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ORIGINAL RESEARCH

Anatomical versus Parenchymal-Sparing Hepatectomy for Early-Stage Perihilar Hepatocellular Carcinoma: A Propensity Score Matching Analysis

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Background: The benefit of anatomical hepatectomy (AR) for patients with early-stage perihilar hepatocellular carcinoma (HCC) remains unclear. This study aimed to compare the clinical efficacy and safety between AR and parenchymal-sparing hepatectomy (PSH) for early-stage perihilar HCC.

Methods: A total of 201 patients with perihilar HCC who underwent hepatectomy between January 2015 and December 2023 were retrospectively analyzed. Among them, 114 patients received AR and 87 patients received PSH. Propensity score matching (PSM) with a 1:1 ratio was used to eliminate selection bias. The survival outcomes and postoperative complications were compared between the two groups.

Results: After PSM, 77 patients were included in each group. The proportion of patients with surgical margins ≥1 cm was higher in the AR group (31.2% vs 11.7%, P=0.003), and the incidence of postoperative liver failure was also higher in the AR group than in the PSH group (14.3% vs 3.9%, P=0.025). The 1-, 3-, and 5-year overall survival (OS) rates were 94.6%, 80.4%, and 75.2% in the AR group and 97.4%, 78.5%, and 66.6% in the PSH group (P=0.292). The 1-, 3-, and 5-year recurrence-free survival (RFS) rates were 76.5%, 59.2% and 50.5% in the AR group and 76.5%, 48.2% and 46.2% in the PSH group, respectively (P=0.415). OS and RFS rates were similar in both groups. Multivariate analysis revealed that AFP ≥400 ng/mL (P<0.001), serum albumin level (P=0.024), tumor diameter (P=0.012), satellite nodules (P=0.006) and overall postoperative complications (P=0.005) were independent risk factors for OS. Viral hepatitis (P=0.012), AFP ≥400 ng/mL (P=0.002), satellite nodes (P=0.031) and postoperative adjuvant therapy (P=0.028) were independent risk factors for RFS.

Conclusion: PSH provides similar short-term and long-term survival outcomes to AR for early-stage perihilar HCC patients. It may represent a safe and feasible treatment option for them.

Keywords: hepatocellular carcinoma, anatomical hepatectomy, parenchymal-sparing hepatectomy, perihilar, propensity score matching

Introduction

Hepatocellular carcinoma (HCC) is the sixth most common malignant tumor in the world and the third leading cause of cancer-related death.[1] Currently, curative hepatectomy is considered the preferred treatment for HCC. However, the postoperative recurrence rate remains high. A study involving 10,996 HCC patients reported that the 5-year recurrence rate after curative hepatectomy reached 69.7%.[2] Intrahepatic dissemination through the portal venous system is the primary pathway of tumor metastasis and recurrence.[3] Anatomical hepatectomy (AR) can effectively remove microscopic intrahepatic metastases by resecting the tumor together with the portal vein branches of the affected liver

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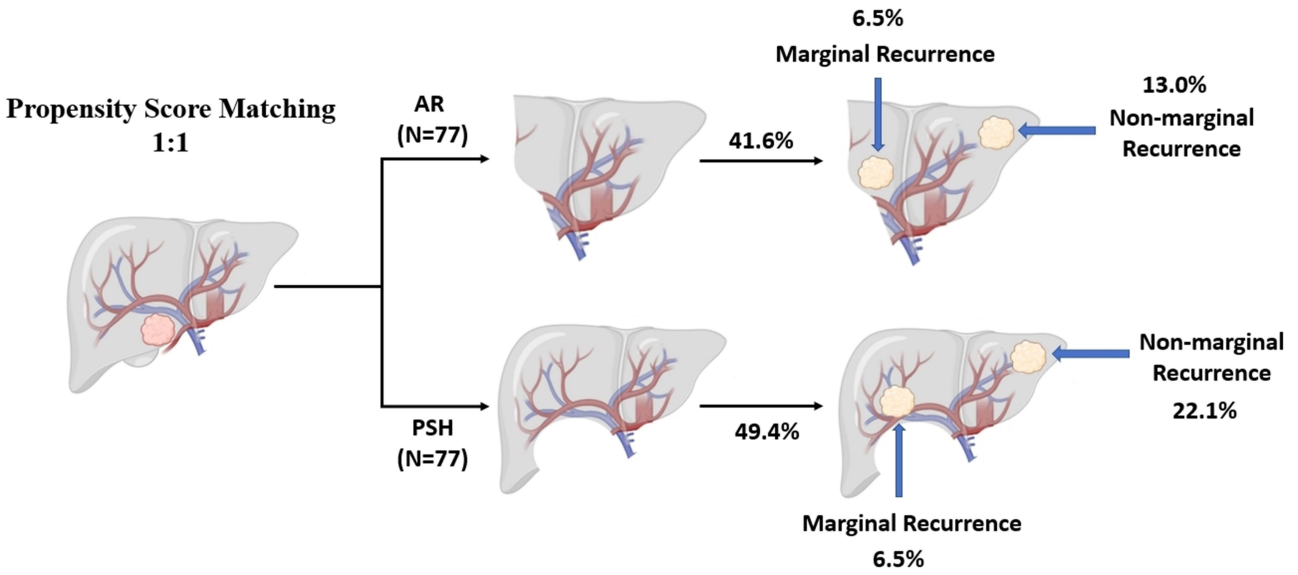
Graphical Abstract



segment.[4,5] Several studies and meta-analyses have shown that, compared with non-anatomical hepatectomy (NAR), AR can improve survival benefit in HCC patients.[6–8] Nevertheless, AR involves resecting a larger volume of normal liver tissue, thereby increasing the risk of insufficient future liver remnant (FLR) and postoperative liver failure. Moreover, some studies have suggested that the long-term prognosis of AR may not be superior to that of NAR.[9,10] Therefore, the choice between AR and NAR remains controversial and may vary depending on clinical and pathological factors, including tumor size, location, liver functional reserve and microvascular invasion.[11]

