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Laparoscopic *vs* open radical resection in the management of gallbladder carcinoma: A systematic review and meta-analysis

LRR *vs* ORR in GBC: Meta-analysis

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Abstract

BACKGROUND

Radical resection offers the only hope for long-term survival in gallbladder carcinoma (GBC) above the T1b stage. However, whether it should be performed under laparoscopy for gallbladder carcinoma (GBC) is still controversial.

AIM

This study aimed to compare laparoscopic radical resection (LRR) with traditional open radical resection (ORR) in managing GBC.

METHODS

A comprehensive search of online databases, including Medline (PubMed), Cochrane Library, and Web of Science, was conducted to identify comparative studies involving LRR and ORR in GBCs till March 2023. A meta-analysis was subsequently performed.

RESULTS

A total of 18 retrospective studies were identified. In the long-term prognosis, the LRR group was comparable with the ORR group in terms of overall survival (OS) and tumor-free survival (TFS) and showed superiority in TFS of the T2/TNMII stage subgroup versus the ORR group (P = 0.04). In the short-term prognosis, the LRR group had superiority over the ORR group in postoperative length of stay (POLS)(P < 0.001). All pooled results were robust in the sensitivity analysis.

CONCLUSION

The meta-analysis results showed that LRR was not inferior to ORR in all measured outcomes and even showed superiority in the TFS of the T2/TNM II stage and the POLS. For surgeons with sufficient laparoscopic experience, LRR can be performed as an alternative surgical strategy to ORR.

Key Words: Gallbladder carcinoma; laparoscopic radical resection; open radical resection; Outcome; systematic review; meta-analysis

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Core Tip: Laparoscopic surgery is still controversial in the treatment of gallbladder cancer(GBC). This is the first meta-analysis to compare Laparoscopic radical resection(LRR) and open radical resection(ORR) in GBC directly. Unlike the previous similar meta-analysis, we excluded interference from simple cholecystectomy(SC) cases in our study and conducted a subgroup analysis. In addition, we also tested the publication bias and conducted a sensitivity analysis.

INTRODUCTION

Gallbladder carcinoma (GBC) is one of the most dismal prognoses among all types of malignancies, and the 5-year survival rates range from 5% to 15%.[1, 2] The most common pathological type of GBC is adenocarcinoma, which accounts for more than 80% of all GBCs.[3, 4] Others include adenosquamous carcinoma, squamous carcinoma and neuroendocrine carcinoma, *etc.* It has a remarkable propensity to spread early by invading the liver and other adjacent organs directly or metastasizing to lymph nodes. Thus, it is generally believed that simple cholecystectomy (SC) is not sufficient for GBC staged T1b and above. A radical resection, which includes partial hepatectomy and lymph node dissection, offers the only hope for long-term survival. [5, 6]

Systemic therapy has always been an important part of the treatment of GBC and biliary tract cancer (BTC), considering the low resection rate at the diagnosis. Cisplatin combined with gemcitabine (CisGem) has been used as the main chemotherapy regimen for advanced gallbladder cancer to this day.[7] In the past decade, immune checkpoint inhibitors (ICIs) have made major breakthroughs in the field of cancer treatment, and have changed the treatment pattern of several malignant tumors, especially for malignancies with dMMR, high TMB or MSI-high. [8-10] However, the role of ICIs in BTC needs to be further studied and clarified, and its combination with other anti-cancer drugs (such as chemotherapy, targeted agents, *etc.*) may be a more promising direction.[10-15] Some scholars are also exploring the relationship between ICIs and other therapeutic targets, such as BRCA 1/2 mutations (BRCAm), in order to provide patients with more personalized and precise treatment.[16]

Laparoscopic surgery has been widely performed in most cancers, including colon cancer, gastric cancer, and liver cancer. Compared with traditional open surgery, laparoscopic radical surgery not only shows the advantages of minimal invasion but also achieves satisfactory long-term survival.[17-20] However, for a long time, laparoscopic surgery has only been recommended for treating benign gallbladder diseases, the staging and biopsy of GBC, or the resection of GBC in very early stages (Tis and T1a). [21-23] It has always been considered contraindicated for GBCs with T1b stage or above, requiring a radical resection. In recent years, many surgeons have tried to apply laparoscopic technology to the management of GBCs. Several meta-analyses have discussed this issue and reached optimistic conclusions.[24-27] However, whether LRR is feasible in treating GBC staged T1b and above still has not been fully demonstrated because the studies included in these meta-analyses contained a large number of SC cases. Thus, we believe that performing a new meta-analysis focused on the feasibility of LRR by excluding all SC cases is necessary.

