

Comparing laparoscopic and open resection in elderly hepatocellular carcinoma: a systematic review and meta-analysis

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Background: Laparoscopic liver resection (LLR) has been accepted as a safe and effective treatment for hepatocellular carcinoma (HCC). However, its impact on elderly patients remains uncertain. This study aimed to compare the efficacy and safety of LLR with open liver resection (OLR) in elderly HCC patients. **Methods:** We conducted a search across the Ovid-Medline, Ovid-EMBASE, and Cochrane Library to identify comparative studies involving primary HCC in elderly patients (≥65 years). Efficacy-related outcomes encompassed overall survival (OS) and disease-free survival (DFS), while safety-related outcomes included post-operative mortality, complications, and length of stay (LOS).

Results: We identified nine eligible cohort studies comprising 1,599 patients. LLR demonstrated comparable 3- and 5-year DFS [hazard ratio (HR) =1.00, 95% confidence interval (CI): 0.98–1.02; HR =1.02, 95% CI: 0.99–1.05] and 3- and 5-year OS (HR =1.01, 95% CI: 0.99–1.02; HR =1.02, 95% CI: 0.99–1.06, respectively) compared to OLR. In terms of safety, there was no significant difference between LLR and OLR in in-hospital mortality [odds ratio (OR) =0.19; 95% CI: 0.02–1.69], 30-day mortality (OR =0.33; 95% CI: 0.03–3.20), and 90-day mortality (OR =0.70; 95% CI: 0.32–1.53). Additionally, LLR presented fewer overall complications (OR =0.53; 95% CI: 0.41–0.67), a lower rate of major complications (OR =0.51; 95% CI: 0.35–0.74), a reduced incidence of liver failure (OR =0.56; 95% CI: 0.33–0.94), and a shorter LOS compared to OLR (mean difference: –14.47 days).

Conclusions: LLR exhibited comparable clinical efficacy and superior safety and fewer complications when compared to OLR in elderly patients with HCC requiring surgery.

Keywords: Elderly; efficacy; safety; resection; laparoscopic

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Introduction

Hepatocellular carcinoma (HCC) poses a significant global health challenge, ranking as the sixth most common malignancy worldwide and serving as a major contributor to cancer-related morbidity and mortality (1). Moreover, the global aging population has contributed to a rising number of elderly individuals diagnosed with HCC, highlighting the importance of this demographic group in disease management (2,3).

The therapeutic approach to HCC varies significantly, encompassing a spectrum of treatments, including transplantation, locoregional therapies, and surgical resection. The choice of treatment depends on factors such as the disease stage, extent, and the patient's overall health (4,5). Among these options, surgical resection has emerged as a primary curative strategy for HCC, offering the potential for long-term survival and disease control (6-9). In the context of an aging population, a critical question arises: "What is the most effective and safest surgical approach for hepatocellular carcinoma in elderly patients?"

Two prominent surgical techniques for HCC resection are laparoscopic liver resection (LLR) and open liver

Highlight box

Key findings

The key findings indicate that laparoscopic liver resection (LLR) is associated with significantly fewer complications, both major and minor, as well as a reduced incidence of postoperative ascites, and shorter length of hospital stay compared to open liver resection (OLR). No significant difference was found in long-term survival rates (overall survival and disease-free survival) between LLR and OLR.

What is known and what is new?

- Surgical resection, including LLR and OLR, is a primary curative strategy for hepatocellular carcinoma (HCC). The effectiveness and safety of these procedures in elderly patients, however, had not been comprehensively analyzed.
- This study provides new insights by specifically comparing LLR and OLR in elderly patients with HCC, highlighting the advantages of LLR in terms of lower complication rates and shorter hospital stays.

What is the implication, and what should change now?

 The findings suggest that LLR may be a safer and more suitable alternative to OLR for elderly patients with HCC. Given the reduced complications and shorter recovery time, clinicians and surgical teams should consider LLR as the preferred surgical approach in this demographic, enhancing patient care and potentially improving outcomes. resection (OLR). LLR, a minimally invasive surgery, has gained popularity over the last two decades due to its potential advantages, including reduced postoperative pain, shorter hospital stays, and faster recovery (9-11). In contrast, OLR represents the conventional surgical approach, affording the surgeon a direct and tactile perception of the liver, which allows for better control of bleeding and potential complications (12). The decision-making process regarding the choice of surgical approach is particularly complex in elderly patients who commonly have a unique set of challenges like comorbidities, compromised physiological reserves, and altered responses to surgical stressors (13). As the elderly population continues to grow, optimizing the management of HCC in this demographic becomes increasingly important.