As a form of NAR, parenchymal-sparing hepatectomy (PSH) preserves a greater amount of functional hepatic parenchyma compared with AR, thereby reducing its impact on postoperative liver function and offering more opportunities for repeat hepatectomy in the event of tumor recurrence.[12] NAR may be more beneficial for patients with severe cirrhosis or impaired liver function.[13]

"Perihilar HCC" is a subtype of HCC characterized by its proximity to the hepatic hilum. It is defined as an HCC located in a 1-cm area extending from the right, left, and common hepatic ducts.[14] Perihilar HCC is not uncommon; however, surgical resection is technically challenging due to its complex anatomical location. AR requires resection of a large volume of normal hepatic parenchyma, whereas NAR may result in inadequate surgical margins. Currently, there is a lack of studies specifically focused on perihilar HCC, and the optimal surgical procedure for achieving greater clinical benefit remains undefined. Therefore, in this retrospective study, we aimed to compare the clinical efficacy and safety of AR versus PSH for early-stage perihilar HCC and to analyze the factors affecting patient prognosis.

Materials and Methods

Study Design and Population

In this single-center, retrospective study, 1085 patients with HCC who underwent hepatectomy at our institution between January 2015 and December 2023 were screened (Figure 1). The inclusion criteria were as follows: (a) age between 18 and 75 years; (b) HCC diagnosed by postoperative pathological histology; (c) Barcelona Clinic Liver Cancer (BCLC) stage 0-A and solitary HCC involving the perihilar region; the minimum anatomical distance from the HCC margin to the main trunk of the left hepatic pedicle, right anterior hepatic pedicle, or right posterior hepatic pedicle was less than 1 cm, as assessed using preoperative CT/MRI; (d) Eastern Cooperative Oncology Group (ECOG) PS score 0–1; (e) Child–Pugh liver function grade A or B (Child B = 7 points); indocyanine green retention rate at 15 minutes was measured in all

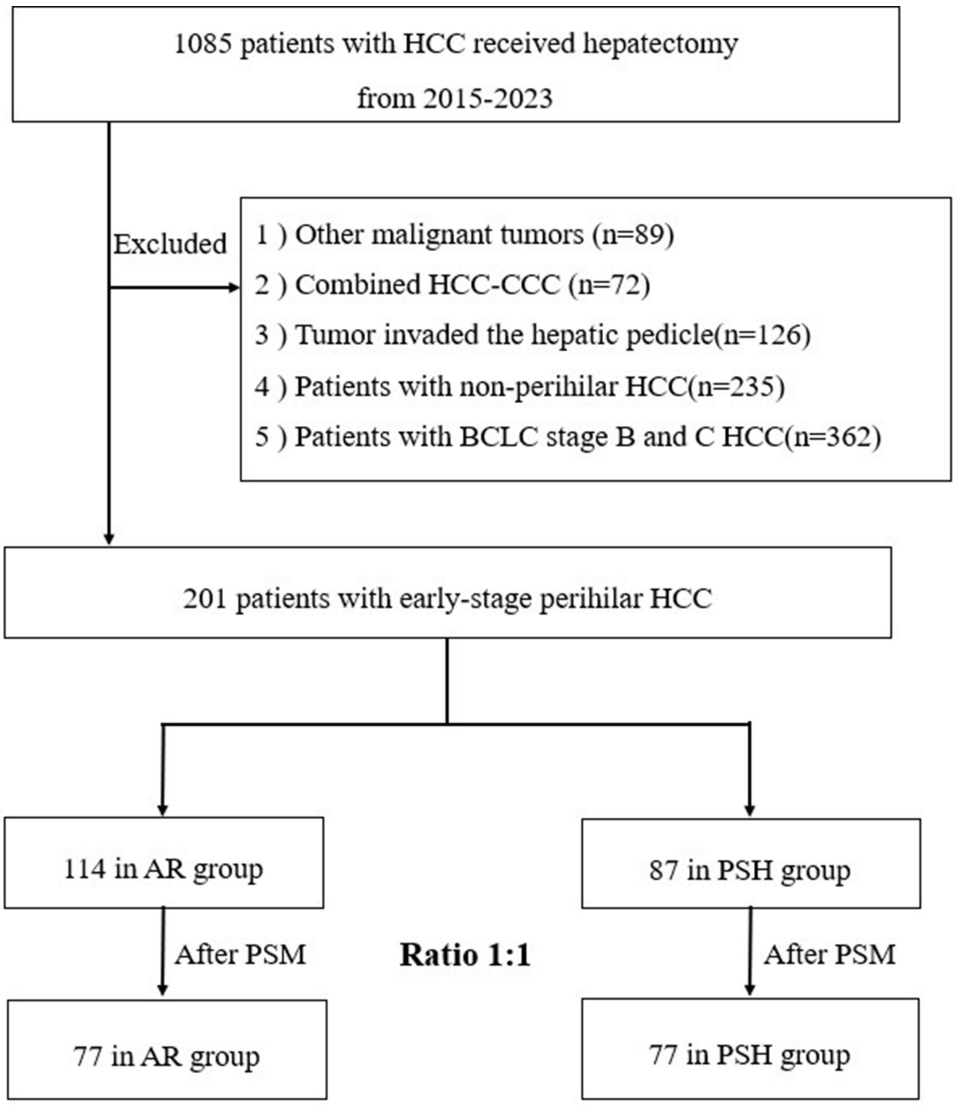


Figure 1 Patient flow chart.
Abbreviations: HCC-CCC, hepatocellular carcinoma-cholangiocarcinoma; AR, anatomical resection; PSH, parenchymal-sparing hepatectomy; PSM, propensity score matching.

patients and was < 20%; (f) adequate FLR (for non-cirrhotic liver: >30% of standardized liver volume; for cirrhotic liver: >40% of standardized liver volume); and (g) normal function of major organs. The exclusion criteria were as follows: (a) had other malignant tumors; (b) had pathological results mixed with hepatocellular carcinoma and cholangiocarcinoma; and (c) had tumors invading the hepatic pedicle. Postoperative complications were assessed according to the Clavien–Dindo classification system, and postoperative liver failure was defined in accordance with the criteria proposed by the International Study Group of Liver Surgery. Grade A liver failure required no change of the patient's clinical management. The clinical management of patients with grade B postoperative liver failure deviated from the regular course but does not require invasive therapy. The need for invasive treatment defined grade C postoperative liver failure.[15] This study was approved by the Ethics Committee of Sichuan Cancer Hospital.

