

# Effect of Different Liver Resection Modalities on the Prognosis of Patients with Hepatocellular Carcinoma on the Left Lateral Lobe

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**Purpose:** To investigate the effect of different liver resection modalities on the prognosis of left lateral lobe hepatocellular carcinoma (HCC) patients.

**Methods:** 315 patients with HCC on left lateral lobe were divided into open left lateral lobectomy (LLL) group (n=249) and open left hepatectomy (LH) group (n=66). The differences in long-term prognosis between two groups were compared.

**Results:** The results showed that narrow resection margin (Hazard Ratio (HR):1.457, 95% Confidential Interval (CI): 1.038–2.047; HR:1.415, 95% CI: 1.061–1.887), tumor diameter > 5 cm (1.645, 1.161–2.330; 1.488, 1.123–1.971), multiple tumors (2.021, 1.330–3.073; 1.987, 1.380–2.861), and microvascular invasion (MVI) (1.753, 1.253–2.452; 1.438, 1.087–1.902) are independent risk factors for overall survival (OS) and tumor recurrence (TR), while liver resection modality is not. After propensity score matching, liver resection modality is not an independent risk factor for OS and TR. Further analysis revealed that wide resection margins were achieved in all patients in the LH group but only 59.0% patients in the LLL group. The OS and TR rates were not significantly different between wide patients with resection margins in LLL group and LH group (P=0.766 and 0.919, respectively), but significantly different between patients with narrow resection margins in LLL group and LH group (P=0.012 and 0.017, respectively).

**Conclusion:** Liver resection modality is not an independent risk factor for the prognosis of patients with HCC on the left lateral lobe as long as wide margins are obtained. Nevertheless, with narrow margins, patients who underwent LH rather than LLL did better.

**Keywords:** hepatocellular carcinoma, left lateral hepatic lobe, left lateral lobectomy, left hepatectomy, prognosis

## Introduction

Hepatocellular carcinoma (HCC) is a common malignant tumor with morbidity and mortality ranking top among all malignant tumors in China.<sup>1</sup> More than 50% world's new liver cancer cases are identified in China each year.<sup>2</sup> Currently, resection is the most effective treatment for HCC,<sup>3,4</sup> but the postoperative prognosis of HCC patients is still very poor.<sup>5,6</sup> The surgical modality can be divided into anatomical liver resection and non-anatomical liver resection or local resection and extended resection. Previous studies have suggested that anatomical hepatectomy can lead to better long-term prognosis than non-anatomical hepatectomy.<sup>7,8</sup> However, regardless of the resection modality, radical resection is the principle for all HCC patients. For patients with HCC on the left lateral lobe, left lateral lobectomy (LLL) and left hepatectomy (LH) are common surgical approaches.<sup>9,10</sup> Both can be performed laparoscopically or openly. Studies have

reported that laparoscopic LH may achieve better overall survival (OS) than open LLL.<sup>11</sup> However, the effects of open LLL or LH on postoperative complications, OS, and tumor recurrence (TR) of patients with HCC on the left lateral lobe are still unclear. Therefore, this study systematically analyzed the effects of different liver resection modalities on postoperative complications, OS, and TR of patients with HCC on the left lateral lobe.

## Patients and Methods

### Patients

A total of 315 patients who had HCC on the left lateral lobe and underwent open LLL or open LH in our hospital from June 2011 to August 2013 were enrolled in the study. These patients were followed up until January 2018. All patients underwent routine preoperative laboratory tests to evaluate their surgical tolerance and tumor resectability. The inclusion criteria were: (1) all patients underwent open LLL or open LH; (2) preoperative liver function assessment indicated Child-Pugh grade A and Child-Pugh score  $\leq$  B7; (3) tumor located only in the left lateral lobe (hepatic segment II or III) but not in other liver segments; (4) single or multiple tumors did not invade the sagittal part of the portal vein; (5) tumor was not involved in large blood vessels, diaphragm and other surrounding organs and did not metastasize; (6) tumor was completely resected, and the surgical resection margin was R0; (7) HCC was pathologically confirmed after the operation; (8) the Clinicopathological and follow-up data are complete. The exclusion criteria were: (1) patients underwent laparoscopic LLL or laparoscopic LH; (2) tumor located on sites other than the left lateral lobe; (3) tumor was accompanied by diaphragmatic invasion or other metastases; (4) patients had received other antitumor therapy before surgery; (5) R0 resection was not achieved in the resection margin;<sup>12</sup> (6) preoperative liver function assessment indicated Child-Pugh score  $>$  B7; and (7) patients had clinically significant portal hypertension.<sup>13</sup> In this study, resection margins were divided into wide margins and narrow margins. The wide margins were defined as the distance of the resection margin to the tumor  $\geq$  1 cm, and the narrow margins were defined as the distance of the resection margin to the tumor  $<$  1 cm.<sup>14</sup>

In accordance with the Declaration of Helsinki, this study was approved by the Institutional Ethics Committee of our hospital. All patients provided written informed consent before participating and allowed the use of their clinicopathological data during diagnosis and treatment for medical research.

