Journal of Hepatocellular Carcinoma

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ORIGINAL RESEARCH

Liver Resection versus Targeted Therapy Plus PD-1 Inhibitors in Hepatocellular Carcinoma with Type I-II Portal Vein Tumor Thrombus: A Comparative Study

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Purpose: The optimal therapeutic strategy of hepatocellular carcinoma (HCC) with portal vein tumor thrombus (PVTT) is debated. This study aimed to compare the survival outcomes of liver resection (LR) versus targeted therapy plus programmed death-1 (PD-1) inhibitors in HCC patients with PVTT.

Patients and Methods: The data of 53 patients with HCC and type I–II PVTT was retrospectively assessed. Among them, 23 underwent LR, and 30 received targeted therapy plus PD-1 inhibitors (TT + PD-1). The baseline characteristics, overall survival (OS) and progression-free survival (PFS) of the two groups were compared. Univariable and multivariable Cox regression analysis were performed to identify independent prognostic factors of OS and PFS.

Results: There were no significant differences in baseline characteristics between the LR and TT + PD-1 groups. The LR group showed a significantly superior median OS (27.3 vs 15.3 months; $P < 0.001$) and PFS (13.8 vs 7.5 months; $P = 0.008$) compared to the TT + PD-1 group. Multivariable Cox regression analysis identified LR was independently associated with a better OS and PFS.

Conclusion: LR may represent an effective therapeutic option for HCC patients with type I–II PVTT.

Keywords: hepatocellular carcinoma, portal vein tumor thrombus, liver resection, targeted therapy, PD-1 inhibitors

Introduction

Hepatocellular carcinoma (HCC) is the third leading cause of cancer-related mortality and the sixth most common cancer globally.[1] Due to the invasive nature of HCC, it frequently results in portal vein tumor thrombus (PVTT). PVTT occurs in 12.5% to 39.7% at the diagnosis of HCC, which is associated with a markedly poor prognosis.[2–4] Treatment strategies for HCC with PVTT differ notably between Western and Eastern guidelines. According to the Barcelona Clinic Liver Cancer (BCLC) staging system, which is widely adopted in Western countries, patients with PVTT are classified as an advanced stage (BCLC-C), for whom liver resection (LR) is generally contraindicated.[5,6] Systemic therapy is typically recommended as the first-line treatment, including targeted therapy and programmed death-1/programmed death ligand-1 (PD-1/PD-L1) inhibitors. However, the survival benefit of systemic therapies in PVTT remains unsatisfied, with a median overall survival (OS) of approximately 10 months.[7–9] The success of IMbrave150 and other Phase 3 trials has made targeted therapy combined with PD-1/PD-L1 inhibitors a standard treatment for advanced HCC, but its efficacy in patients with PVTT still needs real-world validation.[10,11] Meanwhile, there are still unsolved issues regarding the

Received: 6 October 2025
Accepted: 9 December 2025
Published: 16 December 2025

identification of advantageous populations, overcoming resistance, and exploring combinations with other treatment modalities.[12,13]

In contrast to the Western guidelines, LR is considered as a feasible option for patients with PVTT in Asian countries.[14] A recent study on PVTT found that the surgery group had a median OS that was 1.77 years longer than the non-surgery group (2.87 vs 1.10 years, $P < 0.001$). After propensity score matching, the median OS in the surgery group was 2.45 years, compared to 1.57 years in the non-surgery group ($P < 0.001$).[15] Similarly, numerous large-scale studies have shown that LR can provide significant survival benefits for certain subgroups of PVTT patients, as compared to non-surgical treatments.[16–18] Clinical practice guidelines in Japan and China recommend LR as the standard treatment for patients with PVTT involving the first-order branch or higher of the main portal vein.[19,20] Furthermore, a recent study from Japan classified portal vein invasion (Vp) classification 2–3 type PVTT as "borderline resectable 1", suggesting that LR, as the core of the multidisciplinary treatment strategy, may provide survival benefits.[21] In addition, clinical evidence has identified that postoperative adjuvant therapy could improve the prognostic outcomes in patients at high risk of recurrence, especially in those with PVTT after hepatectomy.[22,23]

Given ongoing controversies between Western and Eastern guidelines regarding optimal therapeutic strategies for HCC with PVTT, high-quality studies directly comparing LR with targeted therapy combined with PD-1 inhibitors in patients with type I–II PVTT are still lacking. This study aimed to address this gap by comparing the survival outcomes of these two treatment strategies. The findings are intended to provide novel insights into the optimal treatment strategy for HCC with PVTT and offer scientific evidence for guiding future clinical decision-making.

