Available online at www.sciencedirect.com

ScienceDirect

Journal of the Chinese Medical Association 81 (2018) 429−436

www.jcma-online.com

Original Article

Laparoscopic versus open hepatectomy approach for regional hepatolithiasis: A meta-analysis

Hui Jiang [a], Ou Jiang [a,*], Xianming Xia [b], Song Su [b], Bo Li [b]

[a] Department of Hepatobiliary Pancreatic Surgery, The Second People's Hospital of Neijiang, Sichuan Medical University, Neijiang, Sichuan, China
[b] Department of Hepatobiliary Surgery, First Affiliated Hospital of Sichuan Medical University, Luzhou, Sichuan, China

Received July 16, 2016; accepted September 13, 2017

Abstract

Background: In the present study, we aimed to compare laparoscopic hepatectomy (LH) with open hepatectomy (OH) approach in patients with regional hepatolithiasis (RHL) using meta-analytical techniques.
Methods: A systematic review of the literature was performed to identify studies comparing LH and OH in the management of RHL. Operative parameters, postoperative outcomes, and postoperative complications were evaluated. Meta-analysis was performed using Review Manage Version 5.0 software.
Results: Nine studies matched the selection criteria, which included 719 patients (LH = 333 and OH = 386). LH was associated with shorter hospital stay ($p < 0.00001$), earlier oral intake ($p < 0.00001$), and fewer complications ($p = 0.01$). No significant statistical divergences were found between the LH and OH groups in terms of operative time ($p = 0.48$), blood loss ($p = 0.07$), intraoperative transfusion rate (p = 0.69), initial stone clearance rate ($p = 0.33$), and postoperative stone recurrence rate ($p = 0.23$).
Conclusion: LH for regional hepatolithiasis appears to be a promising treatment modality for patients with intrahepatic stones. However, large numbers of patients and prospective, randomized, controlled studies are required to lead to a more comprehensive comparison of the two procedures.

Keywords: Hepatectomy; Hepatolithiasis; Laparoscopy

1. Introduction

Hepatolithiasis is a disease endemic to Southeast Asian countries.[1] Regional hepatolithiasis (RHL) was defined as stones locally distributed in one or several hepatic segments along the intrahepatic biliary tree, which is often complicated with hepatic duct stenosis in the affected area, as well as with atrophy of the involved hepatic segments.[2] Hepatectomy is deemed to be the most effective strategy for regional hepatolithiasis because it can simultaneously remove stones and biliary stricture, thus reducing the risk of recurring stones.[3,4]

Laparoscopic hepatectomy (LH) was first introduced by Garner et al., in 1992. Since then, laparoscopic surgery has been increasingly reported.[5−7] Although LH has been advocated because of its advantages in the treatment of patients with RHL, only a few firm evidences supporting its safety and usefulness are available. To our knowledge, only a few trials have compared the outcomes of LH with those of OH in patients with RHL,[8−16] and the use of laparoscopic surgery for the treatment of RHL remains controversial because of its technical difficulty and insufficient data associated with stone clearance.

Therefore, in the present study, a systematic review and a meta-analysis were conducted, which aimed to evaluate the technical safety and oncologic feasibility of laparoscopic

Conflicts of interest: The authors declare that they have no conflicts of interest related to the subject matter or materials discussed in this article.

* Corresponding author. Dr. Ou Jiang, Department of Hepatobiliary Pancreatic Surgery, The Second people's Hospital of Neijiang, Sichuan Medical University, Neijiang, Sichuan, China.
E-mail address: jiangouer@163.com (O. Jiang).

https://doi.org/10.1016/j.jcma.2017.09.007

surgery for the treatment of RHL compared with that of conventional OH from published literature.

2. Methods

2.1. Study selection

A systematic review of four databases, including PubMed/Medline, Ovid, Embase, and Cochrane library databases was conducted to identify all studies published up to December 2015 that compared LH with OH for patients with RHL. We adhered to the 2009 preferred reporting items for systematic reviews and meta-analysis (PRISMA) statement. The following MeSH terms were used: "Laparoscopy" or "hepatolithiasis" or "hepatectomy" and "open" or "hepatectomy" and "hepatolithiasis." References from the retrieved articles were also manually reviewed for data extraction. Two authors independently carried out the electronic bibliographic research in accordance with the validated methods of the PRISMA statement.[17]

2.2. Inclusion and exclusion criteria

Inclusion criteria for all eligible studies included that comparison of the outcomes of LH with that of OH for patients with RHL and reporting at least one of the measured outcomes that were referred to as follows: when two studies containing overlapping patients were reported from the same institution or authors, either the higher quality paper or the most recent publication was included in the analysis unless an older publication had more measured outcomes or an RCT publication. The exclusion criteria included studies that contained limited information, cases reports, and results that were not published in English language.

