Propensity Score Analysis of Outcomes Following Laparoscopic or Open Radical Resection for Gallbladder Cancer in T2 and T3 Stages

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Research

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Abstract

Background Although laparoscopic radical resection (LLR) has long been contraindicated in gallbladder cancer (GBC), recent studies have demonstrated laparoscopic surgery did not adversely affect the perioperative and survival outcomes of GBC patients. However, these literatures are mainly focused on GBC of relatively early stages or incidental GBC. This study aimed to investigate the perioperative and long-term outcomes of LRR versus open radical resection (ORR) for GBCs in T2 and T3 stages.

Methods A retrospective study was conducted on 99 patients with GBC of T2 and T3 stages who underwent radical resection at Zhejiang Provincial People's Hospital from January 2010 to December 2020. A 1:1 propensity score matching (PSM), which is the best option to overcome selection bias, was conducted to compare the surgical outcomes and long-term prognosis between LRR and ORR. A logistic regression analysis was performed to identify the predictive risk factors of postoperative overall survival.

Results By using PSM, the two groups were well balanced with 30 patients in each group. In the LRR group, the length of operation was significantly longer than the ORR group, but the intraoperative bleeding and postoperative days of hospital stay were significantly decreased compared to ORR group. Two groups showed comparable outcomes regarding the incidence of biliary reconstruction, lymph node yield, the incidence of postoperative morbidities, the incidence of Clavien–Dindo (C–D) grade III-IV, the days of drainage tubes indwelling, mortality at 30 postoperative days and 90 postoperative days, and the incidence of port sites metastasis. The 1-, 2-, and 3-year overall survival rates were 61.2, 40.1, and 30.1%, respectively, in the LLR group, and 53.3, 40.1, and 40.1%, respectively, in the OLR group (p=0.644). On multivariate analysis, T stage, vascular invasion and tumor differentiation were found to be the independent risk factors for overall survival of GBC in T2 and T3 stages.

Conclusions For GBC in T2 and T3 stages, LRR can achieve comparable perioperative outcomes and long term survival compared to ORR. LRR tend to show advantages over ORR regarding intraoperative bleeding and postoperative days of hospital stay.

Introduction

Gallbladder cancer (GBC), the most common biliary tract malignancy, is known to have a dismal prognosis(1). Curative radical resection remains the gold standard treatment, although patients only have the median survival of 26 months and 5-year survival of 35% after surgical resection(2, 3). Although laparoscopic surgery is widely used in digestive malignancies including liver, colon, gastric and pancreatic cancer(4–7), the application of laparoscopic approach in the curative resection of GBCs remains controversial. The concerns of peritoneal dissemination of cancer cells, port sites metastasis and inadequacies of radical resection during laparoscopic surgery are the main reasons for the limited use of laparoscopic resection for GBC.

Recently, increasing literatures reported encouraging results regarding the application of laparoscopic surgery in GBC. Agarwal et al. demonstrated that there was no significant difference in morbidity,

mortality, lymph nodes yield, and recurrence rate by retrospectively comparing outcomes of 24 cases of laparoscopic radical cholecystectomy and 46 cases of open surgery(8). Itano et al. showed no significant difference regarding postoperative morbidity, mortality, lymph nodes yield, and recurrence rate between laparoscopic and open cases of T2 GBC(9). Yoon et al. reported favorable long-term oncologic results of laparoscopic radical cholecystectomy by including 2 cases of Tis GBC, 10 cases of T1a GBC, 8 cases of T1b GBC and 25 cases of T2 GBC(10). However, these literatures are mainly focused on GBC of relatively early stages or incidental GBC(11). Therefore, investigations examining the efficacy of laparoscopic surgery for advanced GBC remain scare. In this study, the results of laparoscopic radical resection for GBC of T2 and T3 were compared with those carried out by the open approach, focusing on perioperative outcomes and long-term survival.