### Tumor Resection

#### Open Left Lateral Lobectomy

LLL was performed via bilateral subcostal arc incision or reverse L-shaped incision. First, the situation of the liver and the abdominal cavity was explored. Then the left lateral lobe of the liver was fully exposed. Along the left side of the sagittal portion of the portal vein, ultrasonic scalpels or vascular forceps were used to gradually cut off the liver tissues. After the left lateral hepatic lobe was completely sectioned, thorough hemostasis was performed at the liver resection surface.<sup>10</sup> The hepatic portal was occluded during resection by the Pringle maneuver,<sup>15</sup> which involved multiple cycles of 15-min clamping and 5-min release of the portal triad.

#### Open Left Hepatectomy

The left lateral hepatic lobe was fully exposed and the liver tissue was slowly separated along the left of the middle hepatic vein with ultrasonic scalpel and vascular clamp during the hepatic portal occlusion. After left hepatic lobe was completely sectioned, thorough hemostasis was performed at the liver resection surface.<sup>9</sup> During liver resection, the hepatic portal was occluded using the Pringle maneuver. In this study, the caudate lobe was preserved during LH.

### Postoperative Follow-Up and Endpoints

All patients received routine post-operative re-examinations, including blood routine, liver and kidney function examinations, and tumor indicators, including serum alpha-fetoprotein (AFP), carcinoembryonic antigen (CEA), and cancer antigens (CA) 19-9. Additionally, abdominal B-ultrasound, abdominal contrast-enhanced magnetic resonance imaging (MRI), and computerized tomography (CT) were conducted. Patients were re-examined every two months within two years after surgery and every three months after two years of surgery. If recurrence was confirmed, the time when AFP

was abnormally elevated or a new tumor appeared on imaging was defined as the time of recurrence. Patients with a high risk of tumor recurrence based on tumor size, tumor number, and microvascular invasion (MVI) after surgery were recommended to undergo prophylactic transcatheter arterial chemoembolization (TACE) one month after surgery.<sup>16,17</sup> Postoperative complications were assessed according to the Clavien-Dindo criteria.<sup>18</sup>

The primary endpoints were OS and TR. OS was defined as the period from the day of hepatic resection until the patients died or loss to follow-up. TR was defined as the period from the day of hepatic resection until tumor recurrence or metastasis.

## Statistical Analysis

Measurement data were described as median (range) and compared using the independent *t*-test or Mann-Whitney *U*-test. Count data were presented as numbers (percentages) and compared using the chi-square test or Fisher's exact test. Survival and recurrence curves were plotted using the Kaplan-Meier method. Independent risk factors for postoperative OS and TR rates were analyzed using Cox regression analysis. OS was defined as the time from surgery to death or last follow-up, and tumor recurrence was defined as the time from surgery to the first postoperative diagnosis of recurrence or metastasis. The relative risk was presented as a hazard ratio (HR) and 95% confidence interval (CI). A *P* value less than 0.05 was considered statistically significant. All data were analyzed using SPSS version 19 (SPSS Inc, Chicago, IL, USA) and R software version 4.0.0 (<http://www.R-project.org>). In this article a one-to-two propensity score matching (PSM) was used to balance the differences in baseline clinicopathological features between the LLL and LH groups. Covariates included in the PSM analysis were PLT ( $> / \leq 100 \times 10^9/L$ ), CA 19-9 ( $> / \leq 39$  U/mL), Hilar clamping ( $> / \leq 20$  minutes), Tumor diameter ( $> / \leq 5$ cm) to calculate the propensity score by logistic regression.

## Results

### Clinicopathological Features

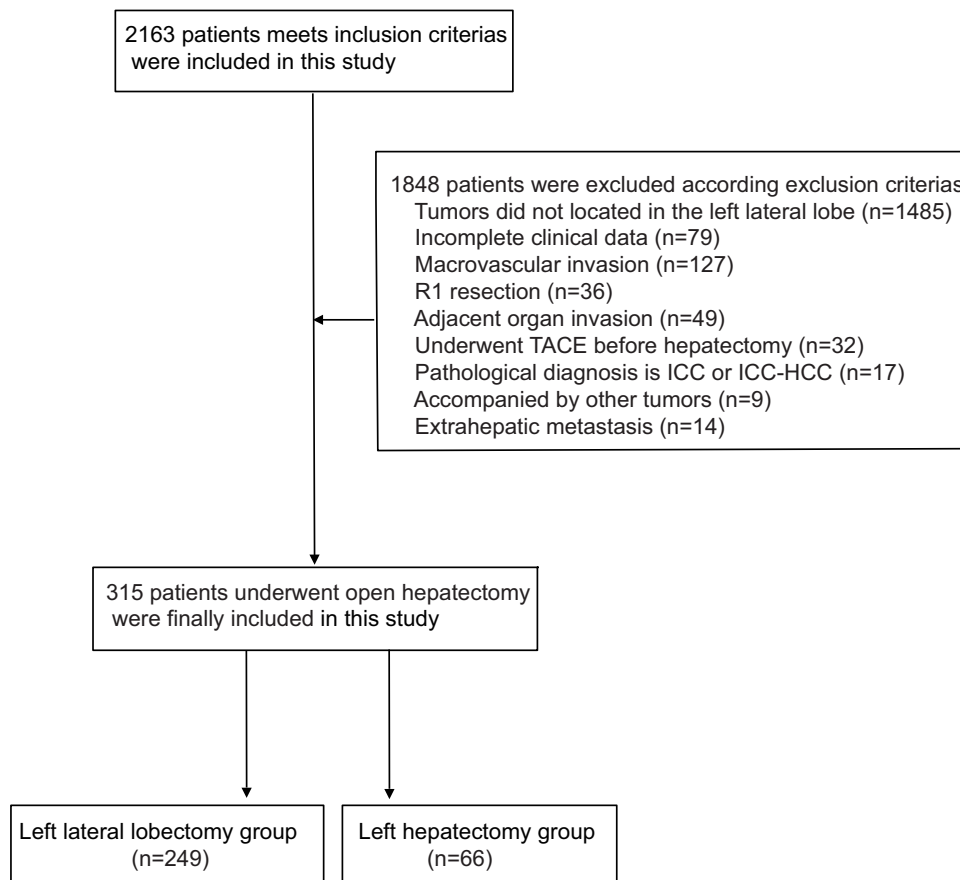
**Figure 1** shows the patient selection flow chart for this study. A total of 315 patients diagnosed with HCC on the left lateral lobe were enrolled in the study and divided into the LLL group ( $n=249$ ) and LH group ( $n=66$ ) based on the resection modality.