2.3. Data extraction

Relevant data including authors' names, published journals, study duration, participant demographics, measured outcomes, and duration of follow-up were extracted and documented on a separate sheet for each publication. If possible, the first or corresponding author was contacted to obtain supplementary information in case of missing data or inaccurate information.

2.4. Outcome of interest

The following outcomes were used to compare LH with OH:

1. Operative parameters: operative time (min), blood loss (ml), transfusion rate, and initial stone clearance rate.
2. Postoperative outcomes: length of hospital stay (day), time to return to oral intake (day), and stone recurrence rate.
3. Postoperative complications

2.5. Quality assessment

Checklists were used for the extraction of data and for the assessment of the methodological quality by the reviewers. The methodological quality of the eligible RCTs was assessed by individual components on the basis of the Cochrane risk of bias tool[18] and that of the non-RCTs was assessed by the modified Newcastle–Ottawa score,[19] which allocates a maximum of nine points each to patient selection, comparability of the two groups (LH and OH), and outcome assessment. Two authors independently examined the studies. The same consensual process mentioned above was used to resolve disagreement.

2.6. Statistical analysis

The Review Manager 5.0 statistical package was used to perform statistical analysis of the data, and heterogeneity was assessed between studies using I2, with $p < 0.10$ for the test level of statistical significance. Meta-analysis of continuous variables was conducted with the inverse–variance statistical method using mean difference (MD), whereas dichotomous variables were analyzed using the Mantel–Haenszel statistical method using odds ratio (OR) as the summary statistic. Both were reported with confidence intervals (CI) of 95%. The MD and OR were both considered to be statistically significant at the level of $p < 0.05$ if the 95% CI did not include the value "1".

3. Results

3.1. Characteristics of all eligible studies

The PRISMA flow chart of literature review is summarized in Fig. 1. A total of 92 potential articles published between 1999 and 2015 were identified from the literature searches. Of these, 13 articles were selected on the basis of their titles and abstracts, and a holistic examination of the text was performed. Nine[8–16] studies including one RCT[14] matched the selection criteria and were suitable for meta-analysis, including 719 patients (LH = 333, OH = 386), respectively. The characteristics of these studies and methodological quality assessment scores are summarized in Table 1.

3.2. Measured outcomes

Meta-analysis results from all eligible studies that compared LH with OH with respect to surgery-related parameters, postoperative parameters, and postoperative complications are summarized in Table 2.

3.3. Surgery-related parameters

All the nine[8–16] studies reported data on operative time, and the meta-analysis revealed that no statistical difference was found between LH and OH (MD = 6.28; 95% CI, from −11.03 to 23.59; Fig. 2A), although there was heterogeneity between studies ($p < 0.0001$) and no difference was found when a fixed-effects model was used. Seven studies[8–12,14,16] reported on the blood loss, which was found to be less in the LH group compared with the OH one by 63.03 ml (95%