Material And Method

Patients' cohort and data collection

Data for a consecutive series of patients who underwent radical resection for GBC, by either open or laparoscopic approach between January 2010 and December 2020 at Zhejiang Provincial People's Hospital, were retrieved retrospectively from a prospectively collected database. Following were the inclusion criteria for this study: (1) histopathologically confirmed diagnosis, (2) patients with advanced GBC (stages T2-T3) underwent radical surgery, (3) no preoperative antitumor therapies, (4) complete perioperative and follow-up information. Exclusion criteria were as follows: patients who received simple cholecystectomy, patients who had another primary malignancy at the time of surgery, and patients who were lost during follow up. The primary aim of the analysis was to compare, in the cohort of patients who underwent radical resection for GBC, short- and long-term outcomes of patients receiving a laparoscopic radical resection (LRR) with those receiving an open radical resection (ORR). The secondary aim was to explore, in the entire cohort of patients, factors affecting the overall survival of GBC patients. Approval for the study was obtained from the Institutional Review Board of Zhejiang Provincial People's Hospital.

Preoperative management

No neoadjuvant locoregional or systemic treatments were applied before operation. Abdominal ultrasonography and contrast-enhanced computed tomography (CT) or magnetic resonance (MR) were routinely performed in patients with advanced GBC. Magnetic resonance cholangiopancreatography (MRCP) was performed in patients with obstructive jaundice. CT angiography was used to evaluate patients with suspected vessel invasion. Positron emission tomography was selectively performed in selected patients to rule out systemic metastasis before radical surgery. Laboratory examinations, including routine blood tests, liver function tests, as well as serum carbohydrate antigen (CA) 19-9 levels were routinely performed in all patients. Endoscopic or percutaneous biliary drainage was performed in patients with obstructive jaundice with total serum bilirubin (TB) >200 μmol/L until TB levels decreased to <80 μmol/L. Indocyanine green (ICG) clearance test at 15 min along with Child-Pugh (CTP) classification was employed to evaluate the liver function and reserve.

Surgical procedure

Patients undergoing laparoscopic surgery were placed in the reverse Trendelenburg position. Routinely, the five-port method was utilized for extended resection of GBC (Figure 1A). For cases requiring bilioenteric anastomosis, the six-port method was used (Figure 1B). Careful inspection of the peritoneal cavity was performed after establishment of pneumoperitoneum to rule out peritoneal or visceral metastasis. Frozen section examination of para-aortic LNs was performed to decide whether radical resection should be terminated. Wedge resection of the GB bed (≥2cm) (Figure 1C) or segment IVb/V resection (Figure 1D) or major hepatectomy was chosen depending on the extent of liver parenchyma invasion. The portal inflow was blocked using the Pringle maneuver when severe intraoperative bleeding occurred. Extra-hepatic bile duct resection and bilioenteric anastomosis (end-to-side method) were performed if the margin of cystic duct was positive. LNs along the extrahepatic bile ducts, the hepatoduodenal ligament, the hilar areas, and the pancreatic head region were dissected (Figure 1E and 1F). Pancreatoduodenectomy was performed for cases with pancreatic parenchymal or intra-pancreatic bile duct infiltration. Resection of adjacent organs including the colon, stomach and duodenum or vessel construction was performed to achieve R0 resection when necessary. Resected specimens were inserted into vinyl bags and extracted through the umbilical port.

Postoperative management and follow-up

Blood routine tests and liver function tests were performed every 3 days after operation. The level of bilirubin in drainage fluid was measured. Bile leakage was defined according to the criteria proposed by ISGLS(12). Morbidity was classified according to the Clavien–Dindo classification. Drainage tubes were removed if contrast-enhanced CT did not show any fluid accumulation in peritoneal cavity. Postoperative chemotherapy was recommended to all GBC patients (T2 and T3) without contradiction to chemotherapy. The postoperative follow-up protocol included clinical examination, liver function tests, serum tumor marker levels (CA199), abdominal ultrasonography, and enhanced CT or MR every month during the first 3 months, followed by every 3 months during the initial 2 years and every 6 months during the next 3 years. Telephone follow-up was conducted to obtain the updated survival status of every patient. OS was calculated as the interval from the date of resection until the date of death, with censoring at the date of the last follow-up.