MATERIALS AND METHODS

Search strategy and study selection

A systematic review of the published studies till March 2023 was performed to screen studies comparing the outcomes of patients who underwent LRR *vs* ORR for GBCs. We searched the abstracts in PubMed, Cochrane Library, and Web of Science using the keywords: laparoscopic or minimally invasive, gallbladder cancer or gallbladder carcinoma or gallbladder neoplasm. Searches were limited to human studies and English-language publications. The citation lists of retrieved studies were manually filtered to identify other studies. Two researchers independently searched for studies and compared the results.

Study selection

Eligible studies were required to meet the following criteria: (1) the study must be a comparative design evaluating LRR and ORR for GBC, and (2) the study should be a human study and published in English.

The study was excluded from the analysis for the following reasons: (1) case report or case series studies; (2) the studies enrolling patients who just underwent laparoscopic SC (LSC) or whose surgical method was unclear; and (3) the studies including other tumors, such as intrahepatic bile duct cancer, in which GBC data could not be extracted separately. The literature search and selection strategy are shown in **Figure 1**.

The modified Newcastle–Ottawa Scale (NOS) was used to assess the quality of included studies.[28]

Data extraction and outcome measures

The data extraction was performed independently by two authors. The following details were extracted: study period, study design, country/region, number of patients, sex, age, type of surgery, tumor stage, operation time, blood loss, complications, postoperative length of stay (POLS), resection margin, and so forth.

The primary outcomes were overall survival (OS) and tumor-free survival (TFS). The hazard ratio (HR) and 95% confidence interval (CI) of survival were extracted from the survival curve using Engauge Digitizer 11.1 software if they were not reported. Then, the HR and 95%CI were calculated and converted into lnHR and SE (lnHR) for analysis.[29] The secondary outcomes included the number of lymph nodes harvested (No. LNH), operation time, blood loss, R0 resection rate, POLS, and complications rate. If the aforementioned information was a continuous variable given in the form of a median (range), it needed to be converted into the form of mean ± standard deviation[30, 31]. Two authors independently extracted and compared the data to eliminate the mistakes. Some data were not available, and hence not all included studies could participate in every outcome analysis.

Statistical analysis

The studies from which valid data could be extracted were included in the final meta-analysis. For dichotomous data, the odds ratio (OR) and 95%CI were calculated; for continuous data, the mean difference (MD) and 95%CI were calculated. For survival data, we calculated HR and 95%CI. The chi-square test and I^2 statistic were used to measure heterogeneity. For example, the chi-square test P <0.05 or I^2 >50% indicated significant heterogeneity. In this case, a random-effects model was adopted; otherwise, a fixed-effects model was used. All meta-analyses were performed using the statistical software Review Manager [(RevMan). Version 5.3. Copenhagen, Denmark: The Nordic Cochrane Centre, The Cochrane Collaboration; 2014]. A P value <0.05 indicated a statistically significant difference.

Risk of Bias

The Begg's test and Egger's test were used to evaluate potential publication bias quantitatively. A P value or corrected P value of <0.05 in the test indicated the presence of significant statistical publication bias. The results are shown in Table 2. Besides, the sensitivity analysis was conducted to assess the stability of the pooled results of major measured outcomes. The results of the sensitivity analysis are presented in Figure 6. Begg's test, Egger's test, and sensitivity analysis were conducted using Stata software (version 17.0).

Subgroup analysis

Subgroup analysis could be conducted to reduce interference from tumor staging and other factors. Based on the available data, we found that there are fewer data in the T1/Tumor-Node-Metastasis(TNM) **I** stage and T3/TNM IIIstage that can be extracted, so we conducted a subgroup analysis for the T1/TNMI + T2/TNM II stage**,** T2/TNM **II** stage and T2/TNM II+ T3/TNM **III**stage respectively. In addition, we also conducted a subgroup analysis of the data after propensity score matching (PSM).

