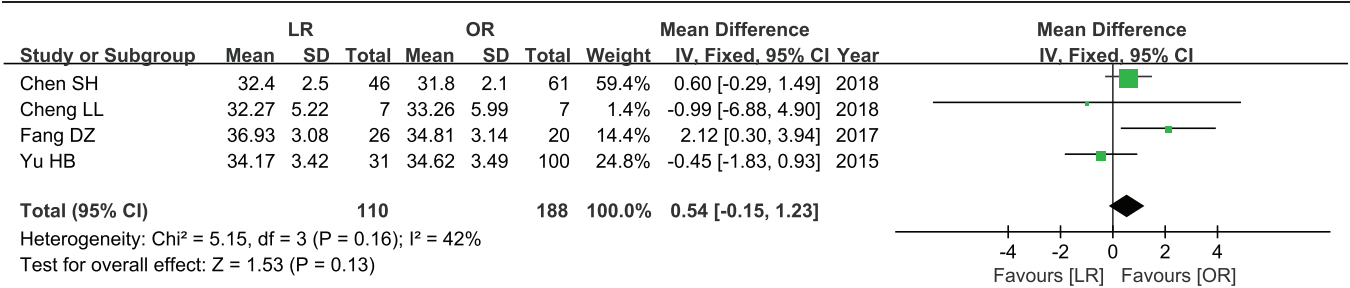


Figure 12. Meta-analysis of the postoperative TBil values.

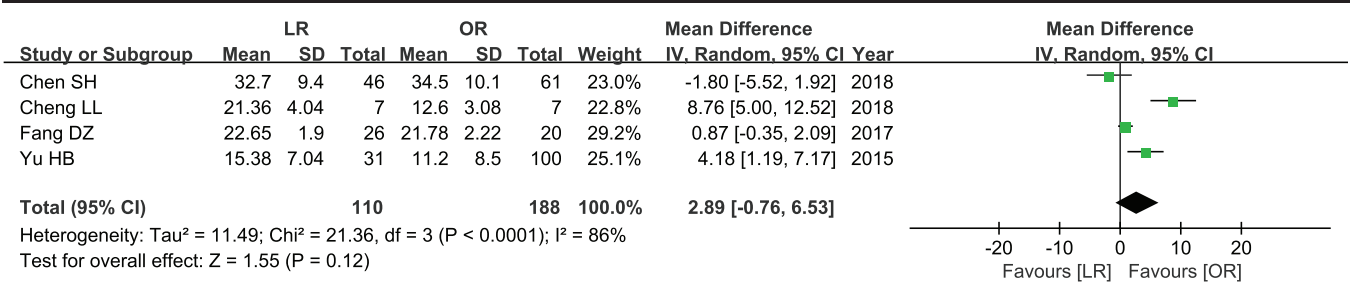


Figure 13. Meta-analysis of the postoperative ALB values.

meta-analysis results showed that laparoscopic hepatectomy effectively reduced the amount of bleeding in patients without prolonging the time of hepatectomy. The reason for this is that the operational field of vision under a laparoscope is clear. In addition, the use of ultrasonic scalpels in laparoscopic surgery is beneficial to hemostasis and prevents the damage to the tissue surrounding the liver. In addition, laparoscopy has the advantage of amplification, which can make the blood vessels completely bare, and instruments such as cutters and titanium clips can be used to ligate blood vessels at their roots. This, to a certain extent, can help in reducing the amount of bleeding during an operation.

The results of the meta-analysis revealed that the incidence of complications after laparoscopic resection was significantly lower than that after open surgery. Among the complications that occurred, the incidence of postoperative celiac infections in the laparoscopic group was significantly lower than that in the open operation group. This is because the laparoscopic operation was performed in a relatively closed environment, which generally provides protection from organ exposure during an

operation, reduces the loss and leakage of fluid, contributes to the stability of the celiac environment, and reduces the risk of postoperative celiac infection. In addition, pain is a common postoperative complication, occurring in more than 90% of the cases, which usually affects the functional state and quality-of-life of many patients. In this study, the VAS pain scores of the patients in the laparoscopic group were significantly lower than those in the open surgery group, suggesting that laparoscopic resection of liver hemangioma is less traumatic to patients. This could be due to the small incision in the abdominal wall in the laparoscopic group, which results in significantly less postoperative pain and is conducive to earlier postoperative activities.

