Laparoscopic versus open hepatectomy for hepatocellular carcinoma with cirrhosis: a single-center propensity score matching analysis

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Background: Laparoscopic hepatectomy (LH) for hepatocellular carcinoma (HCC) remains controversial due to limited research. This study analyzed the oncology prognosis of patients who received LH treatment for HCC compared with conventional open hepatectomy (OH).

Methods: We conducted a retrospective analysis of patients with cirrhosis who underwent hepatectomy for HCC between 2012 and 2018. Patients were divided into LH and OH groups, and the oncology outcomes were compared before and after 1:1 propensity score matching (PSM).

Results: A total of 403 patients with HCC cirrhosis who received LH (n=112) and OH (n=291) were enrolled. After PSM, 106 pairs of patients were matched. Compared with OH before and after PSM, there was no significant difference in overall survival (OS) and relapse-free survival (RFS) between the two groups. Tumor stage, Child-Pugh classification, venous tumor thrombus, tumor size ≥5 cm, and microvascular invasion (MVI) were independent risk factors for postoperative OS in HCC patients with cirrhosis. Tumor size ≥5 cm and MVI were independent risk factors for RFS.

Conclusions: Patients with HCC who underwent LH had a similar OS and RFS compared with those who received traditional open surgery. Therefore, LH can be used as a safe and feasible treatment for patients with HCC.

Keywords: Hepatocellular carcinoma (HCC); laparoscopic hepatectomy (LH); open hepatectomy (OH); prognosis

Introduction

Hepatocellular carcinoma (HCC) is the third leading cause of cancer deaths worldwide. Approximately 50% of new liver cancer patients are from China, making HCC the second most common malignant tumor in China (1-3). Currently, treatment for HCC is divided into surgical treatment and non-surgical treatment, and surgical treatment includes tumor resection and liver

transplantation. Due to the shortage of liver sources and the long waiting time for transplantation, liver transplantation cannot be performed clinically on a large scale. Hence, liver resection remains the primary surgical option for a potential cure. Unfortunately, most HCC patients already have cirrhosis by the time of diagnosis. HCC patients with cirrhosis have a higher risk of intraoperative bleeding, postoperative refractory ascites, and liver failure following tumor resection (4). Therefore, the technique requires a high level of surgical skill and experience.

Reich et al. completed the world's first laparoscopic hepatectomy (LH) in 1991, ushering in a new era of laparoscopic liver resections (5). As a relatively less invasive surgical method, this modified technique has attracted worldwide attention (6). LH has been reported to result in less blood loss, lower rates of postoperative complications, and shorter hospital stays than conventional open hepatectomy (OH) (7). However, most surgeons have expressed concerns about tumor spread in the endoscopy environment, difficulty locating tumor boundaries, and difficulty controlling bleeding when tumors are close to important blood vessels, resulting in the slow promotion and uptake of LH amongst surgeons worldwide. With the popularization of technology and the improvement in endoscopic surgical techniques, the theoretical and technical aspects of LH have become well established, and the feasibility, safety, and effectiveness of LH have been gradually confirmed.

Although significant progress has been made in LH technology, its application in HCC patients remains controversial, with concerns remaining about tumor spread and adverse oncology outcomes (8). In 2018, Ramirez et al. compared open abdominal surgery with laparoscopic or robot-assisted minimally invasive surgery for patients with early cervical cancer and found that minimally invasive resection had no advantage in the treatment prognosis of early cervical cancer but had a higher recurrence rate and increased risk of death (9). The findings have also sparked a fierce debate in the field of hepatobiliary surgery. A study of 2,804 patients undergoing LH showed no significant difference in perioperative complication rates and mortality between LH and OH (10). For HCC patients with cirrhosis, laparoscopic surgery has also demonstrated good short- and long-term outcomes (11,12). However, most of these reports involve small liver resections, and the issue remains controversial.

Our center is located in a region with a high incidence of HCC in China, and the number of hepatectomy performed is increasing year by year. Therefore, this study can help local doctors choose surgical procedures and provide theoretical reference for other doctors. The purpose of this study was to analyze the survival results of patients with HCC complicated with cirrhosis treated with LH and OH in our center. To reduce the potential selection bias inherent in retrospective studies, we used a propensity score matching (PSM) analysis to determine the differences in survival outcomes between the two surgical procedures. We present the following article in accordance with the STROBE reporting checklist (available at https://dx.doi.org/10.21037/atm-21-5833).

Methods

Study subjects

We retrospectively collected data from patients with HCC, without obvious surgical contraindications, who underwent hepatectomy and complicated with cirrhosis from 2012 to 2018 in the First Affiliated Hospital of Guangxi Medical University. A total of 403 patients with HCC complicated with cirrhosis were enrolled and formed the basis of this study. Since our study focused on LH, based on the number of LH cases, after 1:1 PSM, there were 106 patients in the open group and 106 patients in the laparoscopic group (Figure 1). Baseline, clinical, and pathological data and survival outcome data were collected for retrospective analysis.