Surgical Procedure

The extent of resection was selected on the basis of the patient's tumor location, tumor size, FLR, and liver function as assessed by the Child–Pugh classification. All enrolled patients were eligible for both AR and PSH; however, the ultimate selection of the surgical procedure was determined by surgeon preference. AR was defined as systematic

resection of at least one Couinaud segment. In this study, there were six types of AR: anatomic right posterior sectionectomy, right anterior sectionectomy, right hemihepatectomy, middle hepatectomy (segments IV, V, and VIII), left medial sectionectomy, and left hemihepatectomy. The target hepatic pedicle was located and ligated intraoperatively, and the hepatic parenchyma was isolated along the ischemic lines and hepatic veins via a harmonic scalpel or cavitron ultrasonic surgical aspirator (CUSA). PSH was defined as the resection of the primary tumor and liver tissue within a certain distance from the primary tumor, without regard to the liver sections and segments. Depending on the location of the tumor, the resection margin was determined via ultrasound. By occlusion of hepatic blood flow, the liver parenchyma was gradually dissected until the lesion was completely removed. All procedures were designed and performed by the same medical team. Typical cases in both groups are shown in Figure 2.

Follow-Up

All patients were followed up regularly, every 3 months for the first 2 years and every 3–6 months thereafter. The final follow-up date was December 31, 2025. Follow-up items included routine blood tests, liver function tests, serum alpha-fetoprotein (AFP) tests, abdominal ultrasound, and enhanced CT or MRI. Patients at high risk of postoperative recurrence and metastasis received postoperative adjuvant transarterial chemoembolization (TACE). Adjuvant TACE was performed 4 to 8 weeks after radical surgery. The TACE procedure was carried out in the following manners. Hepatic arterial angiography was performed with a 5 Fr RH catheter to insert through femoral artery to access hepatic artery. Subsequently, a microcatheter was inserted into right and left hepatic artery and inject adriamycin (20–30 mg/m2) and lipiodol (3–5 mL). The site of recurrence was divided into intrahepatic recurrence, extrahepatic recurrence and both intrahepatic and extrahepatic recurrence. Intrahepatic recurrence was divided into marginal recurrence (within 2 cm of the surgical margin), nonmarginal recurrence and multiple intrahepatic recurrences. The treatment options for recurrent HCC were determined on the basis of tumor characteristics, patient liver function, and the results of our multiple disciplinary team (MDT) discussion. Overall survival (OS) was defined as the period from the date of surgery to the date of death or the date of last follow-up. Recurrence-free survival (RFS) was defined as the time from the date of surgery to the date of tumor recurrence.

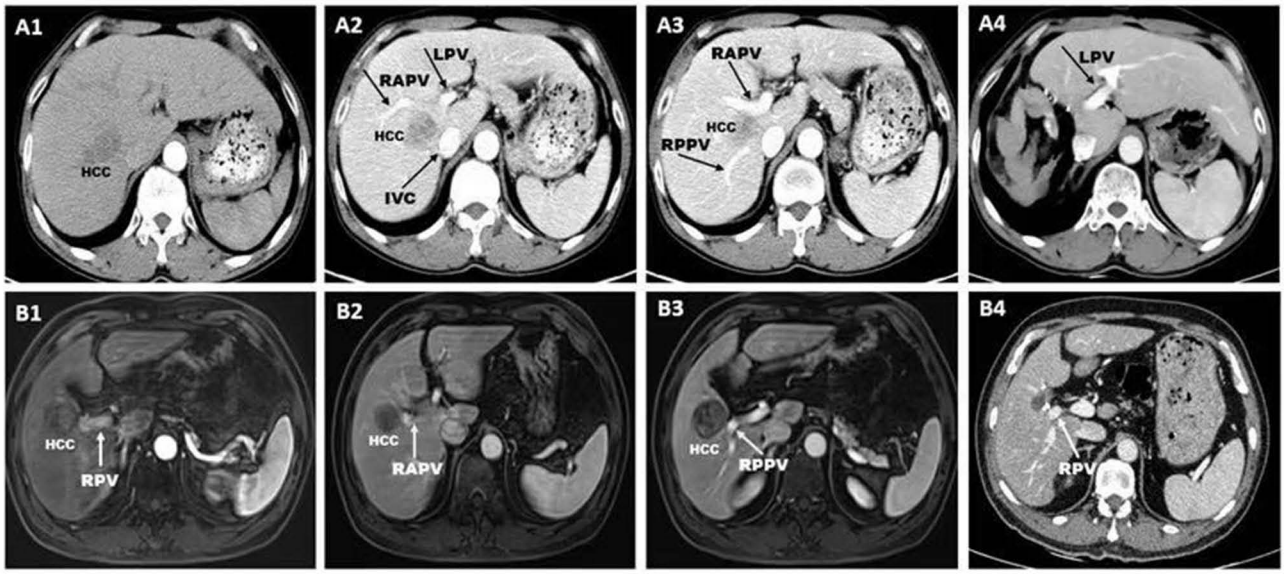


Figure 2 Typical cases of perihilar HCC before and after resection. HCC patients with tumors located in the perihilar region (in the AR group, (**A1**–**A4**)). (**A1**) Arterial phase. (**A2**) The HCC was close to the RAPV and IVC. (**A3**) The HCC was close to the RAPV and RPPV. (**A4**) After hemi-hepatectomy. HCC patients with tumors located in the perihilar region (in the PSH group, (**B1**–**B4**)). (**B1**) Arterial phase. (**B2**) The HCC was close to the RAPV. (**B3**) The HCC was close to the RPPV. (**B4**) After parenchymal-sparing hepatectomy.