Materials and Methods

Patients

Consecutive patients with HCC and type I–II PVTT who underwent LR or received targeted therapy plus PD-1 inhibitors (TT + PD-1) at the General Hospital of Northern Theater Command between January 2019 and June 2024 were enrolled and analyzed. The diagnosis of HCC was confirmed through pathological examination of percutaneous biopsy or postoperative specimens, or in accordance with the clinical imaging criteria established by the American Association for the Study of Liver Diseases (AASLD).[6] The presence and extent of PVTT were assessed using contrast-enhanced computed tomography (CT) or magnetic resonance imaging (MRI). PVTT was classified according to Cheng's classification, which categorizes tumor thrombus involvement in the portal vein into four types: type I, tumor thrombus in the segmental branches of the portal vein or above; type II, tumor thrombus extending to the right or the left portal vein; type III, tumor thrombus extending to the main portal vein; and type IV, tumor thrombus extending to the superior mesenteric vein.[24]

The inclusion criteria were: (1) aged 18–75 years; (2) diagnosed with HCC and type I–II PVTT; (3) Child-Pugh grade A-B7; (4) no macroscopic hepatic vein tumor thrombus; (5) at least one measurable lesion based on the modified Response Evaluation Criteria in Solid Tumors (mRECIST). The exclusion criteria were as follows: (1) prior anti-tumor treatment before hospitalization; (2) extrahepatic or distant metastases before treatment; (3) a history of other malignancies; (4) positive surgical margins; (5) incomplete baseline and follow-up data.

Treatment

In the LR group, the selection of the surgical approach, either laparoscopic or open surgery, was made through a shared decision-making process between surgeons and patients. The extent of LR was determined by the tumor number and size, as well as the degree of cirrhosis. The surgical approach for PVTT was determined intraoperatively, employing either thrombectomy or en bloc resection. In the TT + PD-1 group, treatment began after the diagnosis and comprehensive assessment. The adopted targeted regimen included sorafenib (400 mg orally twice daily), lenvatinib (8 mg for body weight < 60 kg or 12 mg for body weight ≥ 60 kg, orally once daily), apatinib (250 mg orally once daily) and bevacizumab (15 mg/kg by intravenous infusion once every 3 weeks).[10,11,25,26] All PD-1 inhibitors (camrelizumab 200 mg; sintilimab 200 mg; tislelizumab 200 mg; toripalimab 240 mg) were administered by intravenous infusion once every 3 weeks.[11,27–29] The selection of targeted regimens and PD-1 inhibitors was based on the most recent safety

profiles, patient financial status, and drug availability. Treatment-related adverse events (TRAEs) were closely monitored during the therapeutic process. Additionally, if patients experienced any grade 3 or higher TRAEs, the drug dosages were reduced or discontinued until the symptoms were alleviated.

Study Endpoints and Follow-Up

The primary endpoints were OS and progression-free survival (PFS). OS was defined as the period between the initiation of treatment and the patient's death or last follow-up. PFS was defined as the period between the LR and the tumor recurrence or last follow-up for the LR group, and the period between the initiation of treatment and the tumor progression or last follow-up for the TT + PD-1 group. The secondary endpoints were postoperative complications for the LR group, and TRAEs for the TT + PD-1 group. TRAEs and postoperative complications were categorized using the Common Terminology Criteria for Adverse Events (CTCAE) version 5.0 and Clavien-Dindo classification, respectively.

Patients in the LR group were followed up 1 month after surgery, with subsequent follow-ups every 3–6 months for the first 2 years, and every 6 months thereafter. The follow-up surveillance items included laboratory tests (serum tumor biomarkers, liver function and complete blood count), abdominal ultrasound and contrast-enhanced CT or MRI. In the TT + PD-1 group, tumor response was assessed by contrast-enhanced CT or MRI every 12 weeks. When the patients experienced tumor recurrence or progression, they chose the appropriate treatment based on the doctor's recommendation and their own conditions, including second-line systemic therapy, transarterial chemoembolization (TACE), radiotherapy, or best supportive care. All patients were followed up until death or loss to follow-up, and the data were censored on May 31, 2025.