RESULTS

Study selection and characteristics

Eighteen retrospective studies were identified after screening based on the inclusion criteria and assessing the full text of potentially eligible studies.[32-46] The characteristics and quality evaluation of the 18 included studies for meta-analysis are summarized in Table 1. These studies included 3513 patients with GBC who underwent surgery with curative intention, of which 1422 were in the LRR group and 2091 were in the ORR group. The details about these patients are shown in Table S1. One study[33] included 12 cases of LSC; we retained this study and only included data from its T2 and T3 subgroups comprising no LSC cases. Another study[47] included eight LSC cases; however, after matching based on propensity scores, the laparoscopic and open surgery groups comprised four cases each. We believed that it had less impact on the analysis results; therefore, this study was also retained. The data after PSM was available in 6 of the 18 studies.

Long-term outcomes

1. OS and TFS

The OS data were available in 1615 studies, and no significant heterogeneity existed [c^2 = 17.31, df = 15 (P = 0.30); I^2 = 13%]. Therefore, a fixed-effects model was used. The result showed no difference in OS between the LRR and ORR groups (HR: 0.92, 95%CI: 0.80–1.05; P = 0.22; Figure 2A).

The TFS data were available in 10 studies, and no significant heterogeneity existed [c^2 = 9.32, df = 9 (P = 0.41); I^2 = 3%]. Therefore, a fixed-effects model was used. The result showed no difference in TFS between the LRR and ORR groups (HR: 0.93, 95%CI: 0.66–1.31; P = 0.70; Figure 2B).

2. OS and TFS after PSM

The OS data after PSM were available in five studies, and no significant heterogeneity existed [c^2 = 1.15, df = 4 (P = 0.89); I^2 = 0%]. Therefore, and a fixed-effects model was used. The result showed no difference in OS between the LRR and ORR groups (HR: 0.71, 95%CI: 0.39–1.30; P = 0.27; Figure 2C).

The TFS data after PSM were available in four studies, and no significant heterogeneity existed [c^2 = 0.96, df = 3 (P = 0.81); I^2 = 0%]. Therefore, a fixed-effects model was used. The result showed no difference in TFS between the LRR and ORR groups (HR: 1.00, 95%CI: 0.63–1.57; P = 0.99; Figure 2D).

3. OS and TFS in the T2/TNM II subgroup

The OS data of the T2/TNM II stage were available in seven studies, and no significant heterogeneity existed [c^2 = 3.66, df = 6 (P = 0.72); I^2 = 0%]. Therefore, a fixed-effects model was used. The result showed no difference in OS between the LRR and ORR groups for the T2/TNM II subgroup (HR: 0.94, 95%CI: 0.53–1.65; P = 0.83; Figure 3A).

The TFS data of the T2/TNM II stage were available in five studies, and no significant heterogeneity existed [c^2 = 4.12, df = 4 (P = 0.39); I^2 = 3%]. Therefore, a fixed-effects model was used. The LRR group showed a better TFS than the ORR group for the T2/TNM II subgroup (HR: 0.50, 95%CI: 0.26–0.96; P = 0.04; Figure 3B).

4. OS and TFS in the T1/TNM I + T2/TNM II subgroup

The OS data of the T1/TNM I or T2/TNM II stage were available in eleven studies, and no significant heterogeneity existed [c^2 = 7.06, df = 11 (P = 0.79); I^2 = 0%]. Therefore, a fixed-effects model was used. The result showed no difference in OS between the LRR and ORR groups for the T1/TNM I + T2/TNM II subgroup (HR: 1.35, 95%CI: 0.95–1.92; $P = 0.09$; Figure 3C).

The TFS data of the T1/TNM I or T2/TNM II stage were available in seven studies, and no significant heterogeneity existed [$c^2 = 8.23$, df = 6 ($P = 0.22$); $I^2 = 27\%$]. Therefore, a fixed-effects model was used. A significant difference was detected in TFS between the LRR and ORR groups for the T1/TNM I or T2/TNM II subgroup (HR: 0.83, 95%CI: 0.54–1.27; $P = 0.39$; Figure 3D).