Abbreviations: RAPV, right anterior portal vein; RPPV, right posterior portal vein; IVC, inferior vena cava; HCC, hepatocellular carcinoma.

Propensity Score Matching (PSM) and Statistical Analysis

To adjust for the differences in baseline characteristics between the two groups and to decrease potential selection bias, a 1:1 PSM was performed in this study. Baseline characteristics included sex, age, viral hepatitis status, alpha-fetoprotein (AFP) level, white blood cell (WBC) count, platelet count (PLT), albumin (ALB), alanine aminotransferase (ALT), aspartate aminotransferase (AST), liver cirrhosis status, Child–Pugh classification and tumor diameter. Continuous variables are expressed as the mean ± standard deviation (Mean ± SD) or median and interquartile range (IQR). Categorical variables are described as numbers (N) and percentages (%). Continuous variables were analyzed via the independent-sample *t* test or Mann–Whitney test, and categorical variables were analyzed via the chi–square test (χ^2) or Fisher's exact test. The Kaplan–Meier method was used for survival analysis, and the Log rank test was used to compare the OS rate and RFS rate between the two groups. Cox proportional hazards model was used for univariate and multivariate analyses. P<0.05 was considered a statistically significant difference. SPSS 27.0 statistical software was used for data processing and analysis.

Results

Patient Characteristics

We analyzed the data of 1085 HCC patients who underwent hepatectomy between January 2015 and December 2023. A total of 201 patients with BCLC stage 0-A HCC were included in this study, comprising 114 patients in the AR group and 87 in the PSH group. All HCC cases were with solitary tumors. The baseline characteristics are shown in Table 1. Statistical analysis revealed significant differences in the PLT (P=0.026) and tumor diameter (P=0.036) between the two groups. To reduce the confounders of the baseline characteristics, PSM analysis was performed at a 1:1 ratio. Finally, a total of 154 patients were selected, with 77 patients in each group. After matching, no significant differences were observed between the two groups with respect to baseline characteristics. Covariate balance after matching was confirmed by standardized mean differences below 0.1 for all variables, as shown in Supplementary Figure 1.

Table 1 Baseline Characteristics of Patients Before and After Propensity Score Matching

Characteristics	Before PSM			After PSM		
	AR Group N=114	PSH Group N=87	P value	AR Group N=77	PSH Group N=77	P value
Sex, N (%)			0.741			0.676
Female	19 (16.7%)	13 (14.9%)		15 (19.5%)	13 (16.9%)	
Male	95 (83.3%)	74 (85.1%)		62 (80.5%)	64 (83.1%)	
Age (years), Mean ± SD	55.3 ± 10.7	56.5 ±11.5	0.449	55.3 ± 9.6	57.1 ± 11.4	0.293
Viral hepatitis, N (%)	95 (83.3%)	76 (87.4%)	0.428	68 (88.3%)	66 (85.7%)	0.632
AFP≥400 ng/mL, N (%)	37 (32.5%)	25 (28.7%)	0.571	21 (27.3%)	23 (29.9%)	0.721
WBC (10^9/L), M (IQR)	5.5 (4.5–6.5)	5.4 (4.1–6.7)	0.588	5.1 (4.3–6.2)	5.3 (4.0–6.7)	0.877
PLT (10^9/L), M (IQR)	142.0 (100.8–186.3)	123.0 (95.0–163.0)	**0.026**	127.0 (96.0–164.5)	127.0 (96.0–164.0)	0.894
ALB (g/L), Mean ± SD	39.6 ± 4.0	38.9 ± 4.8	0.309	39.3 ± 4.0	38.8 ± 4.6	0.448
ALT (U/L), M (IQR)	37.5 (26.0–72.0)	35.0 (24.0–72.0)	0.775	39.0 (25.5–70.0)	35.0 (24.0–71.0)	0.961
AST (U/L), M (IQR)	38.5 (27.0–59.3)	36.0 (26.0–49.0)	0.376	38.0 (26.5–58.0)	36.0 (26.0–61.0)	0.919
Liver cirrhosis, N (%)	42 (36.8%)	44 (50.6%)	0.051	36 (46.8%)	37 (48.1%)	0.872
Child–Pugh class, N (%)			0.168			0.367
A	113 (99.1%)	83 (95.4%)		76 (98.7%)	73 (94.8%)	
B	1 (0.9%)	4 (4.6%)		1 (1.3%)	4 (5.2%)	
Portal hypertension, N (%)	12 (10.5%)	16 (18.4%)	0.111	8 (10.4%)	14 (18.2%)	0.167
Tumor size (cm), M (IQR)	5.6 (3.5–8.0)	5.0 (3.1–7.0)	**0.036**	5.0 (3.0–7.0)	5.0 (3.5–7.0)	0.599

Note: Bold values indicate statistical significance (P<0.05).

Abbreviations: PSM, propensity score matching; AR, anatomical resection; PSH, parenchymal-sparing hepatectomy; N, number; AFP, alpha-fetoprotein; WBC, white blood cell count; PLT, platelet count; ALB, albumin; ALT, alanine aminotransferase; AST, aspartate aminotransferase; SD, standard deviation; IQR, interquartile range.