Statistical Analysis

Categorical variables were expressed as frequencies and percentages, and inter-group comparisons were performed using Chi-square test or Fisher's exact test. Continuous variables were presented as median (interquartile range) or mean (standard deviation), with inter-group differences assessed using the Mann–Whitney *U*-test or Student's *t* test, as appropriate. OS and PFS were estimated using the Kaplan-Meier method, and survival differences between the groups were compared using the Log rank test. Univariable and multivariable Cox regression analysis were conducted to identify independent prognostic factors of OS and PFS. Variables with a P-value < 0.1 in the univariable analysis were included in the multivariable Cox regression model. All statistical tests were two-tailed, with a P-value < 0.05 considered statistically significant. Statistical analyses were performed using SPSS software (version 27, IBM, Chicago, IL, USA).

Results

Patient Characteristics

Upon inclusion and exclusion criteria, 53 patients with HCC and type I–II PVTT who underwent LR (n = 23) or received TT + PD-1 (n = 30) were included (Figure 1). The mean age of the patients was 56.6 ± 9.7 years, with the majority being male (86.8%). Most patients (90.6%) were hepatitis B virus (HBV)-related HCC, and 24 (45.3%) of patients had baseline alpha-fetoprotein (AFP) ≥ 400 ng/mL. Among the patients, 11 (20.8%) had a maximum tumor diameter ≥ 10 cm, 26 (49.1%) presented multiple tumors, 23 (43.4%) patients had type I PVTT, and 30 (56.6%) patients had type II PVTT. As shown in Table 1, the baseline characteristics were well-balanced between the two groups.

Treatment Outcomes

In the LR group (Table S1), 17 patients (73.9%) underwent open surgery and 19 patients (82.6%) underwent major hepatectomy. En bloc resection of the involved portal vein segment was the predominant approach for PVTT management, performed in most cases (73.9%). The median operative time was 270 minutes, and the median intraoperative blood loss was 400 mL, with 8 (34.8%) patients had intraoperative blood transfusion. The median postoperative stay was 12 days, 17 (73.9%) patients experienced postoperative complications, and only 1 patient occurred Clavien-Dindo grade IIIa ascites requiring therapeutic paracentesis. Additionally, postoperative pathological examination confirmed

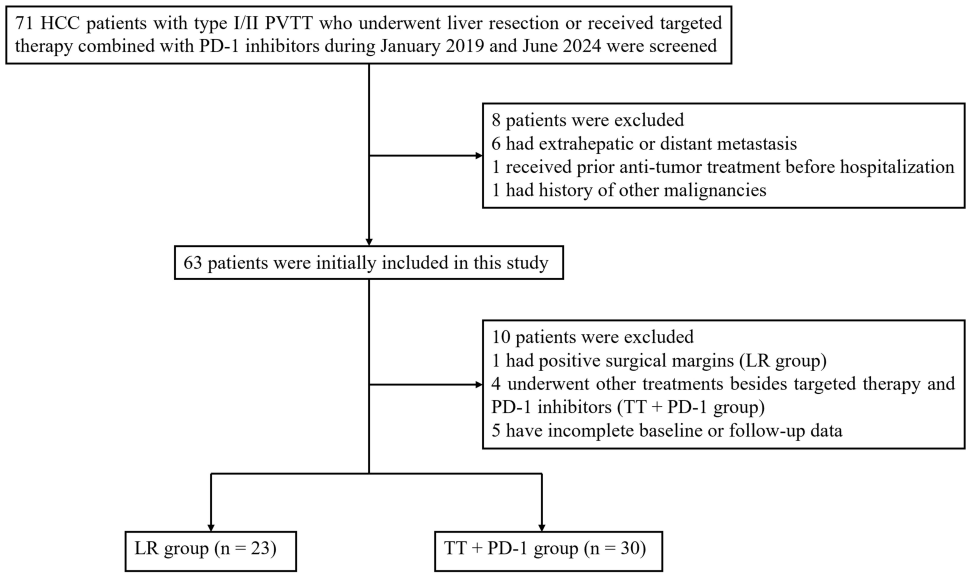

Figure 1 Flowchart of patient selection. PD-1, programmed death-1; LR, liver resection; TT, targeted therapy.

microvascular invasion in 20 (87.0%) patients. Of the 23 patients, 19 (82.6%) patients received postoperative adjuvant therapy, with tyrosine kinase inhibitors (TKIs) as the predominant choice.