Propensity score matching (PSM)

1:1 PSM was performed to overcome bias resulting from lack of randomization due to the different co-variable distribution among patients who received either of the surgical approaches to radical resection. The caliper of 0.05 used in the model. A consensus regarding which variables should be balanced in the model was reached among all authors. The balanced variables included age, gender, body mass index (BMI), the history of gallbladder stone, CA199, total bilirubin, ALT, T stage, N stage, M stage, vascular invasion, neural invasion, pathological type, tumor differentiation, and postoperative chemotherapy.

Risk factors affecting overall survival

The univariate and multivariate analyses were performed on the entire patients' cohort to identify the risk factors affecting overall survival. Variables that might affect the postoperative survival were incorporated into the univariate analysis including age, gender, body mass index (BMI), the history of gallbladder stone, CA199, preoperative total bilirubin, preoperative ALT, the surgical approach, T stage, N stage, M stage, vascular invasion, neural invasion, pathological type, tumor differentiation, operation time, blood loss, and postoperative chemotherapy. The variables (those with $P < 0.05$ in univariate analysis) were incorporated into the multivariate analysis of logistic regression to identify the independent risk factors affecting postoperative overall survival.

Statistical analysis

SPSS statistical software (IBM SPSS, Inc., Chicago, IL, version 25) and Graphpad were used for statistical analysis. Categorical variables which were presented as absolute numbers (percentage) were compared between groups by the $\chi 2$ test. Continuous variables presented as mean ± standard deviation were compared between groups using Student's t test. Log-rank test were used to determine the difference of overall survival between two groups. $P<0.05$ was considered to be statistically significant difference.

Results

During the study period, 99 GBC patients of T2 and T3 underwent radical resection. There were 56 patients underwent LRC and 43 patients received ORC. After a 1:1 PSM, there were 30 patients in each of groups of LRC and ORC.

Baseline and pathological characteristics

In the entire cohort, there were no significant difference in the baseline characteristics including age, gender, BMI, the history of gallstone, preoperative CA199, and preoperative TB (Table 1). The incidence of elevated preoperative ALT was significantly higher in ORR group compared with LRR group (7/56 vs 14/43, $P = 0.024$). Regarding T stage distribution, LRR group tend to have a lower proportion of T3 stage (28/56 vs 27/43), although the difference was not statistically significant ($P = 0.227$). Other pathological characteristics including N stage, M stage, pathological type, tumor differentiation, peri-neural invasion, vascular invasion were comparable between LRR and ORR group.

Table 1
The comparison of baseline and pathological characteristics between LRC and ORC group

	LRC group (n = 56)	ORC group (n = 43)	P
Age			
< 60	15	17	0.199
≥ 60	41	26	
Gender			
Male	12	8	0.804
Female	44	35	
BMI			
< 24	38	27	0.671
≥ 24	18	16	
Gallstone			
Absence	29	26	0.421
Presence	27	17	
Preoperative CA199			
< 37 U/L	33	25	> 0.999
≥ 37 U/L	23	18	
Preoperative TB			
< 24 umolL/L	48	33	**0.092**
≥ 24 umolL/L	8	13	
Preoperative ALT			
< 40U/L	49	29	**0.024**
≥ 40U/L	7	14	
T stage			
T2	28	16	0.227
T3	28	27	
N stage			

	LRC group (n = 56)	ORC group (n = 43)	P
N0	28	22	> 0.999
N1-N2	28	21	
M stage			
M0	53	40	> 0.999
M1	3	3	
Pathological type			
Adenocarcinoma	52	39	0.725
Squamous carcinoma	4	4	
Tumor differentiation			
Poor	23	16	0.836
Well or Moderate	33	27	
Peri-neural invasion			
Absence	27	23	0.686
Presence	29	20	
Vascular invasion			
Absence	34	23	0.541
Presence	22	20	

Table 2
The comparison of perioperative outcomes between LRC and ORC group

	LRC group (n = 56)	ORC group (n = 43)	P
Biliary reconstruction	6	8	0.384
Length of operation	292.35 ± 14.41	249.02 ± 13.30	0.033
Intraoperative bleeding	233.91 ± 26.35	461.25 ± 53.15	< 0.01
Lymph node yield	9.39 ± 0.68	8.26 ± 0.52	0.208
Morbidity			
Bile leakage	6	3	0.521
Postoperative bleeding	3	1	0.448
Abdominal abscess	3	3	0.738
Clavien–Dindo classification grade III-IV	6	5	0.886
Days of drainage tubes indwelling	7.46 ± 0.62	9.30 ± 0.85	0.077
Postoperative days of hospital stay	10.32 ± 0.60	14.74 ± 0.91	< 0.01
Mortality at 30 postoperative days	1	1	0.850
Mortality at 90 postoperative days	3	4	0.527
Port sites metastasis	0	0	> 0.999