5. OS and TFS in T2/TNM II + T3/TNM IIIsubgroup

The OS data of the T2/TNM II or T3/TNM IIIstage were available in nine studies, and no significant heterogeneity existed [$c^2 = 4.56$, df = 10 ($P = 0.92$); $I^2 = 0\%$]. Therefore, a fixed-effects model was used. The result showed no difference in OS between the LRR and ORR groups for the T2/TNM II + T3/TNM IIIsubgroup (HR: 0.82, 95%CI: 0.64–1.05; $P = 0.12$; Figure 3E).

The TFS data of the T2/TNM II or T3/TNM IIIstage was available in seven studies, and no significant heterogeneity existed [$c^2 = 7.79$, df = 6 ($P = 0.25$]; $I^2 = 23\%$]. Therefore, a fixed-effects model was used. A significant difference was detected in TFS between the LRR and ORR groups for the T2/TNM II + T3/TNM IIIsubgroup (HR: 0.81, 95%CI: 0.52–1.24; $P = 0.32$; Figure 3F).

Short-term outcomes

1. Number of lymph nodes harvested

The data of No. LNH were reported in seventeen studies. Significant heterogeneity existed between these studies [$c^2 = 131.34$, df = 16 ($P < 0.001$); $I^2 = 88\%$]. Therefore, a random-effects model was used. The results showed no significant difference in the No. LNH between the LRR and ORR groups (MD: –0.73; 95%CI: –1.87 to 0.41; $P = 0.21$; Figure 4A).

The data of No. LNH after PSM was reported in six studies. Significant heterogeneity was found between these studies [$c^2 = 78.43$, df = 5 ($P < 0.001$); $I^2 = 94\%$]. Therefore, a random-effects model was used. The results showed no significant difference in the No. LNH between the LRR and ORR groups (MD: –1.52; 95%CI: –4.20 to 1.15; P = 0.26; Figure 5A).

2. Operation time

The data of operation time were reported in sixteen studies. Significant heterogeneity existed between these studies [c^2 = 288.26, df = 15 (P < 0.001); I^2 = 95%]. Therefore, a random-effects model was used. The results showed no significant difference in the operation time between the LRR and ORR groups (MD: 7.72; 95%CI: –16.28 to 31.72; P = 0.53; Figure 4B).

The data of operation time after PSM was reported in six studies. Significant heterogeneity existed between these studies [c^2 = 81.27, df = 5 (P < 0.001); I^2 = 94%]. Therefore, a random-effects model was used. The results showed no significant difference in the operation time between the LRR and ORR groups (MD: 22.69; 95%CI: –12.93 to 58.31; P = 0.21; Figure 5B).

3. Intraoperative blood loss

The data of intraoperative blood loss were reported in fourteen studies. Significant heterogeneity existed between these studies [c^2 = 516.12, df = 13 (P < 0.001); I^2 = 97%]. Therefore, a random-effects model was used. The LRR group showed lesser intraoperative blood loss than the ORR group (MD: –60.58; 95%CI: –102.94 to –18.23; P = 0.005; Figure 4C).

The data of intraoperative blood loss after PSM were reported in four studies. Significant heterogeneity existed between these studies [c^2 = 237.8, df = 3 (P < 0.001); I^2 = 99%]. Therefore, a random-effects model was used. The results showed no significant difference in the intraoperative blood loss between the LRR and ORR groups (MD: –94.71; 95%CI: –262.26 to 72.83; P = 0.27; Figure 5C).

4. Postoperative length of stay

The data of POLS were reported in seventeen studies. Significant heterogeneity existed between these studies [c^2 = 212.98, df = 16 (P < 0.001); I^2 = 92%]. Therefore, a random-effects model was used. The LRR group showed a shorter POLS than the ORR group (MD: –3.31; 95%CI: –4.38 to –2.24; P < 0.001; Figure 4D).

The data of POLS after PSM were reported in six studies. Significant heterogeneity was found between these studies [c^2 = 139.03, df = 5 (P < 0.001); I^2 = 96%]. Therefore, a random-effects model was used. The LRR group showed a shorter POLS than the ORR group (MD: –4.11; 95%CI: –6.10 to 2.12; P < 0.001; Figure 5D).