Inclusion and exclusion criteria

This study is a retrospective study. In order to unify terminology and facilitate understanding, so the diagnosis of primary liver cancer is based on The Guidelines for the Diagnosis and Treatment of Primary Liver Cancer in China (2019 Edition) (13). The patient inclusion criteria were as follows: (I) male or female patients aged 18–75 years; (II) a diagnosis of HCC with cirrhosis confirmed by postoperative pathology; (III) a preoperative evaluation confirming the feasibility of HCC resection. The exclusion criteria included (I) secondary HCC, (II) early HCC intervention (e.g., transcatheter arterial embolization, radiofrequency ablation, or portal vein embolization), (III) HCC rupture and hemorrhage, (IV) postoperative follow-up loss, (V) non-radical resection, and (VI) a follow-up time less than 6 months.
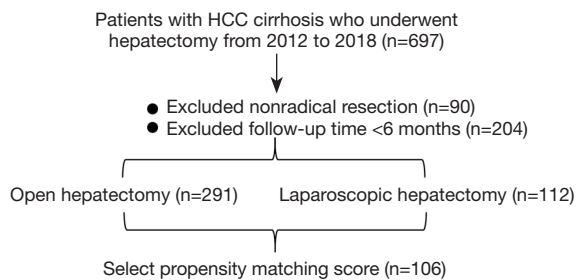
Patients with HCC cirrhosis who underwent
hepatectomy from 2012 to 2018 (n=697)

● Excluded nonradical resection (n=90)
● Excluded follow-up time <6 months (n=204)

Open hepatectomy (n=291)   Laparoscopic hepatectomy (n=112)

Select propensity matching score (n=106)

Figure 1 The screening flow chart of HCC patients with cirrhosis. HCC, hepatocellular carcinoma.

Data collection

Data on 403 cases were obtained through our inpatient and outpatient information management systems and were based on the inclusion and exclusion criteria. The available data included sex, age, hepatitis background, smoking and alcohol intake (alcohol intake >30 g/day for men and >20 g/day for women), tumor assessment (presence of portal vein cancer thrombus, tumor size, and number), intraoperative conditions (surgical method, operative time, blood loss, blood transfusion volume, etc.), pathology [degree of differentiation, cirrhosis, microvascular invasion (MVI), etc.], postoperative complications, and length of hospital stay. Postoperative complications were recorded during hospitalization at the same surgery or within 30 days after discharge and were assessed according to the Clavien-Dindo classification system (14). Patients or family members were followed up through our information management system and by telephone, with OS defined as the time from surgery to death or the date of the last follow-up. RFS was defined as the time from surgery to the date of a diagnosis of HCC recurrence.

Statistical analysis

Continuous variables are presented as mean (standard deviation) and independent sample t-test is used. The categorical variables are presented in terms of numbers (percentage), using the Chi-square test or Fisher's exact probability method as required. Kaplan-Meier method was used to calculate the cumulative mortality and recurrence rates between the open and endoscopic groups, and log-rank method was used to compare the differences in mortality and recurrence rates between the two groups. In this study, propensity score matching was used to eliminate confounding effects of included variables. We matched

patients in the open and endoscopic groups at a ratio of 1:1, and factors related to overall survival (OS) and relapse-free survival (RFS) were included in the propensity scoring model, including age, sex, body mass index (BMI), smoking, alcohol, α-fetoprotein (AFP), diabetes mellitus (DM), hypertension, Barcelona clinic liver cancer stage (BCLC), China liver cancer stage (CNLC), Child-Pugh grade, liver fluke, tumor size and number, hepatitis virus infection, pathological stage, MVI, operation time, and blood loss. we used propensity score for non-replace-matching, and matched parameters were (Method = Nearlyst, CLIper =0.2*SD). COX proportional risk model was used for univariate and multivariate analysis to identify risk factors associated with OS and RFS. P<0.05 was considered statistically significant. All analyses were performed using R software (https://www.r-project.org/).

Ethical statement

The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). This study was approved by the Ethics Committee of the First Affiliated Hospital of Guangxi Medical University (No. 2021-KY-E-277). Individual consent for this retrospective analysis was waived.

Results

Baseline characteristics

We conducted a retrospective analysis of 403 HCC patients with cirrhosis who underwent hepatectomy from 2012 to 2018. There were 291 cases (72.2%) in the laparotomy group and 112 cases (27.8%) in the laparoscopy group. Baseline data before PSM showed that CNLC stage (P=0.021), venous tumor thrombus (P=0.027), hepatitis (P=0.022), duration of surgery (P=0.013), bleeding (P=0.04), and length of hospitalization (P<0.001) were significantly different between the groups (*Table 1*). After 1:1 PSM, 106 patients remained in each group, and all clinicopathological features were well balanced between the two groups (*Table 2*, *Figure 2*).