Surgical and Pathological Outcomes

In the AR group, the surgical procedures included 13 left hemihepatectomies, 17 right hemihepatectomies, 6 middle hepatectomies, and 41 sectionectomies (including right anterior, right posterior, and left medial sections). Table 2 shows the short-term surgical outcomes in the AR and PSH groups after PSM. The proportion of patients with surgical margins ≥1 cm was significantly higher in the AR group (31.2% vs 11.7%, P=0.003), and the incidence of postoperative liver failure was higher in the AR group than in the PSH group (14.3% vs 3.9%, P=0.025). The incidences of postoperative liver failure for grade A, B, and C were 6.5%, 3.9%, and 3.9% in the AR group, and 1.3%, 2.6%, and 0% in the PSH group (P=0.209, 1.000, and 0.245, respectively). No significant differences were observed between the groups in terms of bleeding (P=0.386), blood transfusion (P=0.114), biliary leakage (P=1.000) or severe complications (Clavien–Dindo III–V) (P=0.385). The rates of postoperative recurrence were similar (41.6% vs 49.4%, P=0.332). There were no reported deaths during hospitalization. In terms of pathological findings, the degree of tumor differentiation was comparable between the AR and PSH groups (P=0.196). Additionally, the incidence of microvascular invasion (28.6% vs 31.2%, P=0.725) and satellite nodules (9.1% vs 9.1%, P = 1.000) did not differ significantly between the two groups.

Recurrence

In the PSM cohort, 70 patients experienced recurrence, with 32 patients in the AR group and 38 in the PSH group. Among them, 45 cases were intrahepatic recurrences, including 10 marginal recurrences, 27 non-marginal recurrences, and 8 cases of multiple intrahepatic recurrences. Extrahepatic recurrence was observed in 16 patients, whereas both intrahepatic and extrahepatic recurrence occurred in 9 patients.

After recurrence, a total of 59 patients received secondary treatment, including surgical resection, transarterial chemoembolization (TACE), radiofrequency ablation (RFA), systemic therapy, and combination therapy. The recurrence and treatment details for both groups are presented in Table 3. Among them, 18 recurrent patients underwent re-hepatectomy (6 in the AR group and 12 in the PSH group), and the re-resection rates of the AR and PSH groups were 18.8% and 31.6%, respectively.

Table 2 Postoperative Outcomes of Patients After Propensity Score Matching

Characteristics	AR Group N=77	PSH Group N=77	P value
Surgical margin≥1 cm, N (%)	24 (31.2%)	9 (11.7%)	**0.003**
Blood loss (mL), M (IQR)	300 (200–550)	400 (200–750)	0.386
Transfusion, N (%)	8 (10.4%)	15 (19.5%)	0.114
Complication, N (%)	30 (39.0%)	26 (33.8%)	0.503
Liver failure, N (%)	11 (14.3%)	3 (3.9%)	**0.025**
Grade A	5 (6.5%)	1 (1.3%)	0.209
Grade B	3 (3.9%)	2 (2.6%)	1.000
Grade C	3 (3.9%)	0	0.245
Biliary leakage, N (%)	2 (2.6%)	2 (2.6%)	1.000
Hemorrhage, N (%)	3 (3.9%)	1 (1.3%)	0.620
Clavien–Dindo class III–V, N (%)	8 (10.4%)	5 (6.5%)	0.385
Tumor differentiation, N (%)			0.196
Well	12 (15.6%)	5 (6.5%)	
Moderate	52 (67.5%)	57 (74.0%)	
Poor	13 (16.9%)	15 (19.5%)	
Microvascular invasion, N (%)	22 (28.6%)	24 (31.2%)	0.725
Satellite nodules, N (%)	7 (9.1%)	7 (9.1%)	1.000
Recurrence, N (%)	32 (41.6%)	38 (49.4%)	0.332
Postoperative adjuvant therapy, N (%)	37 (48.1%)	41 (53.2%)	0.519

Note: Bold values indicate statistical significance (P<0.05).
Abbreviations: AR, anatomical resection; PSH, parenchymal-sparing hepatectomy; N, number; IQR, interquartile range.

Table 3 Characteristics and Treatment of Recurrent HCC Patients After Propensity Score Matching

Variables	AR Group N=77	PSH Group N=77	P value
Recurrence, N (%)	32 (41.6%)	38 (49.4%)	0.332
Recurrence site, N (%)			0.573
Intrahepatic	18 (56.3%)	27 (71.1%)	0.198
Marginal	5	5	
Non-marginal	10	17	
Multiple	3	5	
Extrahepatic	10 (31.3%)	6 (15.8%)	0.125
Both	4 (12.5%)	5 (13.2%)	1.000
Treatment for recurrence, N (%)			0.784
Re-resection	6 (18.8%)	12 (31.6%)	0.221
TACE	6 (18.8%)	7 (18.4%)	0.972
RFA	3 (9.4%)	1 (2.6%)	0.325
Systemic therapy	5 (15.6%)	5 (13.2%)	1.000
TACE + Systemic therapy	5 (15.6%)	9 (9.2%)	0.401

Abbreviations: AR, anatomical resection; PSH, parenchymal-sparing hepatectomy; N, number; TACE, transarterial chemoembolization; RFA, radiofrequency ablation.

Survival Outcomes

Before PSM, the median follow-up time for all patients was 37.0 months (range: 1.0–131.0 months). The 1-, 3-, and 5-year OS rates were 94.4%, 80.8%, and 73.4%, respectively, while the 1-, 3-, and 5-year RFS rates were 78.7%, 56.4%, and 50.4%, respectively. In the AR and PSH groups, the 1-, 3-, and 5-year OS rates were 91.9%, 80.6%, and 75.1% in the AR group, and 97.7%, 81.4%, and 72.0% in the PSH group (P=0.659). The 1-, 3-, and 5-year RFS rates were 79.1%, 62.8%, and 54.2% in the AR group, and 78.1%, 49.5%, and 45.9% in the PSH group (P= 0.194). No significant differences in OS or RFS were observed between the two groups (Figure 3A and B).