**Supplement Table 1** lists the baseline characteristics of the 315 patients with HCC on the left lateral lobe. No significant differences were observed between the two groups in clinicopathological features. However, compared to the LH group, patients in the LLL group had lower platelet count (140.0 vs 157.010<sup>9</sup>/L,  $P=0.039$ ), lower CA199 (17.3 vs 20.3 U/mL,  $P=0.040$ ), a lower proportion of hilar clamping  $> 20$  minutes (16.1% vs 30.3%,  $P=0.009$ ), a higher proportion of narrow margins (41.0% vs 0,  $P<0.001$ ), and smaller tumor diameter (4.1cm vs 4.7cm,  $P=0.017$ ). After PSM, no significant differences were observed between the two groups in clinicopathological features (**Table 1**).

### OS and TR in the Whole Cohort and PSM Group

The median follow-up time for the 315 HCC patients was 58.9 months. The 1, 3, and 5-year OS rates were 91.1%, 70.1%, 53.3% and the TR rates were 15.6%, 48.6%, 68.0%, respectively. **Supplement Table 2** lists the results of univariate analyses for postoperative OS and TR. **Supplement Table 3** lists the results of multivariate analyses for postoperative OS and TR. The results of multivariate analyses showed that the liver resection modality was not an independent risk factor for patients' postoperative OS and TR. The postoperative 1, 3, and 5-year OS rates were 90.7%, 68.2%, and 51.5% for patients in the LLL group and 92.4%, 77.3%, and 60.3% for patients in the LH group ( $P=0.176$ ) (**Figure 2A**). The postoperative 1, 3, and 5-year TR rates were 16.5%, 49.8%, and 69.5% for patients in the LLL group and 12.1%, 49.9%, and 62.3% for patients in the LH group ( $P=0.257$ ) (**Figure 2B**).

**Table 2 and 3** show the results of univariate and multivariate analyses of postoperative OS and TR rates after PSM, respectively. The results of multivariate analyses showed that narrow margin (HR:1.838, 95% CI:1.038–3.257; HR:1.875, 95% CI:1.153–3.048), tumor diameter  $> 5$  cm (HR:1.829, 95% CI:1.100–3.041; HR:1.516, 95% CI:1.014–2.268), multiple tumors (HR:2.389, 95% CI:1.369–4.170; HR:2.440, 95% CI:1.516–3.928) and MVI (HR:1.575, 95% CI:1.004–2.471; HR:1.452, 95% CI:1.006–2.095) were independent risk factors for OS and TR, while liver resection modality was



**Figure 1** Flow chart for selecting patients in the LLL group and in the LH group.

not an independent risk factor for OS and TR. The postoperative 1, 3, and 5-year OS rates after PSM were 88.5%, 67.2%, and 51.1% for patients in the LLL group and 93.4%, 80.3%, and 63.7% for patients in the LH group ( $P=0.079$ ) (Figure 2C). The postoperative 1, 3, and 5-year TR rates were 18.0%, 50.0%, and 70.3% for patients in the LLL and 11.5%, 41.0%, and 60.9%, for patients in the LH group ( $P=0.163$ ) (Figure 2D).

## The Differences in OS and TR Rates Between LLL Group and LH Group

The 1-, 3-, and 5-year OS rates were 87.3%, 58.8%, and 41.1%, respectively, for patients with narrow margins in the LLL group and 92.4%, 77.3%, and 60.3%, respectively, for patients in the LH group ( $P=0.012$ ) (Figure 3A). The 1, 3, and 5-year TR rates were 22.5%, 59.8%, and 76.5%, respectively, for patients with narrow margins in the LLL group and 12.1%, 43.9%, and 62.3% for patients in the LH group ( $P=0.017$ ) (Figure 3B). The 1-, 3-, and 5-year OS rates were 93.2%, 74.8%, and 58.7%, respectively, for patients with wide margins in the LLL group and 92.4%, 77.3%, and 60.3%, respectively, for patients in the LH group ( $P=0.766$ ) (Figure 3C). The 1-, 3-, and 5-year TR rates were 12.2%, 42.9%, and 64.6%, respectively, for patients with wide margins in the LLL group and 12.1%, 43.9%, and 62.3%, respectively, for patients in the LH group ( $P=0.919$ ) (Figure 3D).