Perioperative outcomes and long-term survival

The incidence of biliary reconstruction was comparable between two groups. The length of operation in LRR group was significantly longer than that in ORR group (292.35 ± 14.41 vs 249.02 ± 13.30, P = 0.033). Intraoperative bleeding was significantly lower in LRR group than ORR group (233.91 ± 26.35 vs 461.25 ± 53.15, P < 0.01). Lymph node yield was comparable between two groups. Two groups also showed comparable incidence of postoperative morbidities including bile leakage, postoperative bleeding, and abdominal abscess. The incidence of Clavien–Dindo (C–D) grade III-IV was similar between groups. LRR group showed a trend of decreased days of drainage tubes indwelling (7.46 ± 0.62 vs 9.30 ± 0.85), although the difference did not show statistical significance (P = 0.077). Compared with ORR group, the postoperative days of hospital stay was significantly decreased in LRR group (10.32 ± 0.60 vs 14.74 ± 0.91, P < 0.01). Mortality at 30 postoperative days and 90 postoperative days, as well as the incidence port sites metastasis did not differ significantly between two groups. As for long-term survival, the 1-, 2-, and 3-year overall survival rates were 70.1, 50.2, and 44.6%, respectively, in the LLR group, and 52.7, 40.7, and 38.2%, respectively, in the OLR group (p = 0.155, Fig. 2A).

Baseline and pathological characteristics after PSM

After PSM, the baseline and pathological characteristics including age, gender, BMI, history of gallstone, preoperative CA199, preoperative TB, preoperative ALT, T stage, N stage, M stage, pathological type, tumor differentiation, peri-neural invasion, and vascular invasion showed good comparability between two groups as shown in Table 3.

Table 3
The comparison of baseline and pathological characteristics between LRC and ORC group after PSM

	LRC group (n = 30)	ORC group (n = 30)	P
Age			
< 60	9	11	0.785
≥ 60	21	19	
Gender			
Male	7	5	0.748
Female	23	25	
BMI			
< 24	21	20	> 0.999
≥ 24	9	10	
Gallstone			
Absence	18	17	> 0.999
Presence	12	13	
Preoperative CA199			
< 37 U/L	17	18	> 0.999
≥ 37 U/L	13	12	
Preoperative TB			
< 24 umolL/L	24	24	> 0.999
≥ 24 umolL/L	6	6	
Preoperative ALT			
< 40U/L	23	24	> 0.999
≥ 40U/L	7	6	
T stage			
T2	9	10	> 0.999
T3	21	20	

	LRC group (n = 30)	ORC group (n = 30)	P
N stage			
N0	14	16	0.797
N1-N2	16	14	
M stage			
M0	29	29	> 0.999
M1	1	1	
Pathological type			
Adenocarcinoma	27	28	> 0.999
Squamous carcinoma	3	2	
Tumor differentiation			
Poor	15	15	> 0.999
Well or Moderate	15	15	
Peri-neural invasion			
Absence	16	16	> 0.999
Presence	14	14	
Vascular invasion			
Absence	17	17	> 0.999
Presence	13	13	

Perioperative outcomes and long-term survival after PSM

Table 4 shows the perioperative outcomes of two groups after PSM. The incidence of biliary reconstruction was comparable between two groups after PSM. The length of operation in LRR group was significantly longer than that in ORR group (292.35 ± 14.41 vs 249.02 ± 13.30, P = 0.033). LRR group showed significantly decreased intraoperative bleeding (233.91 ± 26.35 vs 461.25 ± 53.15, P < 0.01). Lymph node yield, the incidence of postoperative morbidities, Clavien–Dindo (C–D) grade of III-IV, and the days of drainage tubes indwelling were comparable between groups. Postoperative days of hospital stay was significantly decreased in LRR group (10.32 ± 0.60 vs 14.74 ± 0.91, P < 0.01). Mortality at 30 postoperative days and 90 postoperative days, as well as the incidence port sites metastasis, did not

differ significantly between two groups. As for long-term survival, the 1-, 2-, and 3-year overall survival rates were 61.2, 40.1, and 30.1%, respectively, in the LLR group, and 53.3, 40.1, and 40.1%, respectively, in the OLR group (p = 0.644, Fig. 2B).