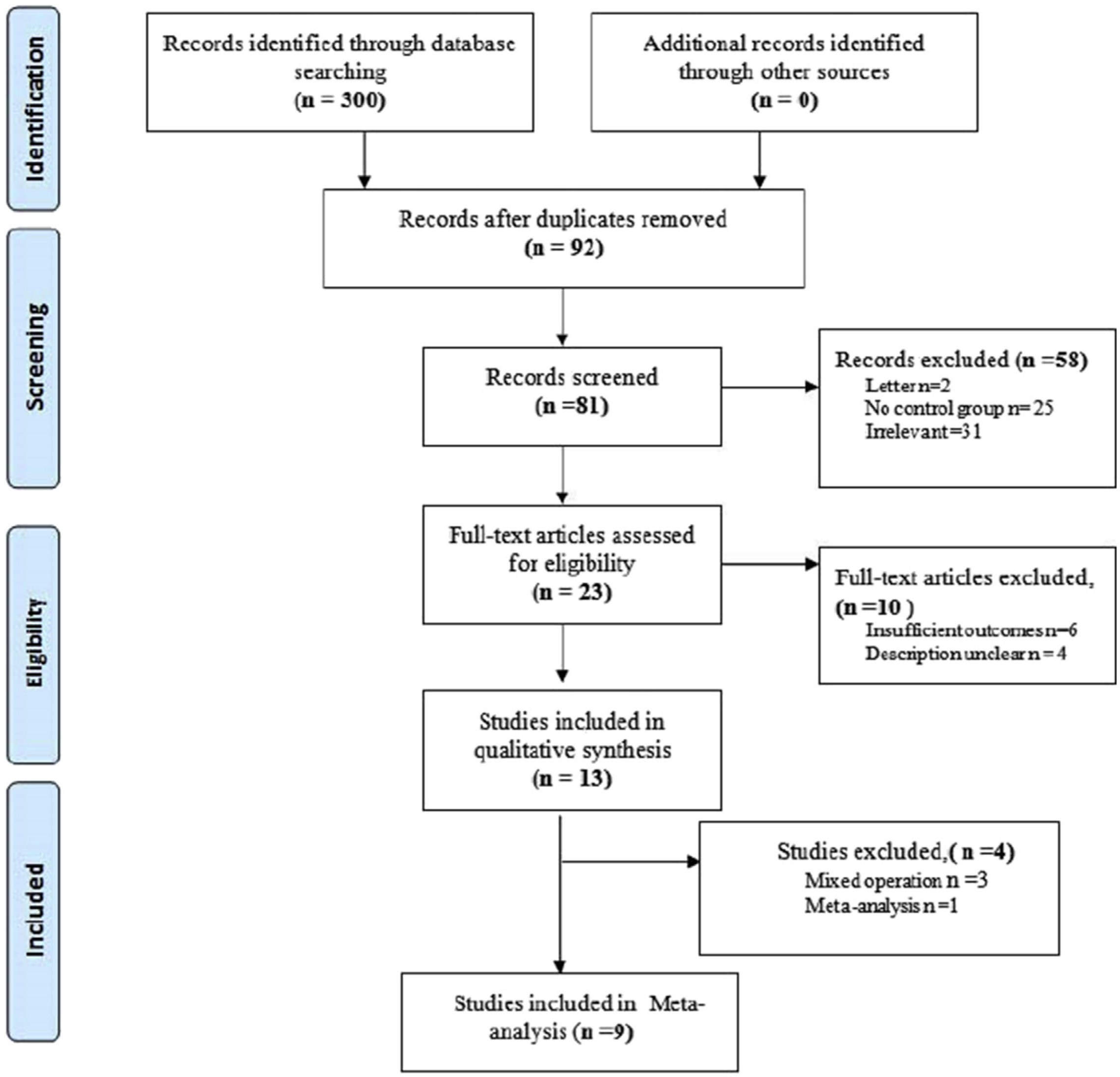

Fig. 1. The PRISMA flowchart of literature review.

Table 1
Patient demographics of all included studies.

Authors (year)	Study type	Patients (n)	Age	Gender	BMI (LH/OH)Kg/m^2	Mortality (LH/OH)	Quality score
Cai *et al*.(2007)	Non-RCT	LH:29 OH:22	LH:47.9 ± 14.2 OH:51.9 ± 11.9	LH:5:24 OH:7:15	N	0/0	****
Jin Fu *et al*. (2010)	Non-RCT	LH:28 OH:33	LH (range 25–63) OH (range31–68)	LH:10/18 OH:12/21	N	0/0	********
Ju Tian *et al*. (2013)	Non-RCT	LH:116 OH:78	LH (49.4 ± 11.9) OH(49.3 ± 11.2)	LH:34/82 OH:29/49	N	N/N	******
Sang lee *et al*. (2014)	Non-RCT	LH:7 OH:9	LH:(56.1 ± 5.9) OH:59.8 ± 9.0	LH:2:5 OH:2/7	LH:24.1 ± 3.9 OH:23.2 ± 3.3	N/N	********
Kim *et al*.(2015)	Non-RCT	LH:17 OH:17	LH:60.6 (mean years) OH: 63.5	LH:5/12 OH:6/11	N	N/N	******
Guoqiang *et al*. (2015).	RCT	LH:49 OH:49	LH:57.53 ± 6.31 OH: 58.42 ± 7.21	LH:22/27 OH:22/26	N	N/N	–
Namoong *et al* (2014)	Non-RCT	LH:37 OH:112	LH:53.0 ± 10.89. OH:59.1 ± 8.40	LH:9/28 OH:40/72	N	0/0	******
Shin *et al* (2016)	Non-RCT	LH:40 OH:54	LH:56.8 ± 8.2 OH:55.6 ± 9.6	LH:8/32 OH:19/35	LH:22.8 ± 2.8 OH:22.9 ± 3.0	N/N	*****
Kun Zhang *et al* (2008)	Non-RCT	LH:10 OH:12	N N	LH:N OH:N	LH:N OH:N	N/N	*****

N = Not obtained, LH = Laparoscopic Hepatectomy; OH = Open Hepatectomy; N = Not obtained.

Table 2
Pooled Analysis Comparing LH versus OH group.

Outcome of interest	Studies (n)	Patients (n)	OR/MD	95% CI	p	Heterogeneity test HG χ^2	p
Operative outcomes							
Operative time	9	719	6.28	−11.03 to 23.59	0.48	323.66	<0.00001
Blood loss	7	681	−63.03	−131.2 to 5.13	0.07	88.07	<0.00001
Transfusion rate	4	498	0.88	0.46 to 1.67	0.69	2.27	0.52
Initial stone clearance rate	6	570	1.36	0.73 to 2.54	0.33	0.72	0.98
Postoperative parameters							
Time to oral intake	2	200	−0.67	−0.91 to −0.42	**<0.00001**	1.36	0.24
Hospital stay	9	719	−4.72	−6.81 to −2.63	**<0.00001**	82.70	<0.00001
Stone recurrence rate	7	605	−0.02	−0.05 to 0.01	0.23	6.52	0.37
Postoperative complications	8	697	0.58	0.38 to 0.88	**0.01**	6.68	0.46

CI = confidence interval; HG = heterogeneity between studies; MD = weighted mean difference; OR = odds ratio; LH = laparoscopic hepatectomy; OH = open hepatectomy.