## The Differences in Postoperative Complications and Liver Function Between LLL Group and LH Group

Of the 315 HCC patients, 55 patients had postoperative complications, 44 patients had one postoperative complication, and 8 patients had two different postoperative complications. The postoperative complication rate was 55/315 (17.5%).

**Table 1** Baseline Characteristics of Patients After PSM

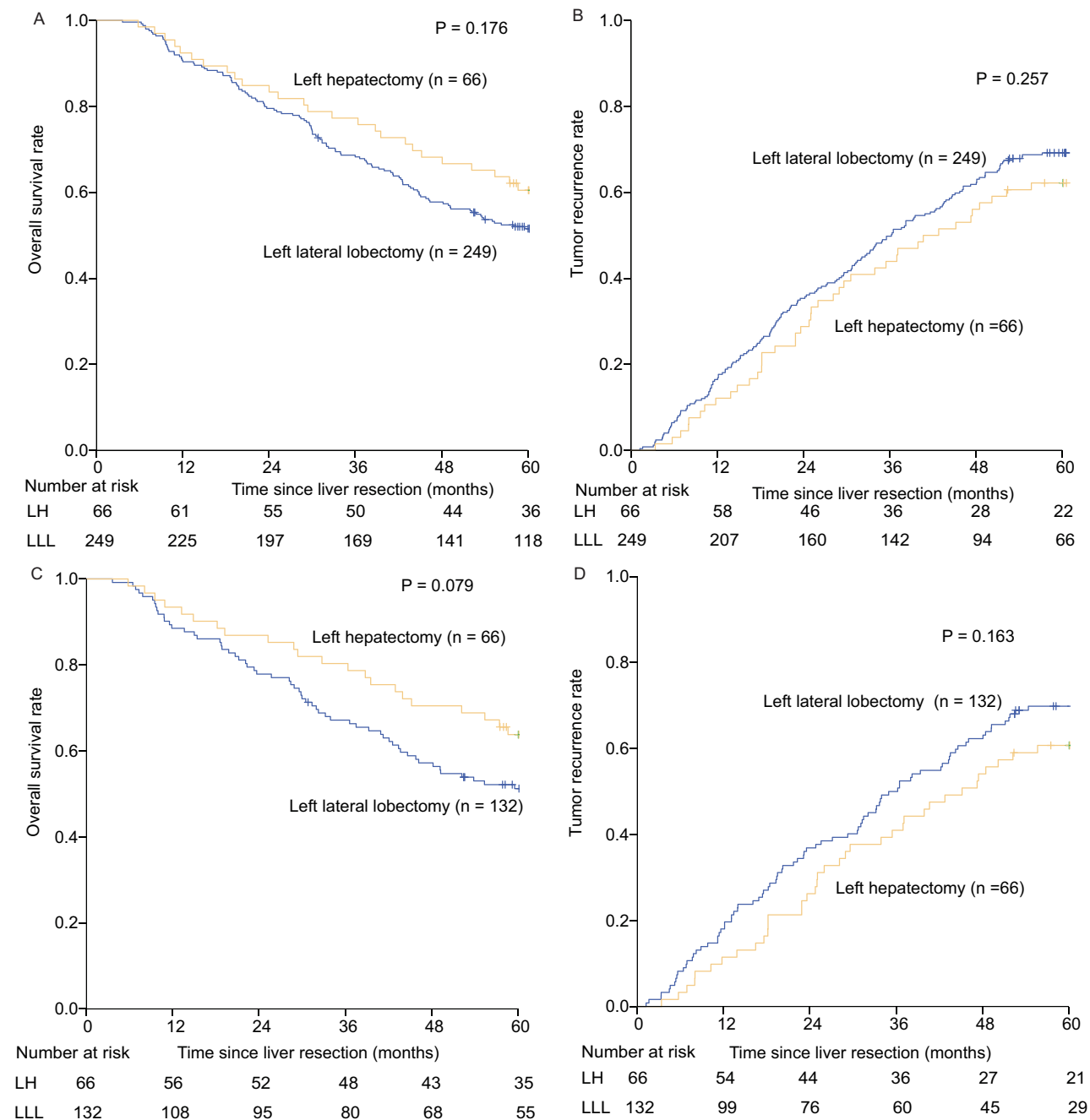
Variable	Number (%) / Median (IQR)		P
	Left Lateral Lobectomy (n =132)	Left Hepatectomy (n =66)	
Age, years	54.0(46.0–61.0)	54.0(43.0–60.0)	0.570
Sex, male	100(82.0)	51(83.6)	0.783
Diabetes, yes	7(5.7)	3(4.9)	0.818
<b>Preoperative</b>			
HBsAg, positive	95(77.9)	53(86.9)	0.144
HBV-DNA level, > 2000 IU/mL	61(50.0)	38(38.4)	0.116
Preoperative antiviral therapy, yes	10(8.2)	5(8.2)	1.000
PLT, 10 <sup>9</sup> /L	137.5(100.0–184.5)	154.0(101.0–199.0)	0.162
PT, seconds	12.2(11.7–13.0)	12.0(11.7–12.8)	0.458
TBIL, μmol/L	14.0(11.4–17.9)	13.7 (11.6–19.4)	0.819
ALB, g/L	40.3(38.3–42.7)	40.3(38.1–42.4)	0.739
ALT, IU/L	30.1(19.8–48.2)	40.8(16.5–53.7)	0.701
AFP, ng/mL	103.7(6.1–1683.5)	114.0(12.1–3438.0)	0.504
CEA, μg/L	2.7(2.0–4.1)	2.6(1.8–4.8)	0.881
CA 19-9, U/mL	17.6(9.9–29.8)	19.4(11.5–35.8)	0.107
<b>Intraoperative</b>			
Blood transfusion, yes	7(5.7)	2(3.3)	0.468
Hilar clamping, > 20 minutes	97(79.5)	43(70.5)	0.175
<b>Postoperative</b>			
Surgical margin <sup>§</sup> , > 1.0 cm	92(75.4)	61(100)	<0.001
Cirrhosis <sup>§</sup>	70(57.4)	30(49.2)	0.294
Tumor diameter <sup>§</sup> , cm	4.8(3.3–6.3)	4.7(3.7–6.6)	0.156
Tumor number <sup>§</sup> , multiple <sup>†</sup>	20(16.4)	9(14.8)	0.775
MVI <sup>§</sup> , presence	43(35.2)	24(39.3)	0.587
Tumor capsule <sup>§</sup> , incomplete	59(48.4)	29(47.5)	0.917
Edmondson-Steiner grade <sup>§</sup> , III/IV	78(63.9)	43(70.5)	0.377
TBIL of postoperative day 1, μmol/L	32.8(22.5–48.8)	35.0(25.7–47.9)	0.742
ALT of postoperative day 1, IU/L	310.0(185.3–529.4)	321.3(175.3–461.5)	0.982
TBIL of postoperative day 3, μmol/L	25.9(17.1–37.6)	30.5(20.6–39.0)	0.147
ALT of postoperative day 3, IU/L	128.8(80.6–201.0)	105.9(41.9–210.8)	0.157
TBIL of postoperative day 5, μmol/L	15.2(12.4–21.9)	14.7(11.6–21.8)	0.251
ALT of postoperative day 5, IU/L	63.2(36.7–114.3)	56.7(34.4–121.2)	0.969
Adjuvant TACE, yes	41(33.6)	22(36.1)	0.741