This systematic review and meta-analysis aimed to fill the knowledge gap by systematically comparing the efficacy and safety of LLR and OLR for HCC in elderly patients (≥65 years). Through a comprehensive review and synthesis of existing evidence, we aimed to offer valuable insights that can assist clinicians and surgical teams in making informed decisions regarding the surgical approach for this specific patient population. We present this article in accordance with the PRISMA reporting checklist (available at https://jgo.amegroups.com/article/view/10.21037/jgo-24-67/rc).

Methods

The methods for selecting articles, conducting data analysis, and reporting the results of the meta-analysis were predetermined in the protocol. The protocol was registered on the PROSPERO (registration number CRD42022301691). Ethics approval for this study was waived from the IRB of National Evidence-based Healthcare Collaborating Agency (NECA).

Search strategy

We conducted a comprehensive search for studies comparing LLR with OLR in the treatment of elderly patients with HCC up until March 2022. We utilized the Ovid-Medline, Ovid-EMBASE, and Cochrane Library databases, with no restrictions on publication year or language. Our search strategy combined Medical Subject Headings (MESH) terms such as "hepatocellular carcinoma", "aged", and "hepatectomy" as well as related terms. To efficiently identify randomized controlled trials and observational studies, we applied the search filter

recommended by the Scottish Intercollegiate Guidelines Network. Furthermore, we scrutinized the bibliographies of relevant articles to identify any additional publications. For a detailed breakdown of our search strategy and results for each database, please refer to the Tables S1-S3.

Inclusion and exclusion criteria

In our study, we focused exclusively on patients undergoing primary surgical treatment for_HCC and did not include cases of re-hepatectomy. Two independent reviewers (I.I.Y. and S.R.) conducted an initial screening of titles and abstracts to exclude irrelevant studies. Subsequently, a thorough fulltext review of potentially relevant articles was performed. The inclusion criteria were defined as follows: (I) studies focusing on elderly patients (≥65 years) with primary HCC; (II) comparative studies between LLR (laparoscopic or robotic) and OLR for elective surgical procedures; (III) studies reporting at least one of our predetermined outcomes of interest; and (IV) original, peer-reviewed articles that had been published. The exclusion criteria encompassed: (I) studies involving inappropriate populations, such as those with stage IV HCC, recurrent HCC or re-hepatectomy, liver metastasis, or specific situations like human immunodeficiency virus (HIV) infection; (II) studies related to emergency surgery or palliative treatment; (III) nonoriginal articles, including reviews, editorials, letters, etc.; (IV) publications consisting solely of abstracts; (V) studies published in languages other than English or Korean; and (VI) duplicate publications. Any discrepancies in the review process were resolved through discussion and consensus, with the involvement of additional reviewers when necessary.

Data extraction and quality assessment

We employed the Methodological Index for Non-randomized Studies (MINORS) (14) to evaluate the quality of non-randomized surgical studies. Quality assessments were conducted independently by two researchers (D.A.P. and S.R.). Any discrepancies in assessment were resolved through consensus among all the authors. The data extraction encompassed the following categories: (I) study characteristics, including study design, country, study center, etc.; (II) participant characteristics, such as the disease, age cutoff point, stage, and proportion of males; (III) intervention details, including the type and scope of surgery; (IV) outcomes, which comprised survival outcomes at 3- and 5-year intervals, encompassing overall survival

(OS) and disease-free survival (DFS), as well as postoperative mortality at 30 days, 90 days, and in-hospital, liver failure-related mortality, overall complication rate, major/minor post-operative complication rate, individual post-operative complications, including liver failure, heart failure, respiratory failure, renal failure, ascites, hemorrhage, wound infection, intra-abdominal abscess, re-operation rate, recurrence rate, re-hospitalization rate, and patient-reported outcomes. Major complications were defined as Clavien-Dindo grade III or higher, while minor complications were defined as Clavien-Dindo grades I-II. Additionally, we considered the descriptions provided by the authors of the primary research papers. Two independent reviewers extracted the variables listed above using a predefined data extraction form, and a double-check was performed to ensure accuracy. In cases where the primary research paper did not provide relevant data, we extracted survival rates and median survival times using the "Ungraph" program. To mitigate selection bias, we gave preference to extracting and utilizing matching data from matched studies.