5. Complications

The data of complications were reported in fifteen studies. No significant heterogeneity existed [c^2 = 7.68, df = 14 (P = 0.91); I^2 = 0%]. Therefore, a fixed-effects model was used. The LRR group showed a lower complication rate than the ORR group (OR: 0.69; 95%CI: 0.49–0.96; P = 0.03; Figure 4E).

The data of complications after PSM were reported in six studies. No significant heterogeneity existed [c^2 = 18.04, df = 15 (P = 0.26); I^2 = 17%]. Therefore, a fixed-effects model was used. The results showed no significant difference in the complications between the LRR and ORR groups (OR: 1.00; 95%CI: 0.78-1.28; P = 1.00; Figure 5E).

6. Complications (Clavien–Dindo 3–4)

The data of complications (Clavien–Dindo 3–4) were reported in eight studies. No significant heterogeneity existed [c^2 = 3.18, df = 4 (P = 0.53); I^2 = 0%]. Therefore, a fixed-effects model was used. The results showed no significant difference in the complications (Clavien–Dindo 3–4) between the LRR and ORR groups (OR: 0.59; 95%CI: 0.26–1.32; P = 0.20; Figure 4F).

The data of complications (Clavien–Dindo 3–4) after PSM were reported in five studies . No significant heterogeneity existed [c^2 = 0.55, df = 1 (P = 0.46); I^2 = 0%]. Therefore, a fixed-effects model was used. The results showed no significant difference in the complications (Clavien–Dindo 3–4) between the LRR and ORR groups (OR: 1.00; 95%CI: 0.24–4.19; P = 1.00; Figure 5F).

7. R0 resection rate

The data of the R0 resection rate were reported in eight studies. No significant heterogeneity existed [c^2 = 1.77, df = 6 (P = 0.94); I^2 = 0%]. Therefore, a fixed-effects model was used. The LRR group showed a significant higher R0 resection rate compared with the ORR group (OR: 1.23; 95%CI: 1.01–1.50; *P* = 0.04; Figure 4G). Data of the R0 resection rate after PSM were not enough for pooled analysis.

Early-staged rate

We defined the T1-2 stage and TNM I –II stage as the early-staged group, and the T3-4 stage and TNM III-IVstage as the late-staged group. Of the eighteen included studies, nine studies comprised only early-staged or late-staged cases. We included the remaining nine studies for analysis. Significant heterogeneity existed between these studies [c^2 = 17.40, df = 8 (*P* = 0.03); I^2 = 54%]. Therefore, a random-effects model was used. The LRR group showed a significant higher early-staged rate compared with the ORR group (OR: 1.54; 95%CI: 1.08–2.18; *P* = 0.02; Figure 4H).

Evaluation of publication bias and sensitivity analysis

Egger's test, Begg's test, and sensitivity analysis were performed to evaluate major measured outcomes, including the No. LNH, operation time, blood loss, POLS, complications, complications (Clavien–Dindo 3–4), R0 resection rate, OS, and TFS. A remarkable asymmetry was detected using Egger's test in the No. LNH, operation time, and POLS; however, no publication bias was detected using Begg's test in all measured outcomes. The results of Egger's test and Begg's test are presented in Table 2. The sensitivity analysis showed that the pooled results of all of the major outcomes were stable and robust. The results of the sensitivity analysis are presented in Figure 6.

DISCUSSION

In the analysis of long-term prognosis, the LRR group was comparable with the ORR group in terms of OS and TFS. The same result was obtained even after the propensity scores were matched. Then, the subgroup analysis about T2/TNM II stage, T1/TNM I + T2/TNM II stage, and T2/TNM II + T3/TNM IIIstage was performed. The results showed that the LRR group had a superiority over the ORR group in terms of TFS only in the T2/II stage subgroup (*P* = 0.04). In the analysis of short-term prognosis, the LRR group had superiority over the ORR group in terms of blood loss (*P* = 0.005), POLS (*P* < 0.001), complication rate (*P* = 0.03), and R0 resection rate (*P* = 0.04). After the propensity scores were matched, the advantage remained in the POLS ($P < 0.001$), but was lost in the blood loss ($P = 0.27$) and complication rate ($P = 0.29$). The R0 resection rate could not be analyzed after PSM due to the unavailability of data. The LRR and ORR groups did not show significant differences in other short-term outcomes, such as No. LNH, surgical time, and complication rate (Clavien-Dindo3-4), regardless of whether the propensity scores were matched or not. Egger's test and Begg's test indicated publication bias, but all of the pooled results were stable and robust in the sensitivity analysis.