**Notes:** <sup>§</sup>Based on postoperative pathology. <sup>†</sup>Tumor nodules  $\geq 2$ .

**Abbreviations:** PSM, propensity score matching; IQR, interquartile range; HBsAg, hepatitis B surface antigen; HBV-DNA, hepatitis B virus deoxyribonucleic acid; TBIL, total bilirubin; ALB, albumin; ALT, alanine transaminase; PT, prothrombin time; PLT, platelet; AFP, alpha fetoprotein; CEA, carcinoembryonic antigen; CA 199, Carbohydrate antigen 199; MVI, microvascular invasion; TACE, transarterial chemoembolization.

The postoperative complication rate was 42/249 (16.8%) for patients in the LLL group and 13/66 (19.7%) for patients in the LH group ( $P=0.590$ ). The rate of grade III/IV postoperative complications was 4/249 (1.6%) and 2/66 (3.0%) for patients in the LLL group and in the LH group, respectively ( $P=0.806$ ) (Table 4).

In terms of postoperative liver function, the TBIL levels and ALT levels on the first postoperative day were 34.9 μmol/L and 35.1 μmol/L, 289.2 IU/L and 319.6 IU/L, respectively, for patients in the LLL group and LH group, which showed no significant differences ( $P=0.965$  and  $P=0.665$ , respectively). The TBIL and ALT levels on postoperative day 3 were 27.7 μmol/L and 126.9 IU/L, respectively, for patients in the LLL group and 31.3 μmol/L and 105.9 IU/L, respectively, for patients in the LH group, showing no significant differences ( $P=0.155$  and  $P=0.087$ , respectively). The TBIL and ALT levels on postoperative day 5 were 15.2 μmol/L and 60.1 IU/L, respectively, for patients in the LLL



**Figure 2** Overall survival and tumor recurrence curves of patients with HCC on the left lateral lobe in the LH group and LLL group before and after propensity score matching. **(A)** Overall survival curve before propensity score matching; **(B)** Tumor recurrence curve before propensity score matching; **(C)** Overall survival curve after propensity score matching; **(D)** Tumor recurrence curve after propensity score matching.

group and 14.9  $\mu\text{mol/L}$  and 59.1 IU/L, respectively, for patients in the LH group, showing no significant differences ( $P=0.155$  and  $P=0.818$ , respectively). ([Supplement Table 1](#)).