Univariate and multivariate analyses of OS and RFS predictions

Before PSM, univariate analysis showed that BCLC stage B–C (P=0.008), CNLC stage III (P=0.009), venous tumor

Page 4 of 15

He et al. Analysis of LH and OH of HCC with liver cirrhosis

Table 1 Patients' baseline characteristics before propensity score matching

Variable	Open hepatectomy (n=291)	Laparoscopic hepatectomy (n=112)	P value
Gender, n (%)			0.222
Female	41 (14.1)	22 (19.6)	
Male	250 (85.9)	90 (80.4)	
Age	49.3 (10.3)	49.1 (10.8)	0.867
BMI	23.0 (3.17)	22.9 (3.12)	0.936
Smoking, n (%)			0.529
No	178 (61.2)	73 (65.2)	
Yes	113 (38.8)	39 (34.8)	
Alcohol, n (%)			0.226
No	193 (66.3)	82 (73.2)	
Yes	98 (33.7)	30 (26.8)	
AFP (ng/mL), n (%)			0.747
<400	196 (67.4)	78 (69.6)	
≥400	95 (32.6)	34 (30.4)	
DM, n (%)			1.000
No	266 (91.4)	102 (91.1)	
Yes	25 (8.59)	10 (8.93)	
Hypertension, n (%)			0.899
No	262 (90.0)	102 (91.1)	
Yes	29 (9.97)	10 (8.93)	
BCLC stage, n (%)			0.416
0-A	255 (87.6)	94 (83.9)	
B-C	36 (12.4)	18 (16.1)	
CNLC stage, n (%)			0.021
I	240 (82.5)	92 (82.1)	
II	42 (14.4)	10 (8.93)	
III	9 (3.09)	10 (8.93)	
Child-Pugh classification, n (%)			0.419
A	277 (95.2)	109 (97.3)	
B	14 (4.81)	3 (2.68)	
Liver fluke, n (%)			0.375
No	254 (87.3)	102 (91.1)	
Yes	37 (12.7)	10 (8.93)	
Venous tumor thrombus, n (%)			0.027
No	282 (96.9)	102 (91.1)	
Yes	9 (3.09)	10 (8.93)	

Table 1 (*continued*)

Table 1 (*continued*)

Variable	Open hepatectomy (n=291)	Laparoscopic hepatectomy (n=112)	P value
Number of tumors, n (%)			0.367
Single	248 (85.2)	100 (89.3)	
Multiple	43 (14.8)	12 (10.7)	
Tumor size, n (%)			0.089
<5 cm	205 (70.4)	89 (79.5)	
≥5 cm	86 (29.6)	23 (20.5)	
Hepatitis, n (%)			0.022
No	33 (11.3)	4 (3.57)	
HBV	251 (86.3)	107 (95.5)	
HCV	7 (2.41)	1 (0.89)	
Degree of differentiation, n (%)			0.342
Well	18 (6.19)	5 (4.46)	
Moderately	267 (91.8)	102 (91.1)	
Poorly	6 (2.06)	5 (4.46)	
MVI, n (%)			0.606
No	217 (74.6)	80 (71.4)	
Yes	74 (25.4)	32 (28.6)	
Duration of operation	225 [104]	257 [118]	0.013
Bleeding	517 [784]	385 [472]	0.040
Length of stay	19.8 [6.51]	15.1 [6.56]	<0.001
Clavien-Dindo, n (%)			0.529
< Grade 3	280 (96.2)	110 (98.2)	
≥ Grade 3	11 (3.78)	2 (1.79)	

MVI, microvascular invasion; BMI, body mass index; AFP, α-fetoprotein; DM, diabetes mellitus; BCLC, Barcelona clinic liver cancer staging; CNLC, China liver cancer staging.

thrombus (P=0.011), tumor size ≥5 cm (P=0.001), MVI (P=0.001), and bleeding (P=0.012) were correlated with OS. BCLC stage B–C (P=0.031), CNLC stage II (P=0.014), multiple tumors (P=0.004), MVI (P=0.022), and bleeding (P=0.003) were correlated with RFS (*Table 3*). We selected clinically common prognostic factors for the multifactorial analysis, which indicated that venous tumor thrombus (P=0.049), tumor size ≥5 cm (P=0.003), and MVI (P=0.032) were independent risk factors for OS. Multiple tumors (P=0.026) and bleeding (P=0.015) were independently correlated with RFS (*Table 4*). After PSM, univariate analysis showed that BCLC stage B–C (P=0.032), CNLC stage III (P=0.018), Child-Pugh classification B (P=0.013), venous

tumor thrombus (P=0.017), tumor size ≥5 cm (P=0.006), and MVI (P=0.026) were correlated with OS, while tumor size ≥5 cm (P=0.033) and MVI (P=0.028) were correlated with RFS (*Table 5*).