Statistical analysis

Survival results were presented using descriptive statistics, relying on median survival time and 5-year survival rate data extracted from the literature. When applicable, we conducted meta-analyses employing a random-effects model, utilizing either the generic inverse variance method or the Mantel-Haenszel method to convey the impact of a variable on survival in terms of hazard ratios (HRs) or odds ratios (ORs) with accompanying 95% confidence intervals (CIs). To assess statistical heterogeneity, we employed Cochran and I² statistics. Statistical heterogeneity was analyzed through a chi-squared test, with a significance threshold set at a P value <0.10 in the I² test (15). An I² value exceeding 50% was considered substantial evidence of statistical heterogeneity (16). Subgroup and sensitivity analyses_were conducted to elucidate any heterogeneity among studies, when statistically significant, or to explore treatment effects based on specific study characteristics. Variables considered in the subgroup or sensitivity analysis included patient characteristics (age cutoff, tumor stage), intervention details [proportion of minor liver resection (LR)], general study characteristics (country, study design, number of adjusted variables), and methodological factors. Subgroup analyses were performed when there were five or more articles, as a small number of studies can

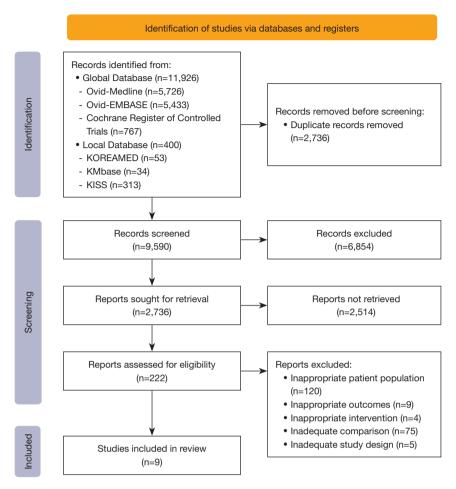


Figure 1 Flow diagram of study selection.

yield misleading results. Sensitivity analysis was executed exclusively on matched studies and those with median MINORS scores. Unfortunately, a sensitivity analysis involving studies exclusively on super-elderly patients (>80 years) was infeasible due to a lack of relevant studies. For analyses involving more than 10 studies, we planned to assess publication bias and utilized the contour-enhanced funnel plot and Egger's test. For conducting the metanalysis, we utilized RevMan version 5.4 (The Cochrane Collaboration, Oxford, UK). The threshold for statistical significance was set at 5%.

Results

Study characteristics

We initially identified 2,736 potentially relevant studies from electronic databases and meticulously screened them, resulting in the selection of 222 studies for full-text review (Figure 1). Of these, 213 were excluded, leaving 9 studies included in this review. Table 1 offers an overview of these 9 studies, encompassing a total of 1,599 patients (17-25). All included studies were retrospective observational cohort studies. Notably, 8 of these studies employed propensity score matching analysis to compare LLR and OLR outcomes. Seven of the studies were conducted in Asian countries. Age criteria for defining elderly patients varied, with five papers (55.6%) using a cutoff of 70 years, while two papers (22.2%) used criteria of 75 and 65 years of age.

Quality assessment

In the quality assessment of the included cohort studies, most of the 12 items received a rating of two points, with the exception of consecutive population sampling and prospective data collection (Figure S1). The median