CI, from −131.20 to 5.13; Fig. 2B). However, this finding was not associated with significant difference between studies ($p = 0.07$). Blood transfusion has been illustrated in four studies,[9,11,12,16] and the meta-analysis revealed that no statistical difference was found between LH and OH in the transfusion rate (OR = 0.88; 95% CI, 0.46−1.67; $p = 0.69$; Fig. 2C), respectively. Six studies[8−12,16] analyzed the initial stone clearance rate, which was not found to be significantly different between groups (OR = 1.36; 95% CI, 0.73−2.54; $p = 0.33$; Fig. 2D).

3.4. Postoperative parameters

Most studies reported on the time to return to oral intake after surgery and suggested earlier in the LH group. Meta-analysis of available data from two studies[8,16] revealed a statistically significant earlier time to oral intake by 0.67 days in LH when compared with the OH group (95% CI, 0.46−1.67; $p < 0.0001$; Fig. 3A), but this finding was not associated with significant heterogeneity when all available studies were used for pooled analysis ($p = 0.27$). All studies[8−16] reported on the duration of hospitalization, which was found to be significantly shorter in LH group compared with the OH group by 4.72 days (95% CI, from −6.81 to −2.63; $p < 0.0001$; Fig. 3B). This finding was associated with significant heterogeneity between studies ($p < 0.0001$). Postoperative stone recurrence rate was recorded in seven studies,[8−13,16] which was found to be not significantly different in the LH group compared with the OH group (OR = −0.02; 95% CI, from −0.05 to 0.01; $p = 0.23$; Fig. 3C), and this finding was not associated with significant heterogeneity between studies ($p = 0.37$).

3.5. Postoperative complications

All included studies reported on postoperative complications. The complication in the LH group was statistically significantly lesser by 0.58 than that in the OH group (95% CI, 1.68−6.89; $p = 0.01$; Fig. 4), without significant heterogeneity between studies ($p = 0.46$).

LH was associated with shorter hospital stay ($p < 0.00001$), earlier oral intake ($p < 0.00001$), and fewer complications ($p = 0.01$). There were no significant statistical divergences observed between the LH and OH groups in terms of operative time ($p = 0.48$), blood loss ($p = 0.07$), intraoperative transfusion rate ($p = 0.69$), initial stone clearance rate ($p = 0.33$), and postoperative stone recurrence rate ($p = 0.23$).

3.6. Publication bias

The funnel plot of the present study based on postoperative overall complications is shown in Fig. 5. All studies lay inside the limits of the 95% CIs and are more evenly vertically distributed, showing no evidence of publication bias.

4. Discussion

4.1. Summary of evidence

During the past decade, the evolution of minimally invasive approaches represents one of the most significant advances in the field of surgery. Several studies have shown that laparoscopic approach to hepatectomy has been associated with a reduction in postoperative pain, morbidity, faster recovery, and early discharge compared with conventional open liver resection.[20,21] However, technological challenges attributable to adhesion to adjacent tissue or altered structure caused by chronic inflammation restrict the laparoscopic approach to hepatolithiasis. Furthermore, initial evidences in support of LH in the management of RHL were mostly in the form of single-institution case series and thus limited by their sample size. A meta-analysis that compared LH and OH had not yet been performed. In the present study, the results of the meta-analysis of the nine studies suggest that patients undergoing LH, compared with those undergoing OH, have earlier oral intake, shorter hospital stay, and fewer complications. The meta-analysis showed no statistically significant differences between the two groups in terms of operative time, estimated blood loss, intraoperative transfusion rate, initial stone clearance rate, as well as postoperative stone recurrence rate.