In recent years, several meta-analyses comparing laparoscopic and open surgery for treating GBC were published, and similar results were obtained.[24-27] However, we believed that conducting this meta-analysis was necessary because it was significantly different from the previous studies. First, all previous meta-analyses included many studies comprising a large number of SC cases. For example, in the study by Jang *et al*,[48] 197 cases were included. However, 94 cases in the laparoscopic group and 30 cases in the open surgery group just underwent SC, and only 73 cases in the open surgery group underwent ORR. This study aimed to explore the feasibility of LSC for T1 GBC. In the study performed by Goetze *et al*.,[49] 837 patients were included. According to the primary access technique, 492 patients underwent LSC, 200 underwent open surgery, and 142 initially underwent LSC, but the approach was converted into open surgery. Then, 300 patients who had re-resection were also stratified according to the primary surgical approach, and whether LRR was performed was not clearly mentioned. Based on the content and era of the research, it is quite possible that the re-resection was carried out under open surgery. This study aimed to explore the impact of the primary access technique (laparoscopy *vs* primary open surgery) on the prognosis of GBCs. The aforementioned two studies were included in all of the previous meta-analyses and made important contributions to the pooled results because of their large sample sizes. Similar situations existed in many other included studies[50-59], and they did not discuss the impact of the approach of radical resection on the prognosis of GBC. Therefore, these studies were not included based on our inclusion criteria. This was the biggest difference between our meta-analysis and the previous meta-analyses. Second, we analyzed the results of TFS, which were not used in the previous meta-analyses. The results of the overall recurrence rate were pooled in the meta-analysis performed by Lv *et al*. [26] and Nakanishi *et al*. [27]. However, we presumed that it was unreasonable to directly pool the overall recurrence rate results because the follow-up times of the included studies were not the same and the HR used in our study was more reasonable. Third, we analyzed the data after propensity scores were matched to minimize the influence of other factors on the results, which was not reported in the previous meta-analyses. Fourth, we pooled the staging data and found that the cases included in the LRR group had an earlier stage than those in the ORR group. Tumor staging is one of the most important factors affecting the prognosis, which suggested that our interpretation of the overall results should be conservative and we should pay more attention to subgroup analysis.

Laparoscopic surgery has been thought to worsen the prognosis of GBC, which was first described in the 1990s.[60-62] Since then, it has been controversial, and the focus is on the possible port-site recurrence and peritoneal metastasis after laparoscopic surgery, which was considered to be associated with intraoperative gallbladder perforation and pneumoperitoneum and suggested a poor prognosis.[63-65] The submucosa of the gallbladder wall is absent, and the muscularis propria is extremely thin. Thus, gallbladder perforation is more likely to occur in laparoscopic surgery. Around the 2000s, the gallbladder perforation rate in laparoscopic surgery was reported to be 20%–36%.[62, 66, 67] However, currently, gallbladder perforation is not as common as earlier, which may be attributed to the improvement in the operation skills of the surgeons. Of the 18 studies included in our meta-analysis, only the study by Feng *et al*[33] reported perforations caused by gallbladder decompression due to incarcerated gallstones or severe inflammation, and the incidence showed no difference between laparoscopic and open surgery groups. Besides, the routine use of retrieval bags, avoiding the direct contact between the surgical specimen and extraction port, significantly reduced the risk of port-site metastasis.[65] In the 1990s, the incidence of port-site metastases in IGBC was reported as high as 17%.[68] However, the incidence decreased to 10% in a recent systematic review, and the recurrence rate of incisions after open surgery remained at about 7%.[69] Further, the incidence of peritoneal carcinomatosis was even higher in the ORR group than in the LRR group in the study by Vega *et al*. [38]

Another concern is about whether laparoscopic surgery is competent for the radical resection of GBC, which includes partial hepatectomy (wedge resection/ IVb +Vsegment resection) and lymph node dissection. In the past, such a complicated surgery was not appropriate to be performed in laparoscopy. However, the development of laparoscopic surgery for other cancers has changed this view. Many reports were available about the use of laparoscopic techniques in complex liver resection, such as right hemi-hepatectomy, caudate lobe resection, and so forth, and a better short-term prognosis and comparable long-term survival were confirmed.[70-72] The laparoscopic techniques have also been reported in a live liver donation.[73, 74] More extensive lymph node dissection has been developed for treating gastric cancer and is widely used under laparoscopy.[17, 75] Thus, from a purely technical perspective, the current laparoscopic techniques can fully meet the requirements of radical resection for elective GBC, and it seems that LRR should no longer be considered a contraindication for GBC.