In the TT + PD-1 group, all patients received at least one cycle of PD-1 inhibitors and underwent a minimum of one radiological evaluation. The median treatment duration was 3 cycles (interquartile range 1–8.3). 23 (76.7%) patients received lenvatinib, and sintilimab (43.3%) was the most commonly used PD-1 inhibitor. According to mRECIST, 7 (23.3%) patients achieved partial response (PR), and 9 (30.0%) patients had stable disease (SD), resulting in an objective response rate (ORR) of 23.3% and a disease control rate (DCR) of 53.3%, respectively (Table S2). Treatment discontinuation occurred in 29 patients, primarily due to radiologically confirmed disease progression (27) and TRAEs (2). At the time of data cutoff, one patient remained on combination therapy. As shown in Table S3, the safety of TT +

Table 1 Baseline Demographics and Clinical Characteristics in Patients with HCC and Type I–II PVTT

Characteristic	Total (n = 53)	LR (n = 23)	TT + PD-1 (n = 30)	P-value
Age (years)	56.6 ± 9.7	56.3 ± 8.3	56.8 ± 10.8	0.843
Sex (male/female)	46(86.8)/7(13.2)	18(78.3)/5(21.7)	28(93.3)/2(6.7)	0.218
Etiology (HBV/HCV/no-viral)	48(90.6)/3(5.7)/2(3.8)	21(91.3)/2(8.7)/0(0)	27(90.0)/1(3.3)/2(6.7)	0.492
Child-Pugh grade (A/B)	47(88.7)/6(11.3)	20(87.0)/3(13.0)	27(90.0)/3(10.0)	1.000
Liver cirrhosis (present/absent))	44(83.0)/9(17.0)	18(78.3)/5(21.7)	26(86.7)/4(13.3)	0.478
TBIL (μmol/L)	14.9(12.6–19.5)	13.8(11.5–16.5)	16.4(13.0–21.7)	0.095
ALT (U/L)	43.8(24.9–65.6)	51.9(28.5–67.9)	42.3(21.9–60.0)	0.236
AST (U/L)	47.8(29.3–75.5)	43.0(28.4–75.1)	51.2(31.4–88.6)	0.554
ALB (g/L)	37.1 ± 4.9	37.5 ± 5.3	36.8 ± 4.7	0.586
PLT (10^9/L)	148.0(108.5–219.5)	157.0(116.0–197.0)	131.5(103.5–232.3)	0.774
PT (s)	14.0(13.3–14.7)	14.1(12.9–14.7)	14.0(13.5–14.7)	1.000
Baseline AFP (≥ 400 ng/mL/< 400 ng/mL)	24(45.3)/29(54.7)	10(43.5)/13(56.5)	14(46.7)/16(53.3)	1.000
Tumor number (multiple/single)	26(49.1)/27(50.9)	9(39.1)/14(60.9)	17(56.7)/13(43.3)	0.206
Tumor diameter (cm)	8.3(7.1–9.5)	7.7(6.1–9.5)	8.5(7.4–9.5)	0.172
Tumor diameter (≥ 10cm/< 10cm)	11(20.8)/42(79.2)	5(21.7)/18(78.3)	6(20.0)/24(80.0)	1.000
PVTT type (I/II)	23(43.4)/30(56.6)	10(43.5)/13(56.5)	13(43.3)/17(56.7)	0.992

Abbreviations: HBV, hepatitis B virus; HCV, hepatitis C virus; TBIL, total bilirubin; ALT, alanine aminotransferase; AST, aspartate aminotransferase; ALB, albumin; PLT, platelet; PT, prothrombin time; AFP, alpha-fetoprotein.

PD-1 was favorable. The incidence of TRAEs was 76.7%, and only 2 (6.7%) patients occurred Grade III gastrointestinal hemorrhage necessitating endoscopic hemostatic intervention.

Survival Outcomes

At the time of data cutoff on May 31, 2025, 36 (67.9%) patients had died, and 47 (88.7%) patients had the disease recurrence or progression. The patients who underwent LR had a better OS (P < 0.001) and PFS (P = 0.008) compared with those who received TT + PD-1. The median OS and PFS of the LR group were 27.3 and 13.8 months, respectively, while the median OS and PFS of the TT + PD-1 group were 15.3 and 7.5 months, respectively (Figure 2). Then, subgroup survival analysis was performed according to the type of PVTT. In patients with type I PVTT, the OS in the LR group was significantly better than TT + PD-1 group (P = 0.003), whereas the PFS between the two groups was comparable (P = 0.183). Specifically, the median OS and PFS of the LR group were 34.9 and 15.8 months, respectively, and the median OS and PFS of the TT + PD-1 group were 18.4 and 9.4 months, respectively (Figure 3). In patients with type II PVTT, patients in the LR group showed a better OS (P = 0.039) and PFS (P = 0.026) compared with those in the TT + PD-1 group. Specifically, the median OS and PFS of the LR group were 20.8 and 11.4 months, respectively, and the median OS and PFS of the TT + PD-1 group were 13.6 and 7.3 months, respectively (Figure 4).