Table 4
The comparison of perioperative outcomes between LRC and ORC group after PSM

	LRC group (n = 30)	ORC group (n = 30)	P
Biliary reconstruction	4	3	> 0.999
Length of operation	328.12 ± 21.53	245.82 ± 15.18	**< 0.01**
Intraoperative bleeding	256.74 ± 39.21	484.36 ± 64.67	**< 0.01**
Lymph node yield	10.12 ± 0.90	7.92 ± 0.57	**0.04**
Morbidity			
Bile leakage	3	2	0.640
Postoperative bleeding	1	0	0.313
Abdominal abscess	2	2	> 0.999
Clavien–Dindo Classification Grade III-IV	3	2	0.640
Days of drainage tubes indwelling	7.43 ± 0.71	8.37 ± 0.87	0.41
Postoperative days of hospital stay	10.43 ± 0.97	14.23 ± 1.07	**0.01**
Mortality at 30 postoperative days	1	1	> 0.999
Mortality at 90 postoperative days	3	3	> 0.999
Port sites metastasis	0	0	> 0.999

Risk factors of overall survival after operation

As shown in Table 5, univariate analysis identified T stage, N stage, vascular invasion, tumor differentiation and biliary reconstruction to be the risk factor for overall survival. Multivariate analysis further identified the T stage, vascular invasion and tumor differentiation to be the independent risk factors of overall survival for GBC of T2 and T3 stages.

Table 5
Univariable and multivariable logistic regression of factors associated with the overall survival of GBC in T2 and T3 stages

	Univariable logistic regression		Multivariable logistic regression	
	OR (95% CI)	P	OR (95% CI)	P
Age (< 60 vs. ≥60)	1.354 (0.754–2.431)	0.310		
Gender (Male vs. Female)	1.085 (0.544–2.163)	0.818		
BMI (< 24 vs. ≥24)	0.597 (0.324–1.098)	0.085		
History of Gallstone (Presence vs Absence)	1.476 (0.856–2.543)	0.162		
CA199 (< 37 vs ≥ 37)	1.675 (0.965–2.845)	0.070		
Total bilirubin (< 24 vs ≥ 24)	1.274 (0.655–2.480)	0.486		
ALT (< 50 vs ≥ 50)	1.190 (0.636–2.225)	0.592		
Surgical Type (ORR vs LRR)	0.678 (0.392–1.172)	0.162		
T stage (T2 vs T3)	4.049 (2.181–7.515)	**< 0.001**	2.677 (1.386–5.171)	**0.003**
N stage (N0 vs N1-2)	2.368 (1.361–4.122)	**0.002**	1.592 (0.878–2.886)	0.126
M stage (M0 vs M1)	1.486 (0.535–4.130)	0.472		
Vascular invasion (Presence vs Absence)	2.472 (1.433–4.264)	**0.001**	1.646 (0.912–2.971)	0.098
Neural invasion (Presence vs Absence)	1.228 (0.710–2.124)	0.463		
Pathological type (Adenocarcinoma vs Squamous carcinoma)	1.629 (0.693–3.828)	0.292		
Tumor differentiation (Poor vs Well or Moderate)	4.211 (2.365–7.499)	**< 0.001**	3.702 (2.021–6.781)	**< 0.001**
Biliary reconstruction (Presence vs Absence)	2.117 (1.107–4.051)	**0.035**	1.494 (0.770–2.900)	0.235

Discussion

With the development of laparoscopic techniques and equipment, the laparoscopic surgery has been widely applied in gastric cancer, liver cancer, pancreatic cancer and colon cancer. In the case of GBC, the development and application of laparoscopic surgery is still in initial stage compared with that of laparoscopic surgery in other digestive cancers. During recent years, several studies with limited case numbers reported the perioperative and survival outcomes of laparoscopic approach for early GBC or incidental GBC(6, 8–10). A recent survey of surgical experts revealed that laparoscopic surgery has been gradually accepted for suspicious or early GBC(13). However, the role of laparoscopic radical resection for GBC in relatively late stages remains uncovered.