Survival analysis before and after PSM

Before PSM, there was no significant difference in oncology outcomes between the two groups in OS (P=0.69) and RFS (P=0.25). The OS and RFS rates at 1, 3, and 5 years in OH were 95.7%, 81.4%, 67.7%, 87.4%, 68.9%, and 54.9%, respectively. The OS and RFS rates at 1, 3, and 5 years in LH group were 94.6%, 79.8%, 58%, 91.0%, 73.3%, and

Table 2 Patients' baseline characteristics after propensity score matching

Variable	Open hepatectomy (n=106)	Laparoscopic hepatectomy (n=106)	P value
Gender, n (%)			1.000
Female	21 (19.8)	20 (18.9)	
Male	85 (80.2)	86 (81.1)	
Age	48.8 (11.0)	48.7 (10.7)	0.970
BMI	23.1 (2.98)	23.0 (3.07)	0.912
Smoking, n (%)			0.887
No	66 (62.3)	68 (64.2)	
Yes	40 (37.7)	38 (35.8)	
Alcohol, n (%)			1.000
No	76 (71.7)	76 (71.7)	
Yes	30 (28.3)	30 (28.3)	
AFP (ng/mL), n (%)			1.000
<400	74 (69.8)	73 (68.9)	
≥400	32 (30.2)	33 (31.1)	
DM, n (%)			0.795
No	99 (93.4)	97 (91.5)	
Yes	7 (6.6)	9 (8.5)	
Hypertension, n (%)			0.613
No	99 (93.4)	96 (90.6)	
Yes	7 (6.6)	10 (9.4)	
BCLC stage, n (%)			0.834
0-A	94 (88.7)	92 (86.8)	
B-C	12 (11.3)	14 (13.2)	
CNLC stage, n (%)			0.924
I	92 (86.8)	90 (84.9)	
II	8 (7.5)	9 (8.49)	
III	6 (5.7)	7 (6.60)	
Child-Pugh classification, n (%)			1.000
A	103 (97.2)	103 (97.2)	
B	3 (2.83)	3 (2.83)	
Liver fluke			0.805
No	98 (92.4)	96 (90.6)	
Yes	8 (7.6)	10 (9.4)	
Venous tumor thrombus, n (%)			1.000
No	100 (94.3)	99 (93.4)	
Yes	6 (5.7)	7 (6.6)	

Table 2 (*continued*)

Table 2 (*continued*)

Variable	Open hepatectomy (n=106)	Laparoscopic hepatectomy (n=106)	P value
Number of tumors, n (%)			0.814
Single	97 (91.5)	95 (89.6)	
Multiple	9 (8.5)	11 (10.4)	
Tumor size, n (%)			0.728
<5 cm	87 (82.1)	84 (79.2)	
≥5 cm	19 (17.9)	22 (20.8)	
Hepatitis, n (%)			0.873
No	6 (5.7)	4 (3.77)	
HBV	99 (93.4)	101 (95.3)	
HCV	1 (0.9)	1 (0.94)	
Degree of differentiation, n (%)			1.000
Well	4 (3.8)	5 (4.7)	
Moderately	98 (92.4)	97 (91.5)	
Poorly	4 (3.8)	4 (3.8)	
MVI, n (%)			1.000
No	76 (71.7)	75 (70.8)	
Yes	30 (28.3)	31 (29.2)	
Duration of operation	250 [117]	255 [116]	0.734
Bleeding	376 [340]	389 [482]	0.825
Length of stay	19.3 [6.76]	14.9 [6.27]	<0.001
Clavien-Dindo, n (%)			0.280
< Grade 3	100 (94.3)	104 (98.1)	
≥ Grade 3	6 (5.7)	2 (1.9)	

AFP, α-fetoprotein; DM, diabetes mellitus; BCLC, Barcelona clinic liver cancer; CNLC, China liver cancer; HBV, Hepatitis B virus; HCV, Hepatitis C virus; MVI, microvascular invasion.

46.4%, respectively. After PSM, there was no significant difference in OS (P=0.7) and RFS (P=0.066) between the two groups. The rates of OS and RFS at 1, 3, and 5 years in OH were 93.2%, 80.2%, 72.4%, 83.5%, 65.3%, and 41.7%, respectively. The rates of OS and RFS at 1, 3, and 5 years in LH group were 94.3%, 79.9%, 57.5%, 90.5%, 74.1%, and 53.0%, respectively (*Figure 3*).