Our meta-analysis confirmed that the patients in the laparoscopic group had shorter postoperative exhaust and hospitalize length than the patients in the laparotomy group, which indicated that laparoscopic hemangioma resection caused less damage. Furthermore, the patients in the laparoscopic group were able to get out of bed earlier and showed better gastrointestinal peristalsis and gastrointestinal function recovery.

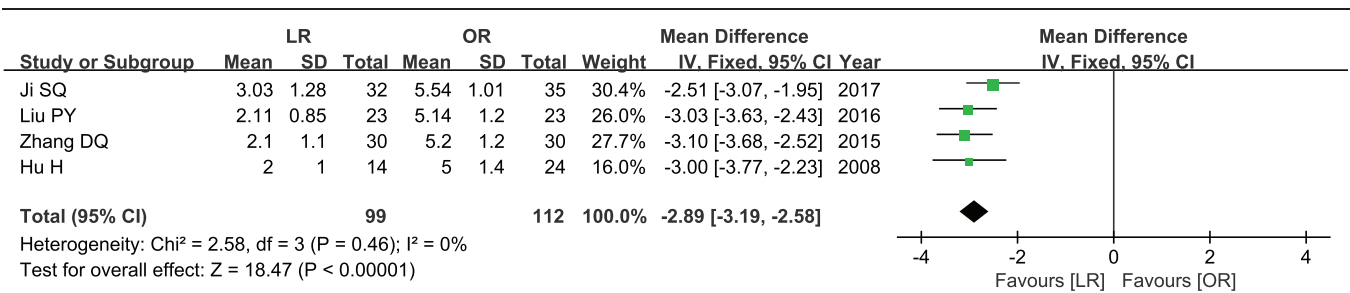


Figure 14. Meta-analysis of the postoperative VAS score.