In this study, we retrospectively analyzed the outcomes of 99 GBC cases in T2 and T3 stages who underwent laparoscopic (n = 56) or open (n = 43) radical resection. Our data showed that laparoscopic surgery achieved comparable perioperative outcomes and long-term survival with open surgery. Laparoscopic surgery even demonstrated advantages over open surgery regarding intraoperative bleeding and postoperative hospital stay. As in many other surgical centers, the LRR in our institution started with GBC in relatively early stages and moved progressively to advanced lesions. Therefore, the LLR and ORR groups in current study were different regarding preoperative TB level, preoperative ALT level, T stage distribution, as a result of the decision-making in surgical approach that considered characteristics of individual GBC case, surgeon attitude and experience. To overcome this selection bias, 1:1 PSM was performed and created two comparable groups of GBC patients in T2 and T3 stage who underwent LLR (n = 30) versus ORR (n = 30). After PSM, LRR and ORR groups showed better comparability in baseline and pathological characteristics. The data of perioperative and long-term survival further validated that compared with open surgery, laparoscopic approach did not adversely affect the perioperative safety, oncological outcomes and overall survival of GBC in T2 and T3 stages.

One issue preventing the application of laparoscopic approach in GBC is the possible of risk of port-site implantation or metastasis due to intraoperative gallbladder perforation. Although previous study reported high incidence of port-site metastasis, there was no case of port-site metastasis in the present study. This data was consistent with recently published literatures(14, 15). Preoperative recognition of malignancy, precautionary operative manipulation, en-bloc resection of gallbladder and liver parenchymal, and use of plastic bag for specimen removal are probably attributable to this low incidence of port-site metastasis. Therefore, concern about port-site metastasis should not be an obstacle for the application of laparoscopic approach for GBC.

Another concern counting against the application of LRR for GBC is regarding its oncologic adequacy and intraoperative safety. Lymph node dissection is a key procedure during radical resection of GBC(16). The extent of lymph node dissection for GBC includes removal of lymph nodes around the hepatoduodenal ligament and the posterior superior pancreaticoduodenal area. The experience of laparoscopic surgery for the treatment of gastrointestinal cancers and pancreatic cancer has provided a foundation for complete lymph node dissection for GBC. Our data showed that laparoscopic approach

was feasible for required lymph node dissection (Fig. 1E-1F) and LRR group had comparable lymph node yield with ORR group, which was consistent with other studies. Although the length of operation was increased in LRR group, laparoscopic surgery was associated with significantly decreased intraoperative bleeding. The incidence of postoperative morbidity, the mortality at 30 and 90 postoperative days were comparable between LRR and ORR group. Moreover, laparoscopic resection was associated with decreased days of drainage tubes indwelling and postoperative days of hospital stay. These data demonstrate that laparoscopic approach can achieve satisfactory oncologic adequacy and intraoperative safety.

To explore the influence of various co-factors on the overall survival of GBC in T2 and T3 stage, a multivariable logistic regression analysis was carried out on the entire cohort of patients. The analysis confirmed T stage, vascular invasion and tumor differentiation to be the independent risk factors of overall survival for GBC in T2 and T3 stages. These indicate the pathological characteristics, instead of the surgical approach (LRR vs. ORR), are the key factors determining the long-term prognosis of GBC patients.

There are some limitations to the present study. First, this study is a retrospective, nonrandomized, single-institution investigation, which limit the strength of the results. Although this is the largest retrospective study examining the perioperative and long-term outcomes of laparoscopic resection for GBC in T2 and T3 stages, the confidence level of this study will be improved by including more GBC cases from multiple surgical centers. Second, the intrinsic variability in baseline patient characteristics, pathological features could not be fully captured by the categorical variables described. This means other hidden differences could possible exist between groups, even in the propensity score-matched series, that may have influenced the choice of surgical approach and clinical outcomes. Finally, an intrinsic limitation of 1:1 PSM is that many control subjects (ORR) or treated subjects (LRR) are excluded from statistical analysis, which can result in loss of information and decrease the precision of the estimated association between surgical approach and clinical outcomes.