Discussion

Different stages of HCC lead to various treatment options, including hepatectomy, ablation, transarterial chemoembolization (TACE), targeted drug therapy, and liver transplantation (15,16). For early HCC, hepatectomy is the best treatment. For unresectable tumors, neoadjuvant therapy and comprehensive treatment can be used to reduce the size of the tumor and classification stage so that surgical resection is possible. Hepatectomy as a radical resection can achieve a satisfactory outcome in oncology and can be used as a first-line treatment for early and intermediate HCC or as a pretransplant bridging therapy (17). The significance of translational therapy, which has emerged in recent years, is to provide patients with the opportunity for radical treatment, which may enable patients to achieve longer disease-free survival and OS. Advances in laparoscopic instruments and techniques have greatly improved
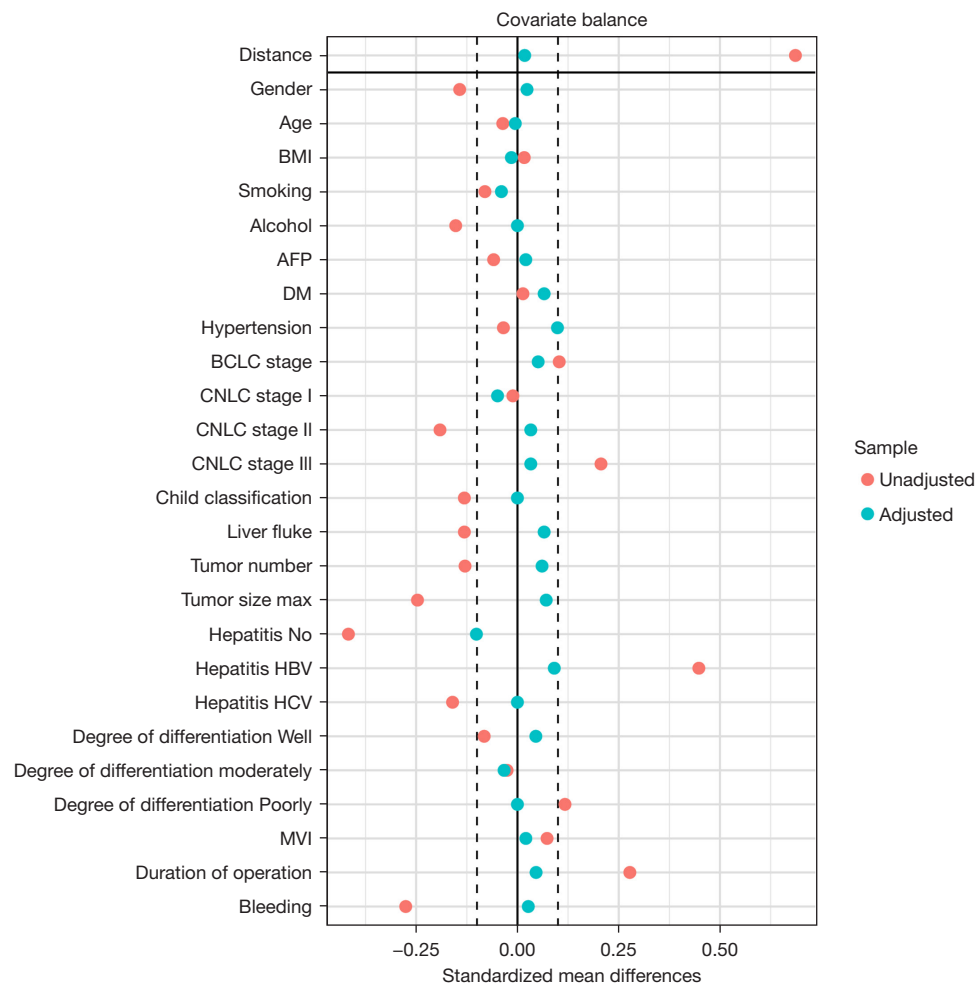
Page 8 of 15

He et al. Analysis of LH and OH of HCC with liver cirrhosis

Figure 2 The balance test of propensity score matching. AFP, α-fetoprotein; DM, diabetes mellitus; BCLC, Barcelona clinic liver cancer; CNLC, China liver cancer; HBV, Hepatitis B virus; HCV, Hepatitis C virus; MVI, microvascular invasion.

laparoscopic surgery and promoted the development of LH, but the liver has a unique anatomical structure, and the procedure remains complex and challenging, especially for HCC patients with cirrhosis who need resection (18). Compared with OH, LH has high-definition anatomical vision, and is also convenient for communication and learning among physicians. However, for tumors near large vessels or special parts, it is not convenient for laparoscopic instrument operation, and doctors with low experience need to master it after long-term practice.

The shortcomings of LH can be overcome to some extent by strengthening the training of surgical skills by senior or experienced physicians.

Clinical consensus is that cirrhosis is a high-risk factor for primary liver cancer, and the occurrence of cirrhosis can

further shorten the survival of liver cancer patients (19). The degree of cirrhosis is closely related to the reserve function of the liver, especially the coagulation function. Patients with cirrhosis are prone to have complications, such as portal hypertension and impaired coagulation function. It is difficult to separate hardened liver tissue, and uncontrolled bleeding increases the risk of surgery in patients with cirrhosis (20). The majority of liver cancers in Guangxi are complicated by cirrhosis and require safe and effective surgical methods. The radical treatment of HCC may afford greater benefits for patients who have complex underlying liver diseases. With the widespread use of laparoscopy in general surgery, a large number of recent studies have reported the advantages of LH, which can achieve complete tumor resection and tumor-free