Table 1 General characteristics of included studies

Author, year	Country/	Study	Study center	Enroll period	Study populations	Elderly	Z (Proportion of minor LR [†]	tion of	MINORS	Robotic	Hybrid
•	region	design	•			(years)	(LLR/OLR)	LLR	OLR	score	surgery	approach
Monden, 2022 (17)	Japan	RC, PSM	Single center	2010–2021	Aged ≥70 years newly diagnosed with HCC who underwent LLR and OLR	20	75/75	%2'06	92.0%	23	Not mentioned	Excluded
Delvecchio, 2021 (18)	Europe	RC, PSM	Multi-center (n=8)	2009–2019	Elderly patients with HCC	20	219/219	81.7%	80.8%	21	Not mentioned	Not mentioned
Wen, 2021 (19)	China	RC, PSM	Single center	2015–2018	Patients over 65 years old who underwent liver resection	92	71/71	94.4%	91.5%	21	Not mentioned	Not mentioned
Chen, 2020 (20)	China	RC, PSM	Single center	2013–2018	Patients with primary HCC aged 70 years or older who underwent radical hepatectomy	70	64/64	100%	100%	20	Not mentioned	Not mentioned
Dumronggittigule, 2020 (21)	Korea	RC, PSM	Single center	2003–2018	HCC patients aged ≥70 years after hepatectomy	20	41/41	53.7%	56.1%	21	Excluded	Not mentioned
Kim, 2020 (22)	Korea	RC, PSM	Single center	2013–2017	Elderly patients with solitary treatment-naive HCC underwent liver resection	92	96/160	51.1%	%0.99	2	Excluded	Not mentioned
Nomi, 2020 (23)	Japan	RC, PSM	Multi-center (n=9)	2010–2017	Elderly patients who underwent liver resection for HCC	75	155/155	Mixed	Mixed	21	Not mentioned	Not mentioned
Goh, 2018 (24)	Singapore	Singapore RC, PSM	Single center	2005–2016	Consecutive patients who underwent LMH for HCC	20	32/32	100%	100%	12	Not mentioned	Not mentioned
Amato, 2017 (25)	Italy	RC	Single center	2010–2014	Elderly patients underwent hepatic resections for HCC	75	11/18	100%	88.9%	6	Not mentioned	Excluded

⁺, minor LR: <3 adjacent segment resection. LLR, laparoscopic liver resection; OLR, open liver resection; LR, liver resection; MINORS, Methodological Index for Nonrandomized Studies; RC, retrospective cohort; PSM, propensity score match; HCC, hepatocellular carcinoma; LMH, laparoscopic major hepatectomy.

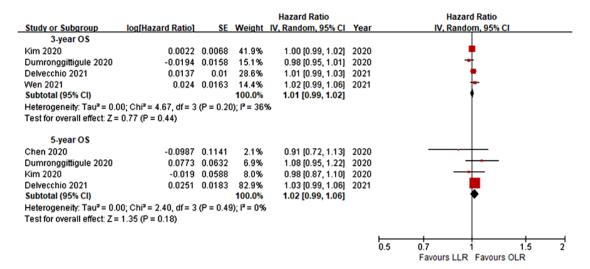


Figure 2 Meta-analysis results on overall survival. SE, standard error; CI, confidence interval; OS, overall survival; LLR, laparoscopic liver resection; OLR, open liver resection.

MINORS score for the assessed values in the 9 studies was 21 points.

 I^2 =0%) and 5-year DFS (HR =1.02; 95% CI: 0.99–1.05; I^2 =0%) (*Figure 3*).

OS

OS data were available in 5 papers, with median survival times identified in four of them, although the 50% survival rate reference point was not reached. In one study, the survival range was reported as 41.1 months in the LLR group and 39.1 months in the OLR group. Four papers provided data on the 3-year survival rates, ranging from 66.9% to 91.0% in the LLR group and 60.5% to 94.6% in the OLR group. For the 5-year survival rate, it ranged from 62.0% to 86.7% in the LLR group and 59.0% to 87.0% in the OLR group. Pooled analyses showed no significant difference between the two groups for both 3-year (HR =1.01; 95% CI: 0.99–1.02; I²=36%) and 5-year survival rates (HR =1.02; 95% CI: 0.99–1.06; I²=0) (Figure 2).

DFS

DFS data were available in five papers, and we extracted the 3- and 5-year DFS rates from papers. The 3-year DFS rate ranged from 48.1% to 71.5% in the LLR group and 49.3% to 58.1% in the OLR group. For the 5-year DFS rate, it varied from 43.4% to 66.0% in the LLR group and 30.8% to 57.0% in the OLR group. Pooled analyses indicated no significant difference between the two groups for both 3-year DFS (HR =1.00; 95% CI: 0.98–1.02;

Post-operative short-term mortality

Eight studies provided data on the 90-day post-operative mortality rate, while two studies reported 30-day mortality, and one study reported in-hospital mortality. No significant differences were observed between the two groups in terms of 90-day post-operative mortality (OR =0.70; 95% CI: 0.32–1.53; I²=0%), 30-day mortality [OR =0.33; 95% CI: 0.03–3.20; I²= not available (NA)], and in-hospital mortality (OR =0.19; 95% CI: 0.02–1.69; I²= NA) (*Figure 4*). Subgroup analysis results for 90-day mortality across all subgroups based on cutoff age and LR type were consistent with the main findings (Table S4).