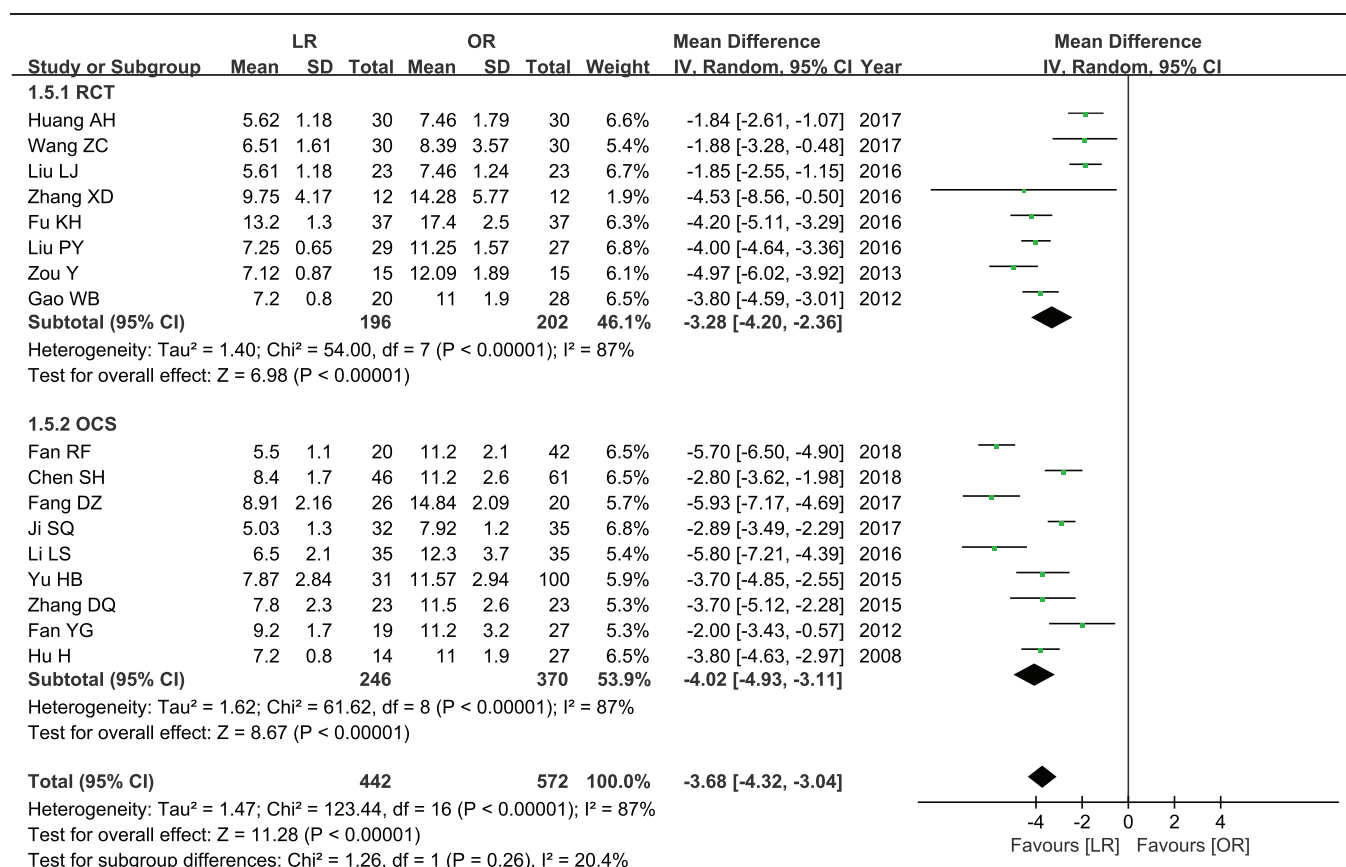


Figure 15. Meta-analysis of the postoperative hospitalize length.

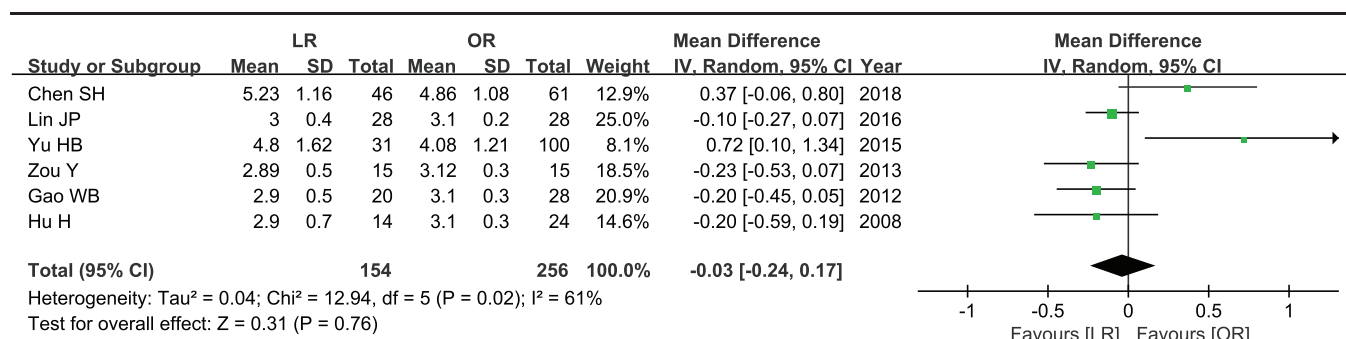


Figure 16. Meta-analysis of the hospitalized cost.