## Discussion

The common surgical modality for patients with HCC on the left lateral hepatic lobe is LLL and LH.<sup>9,10</sup> The LLL involves cutting off liver tissues sequentially along the left side of the sagittal portion of the portal vein, while the LH involves cutting off the liver tissues gradually along the line 0.5 cm away from the left side of the middle hepatic vein to the first hepatic hilum. Due to the anatomical limits of the LLL, wide resection margins cannot be obtained for some

**Table 2** Univariate Analysis of OS and TR for HCC of Left Lateral Lobe After PSM

Variable	OS			TR		
	P	HR	95% CI	P	HR	95% CI
Age, years, > vs ≤ 60	0.716	0.918	0.579–1.455	0.851	1.036	0.713–1.506
Sex, male vs female	0.581	1.166	0.675–2.014	0.476	0.837	0.513–1.365
Diabetes, yes vs no	0.120	1.936	0.842–4.449	0.784	1.122	0.493–2.550
HBsAg, positive vs negative	0.156	1.558	0.844–2.876	0.149	1.415	0.883–2.266
HBV-DNA, IU/mL, > vs ≤ 2000	0.545	0.875	0.567–1.350	0.523	0.891	0.624–1.271
Preoperative antiviral therapy, yes vs no	0.293	0.615	0.249–1.521	0.140	0.563	0.262–1.207
PLT, 10 <sup>9</sup> /L, ≤ vs > 100	0.092	0.618	0.353–1.081	0.205	0.756	0.490–1.166
PT, seconds, > vs ≤ 12	0.526	0.847	0.507–1.415	0.677	0.915	0.603–1.389
TBIL, μmol/L, > vs ≤ 17.1	0.802	1.061	0.666–1.691	0.051	1.449	0.999–2.103
ALB, g/L, > vs ≤ 35	0.886	1.068	0.432–2.639	0.817	0.919	0.448–1.883
ALT, IU/L, > vs ≤ 40	0.155	1.372	0.887–2.123	0.265	1.227	0.856–1.759
AFP, ng/mL, > vs ≤ 200	0.021	1.742	1.088–2.789	0.086	1.380	0.955–1.995
CEA, μg/L, > vs ≤ 10	0.468	0.482	0.067–3.464	0.963	1.027	0.326–3.233
CA 19-9, U/mL, > vs ≤ 39	0.658	1.135	0.648–1.987	0.797	1.062	0.670–1.686
Hilar clamping, minutes, > vs ≤ 20	0.109	0.624	0.351–1.110	0.102	0.684	0.434–1.078
Hepatectomy, left hepatectomy vs left lateral lobectomy	0.079	0.646	0.396–1.053	0.163	0.760	0.516–1.118
Blood transfusion, yes vs no	0.921	0.951	0.348–2.597	0.603	0.789	0.322–1.930
Surgical margin <sup>§</sup> , cm, ≤ vs >1.0	0.006	2.049	1.226–3.426	0.002	1.994	1.282–3.101
Cirrhosis <sup>§</sup> , yes vs no	0.979	1.006	0.652–1.552	0.815	1.044	0.930–1.491
Tumor diameter <sup>§</sup> , cm, > vs ≤ 5	<0.001	2.358	1.506–3.690	<0.001	1.915	1.338–2.741
Tumor number <sup>§</sup> , multiple <sup>†</sup> vs single	<0.001	2.566	1.545–4.261	<0.001	2.316	1.487–3.608
MVI <sup>§</sup> , presence vs absence	0.006	1.834	1.186–2.835	0.025	1.515	1.054–2.178
Tumor capsule <sup>§</sup> , incomplete vs complete	0.177	0.741	0.480–1.144	0.527	0.891	0.624–1.273
Edmondson-Steiner grade <sup>§</sup> , III/IV vs I/II	0.015	1.867	1.127–3.093	0.031	1.535	1.039–2.267
Adjuvant TACE, yes vs no	0.268	1.284	0.825–1.999	0.380	1.179	0.816–1.705

Notes: <sup>§</sup>Based on postoperative pathology. <sup>†</sup>Tumor nodules ≥ 2.

Abbreviations: OS, overall survival; TR, tumor recurrence; HCC, hepatocellular carcinoma; PSM, propensity score matching; HR, hazard ratio; CI, confidence interval; HBsAg, hepatitis B surface antigen; HBV-DNA, hepatitis B virus deoxyribonucleic acid; TBIL, total bilirubin; ALB, albumin; ALT, alanine transaminase; PT, prothrombin time; PLT, platelet; AFP, alpha fetoprotein; CEA, carcinoembryonic antigen; CA 199, Carbohydrate antigen199; MVI, microvascular invasion; TACE, transarterial chemoembolization.