Post-operative complication rate

The overall complication rate was significantly lower in the LLR group compared to the OLR group (OR =0.53; 95% CI: 0.41–0.67; I^2 =0%, *Figure 5A*). Also, incidence of major complication was significantly lower in LLR group (OR =0.51; 95% CI: 0.35–0.74; I^2 =0%, *Figure 5B*). Subgroup analysis based on age cutoff, type of LR, and countries also showed consistent results (Table S5). Additionally, the post-operative minor complication rate was significantly lower in the LLR group than in the OLR group (OR =0.72; 95% CI: 0.54–0.94; I^2 =0%, *Figure 5C*).

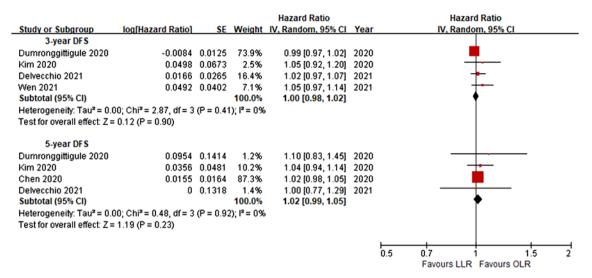


Figure 3 Meta-analysis results on disease-free survival. SE, standard error; CI, confidence interval; DFS, disease-free survival; LLR, laparoscopic liver resection; OLR, open liver resection.

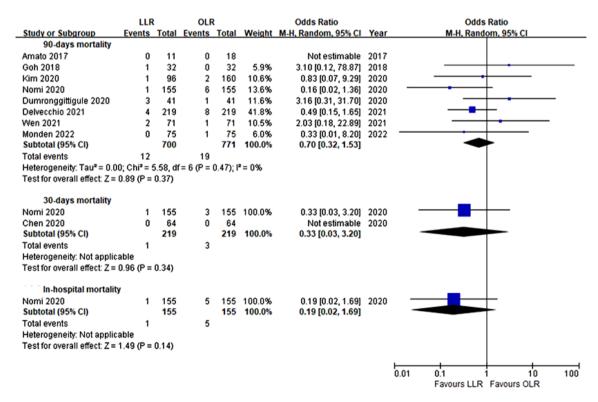


Figure 4 Meta-analysis results on post-operative short-term mortality. LLR, laparoscopic liver resection; OLR, open liver resection; M-H, Mantel-Haenszel; CI, confidence interval.