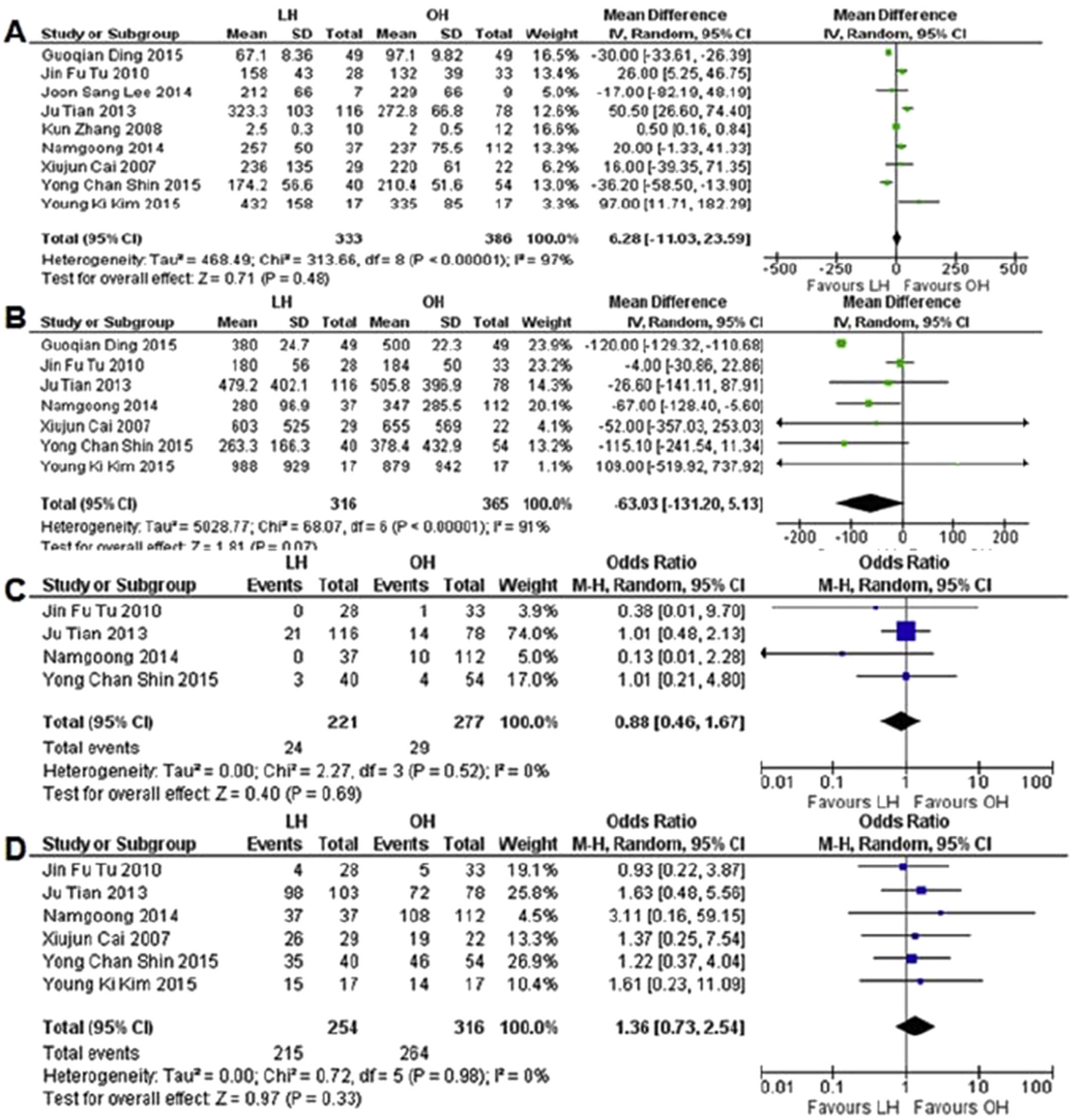

Fig. 2. Meta-analysis for operative outcomes comparing LH with Conventional OH. A operative time, B blood loss, C transfusion rate, D initial stone clearance rate. CI = confidence interval; IV = inverse variance; SD = standard deviation.

4.2. Safety and feasibility

Generally, the left lobe of the liver is vulnerable to hepatolithiasis. In cases where hepatolithiasis is restricted to only the left lobe, left hemihepatectomy is undoubtedly a suitable procedural choice. It possesses the low risk of severe operative complications and eliminates the sources of left-sided hepatolithiasis, such as strictures.[22,23] In contrast, right-sided hepatolithiasis incorporates a low incidence and commonly characterizes bile duct strictures throughout the hilar area. In addition, it carries a higher frequency of bilateral stones, thus reducing the suitability of hepatectomy as an alternative therapy.[24]

Depending on the position of the lesions, most laparoscopic hepatectomies are in fact constrained to cases when only one or two segments exist from the lateral area incorporating to