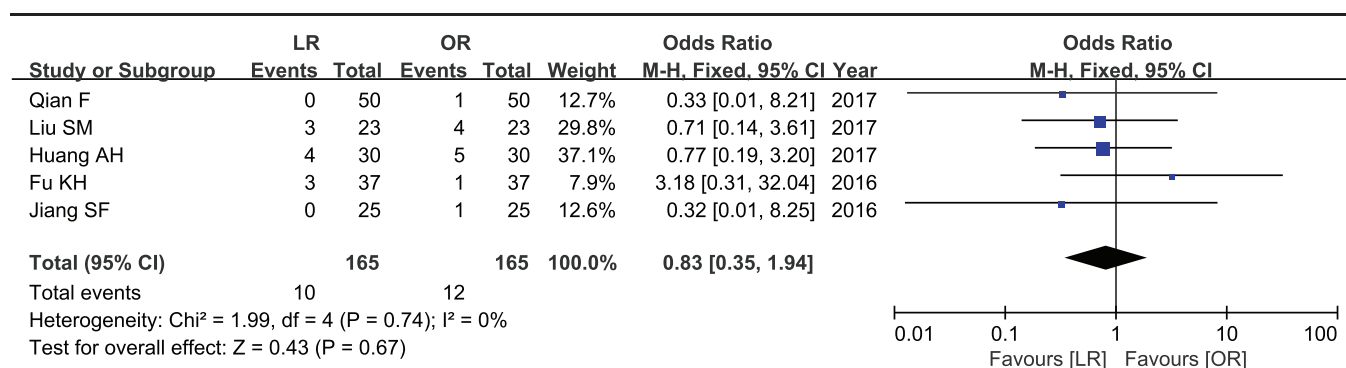


Figure 17. Meta-analysis of the postoperative hemangioma recurrence.