Table 3 Single analysis of OS and RFS before propensity score matching

Factor	OS			RFS		
	HR	95% CI	P value	HR	95% CI	P value
Gender (male)	1.834	0.883–3.809	0.104	1.433	0.834–2.461	0.192
Age	0.998	0.977–1.019	0.840	1.014	0.996–1.032	0.130
BMI	1.025	0.959–1.096	0.461	1.015	0.961–1.072	0.585
Smoking (yes vs. no)	0.959	0.611–1.506	0.857	0.689	0.47–1.011	0.057
Alcohol (yes vs. no)	0.703	0.42–1.176	0.179	0.696	0.461–1.051	0.085
AFP (≥400 vs. <400 ng/mL)	1.051	0.659–1.676	0.836	1.026	0.703–1.496	0.896
DM (yes vs. no)	1.543	0.795–2.993	0.200	1.346	0.757–2.393	0.311
Hypertension (yes vs. no)	0.497	0.182–1.359	0.173	0.519	0.242–1.112	0.092
BCLC stage (B-C vs. 0-A)	2.161	1.228–3.804	0.008	1.702	1.05–2.759	0.031
CNLC stage (II vs. I)	1.320	0.712–2.447	0.377	1.779	1.126–2.81	0.014
CNLC stage (III vs. I)	3.487	1.365–8.91	0.009	1.429	0.521–3.919	0.488
Child-Pugh classification (B vs. A)	2.063	0.95–4.482	0.067	1.900	0.927–3.896	0.080
Liver fluke (yes vs. no)	0.692	0.333–1.437	0.323	1.286	0.78–2.121	0.324
Venous tumor thrombus (yes vs. no)	3.345	1.317–8.497	0.011	1.295	0.474–3.536	0.614
Number of tumors (multiple vs. single)	1.458	0.819–2.595	0.200	1.901	1.222–2.955	0.004
Tumor size (≥5 vs. <5 cm)	2.217	1.425–3.45	0.001	1.088	0.727–1.628	0.683
Hepatitis (HBV vs. no)	1.366	0.627–2.976	0.433	1.012	0.567–1.804	0.969
Hepatitis (HCV vs. no)	1.439	0.299–6.935	0.650	1.664	0.472–5.863	0.428
Degree of differentiation (moderately vs. well)	1.225	0.447–3.353	0.693	1.306	0.574–2.969	0.525
Degree of differentiation (poorly vs. well)	2.182	0.545–8.73	0.270	1.499	0.423–5.313	0.531
MVI (yes vs. no)	2.246	1.436–3.514	0.001	1.568	1.068–2.302	0.022
Duration of operation	1.001	0.999–1.003	0.266	1.001	1–1.003	0.157
Bleeding	1.000	1–1	0.012	1.000	1–1	0.003
Surgical approach (open hepatectomy vs. laparoscopic hepatectomy	0.899	0.53–1.525	0.694	0.779	0.507–1.196	0.254

HR, hazard ratio; CI, confidence interval; OS, overall survival; RFS, relapse-free survival; AFP, α-fetoprotein; DM, diabetes mellitus; BCLC, Barcelona clinic liver cancer; CNLC, China liver cancer; MVI, microvascular invasion.

resection margins (21). Accurate LH can reduce trauma and recurrence rates compared with early OH (22). In addition, laparoscopic robotic surgery, with its greater flexibility, can overcome the limitations of laparoscopic surgery alone and improve surgical accuracy. Furthermore, compared with open surgery, robotic surgery can shorten the length of hospital stay and reduce postoperative complications (23). However, prospective and randomized controlled studies comparing LH and OH have not been carried out.

This study retrospectively analyzed the prognosis of HCC patients with cirrhosis treated by laparoscopic and conventional OH from a single center.

Using PSM in this study, we found that tumor stage, Child-Pugh classification, venous tumor thrombus, tumor size ≥5 cm, and MVI were independent risk factors affecting postoperative OS in HCC patients. Tumor size ≥5 cm and MVI were also correlated with RFS. It has been reported that Child-Pugh classification is associated with

Page 10 of 15

He et al. Analysis of LH and OH of HCC with liver cirrhosis

Table 4 Univariate analysis of OS and RFS before propensity score matching

Factors	OS			RFS		
	HR	95% CI	P value	HR	95% CI	P value
Gender (male *vs.* female)	1.625	0.747–3.536	0.221	1.371	0.776–2.424	0.278
Age	0.997	0.975–1.021	0.829	1.015	0.996–1.034	0.128
DM (yes *vs.* no)	1.677	0.836–3.363	0.145	1.155	0.630–2.115	0.641
AFP (≥400 *vs.* <400 ng/mL)	0.951	0.574–1.574	0.844	1.062	0.173–1.583	0.766
Child-Pugh classification (B *vs.* A)	1.833	0.791–4.249	0.157	1.359	0.642–2.876	0.423
Tumor size (≥5 *vs.* <5 cm)	2.064	1.276–3.338	0.003	0.985	0.643–1.507	0.943
Number of tumors (multiple *vs.* single)	1.177	0.645–2.148	0.596	1.676	1.063–2.643	0.026
Bleeding	1.000	1–1	0.093	1.000	1.000–1.000	0.015
Degree of differentiation (moderately *vs.* well)	1.163	0.416–3.253	0.773	1.274	0.553–2.937	0.570
Degree of differentiation (poorly *vs.* well)	2.290	0.521–10.071	0.273	1.309	0.349–4.905	0.690
MVI (yes *vs.* no)	1.705	1.047–2.776	0.032	1.376	0.918–2.062	0.122
Venous tumor thrombus (yes *vs.* no)	2.608	1.004–6.777	0.049	1.284	0.466–3.536	0.628

OS, overall survival; RFS, relapse-free survival; DM, diabetes mellitus; AFP, α-fetoprotein; MVI, microvascular invasion.