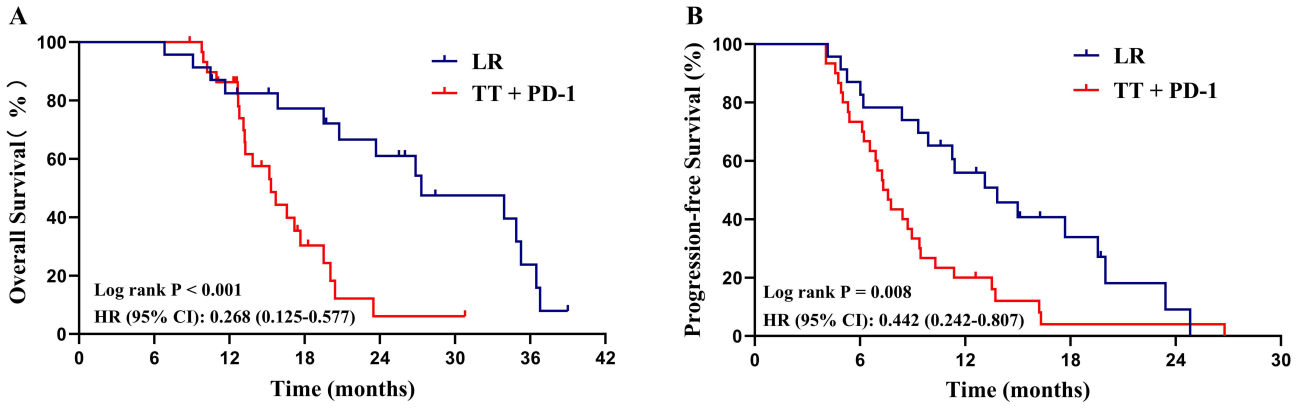

Figure 2 Survival analysis of OS (**A**) and PFS (**B**) between the LR (n = 23) and TT+ PD-1 (n = 30) groups. HR, hazard ratio; CI, confidence interval.

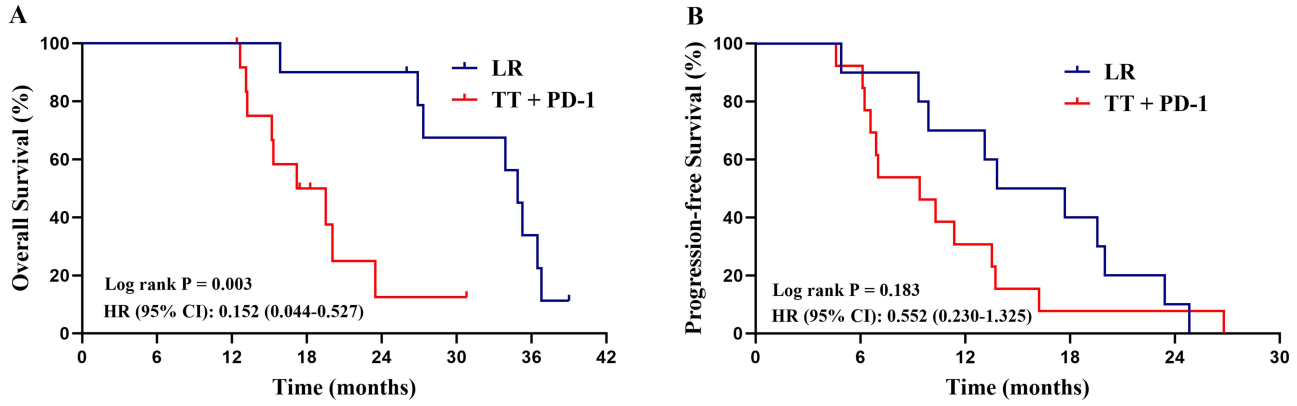

Figure 3 Survival analysis of (**A**) OS and (**B**) PFS: LR group (n = 10) vs TT+ PD-1 group (n = 13) in patients with type I PVTT. HR, hazard ratio; CI, confidence interval.