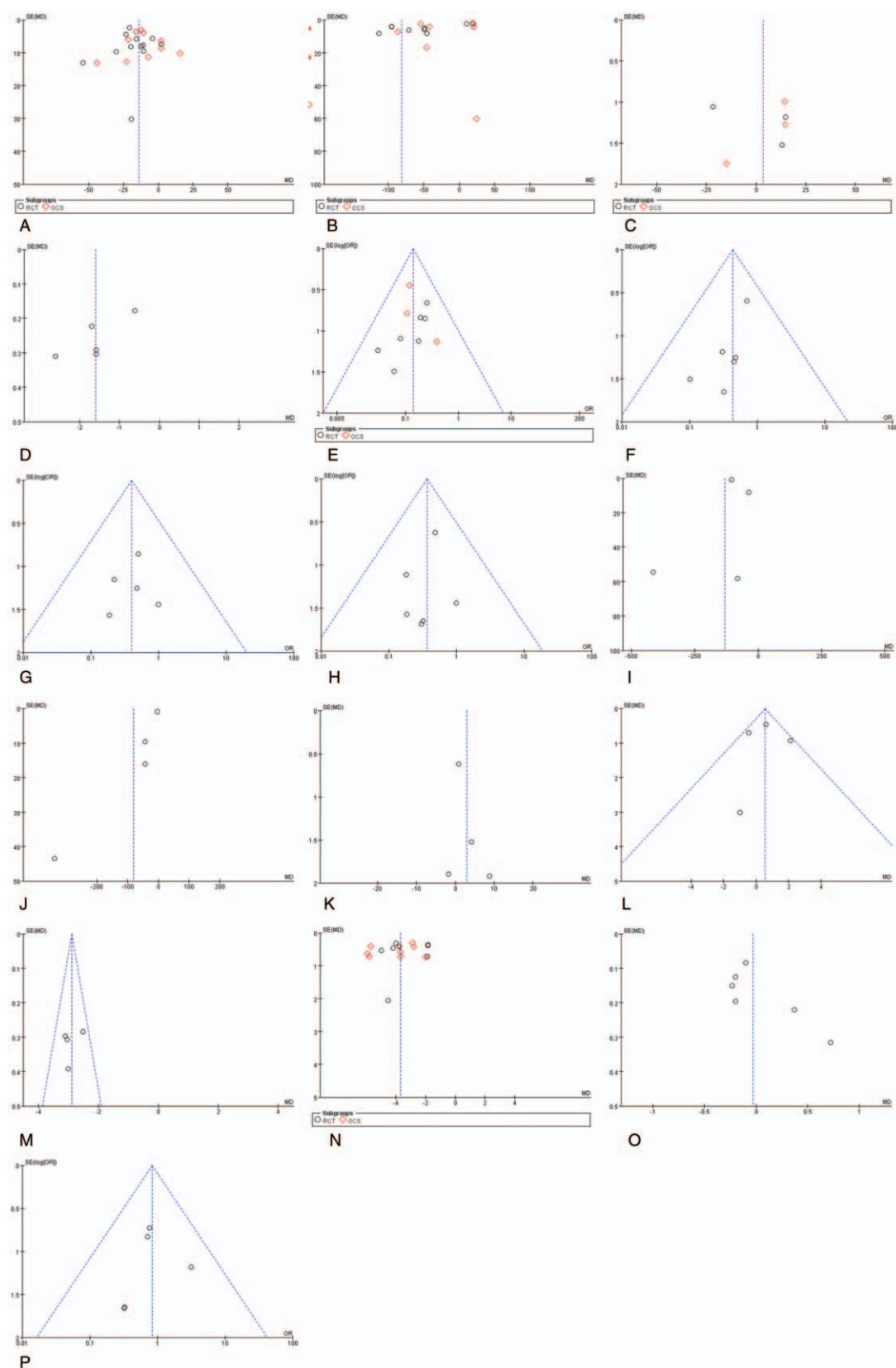


Figure 18. Funnel plots were created to assess the publication bias in our meta-analysis. A=operation time B=intraoperative blood loss, C=hepatectomy time, D=exhaust time, E=postoperative complications, F=bile leak, G=postoperative intra-abdominal hemorrhage, H=postoperative intra-abdominal infection, I=ALT, J=AST, K=TBil, L=ALB, M=VAS score, N=postoperative hospitalize length, O=hospitalized cost, P=postoperative hemangioma recurrence.

In addition, the levels of ALT and AST in the 3 days after the operation were significantly lower in the laparoscopic group than in the open group, indicating that the use of an ultrasonic scalpel during laparoscopic resection of liver hemangioma causes less damage to the normal liver tissue, which is conducive to the recovery of liver function. Analyses of the hospitalized costs revealed that, although the material and operation costs of laparoscopic hepatectomy were higher than those of open hepatectomy, the total hospitalized cost of the laparoscopic group was similar to that of the open hepatectomy group. This was mainly caused by the shortened postoperative time and accelerated recovery of the patients in the laparoscopic resection of liver hemangioma.

Residual remains and recurrence of hepatic hemangioma after resection is rare, with an incidence of approximately 2%.^[32] In this meta-analysis, the recurrence rates in the laparoscopic surgery patients were not significantly different from those in the open surgery group patients, which showed that the long-term effect of laparoscopic surgery was similar to that of open surgery. Actually, most of the clinical “recurrences” are in fact residual tumor tissues which are caused by incomplete resection. Therefore, accurate preoperative imaging evaluation is absolutely critical for the prevention of residual tumor cases and recurrence of hepatic hemangioma after resection. This preoperative examination would determine whether small hemangioma coexists with large hemangioma, which will prevent missed diagnosis and resection. In addition, complete tumor resection is the key to avert postoperative recurrence, especially in the cases of hemangioma without an obvious fibrous capsule, in which a small amount of residual tumor may be the source of postoperative hemangioma recurrence. It is noteworthy that estrogen replacement therapy may accelerate the recurrence of hepatic hemangioma.^[33] Postoperative follow-up revealed solitary small hemangiomas in the liver, most of them were residual small hemangiomas, which could be followed up regularly or treated by microwave/radio-frequency ablation. Reoperation or interventional therapy should be considered if rapid growth of the residual tumor is observed, clinical symptoms appear, or Kasabach–Merritt syndrome is complicated.

A major limitation to our meta-analysis is that all included studies were conducted in China. Thus, our conclusions may not be fully applicable or generalizable to other ethnic populations. Another potential limitation is that the specific surgical experience and methods of perioperative management used at different hospitals could have produced various outcomes, increasing the heterogeneity among the included studies. Furthermore, the liver texture, the anastomotic technique of the surgeon, and hemangioma location might have affected the study outcomes. Hence, further well-designed, large, multicenter RCTs are needed to assess and compare the application of laparoscopic and open surgery in the treatment of hepatic hemangioma.

6. Conclusion

Laparoscopic surgery was superior over open surgery with advantages, including less trauma, quicker recovery, less postoperative pain, shorter hospitalize length, and less postoperative complications in the background of a similar treatment effect. Therefore, laparoscopic resection of liver hemangioma is a safe, effective, and feasible surgical method, which is worthy of clinical application.

Author contributions

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