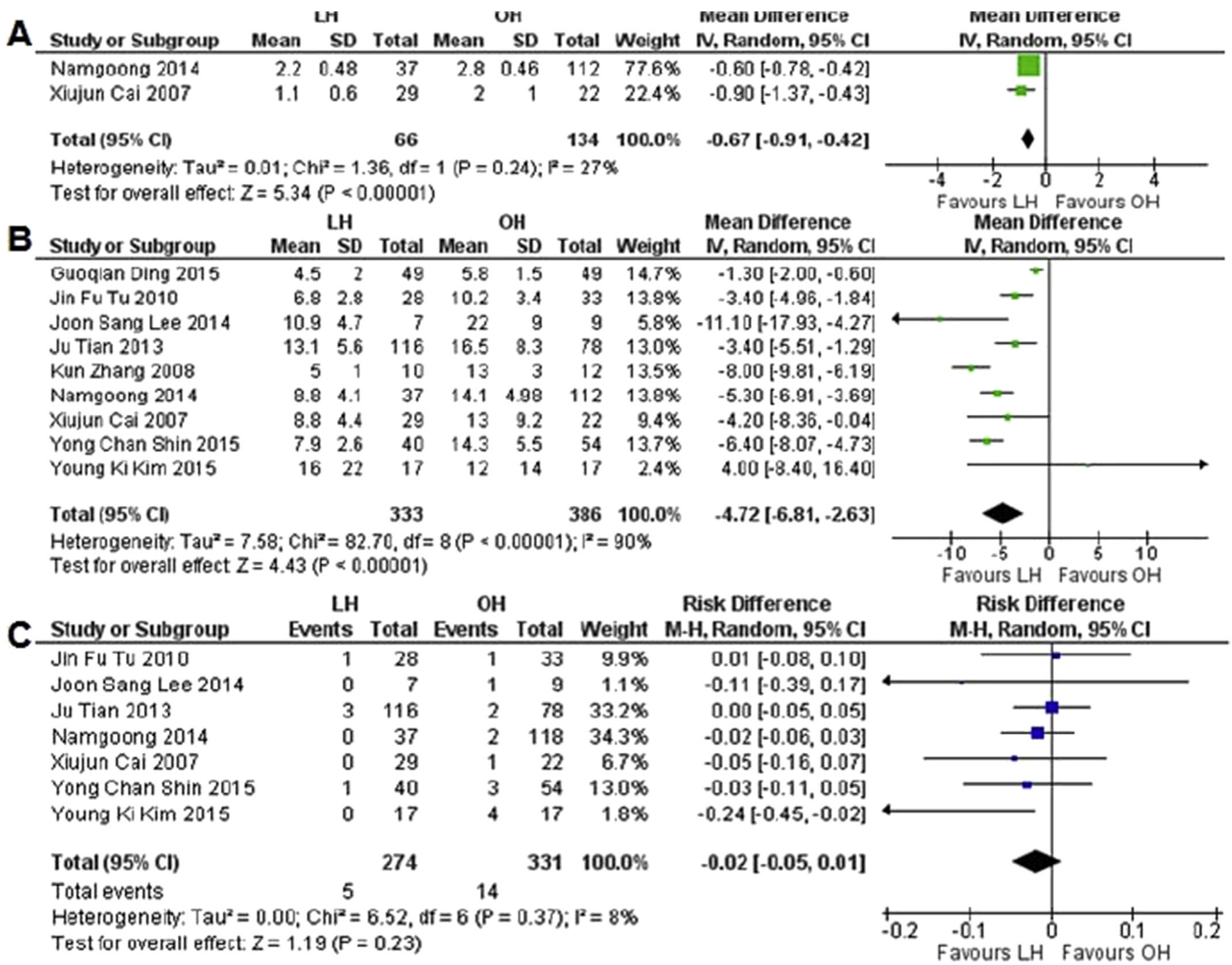

Fig. 3. Meta-analysis for Postoperative parameters comparing LH with Conventional OH. A oral intake, B hospital stay, C stone recurrence. CI = confidence interval; IV = inverse variance; SD = standard deviation.