A Overall complication Experimental Laparoscopic Control Open Odds Ratio Odds Ratio Study or Subgro Events Total Events Total Weight M Random, 95% CI Year M-H, Random, 95% Amato 2017 11 18 0.7% 0.08 (0.00 1.66) 2017 Goh 2018 32 64 5.0% 0.64 [0.22, 1.88] 2018 Chen 2020 10 11 6.7% 0.89 [0.35, 2.28] 155 41 96 57 17 27 Nomi 2020 27 155 21.2% 0.36 [0.21, 0.61] 2020 Dumronggittigule 2020 14 Kim 2020 9.8% 160 0.57 (0.26. 1.24) 2020 Delvecchio 2021 Wen 2021 82 219 110 219 40.7% 0.59 [0.41, 0.87] 2021 0.34 [0.15, 0.79] 2021 71 61 8.5% Total (95% CI) 680 760 100.0% 0.53 [0.41, 0.67] Total events 199 300 Heterogeneity Tau* = 0.00: Chi* = 6.69 df = 7 (P = 0.46): 12 = 0% 100 Test for overall effect: Z = 5.19 (P Favours Laparoscopic LR Favours Open LR **B** Major complication Experimental Laparoscopic Control Open Odds Ratio Odds Ratio Total Events I, Random, 95% CI Year Study or Subgroup Events Total M-H, Random, 95% CI Amato 2017 18 Not estimable 2017 Goh 2018 .55 [0.24, 9.97] Kim 2020 96 10 160 9.9% 0.65 [0.20, 2.14] 2020 15.1% 0.62 [0.24, 1.63] 0.49 [0.04, 5.57] Dumronggittigule 2020 Chen 2020 41 64 41 64 2020 2020 Nomi 2020 12 155 35 26 155 28.5% 0.29 (0.14, 0.58) 2020 Wen 2021 71 75 3.5% 1.00 (0.14, 7.30) 2021 Monden 2022 1.27 [0.33, 4.92] 2022 Total (95% CI) 764 835 100.0% 0.51 [0.35, 0.74] 95 Heterogeneity: Tau² = 0.00; Chi² = 6.51, df = 7 (P = 0.48); I² = 0% 0.01 100 0 1 Test for overall effect: Z = 3.52 (P = 0.0004) Favours Laparoscopic LR Favours Open LR C Minor complication Experimental Laparoscopic Control Open Odds Ratio Odds Ratio H, Random, 95% Cl Year 0.08 [0.00, 1.66] 2017 Study or Subgrou Events Total Events Weight M-H, Random, 95% C Amato 2017 11 18 0.8% Goh 2018 32 32 5.0% 0.47 [0.14, 1.61] 2018 Nomi 2020 22 Dumronggittigule 2020 41 41 3.1% 1.37 [0.29, 6.54] 2020 Kim 2020 Chen 2020 96 64 17 160 8.1% 7.6% 0.56 [0.21, 1.48] 2020 64 Wen 2021 46 71 58 12.6% 0.41 (0.19 0.89) 2021 Delvecchio 2021 219 74 219 0.88 [0.59, 1.32] 2021 Total (95% CI) 0.72 [0.54, 0.94] 689 760 100.0% Total events 153 Heterogeneity: Tau2 = 0.00: Chi2 = 6.86. df: $(P = 0.44): I^2 = 0\%$ 0.01 0 1 10 100 Test for overall effect: Z = 2.38 (P Favours Laparoscopic LR Favours Open LR D Post-operative liver failure Experimental Laparoscopic Control Open Odds Ratio Odds Ratio Study or Subgroup Total Events , Random, 95% CI Year M-H, Random, 95% CI Dumrongaittiqule 2020 41 41 13.6% 0.78 [0.19, 3.13] 2020 64 155 5.0% 27.3% 3.10 [0.31, 30.61] 2020 0.41 [0.15, 1.08] 2020 Chen 2020 155 Nomi 2020 Wen 2021 71 71 4.5% 0.49 (0.04.5.56) 2021 Delvecchio 2021 22 49.6% Monden 2022 0 75 0 Not estimable 2022 625 625 100.0% 0.56 [0.33, 0.94] Total events 26 Heterogeneity: Tau* = 0.00; Chi* = 2.83, df: Test for overall effect: Z = 2.21 (P = 0.03) 100 Favours Laparoscopic LR Favours Open LR E Length of stay Mean Difference Experimental Control Mean Difference Study or Subgroup SD Total Mean SD Total Weight IV. Random, 95% CI Year IV. Random, 95% C Amato 2017 5.7 -2.52 [-3.00, -2.04] 2017 3.18 0.4 11 0.9 18 16.1% Goh 2018 9.25 6.25 32 11.75 32 15.1% -2.50 [-5.56, 0.56] -3.25 [-4.70. -1.80] Chen 2020 12 3.5 64 15.25 4.75 64 15.9% 2020 2.47 41 -2.00 [-3.25, -0.75] Dumronggittigule 2020 16.0% Nomi 2020 30.75 15.5 155 105 63.33 155 9.2% -74.25 [-84.51.-63.99] 2020 14.75 28.67 Delvecchio 2021 Monden 2022 18.25 8.5 75 28.5 13 75 14.8% -10.25 [-13.77, -6.73] Total (95% CI) 469 476 100.0% -14.47 [-19.20, -9.74] Heterogeneity: Tau2 = 36.03; Chi2 = 317.85, df = 6 (P < 0.00001); I2 = 98% -100 100 -50 Test for overall effect: Z = 6.00 (P < 0.00001) Favours LLR

Figure 5 Meta-analysis results on post-operative complication and hospital stay. (A) Overall complication. (B) Major complication. (C) Minor complication. (D) Post-operative liver failure. (E) Length of stay. M-H, Mantel-Haenszel; CI, confidence interval; LR, liver resection; LLR, laparoscopic liver resection; OLR, open liver resection.