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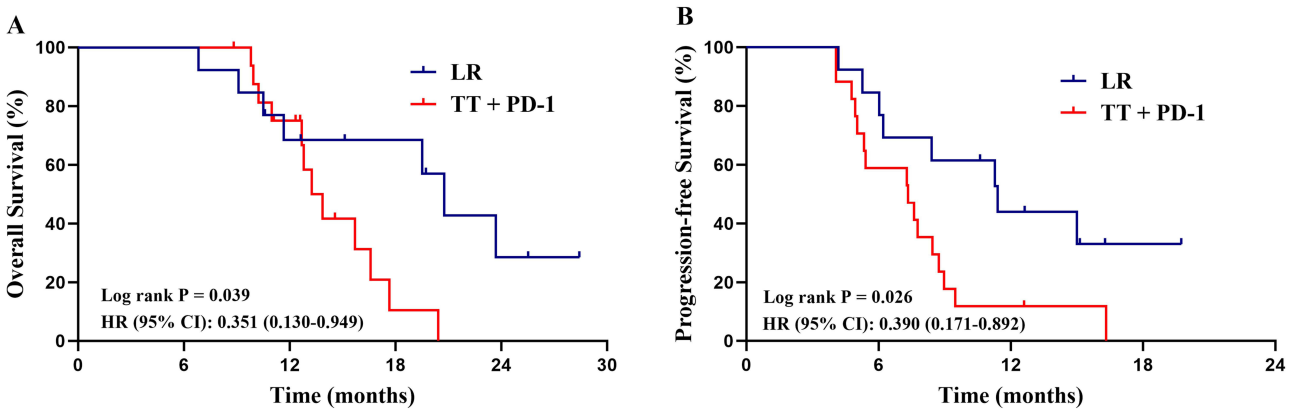

Figure 4 Survival analysis of (**A**) OS and (**B**) PFS: LR group (n = 13) vs TT + PD-1 group (n = 17) in patients with type II PVTT. HR, hazard ratio; CI, confidence interval.

Independent Prognostic Factors of OS and PFS

Multivariable Cox regression analysis demonstrated that PVTT type (hazard ratio (HR): 0.319; 95% confidence interval (CI): 0.148–0.689; P = 0.004) and treatment option (HR: 0.214; 95% CI: 0.079–0.582; P = 0.003) were independent prognostic factors of OS (Table 2). Treatment option (HR: 0.475; 95% CI: 0.255–0.887; P = 0.019) was independent prognostic factor of PFS (Table 3).

Discussion

Our study found that the patients in the LR group had a superior OS and PFS compared with those in the TT + PD-1 group. Multivariable Cox regression analysis further identified that LR was independently associated with a better OS and PFS. Notably, LR achieved a median OS exceeding two years in appropriately selected patients, challenging the conventional paradigm of exclusive systemic therapy. Furthermore, safety profiles of both groups were acceptable Postoperative complications and TRAEs were minor and controllable with symptomatic treatment.

Table 2 Univariable and Multivariable Analysis of Factors Associated with OS

Characteristic	Univariate Analysis			Multivariate Analysis		
	HR	95% CI	P-value	HR	95% CI	P-value
Age, ≥ 60 vs < 60, years	0.805	0.401–1.615	0.542			
Sex, male vs female	1.571	0.551–4.483	0.398			
Child-Pugh grade, A vs B	0.569	0.233–1.391	0.216			
Liver cirrhosis, present vs absent	1.452	0.557–3.782	0.445			
TBIL, ≥ 17.1 vs < 17.1, μmol/L	1.929	0.957–3.888	**0.066**	0.874	0.380–2.013	0.752
ALT, ≥ 40 vs < 40, U/L	1.006	0.517–1.957	0.986			
AST, ≥ 40 vs < 40, U/L	1.481	0.754–2.910	0.254			
ALB, ≥ 35 vs < 35, g/L	0.668	0.340–1.314	0.243			
PLT, ≥ 100 vs < 100, 10^9/L	1.080	0.516–2.262	0.838			
PT, ≥ 14 vs < 14, s	1.032	0.515–2.071	0.928			
Baseline AFP, ≥ 400 vs < 400, ng/mL	1.723	0.881–3.373	0.112			
Tumor number, multiple vs single	1.656	0.844–3.251	0.143			
Tumor diameter, ≥ 10 vs < 10, cm	1.586	0.732–3.436	0.242			
PVTT type, I vs II	0.363	0.171–0.768	**0.008**	0.319	0.148–0.689	**0.004**
Treatment option, LR vs TT + PD-1	0.262	0.115–0.594	**0.001**	0.214	0.079–0.582	**0.003**

Notes: The bolded values indicate statistical significance.
Abbreviations: HR, hazard ratio; CI, confidence interval; TBIL, total bilirubin; ALT, alanine aminotransferase; AST, aspartate aminotransferase; ALB, albumin; PLT, platelet; PT, prothrombin time; AFP, alpha-fetoprotein.