The treatment of GBC will be a comprehensive pattern based on surgery and combined with chemotherapy, immunotherapy and targeted therapy. And it is developing towards the trend of minimally invasive, precise and individualized. In this study, LRR not only provided satisfactory survival, but also showed the characteristics of minimally invasive and enhanced postoperative recovery. It will inevitably play a more important role in the treatment of GBC. In addition, the rapid development of targeted and immunotherapy may provide more treatment options for GBC.

This meta-analysis had some limitations. First, all included studies were retrospective, and no randomized controlled studies or prospective studies were included. Second, significant heterogeneities were found in some analyses, the reasons for which were difficult to find; we could only reduce their impact by choosing random-effects models. Third, we found using Egger' test that a publication bias might exist, but this was difficult to eliminate. Fourth, the estimated HR extracted from the survival curve was rough and might introduce bias. Fifth, related confounding factors were difficult to extract from the study, and few studies were included in the subgroup analysis of staging and the analysis after PSM. Sixth, most of the included studies did not report detailed adjuvant therapy data, so it is difficult to judge the impact of adjuvant therapy on long-term prognosis. This study was not impeccable; however, it truly described the current state in this field and provided reasonable support for the further exploration of LRR in treating GBC.

CONCLUSION

Our analysis enrolled a large number of comparative studies. This was the first study to date to compare LRR and ORR in treating GBC. While excluding the interference of SC cases, the data after PSM was analyzed for the first time. The results of the meta-analysis showed that LRR was not inferior to ORR in all measured outcomes and even showed superiority in the DFS of T2/TNM II stage and the POLS. For surgeons with sufficient laparoscopic experience, LRR could be performed as an alternative surgical strategy to ORR. This might not be the final conclusion, and performing a more comprehensive meta-analysis again is necessary.

ARTICLE HIGHLIGHTS

Research background

Laparoscopic surgery has been widely used in the treatment of a variety of tumors, but it is still controversial in the treatment of gallbladder cancer. This is the first meta-analysis to compare Laparoscopic radical resection(LRR) and open radical resection(ORR) in gallbladder carcinoma(GBC) directly.

Research motivation

This study compared laparoscopic radical resection(LRR) with traditional open radical resection (ORR) in the management of GBC. It aims to resolve the disputes faced by LRR and provide support for further research.

Research objectives

This study aims to clarify the feasibility of LRR in GBC treatment, and encourage more surgeons to further carry out research on LRR, and move the minimally invasive treatment of gallbladder cancer forward.

Research methods

We systematically reviewed literatures on the LRR and ORR in GBC, and integrated the available data for meta-analysis. The Begg's test and Egger's test were used to assess potential publication bias, and sensitivity analysis was used to evaluate the stability of the results.

Research results

This study found that LRR group was comparable with the ORR group in long-term and short-term prognosis, and even showed advantages in some aspects, such as tumor-free survival(TFS) of the T2/TNMII stage subgroup and postoperative length of stay (POLS). Although there is still a lack of support from randomized controlled trial(RCT), this result will encourage surgeons to conduct further and more in-depth research.

Research conclusions

The meta-analysis results showed that LRR was not inferior to ORR in all measured outcomes and even showed superiority in the TFS of the T2/TNM II stage and the POLS. It is the first meta-analysis that excluded interference from simple cholecystectomy(SC) cases, it is also the first time to conduct a subgroup analysis of the data after propensity score matching(PSM).

Research perspectives

LRR will inevitably play a more important role in the treatment of GBC, considering its minimally invasive characteristics and the advantages of enhanced postoperative recovery. But it requires further research, such as RCT research, or research on the combination of LRR and adjuvant therapy.

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SIMILARITY INDEX

PRIMARY SOURCES

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