Post-operative individual complication rate

When considering specific complications, the incidence of post-operative liver failure was significantly lower in the LLR group compared to the OLR group (OR =0.56; 95% CI: 0.33–0.94; I²=0%, *Figure 5D*). In addition, it was possible to analyze the occurrence of ascites, wound infection, respiratory complication, bile leak, and bleeding (Table S6). The occurrence of ascites (OR =0.63), wound infection (OR =0.47), respiratory complication (OR =0.31), bile leak (OR =0.45), and bleeding (OR =0.65) all tended to be lower in the LLR group compared to the OLR group. Among these, the incidence of respiratory complications was statistically significantly lower in the LLR group (OR =0.31; 95% CI: 0.16–0.59; I²=0%).

Length of hospital stay

Regarding the length of stay (LOS), we identified 8 papers; however, a meta-analysis was not feasible due to most of them reporting median and range data. Nevertheless, all the studies consistently reported a significantly shorter hospitalization duration in the LLR group. Specifically, the median hospitalization periods for the LLR and OLR groups were 7 (range, 1–97) and 10 (range, 4–386) days, respectively. In an exploratory integrated analysis following data conversion, the LLR group exhibited a significantly shorter hospitalization period compared to the OLR group, although there was a high degree of heterogeneity among the studies (mean difference: –14.47 days; 95% CI: –19.20 to –9.74 days; I^2 =98%, *Figure 5E*).

Re-operation rate and re-hospitalization rate

Re-operation rates were reported in three studies. The meta-analysis showed no significant difference between the two groups, and there was moderate heterogeneity among the studies (OR =1.52; 95% CI: 0.12–18.96; I²=62%). Re-hospitalization rates were reported in one study, and no significant difference was observed between the two groups (OR =0.66; 95% CI: 0.11–4.02).

Sensitivity analyses

Sensitivity analysis limited to super-aged patients could not be conducted due to the absence of relevant studies. However, we proceeded with planned sensitivity analyses, which excluded two studies, resulting in outcomes similar to those observed in the main analysis (Figure S2). Notably, in these matched studies, the LLR group exhibited a significantly lower incidence of post-operative ascites compared to the OLR group (n=4 studies; OR =0.51; 95% CI: 0.34–0.76; I²=3%) (Figure S2). Finally, sensitivity analyses using studies with MINORS scores above the median (21 points), yielded results consistent with the findings of the overall analysis (Figure S3).

Discussion

This systematic review and meta-analysis aimed to assess the long-term prognosis and short-term post-operative outcomes of LLR in comparison to OLR in elderly patients with HCC. While previous meta-analyses have addressed HCC in elderly populations, our study specifically focused on patients aged ≥65 years, as defined by the World Health Organization, with primary HCC. We excluded studies with mixed populations, encompassing patients under 65 years of age or those with other liver malignancies like intrahepatic cholangiocarcinoma, liver metastases, or recurrent liver cancer. Previously, Jiang et al. (10) conducted a review and meta-analysis encompassing 14 studies comparing laparoscopic hepatectomy to open hepatectomy, while Wang et al. (9) performed meta-analyses using 12 propensity score-matched studies. Brolese et al. (11) reviewed eight studies comparing minimally invasive LRs (laparoscopic or robotic) to OLR. However, these previous systematic reviews included studies involving both adults and patients with primary or metastatic liver malignancies, potentially introducing variations in effectiveness and prognosis following surgical resection. Consequently, they do not offer precise insights into the clinical benefits of LLR compared to OLR in elderly HCC patients. Our study comprehensively assessed surgical safety, perioperative outcomes, long-term prognosis, and patient-reported outcomes associated with LLR versus OLR specifically for elderly HCC patients. We achieved this by selecting comparative studies, including recently published articles comparing LLR to OLR. As a result, our study incorporated the most up-to-date comparative surgical data, potentially providing valuable insights for surgical decision-making.