hepatectomy (Child-Pugh B score) and a high incidence of postoperative complications in advanced cirrhotic HCC (24). The mortality rate of hepatectomy in Child-Pugh grade A, B, and C cirrhosis patients was 10%, 17%, and 63%, respectively (25). Portal vein cancer thrombus can easily form intrahepatic metastasis, and some researchers claim it should be listed as a contraindication for surgery (26). However, some scholars believe that in cases with good liver function and comprehensive preoperative planning and evaluation, HCC complicated by portal vein cancer thrombus or portal hypertension can also be treated with surgery, and some patients can still benefit from surgical resection. Results have also shown that long-term postoperative survival was better than other treatments (27-30). MVI is common in HCC and has been repeatedly shown to be a poor long-term prognostic factor associated with early tumor recurrence and reduced survival (31-33). Studies have identified tumor size (>2–3 cm), number of tumors, and MVI as risk factors for HCC recurrence (34,35). MVI is an important risk factor for early postoperative recurrence, and there are significant differences in the early RFS rates of patients with or without MVI or mild versus severe MVI. Even for patients with small HCC, MVI will increase the recurrence rate of HCC, which is not conducive to the long-term survival of patients (36-40). Our results are similar to those previously reported, which

attests to the reliability of the current study analysis.

Long-term oncology prognosis and disease-free survival are critical in determining the role of LH in HCC management. Most of the current reports on long-term prognosis show no significant differences between LH and OH surgical procedures and 5-year OS and RFS, even in patients with cirrhosis (41-44). However, a previous meta-analysis compared the results of LH and OH in liver cancer patients with cirrhosis and found that the 5-year OS of LH was better than that of OH (45), which may be related to the number of studies included and the lack of long-term prognostic data. In our study, there was no significant difference between the OS and RFS of patients in the LH and OH groups, whether before or after PSM. Similar to most results from recent studies, it also reflects the reliability of the oncology outcome analysis in our study. Therefore, we suggest that LH can be used to shorten the operation time for tumors located in the left half of the liver or superficial. For patients with special tumor location or portal hypertension, OH can be used to improve surgical safety. Our study focused on patient outcomes, so hospitalization costs were not explored in depth.

The retrospective nature of the current study contains inherent flaws due to the lack of randomization, the small sample size, and the single-center design, which may have affected the strength and validity of our results. In addition,

Table 5 Single-factor analysis of OS and RFS after propensity score matching

Factors	OS			RFS		
	HR	95% CI	P value	HR	95% CI	P value
Gender (male *vs.* female)	1.273	0.533–3.038	0.587	1.359	0.693–2.666	0.372
Age	0.996	0.967–1.026	0.804	1.006	0.984–1.03	0.584
BMI	0.990	0.893–1.098	0.846	0.954	0.878–1.037	0.269
Smoking (yes *vs.* no)	0.692	0.35–1.366	0.289	0.647	0.383–1.095	0.105
Alcohol (yes *vs.* no)	0.562	0.248–1.274	0.167	0.676	0.375–1.221	0.194
AFP (≥400 *vs.* <400 ng/mL)	1.597	0.842–3.029	0.152	1.525	0.927–2.51	0.097
DM (yes *vs.* no)	1.872	0.662–5.296	0.237	1.561	0.671–3.631	0.301
Hypertension (yes *vs.* no)	1.328	0.404–4.361	0.640	0.890	0.322–2.458	0.822
BCLC stage (B-C *vs.* 0-A)	2.344	1.074–5.116	0.032	1.690	0.859–3.325	0.128
CNLC stage (II *vs.* I)	0.810	0.248–2.651	0.728	1.298	0.59–2.859	0.517
CNLC stage (III *vs.* I)	3.627	1.242–10.597	0.018	2.149	0.767–6.02	0.145
Child-Pugh classification (B *vs.* A)	4.502	1.377–14.721	0.013	1.001	0.138–7.268	1.000
Liver fluke (yes *vs.* no)	1.296	0.46–3.65	0.624	2.028	0.963–4.27	0.063
Venous tumor thrombus (yes *vs.* no)	3.693	1.269–10.748	0.017	2.091	0.75–5.831	0.159
Number of tumors (multiple *vs.* single)	1.234	0.482–3.159	0.662	1.566	0.773–3.172	0.213
Tumor size (≥5 *vs.* <5 cm)	2.532	1.299–4.938	0.006	1.851	1.052–3.257	0.033
Hepatitis (HBV *vs.* no)	2.504	0.341–18.38	0.367	1.376	0.428–4.422	0.593
Hepatitis (HCV *vs.* no)	0.000	0–Inf	0.997	0.000	0–Inf	0.996
Degree of differentiation (moderately *vs.* well)	1.691	0.232–12.346	0.604	3.489	0.484–25.17	0.215
Degree of differentiation (poorly *vs.* well)	3.065	0.318–29.525	0.332	3.511	0.365–33.782	0.277
MVI (yes *vs.* no)	2.078	1.094–3.948	0.026	1.768	1.062–2.942	0.028
Duration of operation	1.000	0.998–1.003	0.773	1.001	0.999–1.003	0.466
Bleeding	1.000	1–1.001	0.204	1.000	1–1.001	0.289
Surgical approach (open hepatectomy *vs.* laparoscopic hepatectomy	0.883	0.466–1.674	0.704	0.628	0.381–1.036	0.069