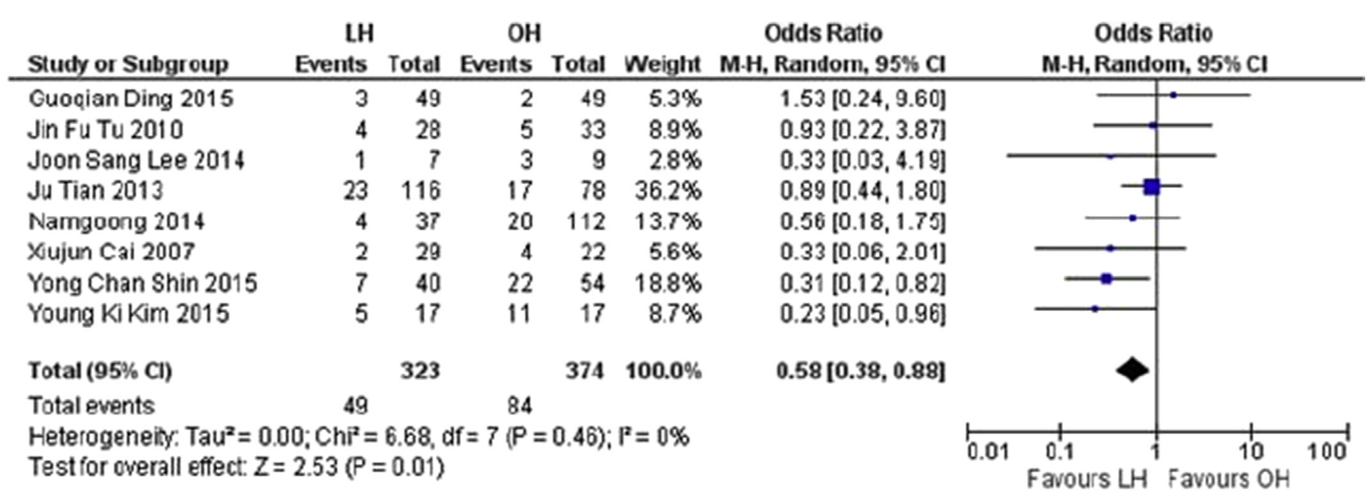

Fig. 4. Meta-analysis for Postoperative morbidity comparing LH with Conventional OH. CI = confidence interval; IV = inverse variance; SD = standard deviation.

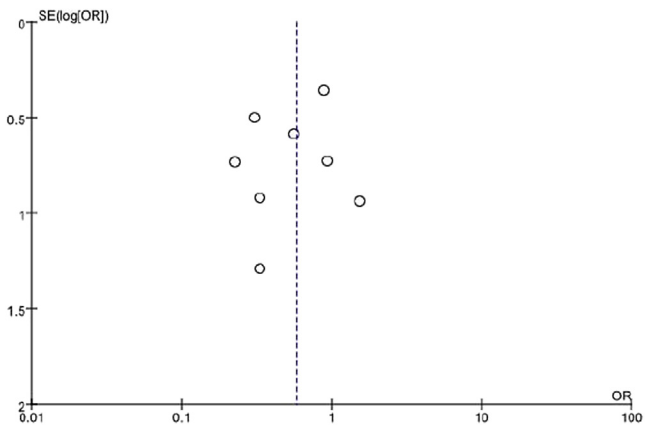

Fig. 5. Funnel plot of overall complications in included studies, showing no publication bias. OR indicates odds ratio.

Couinaud from the second to sixth segment.[16] In addition, significant laparoscopic liver resection, including right hemi-hepatectomy, was conducted by a small number of specialists, with comparable safety and effectiveness to open surgery being previously revealed only in some extremely specialized centers. Nevertheless, laparoscopic left lateral liver resection is usually recommended as a gold standard for resection of lesions positioned in the second and third segments.[25]

4.3. Limitation and recommendation

The strength of this review is acknowledged in that it provides a comprehensive comparison of LH with OH. To our knowledge, this is the first meta-analysis to expound this important issue. However, this meta-analysis has some limitations that should be taken into consideration. The strengths and limitations of meta-analytical techniques have been a source of considerable debate. Besides, only one RCT was included in the meta-analysis, and the calculated results from such non-randomized comparative studies may have numerous biases. In addition, the retrieval is limited by the language and the search terms. The retrieval may be incomplete, and some of the conclusions may require to be further validated by large sample and high-quality clinical research. Significant differences were found between the evaluation measures and measurement tools in the study group (operative time, blood loss, hospital stay), which may lead to heterogeneity among the studies. Finally, some important parameters were measured in an even smaller proportions of articles, which may lead to uncertainty of the credibility of the results.

In conclusion, pooled analysis confirmed that LH is feasible and safe for the management of RHL. In the present study, LH did not significantly differ from open surgery in terms of operative time and stone clearance rate, and it has several advantages of rapid postoperative resumption, such as earlier oral intake, shorter hospital stay, and fewer complications. However, further prospective controlled studies are required for a more comprehensive study between the two procedures in the future.