Our primary outcome of interest in this surgical treatment analysis was the OS rate among elderly patients with primary HCC. We aimed to gather comprehensive data by extracting results from survival curve plots for both the OS rate and DFS rates at the 3-year and 5-year points. Subsequently, we conducted descriptive statistics and an

exploratory meta-analysis. Our analysis indicated that there was no significant difference in long-term survival between the two surgical approaches. These findings align with those of previous studies (9-11). However, it is important to note that further research is necessary to provide more detailed survival data and adjusted HR as time-to-event data, which can enhance the precision and depth of our understanding in this context.

In terms of overall and post-operative major complications, our meta-analysis indicated a decreasing trend in complications associated with LLR, which aligns with the findings of previous systematic reviews (9,10). Additionally, our analysis revealed that LLR was significantly linked to a lower rate of postoperative minor complications, a result consistent with the findings of Wang et al. (9). The smaller abdominal incision used in LLR can help maintain pulmonary function, facilitate early resumption of diet and ambulation, potentially contributing to reduced wound and pulmonary complications (26). In the realm of postoperative individual complications, our meta-analysis notably reported that LLR was associated with a lower rate of liver failure and ascites compared to OLR. These findings were further emphasized in sensitivity analysis, specifically when considering matching-design studies exclusively. During LLR, there is typically no need for complete mobilization of the liver, except in major LRs. This approach preserves collateral vessels and lymphatic channels around the liver. Additionally, LLR requires less manipulation, traction, and compression of the liver than OLR. All these factors contribute to the preservation of liver integrity and likely account for the lower rate of liver failure associated with LLR when compared to OLR (27).

This study found that the incidences of readmission and re-operation have been reported in very few studies. Specifically, regarding the re-operation rate, one out of the three results was contradictory, possibly attributed to the complexity of cases in the open surgery group and limitations in research design after matching. Thus, it is crucial to minimize the impact of selection bias on the outcome variable in future research. Furthermore, we observed that LLR was associated with significantly shorter hospitalization periods compared to OLR, with a difference of approximately 7 and 10 days, respectively. While this finding aligns with reports from previous meta-analyses, it is important to highlight that there was considerable heterogeneity in the exploratory meta-analysis that involved data conversion based on median and interquartile range,

revealing an approximate difference of 14.5 days and an I² statistic of 98%.

This systematic review and meta-analysis have several limitations that warrant acknowledgment. First, the inclusion of only non-randomized studies in the evaluation and pooled analysis posed challenges in obtaining results of optimal clinical relevance. Although many of the studies were matched retrospective cohort studies, it is important to recognize that this approach may not completely mitigate the inherent limitations and risk of selection bias associated with observational studies. Second, we encountered difficulty in clearly defining the age cutoff for elderly patients with HCC. While our intention was to conduct subgroup and sensitivity analyses with a cutoff age of >80 years, as defined in the primary studies, the scarcity of relevant literature limited our ability to explore age-specific effects thoroughly. Third, the majority of the included studies were single-center studies (80%) or conducted in Asian countries (70%). This imbalance in study settings and geographical locations can pose challenges to the generalizability of findings to broader populations. Fourth, our analysis faced limitations due to the lack of inclusion of non-elderly groups in many of the studies we reviewed. Consequently, a direct comparison between these two demographics was not feasible within the scope of our research. Regarding this topic, we are planning to publish a paper based on the results of additional metaanalysis research. Lastly, although we had intended to assess the impact of surgeon bias and operative variability in detail, most studies did not provide comprehensive details or standardized data in this regard. Consequently, it is advisable to interpret the findings of our study with caution, considering these limitations and potential drawbacks in the review process.

Conclusions

In conclusion, this study suggests that LLR may offer a safer and more suitable alternative to open surgery for elderly patients with HCC. LLR is associated with significantly fewer complications, both major and minor, as well as a reduced incidence of postoperative ascites, along with a shorter LOS compared to OLR. To establish the definitive advantages and risks of LLR over OLR in the treatment of elderly patients with HCC, future research should encompass long-term prospective controlled studies and randomized controlled trials that comprehensively assess clinical, oncological, and patient-reported outcomes.

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Footnote

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Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://jgo.amegroups.com/article/view/10.21037/jgo-24-67/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. Ethics approval for this study was waived from the IRB of National Evidence-based Healthcare Collaborating Agency (NECA).

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