Table 3 Univariable and Multivariable Analysis of Factors Associated with PFS

Characteristic	Univariate Analysis			Multivariate Analysis		
	HR	95% CI	P-value	HR	95% CI	P-value
Age, ≥ 60 vs < 60, years	0.997	0.552–1.802	0.992			
Sex, male vs female	2.119	0.829–5.416	0.117			
Child-Pugh grade, A vs B	0.662	0.278–1.578	0.353			
Liver cirrhosis, present vs absent	1.485	0.658–3.348	0.341			
TBIL, ≥ 17.1 vs < 17.1, μmol/L	1.375	0.759–2.490	0.294			
ALT, ≥ 40 vs < 40, U/L	1.086	0.598–1.970	0.786			
AST, ≥ 40 vs < 40, U/L	0.992	0.543–1.810	0.978			
ALB, ≥ 35 vs < 35, g/L	0.771	0.416–1.428	0.409			
PLT, ≥ 100 vs < 100, 10^9/L	1.590	0.757–3.341	0.220			
PT, ≥ 14 vs < 14, s	0.788	0.431–1.439	0.438			
Baseline AFP, ≥ 400 vs < 400, ng/mL	1.139	0.634–2.045	0.663			
Tumor number, multiple vs single	1.918	1.064–3.457	**0.030**	1.746	0.963–3.166	0.066
Tumor diameter, ≥ 10 vs < 10, cm	0.930	0.445–1.942	0.847			
PVTT type, I vs II	0.641	0.346–1.187	0.157			
Treatment option, LR vs TT + PD-1	0.445	0.241–0.820	**0.009**	0.475	0.255–0.887	**0.019**

Notes: The bolded values indicate statistical significance.
Abbreviations: HR, hazard ratio; CI, confidence interval; TBIL, total bilirubin; ALT, alanine aminotransferase; AST, aspartate aminotransferase; ALB, albumin; PLT, platelet; PT, prothrombin time; AFP, alpha-fetoprotein.

PVTT represents as an invasive and progressive pattern of HCC, which is associated with an extremely poorer prognosis than the early-stage HCC. In the past, HCC with PVTT has been considered as a contraindication for LR, with only systemic therapy recommended. However, with the evolution and development of surgical concepts, locoregional therapy techniques, targeted and immunotherapeutic regimens, patients with HCC and PVTT have more treatment options, with improved prognostic outcomes.[20] In the field of systemic treatment, targeted therapy combined with immunotherapy has emerged as the most promising treatment modality for HCC and PVTT. Targeted therapy reduces tumor burden by inhibiting cell proliferation and angiogenesis, while immunotherapy enhances systemic anti-tumor immunity. Systemic combination therapy can overcome the limitations of the monotherapy and potentially improve survival outcomes for advanced HCC. Yuan et al reported that the median OS of HCC patients with type I and II PVTT who received camrelizumab plus apatinib were 16 and 15.9 months, respectively, and the median PFS of these patients were 14.9 and 14 months, respectively.[30] Despite the absence of a control group, these survival outcomes surpassed the previously published data.[7] Furthermore, a multicenter study indicated that the group of atezolizumab plus bevacizumab was associated with a better 1-year OS (P = 0.02) and PFS (P = 0.01) than the group of TACE + radiotherapy in patients with PVTT.[31]

In the past few decades, researchers from Asian countries generally advocate for radical treatment strategies, insisting that the presence of PVTT should not be regarded as the contraindication for LR. Several guidelines support LR as a feasible treatment option for patients with HCC and PVTT, especially for those with type I–II PVTT.[14,19,20] Compared to systemic treatment, the resection of both the primary tumor and tumor thrombus can significantly reduce the tumor burden, potentially prevent distant metastasis and improved liver function by restore portal venous flow. Furthermore, postoperative adjuvant therapies, such as TACE and radiotherapy, have been shown to further prolong the survival time after surgery.[32,33] Thus, LR have been adopted as one of the most effective treatment modalities among Eastern medical centers. Nevertheless, the comparisons between LR and targeted therapy combined with immunotherapy in patients with HCC and PVTT remains largely unknown in real-world practice. Our findings demonstrated that LR was a superior therapeutic strategy, which was associated with a significantly improved OS in both type I and II PVTT subgroups. While a favorable trend toward prolonged PFS was observed for the entire cohort with LR, the benefit reached statistical significance only in type II PVTT. For type I PVTT specifically, the PFS difference between the two groups was not statistically significant (P = 0.183), which was potentially attributable to the limited sample size and consequent

insufficient statistical power. Furthermore, multivariable analysis confirmed the treatment option as an independent prognostic factor of both OS and PFS.