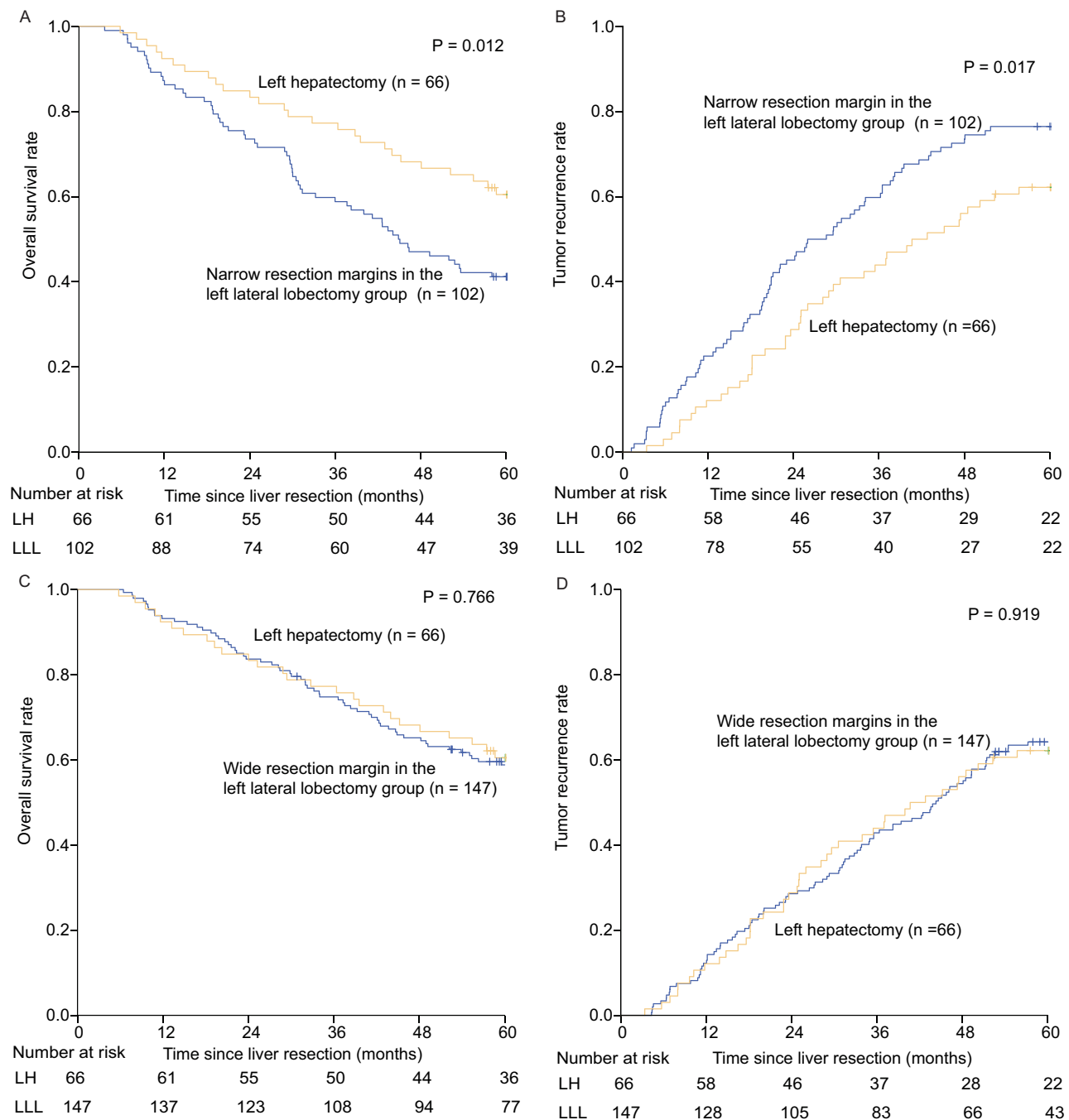
**Table 3** Multivariate Analysis of OS and TR for HCC of Left Lateral Lobe After PSM

Variable	OS			TR		
	P	HR	95% CI	P	HR	95% CI
AFP, ng/mL, > vs ≤ 200	0.196	1.418	0.835–2.407	–	–	–
Surgical margin <sup>§</sup> , cm, ≤ vs >1.0	0.037	1.838	1.038–3.257	0.011	1.875	1.153–3.048
Tumor diameter <sup>§</sup> , cm, > vs ≤ 5	0.020	1.829	1.100–3.041	0.043	1.516	1.014–2.268
Tumor number <sup>§</sup> , multiple <sup>†</sup> vs single	0.002	2.389	1.369–4.170	<0.001	2.440	1.516–3.928
MVI <sup>§</sup> , presence vs absence	0.048	1.575	1.004–2.471	0.046	1.452	1.006–2.095
Edmondson-Steiner grade <sup>§</sup> , III/IV vs I/II	0.701	1.122	0.623–2.019	0.618	1.114	0.728–1.706

Notes: <sup>§</sup>Based on postoperative pathology. <sup>†</sup>Tumor nodules ≥ 2.

Abbreviations: OS, overall survival; TR, tumor recurrence; HCC, hepatocellular carcinoma; PSM, propensity score matching; HR, hazard ratio; CI, confidence interval; AFP, alpha fetoprotein; MVI, microvascular invasion.

patients whose tumors are adjacent to the sagittal portion of the portal vein. Comparing with LLL, LH involves more liver tissues and could lead to greater damage to the liver. However, wide resection margins can be obtained for some HCC patients, resulting in more thorough treatment.



**Figure 3** Overall survival and tumor recurrence of patients with HCC on the left lateral lobe who had wide resection margins and narrow resection margins in the LLL group and in the LH group. **(A)** Postoperative overall survival curve of patients with wide resection margin in the LLL and LH groups; **(B)** Postoperative tumor recurrence curve of patients with wide resection margin in the LLL and LH groups; **(C)** Postoperative overall survival curve of patients with narrow resection margin in the LLL and LH groups; **(D)** Postoperative tumor recurrence curve of patients with narrow resection margin in the LLL and LH groups.