A total of 154 patients were enrolled after PSM, with a median follow-up of 36.5 months (range: 6.0–124.0 months). The 1-, 3-, and 5-year OS rates were 94.6%, 80.4%, and 75.2% in the AR group, and 97.4%, 78.5%, and 66.6% in the PSH group, respectively (P=0.292). The 1-, 3-, and 5-year RFS rates were 76.5%, 59.2%, and 50.5% in the AR group, and 76.5%, 48.2%, and 46.2% in the PSH group, respectively (P=0.415). No significant differences in OS or RFS were observed between the two groups (Figure 3C and D).

Univariate and Multivariate Analyses of Overall Survival and Recurrence-Free Survival

After PSM, univariate and multivariate analyses were performed to determine the independent risk factors for OS and RFS, and the results are presented in Tables 4 and 5. Univariate analysis revealed that the preoperative AFP level (≥ 400 ng/mL), the serum ALB level, the tumor diameter, microvascular invasion (MVI), satellite nodules, and overall postoperative complications were significantly associated with OS. Multivariate analysis revealed that AFP ≥ 400 ng/mL (P < 0.001), the serum ALB level (P=0.024), the tumor diameter (P=0.012), satellite nodules (P=0.006), and overall postoperative complications (P=0.005) were independent risk factors for OS. With respect to RFS, univariate analysis revealed that viral hepatitis, AFP ≥ 400 ng/mL, tumor diameter, MVI, satellite nodules, and postoperative adjuvant therapy were significantly associated with RFS. Multivariate analysis revealed that viral hepatitis (P=0.012), AFP ≥ 400 ng/mL (P=0.002), satellite nodules (P=0.031), and postoperative adjuvant therapy (P=0.028) were independent risk factors for RFS. The surgical procedure (AR/PSH) was not an independent risk factor for OS or RFS.

Discussion

Surgical resection of perihilar tumors is challenging because of their proximity to the main hepatic pedicle. Currently, studies focusing on the surgical treatment of early-stage perihilar HCC remain limited; the optimal surgical approach is still undefined.

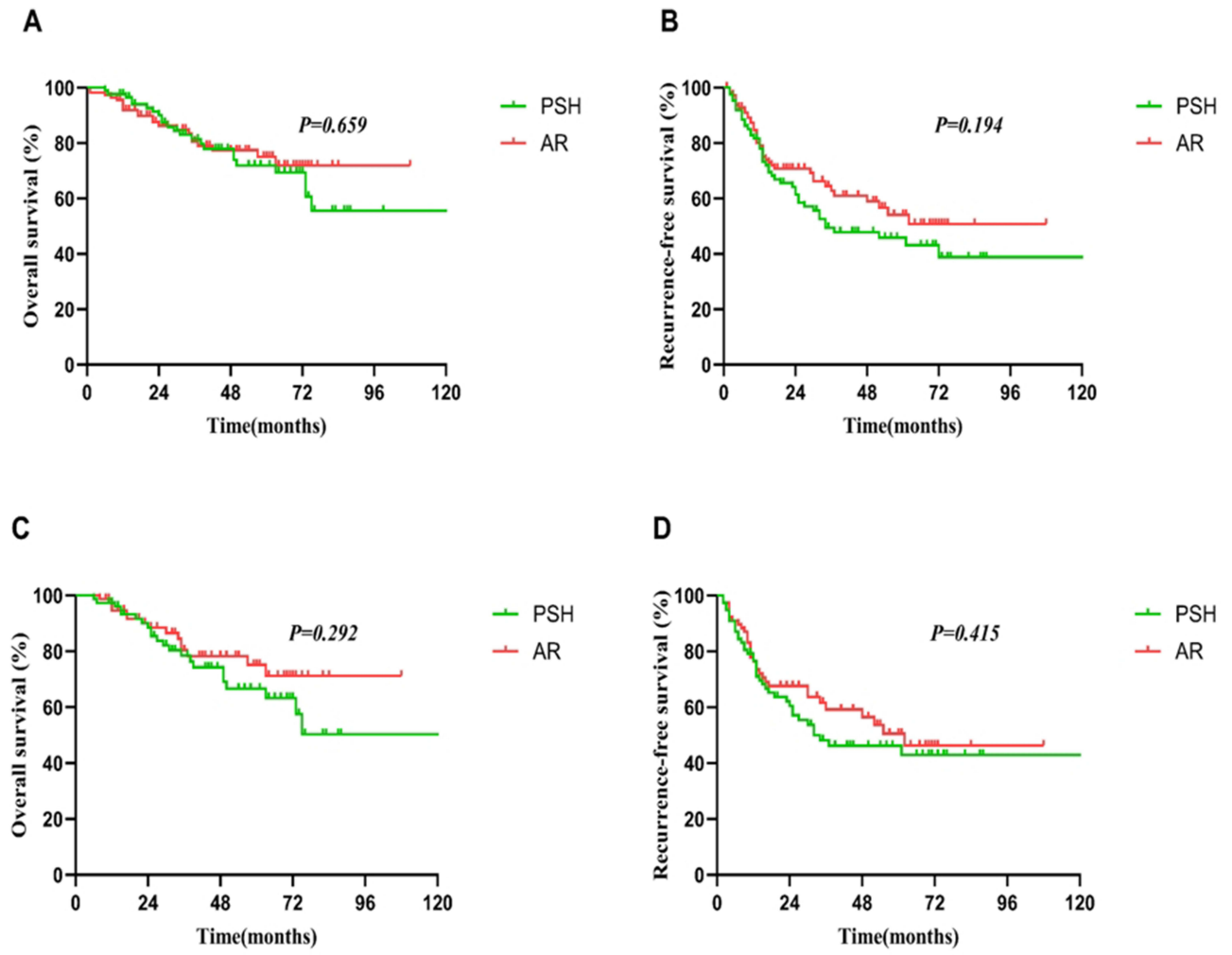


Figure 3 Overall survival (**A**) and recurrence-free survival (**B**) curves of patients in the AR and PSH groups before propensity score matching analysis. Overall survival (**C**) and recurrence-free survival (**D**) curves of patients in the AR and PSH groups after propensity score matching analysis.
Abbreviations: AR, anatomical resection; PSH, parenchymal-sparing hepatectomy.