Although our results suggested that LR offered a survival advantage for HCC patients with type I–II PVTT, careful patient selection and postoperative monitoring are paramount to ensure the efficacy. The Eastern Hepatobiliary Surgery Hospital/Portal Vein Tumor Thrombus (EHBH/PVTT) scoring system proposed by Zhang et al identified subgroups of type I–II PVTT patients who may not obtain substantial survival benefit from LR, including those with preoperative total bilirubin (TBIL) $\geq$ 17.1 μmol/L, AFP $\geq$ 20 ng/mL, tumor diameter > 5 cm, or the presence of satellite nodules.[17] These factors are associated with poorer liver function and more aggressive tumor behavior, highlighting the importance of comprehensive preoperative evaluation to guide decisions regarding hepatectomy. Moreover, Chen et al emphasized the importance of close postoperative monitoring and adjuvant therapy for patients with PVTT to improve long-term postoperative survival outcomes.[34] In our study, patients who underwent LR had dramatically better survival outcomes. However, due to the limited sample size, the actual benefit of LR may be overestimated. Future research directions should include conducting multi-center, prospective cohort studies or randomized controlled trials (RCTs) to validate our conclusions, and utilizing biomarkers to precisely identify patient subgroups that can benefit most from surgery or systemic therapy. Especially, emerging technologies such as proteomics to discover new therapeutic targets may provide insights for developing more effective systemic treatment regimens and even new neoadjuvant/adjuvant strategies combined with surgery in the future.[35]

Our study has several limitations. Firstly, the main limitation of this study is its non-randomized design. Patients who underwent LR may inherently have better liver function reserve, more favorable tumor anatomical location, or better performance status. Although baseline characteristics appeared balanced, these unmeasured confounding factors might have influenced treatment allocation and ultimately outcomes. Larger, multicenter prospective studies across diverse populations are needed to confirm the generalizability of our study results. Secondly, the heterogeneity of targeted regimen and PD-1 inhibitors may potentially influence the results. Thirdly, given this study primarily focused on HBV-related HCC, the effectiveness of LR in HCC of other etiologies, such as hepatitis C virus (HCV) or alcohol-related HCC, requires further investigation.

Conclusion

In conclusion, LR may represent a more effective therapeutic option than TT + PD-1 in patients with HCC and type I–II PVTT. Future research directions should include conducting multi-center, prospective cohort studies or RCTs to validate our results, and utilizing biomarkers to precisely identify patient subgroups that can benefit most from LR or systemic therapy.

Abbreviations

HCC, Hepatocellular Carcinoma; PVTT, Portal Vein Tumor Thrombus; BCLC, Barcelona Clinic Liver Cancer; PD-1, Programmed Death-1; PD-L1, Programmed Death-Ligand 1; OS, Overall Survival; AASLD, American Association for the Study of Liver Diseases; CT, Computed Tomography; MRI, Magnetic Resonance Imaging; mRECIST, modified Response Evaluation Criteria in Solid Tumors; TRAE, Treatment-related Adverse Event; PFS, Progression-free Survival; CTCAE, Common Terminology Criteria for Adverse Event; TACE, Transcatheter Arterial Chemoembolization; HBV, Hepatitis B Virus; AFP, Alpha-fetoprotein; TKI, Tyrosine Kinase Inhibitor; PR, Partial Response; SD, Stable Disease; ORR, Objective Response Rate; DCR, Disease Control Rate; HR, Hazard Ratio; CI, Confidence Interval; TBIL, Total Bilirubin; RCT, Randomized Controlled Trial; HCV, Hepatitis C Virus.

Data Sharing Statement

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Ethics Approval and Informed Consent

This study was approved by the Ethics Committee of the General Hospital of Northern Theater Command (Approval No. 2025064) and conducted in strict compliance with the Declaration of Helsinki. Due to its retrospective design, written informed consent was formally waived by the aforementioned committee, as the study only used de-identified, untraceable medical records without additional risks to patients' rights or privacy. All personal and medical data of patients were strictly protected.

Funding

This study was supported by the Science and Technology Plan Joint Program of Liaoning Province (2024JH2/102600286) and Independent Scientific Research Project of General Hospital of Northern Theater Command (ZZKY2024052).

Disclosure

The authors confirm that there are no conflicts of interest.

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