Our results firstly compared the difference of open LLL and open LH. The results showed that the resection margin can affect patients' postoperative OS and TR. Wide resection margins can improve patients' prognosis, consistent with the results of previous studies.<sup>14,19–21</sup> The liver resection modality is not an independent risk factor for prognosis. In other words, LH is not a protective factor for prognosis compared with LLL. The reason may be the high proportion (59.0%) of wide margins in the LLL group in this study. A high proportion of wide margins results in a better long-term prognosis of patients in the LLL group. Therefore, no significant difference in prognosis was found between the LH



**Table 4** Complication of Patients Underwent Hepatectomy

Complication <sup>‡</sup>	Left Lateral Lobectomy (n =249)	Left Hepatectomy (n =66)	P
Overall complication vents	50	16	0.460
Number of patients (n)	42*	13**	0.590
Grade III/IV (n) <sup>‡</sup>	4***	2****	0.806

**Notes:** \*42 patients occurred complications, 34 patients occurred 1 complication, 8 patients occurred 2 different complications. \*\*13 patients occurred complications, 10 patients occurred 1 complication, 3 patients occurred 2 different complications. \*\*\*4 patients occurred 1 complication. \*\*\*\*2 patients occurred 1 complication. <sup>‡</sup>Graded according to the Clavien-Dindo classification.

group and the LLL group. We further divided these patients in the LLL group into the wide resection margin group and the narrow resection margin group and compared them with patients with LH. The results showed that the prognosis of patients with wide resection margin in the LLL group is similar to that of patients in the LH group. In other words, the liver resection modality has no significant effect on the prognosis of these patients. However, patients with narrow resection margins in the LLL group have a significantly worse prognosis than patients in the LH group. The underlying reason may be that only narrow margin can be obtained for left lateral lobe HCC patients with the tumors adjacent to the sagittal portion of the portal vein during LLL due to the anatomical limits. To obtain wide margins, these patients must undergo LH. Therefore, LH can improve their prognosis. That is, the liver resection modality has an impact on the prognosis of these patients. This may be related to paracancerous foci and MVI, which are collectively referred to as peritumoral micrometastasis and are important factors for postoperative recurrence of HCC, especially early recurrence.<sup>22,23</sup> Studies have shown that pericancerous micrometastasis is also associated with tumor metastasis, recurrence, and poor prognosis.<sup>24,25</sup> Our results also showed that MVI is an independent risk factor for postoperative OS and TR, consistent with previous studies.<sup>22,23</sup> A study showed that micrometastasis could also occur in the liver tissues adjacent to the tumor HCC patient with small tumors, while the probability of micrometastasis was significantly higher in HCC patients with larger tumors.<sup>26</sup> Our results showed that patients in the LH group had a significantly larger tumor diameter than patients in the LLL group (4.7 vs 4.1 cm,  $P=0.016$ ). In addition, more patients in the LH group were MVI positive, which may be related to the larger tumor diameter, consistent with the findings of a previous study.<sup>26</sup> Moreover, studies have found that patients with multiple tumors have a poor prognosis,<sup>27–29</sup> which may be related to tumor origin and MVI rate.

MVI rate is significantly higher in patients with multiple tumors than in patients with a single tumor.<sup>30</sup> A wide resection margin can increase the probability of resecting potential peritumoral micro-metastasis, thereby reducing the possibility of postoperative recurrence of intrahepatic metastasis<sup>31</sup> and improving patients' prognosis. In addition, liver function assessment is an important factor affecting the choice of surgical modality.<sup>32</sup> For patients with severe liver cirrhosis, if preoperative evaluation suggests severe liver function damage after surgery, even if the tumor is adjacent to the sagittal portal vein, more clinicians will consider performing LLL. In addition, the risk of postoperative complications also affects surgical modality selections. Our results showed that LH does not increase the incidence of postoperative complications compared with LLL. That is, although LH involves more liver tissue, it does not significantly increase the probability of postoperative complications compared with LLL, which is consistent with previous studies.<sup>11</sup> In terms of postoperative liver function, our results showed that no significant difference in the levels of TBIL and ALT on the postoperative day 1, 3, and 5 between the LLL group and the LH group, indicating no significant difference in postoperative liver function between the two groups. This may be benefited from stricter preoperative screening in patients in the LH group.

Our study has some limitations. First, the size of patients included in this study is relatively small. Second, the study is a single-center retrospective study. Although it is a real-world study, the results need to be further validated in multi-center prospective studies with larger sample sizes.

## Conclusion

The modality of liver resection is not an independent prognostic risk factor for patients with HCC on the left lateral lobe. As long as the wide surgical margins are ensured, the choice of surgical modality has no significant effect on their long-term prognosis. However, for left lateral lobe HCC patients with tumors adjacent to the sagittal portion of the portal vein, it is crucial to ensure adequate margins, and LH is recommended to achieve a better prognosis.

## Data Sharing Statement

The data supporting the findings of this study are available upon request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

## Ethics Statements

This study was approved by the Ethics Committee of Eastern Hepatobiliary Surgery Hospital. All patients provided written informed consent before participating and allowed the use of their clinicopathological data during diagnosis and treatment for medical research.

## Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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## Disclosure

The authors report no conflicts of interest in this work.

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