In this retrospective study, we found that although AR was associated with a wider surgical margin, it did not significantly reduce tumor recurrence or improve long-term survival outcomes.

Anatomic liver resection of the tumor-bearing portal territory is considered to achieve a better curative effect because it can eliminate the surrounding micro-metastases and satellite nodules.[4] A prospective randomized controlled trial

Table 4 Univariate and Multivariate Analyses of Risk Factors for Overall Survival After Propensity Score Matching

Variables	Univariate HR (95% CI)	P value	Multivariate HR (95% CI)	P value
Sex (male/female)	2.390 (0.732–7.799)	0.149		
Age (years)	1.005 (0.975–1.037)	0.731		
Viral hepatitis (positive/negative)	2.736 (0.835–8.960)	0.096		
AFP≥400 ng/mL (yes/no)	3.533 (1.842–6.774)	**<0.001**	4.674 (2.355–9.280)	**<0.001**
PLT (10^9/L)	0.996 (0.989–1.002)	0.185		
ALB (g/L)	0.925 (0.864–0.990)	**0.025**	0.924 (0.862–0.990)	**0.024**

(*Continued*)

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Table 4 (Continued).

Variables	Univariate HR (95% CI)	P value	Multivariate HR (95% CI)	P value
ALT (U/L)	1.001 (0.997–1.005)	0.563		
AST (U/L)	1.004 (1.000–1.008)	0.077		
Liver cirrhosis (yes/no)	0.530 (0.261–1.078)	0.080		
Child–Pugh class		0.141		
A	1 (Reference)			
B	2.434 (0.745–7.949)			
Portal hypertension (yes/no)	1.141 (0.476–2.739)	0.767		
Tumor size (cm)	1.128 (1.006–1.265)	**0.039**	1.182 (1.037–1.348)	**0.012**
Surgical procedure (AR/PSH)	0.705 (0.365–1.359)	0.296		
Blood loss (mL)	1.000 (1.000–1.001)	0.414		
Transfusion (yes/no)	1.029 (0.449–2.362)	0.945		
Tumor differentiation		0.164		
Well	1 (Reference)			
Moderate	1.321 (0.396–4.401)	0.651		
Poor	2.489 (0.693–8.934)	0.162		
Surgical margin (cm)	1.293 (0.876–1.907)	0.196		
Microvascular invasion (yes/no)	2.022 (1.048–3.903)	**0.036**	1.008 (0.491–2.071)	0.982
Satellite nodules (yes/no)	4.249 (1.831–9.860)	**<0.001**	3.652 (1.437–9.281)	**0.006**
Complication (yes/no)	2.450 (1.269–4.732)	**0.008**	2.748 (1.356–5.569)	**0.005**
Clavien–Dindo Class III–V (yes/no)	1.609 (0.623–4.153)	0.326		
Postoperative adjuvant therapy (yes/no)	0.774 (0.404–1.484)	0.440		

Note: Bold values indicate statistical significance (P<0.05).

Abbreviations: PSM, propensity score matching; HR, hazard ratio; CI, confidence interval; AFP, alpha-fetoprotein; WBC, white blood cell count; PLT, platelet count; ALB, albumin; ALT, alanine aminotransferase; AST, aspartate aminotransferase; AR, anatomical resection; PSH, parenchymal-sparing hepatectomy.

Table 5 Univariate and Multivariate Analyses of Risk Factors for Recurrence-Free Survival After Propensity Score Matching

Variables	Univariate	P value	Multivariate	P value
	HR (95% CI)		HR (95% CI)	
Sex (male/female)	1.207 (0.634–2.299)	0.567		
Age (years)	0.996 (0.974–1.018)	0.703		
Viral hepatitis (positive/negative)	2.339 (1.009–5.419)	**0.048**	3.028 (1.278–7.176)	**0.012**
AFP≥400 ng/mL (yes/no)	1.850 (1.137–3.010)	**0.013**	2.178 (1.321–3.592)	**0.002**
PLT (10^9/L)	0.998 (0.994–1.003)	0.458		
ALB (g/L)	0.969 (0.919–1.021)	0.238		
ALT (U/L)	0.999 (0.996–1.003)	0.638		
AST (U/L)	1.002 (0.998–1.006)	0.367		
Liver cirrhosis (yes/no)	1.202 (0.750–1.924)	0.444		
Child–Pugh class		0.797		
A	1 (Reference)			
B	1.164 (0.366–3.704)			
Portal hypertension (yes/no)	1.984 (0.859–4.584)	0.109		
Tumor size (cm)	1.105 (1.015–1.204)	**0.022**	1.079 (0.980–1.189)	**0.120**
Surgical procedure (AR/PSH)	0.824 (0.515–1.319)	0.420		
Blood loss (mL)	1.000 (1.000–1.001)	0.056		
Transfusion (yes/no)	1.378 (0.766–2.479)	0.284		

(*Continued*)

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Table 5 (Continued).