OS, overall survival; RFS, relapse-free survival; AFP, α-fetoprotein; DM, diabetes mellitus; BCLC, Barcelona clinic liver cancer; CNLC, China liver cancer; MVI, microvascular invasion.
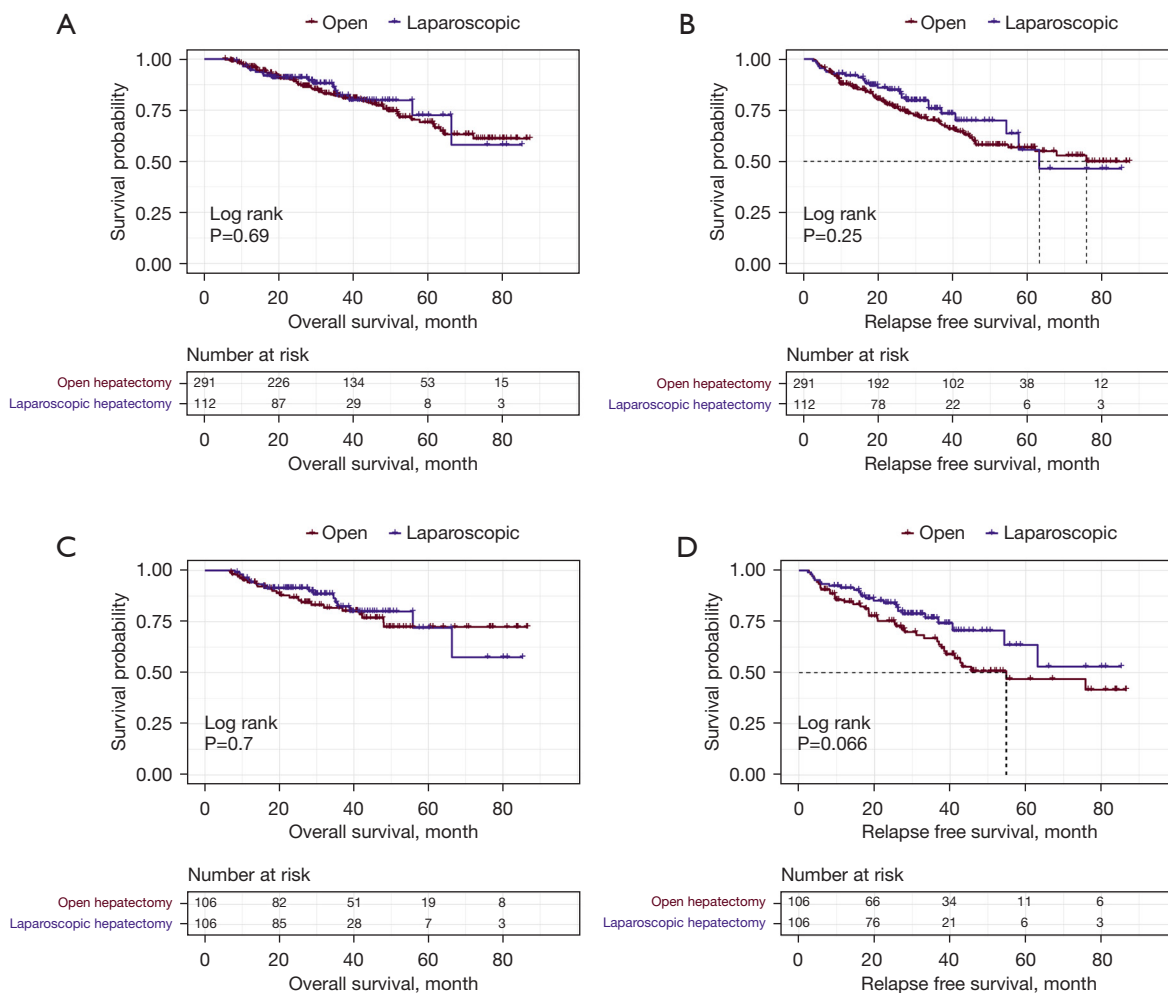
Figure 3 Analysis of the survival curve before and after PSM. (A,B) OS and RFS before PSM; (C,D) OS and RFS after PSM. PSM, propensity score matching; OS, overall survival; RFS, relapse-free survival.

the primary etiology of HCC in our region is the hepatitis B virus infection, which differs from that in European and American countries. Bias matching can minimize selection bias and the effect of potential covariates, but randomized controlled trials are still needed to investigate short - and long-term patient outcomes.

Conclusions

In conclusion, our study showed that LH had a similar postoperative OS and RFS compared with traditional open surgery for HCC patients with cirrhosis. LH can be used as a feasible treatment option for HCC patients with cirrhosis.

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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. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). This study was approved by the Ethics Committee of the First Affiliated Hospital of Guangxi Medical University (No. 2021-KY-E-277). Individual consent for this retrospective analysis was waived.

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Page 14 of 15

He et al. Analysis of LH and OH of HCC with liver cirrhosis

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