In all, even considering these limitations, this study suggests that laparoscopic resection for GBC in T2 and T3 stages shows perioperative outcomes and long-term survival comparable to those of open surgery, and reduces the intraoperative bleeding and the duration of postoperative hospital stay.

Declarations

Ethics approval and consent to participate

Ethics approval for the study was obtained from the Institutional Review Board of Zhejiang Provincial People's Hospital. Informed consent for collecting clinical data were obtained from every patient or, their parent or legal guardian enrolled in this study.

Consent for publication

All authors including Dr. Changwei Dou, Dr. Chunxu Zhang, Dr. Chengwu Zhang and Dr. Jie Liu, agreed the submission and publication of this manuscript. The consent to publish were obtained from every patient or, their parent or legal guardian enrolled in this study.

Availability of data and materials

The data supporting the findings of the article is available from the corresponding author upon reasonable request.

Competing interests

All authors including Dr. Changwei Dou, Dr. Chunxu Zhang, Dr. Chengwu Zhang and Dr. Jie Liu, have no conflicts of interest or financial ties to disclose.

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Authors' contributions

Dr. Changwei Dou designed the study and wrote the manuscript; Dr. Chunxu Zhang collected the clinical data; Dr. Jie Liu designed the study and performed the statistical analysis; Dr. Chengwu Zhang designed the study and wrote the manuscript.