Variables	Univariate	P value	Multivariate	P value
	HR (95% CI)		HR (95% CI)	
Tumor differentiation		0.273		
Well	1 (Reference)			
Moderate	1.481 (0.634–3.459)	0.364		
Poor	2.093 (0.811–5.400)	0.127		
Surgical margin (cm)	0.983 (0.686–1.407)	0.924		
Microvascular invasion (yes/no)	1.847 (1.139–2.995)	**0.013**	1.470 (0.848–2.549)	**0.170**
Satellite nodules (yes/no)	2.693 (1.325–5.475)	**0.006**	2.398 (1.084–5.306)	**0.031**
Complication (yes/no)	1.231 (0.756–2.005)	0.403		
Clavien–Dindo Class III–V (yes/no)	1.142 (0.523–2.496)	0.739		
Postoperative adjuvant therapy (yes/no)	0.564 (0.347–0.915)	**0.021**	0.559 (0.332–0.939)	**0.028**

Note: Bold values indicate statistical significance (P<0.05).
Abbreviations: PSM, propensity score matching; HR, hazard ratio; CI, confidence interval; AFP, alpha-fetoprotein; WBC, white blood cell count; PLT, platelet count; ALB, albumin; ALT, alanine aminotransferase; AST, aspartate aminotransferase; AR, anatomical resection; PSH, parenchymal-sparing hepatectomy.

demonstrated that, compared with NAR, AR significantly reduced the early (within 2 years) local recurrence rate in HCC patients (30.0% vs 59.0%) and markedly prolonged the time to local recurrence (53 vs 10 months, P=0.010).[16] However, the safety of AR has always been of great concern due to the extensive resection required (typically sectionectomy or hemihepatectomy), which results in greater loss of functional hepatic parenchyma and may increase the risk of post-operative liver failure. A multicenter study reported that the incidence of liver failure after AR reached 24.0%.[17] Additionally, many studies have also confirmed that PSH does not lead to worse therapeutic outcomes than AR.[18]

The primary advantage of PSH, which involves a less extensive resection than AR, is the preservation of the main hepatic pedicle and a greater amount of hepatic parenchyma, thereby increasing the possibility of multimodal treatment after tumor recurrence. Several studies have shown that PSH reduces the incidence of postoperative liver failure and provides similar short-term and long-term survival outcomes to AR.[12,19] PSH may be considered for patients at high risk of perioperative liver failure, especially those with cirrhosis.[20] However, PSH may result in inadequate surgical margins (<1 cm) and the inability to remove micro-metastases, leading to a higher risk of tumor recurrence and metastasis compared with AR. Therefore, there is still controversy over whether to perform AR or PSH during the operation.

In our study, we focused on a specific subtype of HCC. Owing to the special anatomical location of perihilar HCC, characterized by its proximity to the main hepatic pedicle and major vessels, surgical resection of tumors in this area is more challenging than resection in other parts of the liver. The resection extent of AR is relatively large, whereas PSH preserves more liver parenchyma, which is favorable for subsequent liver resection in the event of recurrence. Although the proportion of surgical margin ≥1 cm was higher in the AR group than in the PSH group (31.2% vs 11.7%, P=0.003), the recurrence rate was similar between the two groups (41.6% vs 49.4%, P=0.332). However, the recurrence patterns did not differ, and both groups showed similar marginal recurrence rates (5/77).

Despite achieving wider surgical margins in the AR group, increasing the margin width did not significantly improve RFS in this study. Research by Poon et al[21] supports our findings, and Okamura's study yielded similar conclusions.[22] The possible reasons are as follows. First, the hepatic pedicle may represent a boundary for tumor spread and ensure a negative margin along the preserved pedicle wall. Second, most HCCs are surrounded by a typical pseudocapsule that separates the tumor from the vein and can prevent tumor invasion, a phenomenon attributed to the host immune response against tumor cells.[23] Third, the main hepatic pedicle possesses the entire Laennec capsule, which appears to represent a safe anatomic boundary against tumoral spread.[24] Therefore, a narrow resection margin may still achieve preferable results for this particular type of HCC because of the protective effect of hepatic pedicles on limiting tumor spread.

The AR group showed a trend toward improved RFS, but the difference was not statistically significant, and the OS rates were comparable between the two groups. In our study, the re-resection rate was higher in the PSH group than in the AR

group (31.6% vs 18.8%, P=0.221), which may explain the comparable OS between the two groups. Consistently, a study by Lee et al[25] reported that the re-resection rate after PSH was significantly higher than that after AR (45.0% vs 0%).

Our research has confirmed that PSH can achieve the same survival benefit as AR. Katagiri et al[26] demonstrated that PSH is a safe and effective treatment for posterior-superior HCC adjacent to major blood vessels. Postoperative severe complications were comparable between the two groups. However, the incidence of postoperative liver failure was higher in the AR group (14.3% vs 3.9%, P=0.025), which reflects the complications associated with its surgical characteristics. The overall incidence of liver failure and biliary leakage remained low in the PSH group, suggesting that PSH may be safely performed in patients with perihilar HCC.

There are several limitations to this study. First, this was a retrospective, single-center study. The selection between PSH and AR was determined by ICG results, imaging evaluations, and surgeon preference. This non-random selection of surgical procedures may introduce a degree of inherent bias, and although PSM was employed to mitigate this, the possibility of residual confounding cannot be entirely excluded. Moreover, although the clinical baseline characteristics of the two groups were balanced by PSM, the small sample size limited our ability to perform a fully valid statistical analysis. Therefore, multicenter, large-scale prospective studies are essential to further confirm our findings.

Conclusions

PSH provides similar short-term and long-term survival outcomes to AR for early-stage perihilar HCC patients. It may represent a safe and feasible treatment option for them.

Data Sharing Statement

The manuscript incorporates all the data related to this study. Additional data may be made available from the corresponding author upon reasonable request.

Ethics Approval and Consent to Participate

The study was approved by the Clinical Research Ethics Committee of the Sichuan Cancer Hospital and was performed in accordance with the ethical guidelines of the Declaration of Helsinki (Ethical number: KY-2023-116-01). Written informed consent was obtained from all participants.

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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 declare no competing interests in this work.

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