References

1. Uchiyama K, Onishi H, Tani M, Kinoshita H, Ueno M, Yamaue H. Indication and procedure for treatment of hepatolithiasis. *Arch Surg* 2002;**137**:149–53.
2. Li X, Shi L, Wang Y, Tian FZ. Middle and long-term clinical outcomes of patients with regional hepatolithiasis after subcutaneous tunnel and hepatocholangioplasty with utilization of the gallbladder. *Hepatobiliary Pancreat Dis Int* 2005;**4**:597–9.
3. Sakpal SV, Babel N, Chamberlain RS. Surgical management of hepatolithiasis. *HPB Oxf* 2009;**11**:194–202.
4. Uenishi T, Hamba H, Takemura S, Oba K, Ogawa M, Yamamoto T, et al. Outcomes of hepatic resection for hepatolithiasis. *Am J Surg* 2009;**198**:199–202.
5. Qiu J, Chen S, Pankaj P, Wu H. Laparoscopic hepatectomy for hepatic colorectal metastases–a retrospective comparative cohort analysis and literature review. *PloS one* 2013;**8**:e60153.
6. Qiu J, Chen S, Pankaj P, Wu H. Laparoscopic hepatectomy is associated with considerably less morbidity and a long-term survival similar to that of the open procedure in patients with hepatic colorectal metastases. *Surg Laparosc Endosc Percutan Tech* 2014;**24**:517–22.
7. Jin RA, Wang Y, Yu H, Liang X, Cai XJ. Total laparoscopic left hepatectomy for primary hepatolithiasis: eight-year experience in a single center. *Surgery* 2016;**159**:834–41.
8. Cai X, Wang Y, Yu H, Liang X, Peng S. Laparoscopic hepatectomy for hepatolithiasis: a feasibility and safety study in 29 patients. *Surg Endosc* 2007;**21**:1074–8.
9. Tian J, Li JW, Chen J, Fan YD, Bie P, Wang SG, et al. Laparoscopic hepatectomy with bile duct exploration for the treatment of hepatolithiasis: an experience of 116 cases. *Dig Liver Dis* 2013;**45**:493–8.
10. Kim YK, Han HS, Yoon YS, Cho JY, Lee W. Laparoscopic approach for right-sided intrahepatic duct stones: a comparative study of laparoscopic versus open treatment. *World J Surg* 2015;**39**:1224–30.
11. Shin YC, Jang JY, Kang MJ, Jung W, Chang J, Chang YR, et al. Comparison of laparoscopic versus open left-sided hepatectomy for intrahepatic duct stones. *Surg Endosc* 2016;**30**:259–65.
12. Tu JF, Jiang FZ, Zhu HL, Hu RY, Zhang WJ, Zhou ZX. Laparoscopic vs open left hepatectomy for hepatolithiasis. *World J Gastroenterol* 2010;**16**:2818–23.
13. Lee JS, Choi YS, Lee SE. Initial experience of laparoscopic hepatectomy for intrahepatic duct (IHD) stones: comparison with open hepatectomy. *J Minim Invasive Surg* 2014;**17**:68–70.
14. Ding G, Cai W, Qin M. Pure laparoscopic versus open liver resection in treatment of hepatolithiasis within the left lobes: a randomized trial study. *Surg Laparosc Endosc Percutan Tech* 2015;**25**:392–4.
15. Zhang K, Zhang SG, Jiang Y, Gao PF, Xie HY, Xie ZH. Laparoscopic hepatic left lateral lobectomy combined with fiber choledochoscopic exploration of the common bile duct and traditional open operation. *World J Gastroenterol* 2008;**14**:1133–6.
16. Namgoong JM, Kim KH, Park GC, Jung DH, Song GW, Ha TY, et al. Comparison of laparoscopic versus open left hemihepatectomy for left-sided hepatolithiasis. *Int J Med Sci* 2014;**11**:127–33.
17. Moher D, Liberati A, Tetzlaff J, Altman DG. PRISMA Group. Reprint–preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *Phys Ther* 2009;**89**:873–80.
18. Higgins JPT, Green S. *Cochrane handbook for systematic reviews of interventions. Version 5.0.2. Cochrane Collaboration 2009*. Available at: http://www.cochrane-handbook.org. [Accessed 30 January 2012].
19. Stang A. Critical evaluation of the Newcastle-Ottawa scale for the assessment of the quality of nonrandomized studies in meta-analyses. *Eur J Epidemiol* 2010;**25**:603–5.
20. Luo L, Zou H, Yao Y, Huang X. Laparoscopic versus open hepatectomy for hepatocellular carcinoma: short- and long-term outcomes comparison. *Int J Clin Exp Med* 2015;**8**:18772–8.
21. Wang XT, Wang HG, Duan WD, Wu CY, Chen MY, Li H, et al. Pure laparoscopic versus open liver resection for primary liver carcinoma in elderly patients: a single-center, case-matched study. *Med Baltim* 2015;**94**:e1854.

22. Cheong O, Hwang S, Song GW, Kim JH, Ha TY, Lee YJ, et al. Analysis on the clinical significance of biliary exploration through the left hepatic duct opening during left hepatectomy for the patients with hepatolithiasis. *Korean J Hepatobiliary Pancreat Surg* 2005;**9**:203−9.
23. Hwang JH, Yoon YB, Kim YT, Cheon JH, Jeong JB. Risk factors for recurrent cholangitis after initial hepatolithiasis treatment. *J Clin Gastroenterol* 2004;**38**:364−7.
24. Ha TK, Choi CS, Choi YK, Paik NW. Hepatic resection for right sided intrahepatic stones. *Korean J HBP Surg* 2005;**9**:31−5.
25. Dokmak S, Raut V, Aussilhou B, Ftériche FS, Farges O, Sauvanet A, et al. *Laparoscopic left lateral resection is the gold standard for benign liver lesions: a case-control study.* Oxford: HPB; 2013.