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None

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Figures

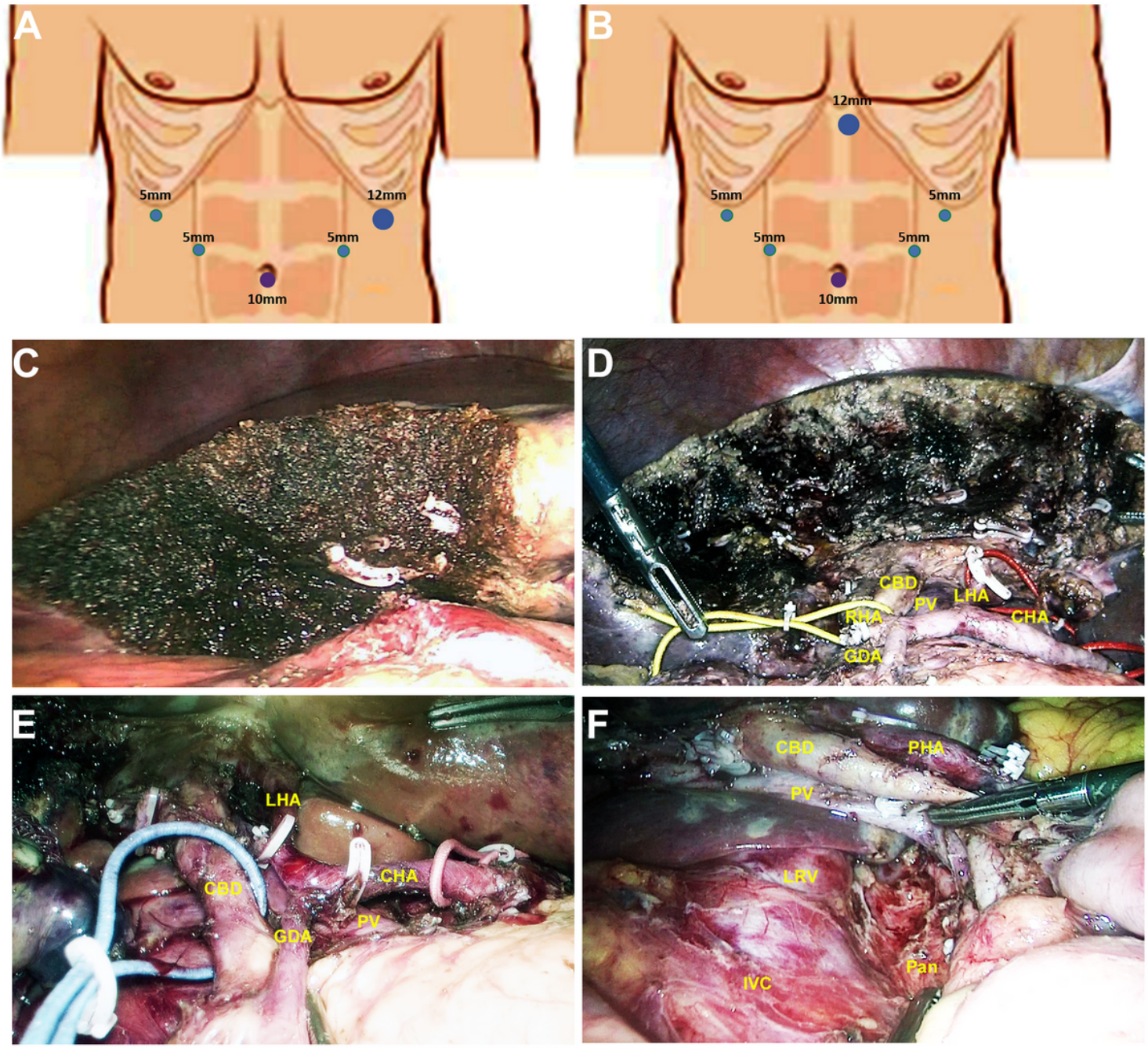

Figure 1

Key procedures of LRR for GBC. (A) Schematic diagram of the five-pore method for radical resection of GBC. (B) Schematic diagram of the six-pore method for radical resection of GBC. (C) The view of liver cross section after wedge resection. (D) The view of liver cross section after resection of segments IVb and V. (E) Dissection of lymph nodes along the extrahepatic bile ducts, the hepatoduodenal ligament and the hilar areas. (F) Dissection of lymph nodes around the retro-pancreatic head region. CBD, common bile duct; CHA, common hepatic artery; LHA, left hepatic artery; RHA, right hepatic artery; GDA, gastroduodenal artery; PV, portal vein; IVC, inferior vena cava; LRV, left renal vein; PHA, proper hepatic artery; Pan, pancreas.

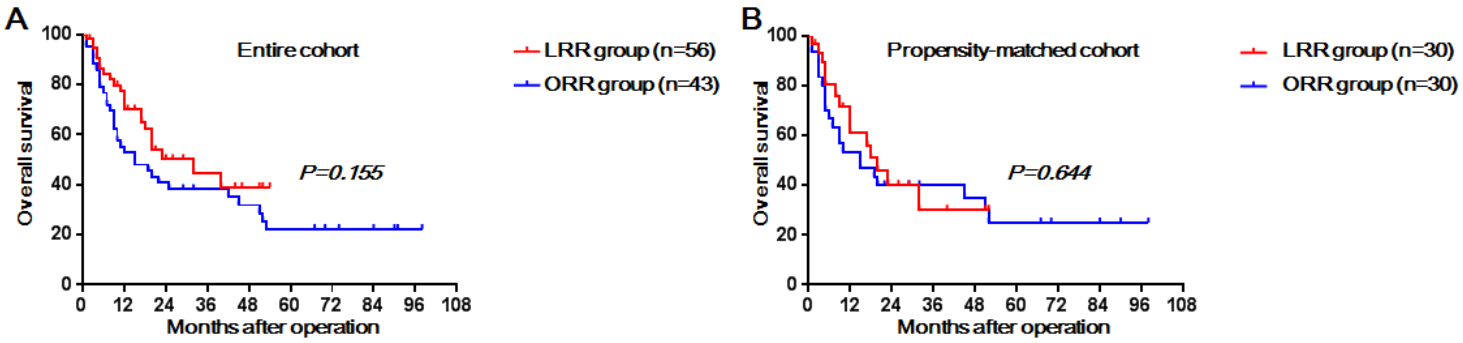

Figure 2

Comparison of Overall survival (OS) for GBCs in T2-T3 stages between LRR and ORR group. (A) OS of GBC patients in T2-T3 stages was compared between LRR and ORR group before PSM. (B) OS of GBC patients in T2-T3 stages was compared between LRR and ORR group after PSM.