Original Article

# The clinical outcomes of patients with vascular invasion after deceased donor liver transplantation

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**Background:** Vascular invasion is a major risk factor for poor prognosis of liver transplantation (LT) for hepatocellular carcinoma (HCC), and this study aimed to evaluate the feasibility and efficacy of deceased donor LT (DDLT) for the treatment of microvascular invasion (MVI) and segmental portal vein tumor thrombus (PVTT).

**Methods:** We retrospectively analyzed 141 patients who received DDLT for HCC combined with vascular invasion from January 2016 to December 2023 at Shulan (Hangzhou) Hospital. To assess the risk of vascular invasion associated with the LT prognosis, we evaluated various clinicopathologic variables. The recurrence-free survival (RFS) and overall survival (OS) based on different types of vascular invasion were also analyzed.

**Results:** A total of 141 patients were enrolled in this study, including patients with MVI (MVI group, n=60), segmental PVTT with segmental branches of the portal vein or above (segmental PVTT group, n=13), and lobar PVTT involving the left and right branches of the portal vein or the main portal vein (lobar PVTT group, n=68). Between the tumor recurrence group and the no recurrence group, there were significant differences in alpha-fetoprotein (AFP) level, tumor total diameter, pretransplant treatment, histological grade, and types of vascular invasion. Subgroup analyses were performed according to the types of vascular invasion, the lobar PVTT group had a significantly higher recurrence rate (lobar *vs.* MVI: 88.2% *vs.* 35.0%, lobar *vs.* segmental: 88.2% *vs.* 30.8%, both P<0.001), but there was no difference in recurrence rate between the MVI group and the segmental PVTT group (35.0% *vs.* 30.8%, P>0.99). The 3-year RFS rate and OS rate were as low as 9.1% and 45.9% in the lobar PVTT group, compared with 65.5% and 76.0% in the MVI group, 58.3% and 75.0% in the segmental PVTT group. Multivariate analysis showed that Child-Pugh classification, tumor total diameter, histological grade, and lobar PVTT were the main risk factors affecting RFS, whereas Child-Pugh classification, tumor total diameter, and lobar PVTT were the main risk factors affecting OS. Finally, analysis of the segmental PVTT group revealed that RFS was significantly higher in well and moderately-differentiated patients than in poor-differentiated patients (P=0.01).

**Conclusions:** Lobar PVTT remains a contraindication to LT, whereas segmental PVTT can still be considered for LT after careful screening.

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**Keywords:** Hepatocellular carcinoma (HCC); liver transplantation (LT); vascular invasion; portal vein tumor thrombus (PVTT)

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## Introduction

Liver cancer is the fourth most common cancer and the second leading cause of cancer-related deaths in China, hepatocellular carcinoma (HCC) accounts for 85–90% of primary liver cancers, and the main risk factor for HCC is chronic hepatitis B virus (HBV) infection (1). Due to the lack of obvious clinical symptoms in the early stage, 70–80% of patients are found in the middle to advanced stage, and even 44–62.2% of patients are complicated with portal vein tumor thrombus (PVTT) (2). The median survival time for patients with untreated intermediate-stage HCC is about 16 months, and for patients with advanced-stage HCC, especially with macrovascular invasion, the median survival time is 6–8 months, with a 1-year survival rate of only about 25% (3). Once PVTT is formed, it can cause portal hypertension and related complications such as gastrointestinal bleeding, refractory ascites, and even leads to hepatocellular jaundice, the prognosis is extremely poor (4).

Liver transplantation (LT) can simultaneously treat malignant tumors, cirrhosis, portal hypertension, and other symptoms. Scholars have discovered that expanding the transplantation criteria based on the Milan criteria (MC) can also achieve a prognosis approximating the MC, resulting in more patients benefiting from LT (5,6).

Vascular invasion is considered a risk factor for poor prognosis in LT, and in particular, the combination of PVTT is considered contraindicated. However, a recent study has shown that LT is superior to hepatectomy in patients with PVTT, and LT is the only independent predictor of overall survival (OS) (7). Some scholars believe that after the formation of PVTT, it exists in the portal vein for a while in a continuous spreading way without hematogenous metastasis to distant sites immediately (8,9). Based on this theory, we conducted the present study to evaluate the feasibility and efficacy of deceased donor LT (DDLT) in treating patients with HCC combined with different types of vascular invasion and to investigate the survival outcomes. We present this article in accordance with the STROBE reporting checklist (available at https://jgo.amegroups.com/article/view/10.21037/jgo-24-328/rc).

### Highlight box

**Key findings**

- Child-Pugh classification, tumor total diameter, histological grade, and lobar portal vein tumor thrombus (PVTT) were independent risk factors of tumor recurrence after liver transplantation (LT).
- Patients with microvascular invasion and segmental PVTT, especially those with well and moderately differentiated histological grade, had a better prognosis after LT.

**What is known and what is new?**

- Vascular invasion is an important risk factor for poor prognosis of LT for hepatocellular carcinoma, PVTT is contraindicated for LT.
- We believe that carefully selected patients with segmental PVTT can have a good prognosis and should be potential candidates for LT.

**What is the implication, and what should change now?**

- Patients with segmental PVTT can also achieve long-term recurrence-free survival after LT by careful screening and evaluation. We can indirectly screen patients with favorable tumor histology and biological behavior by preoperative alpha-fetoprotein level and response to neoadjuvant therapy.

## Methods

### *Patients*

We retrospectively analyzed the data of HCC patients who underwent DDLT in Shulan (Hangzhou) Hospital from January 2016 to December 2023 (*Figure 1*). Only adult patients with HCC combined with vascular invasion were included in this study. The exclusion criteria included (I) no vascular invasion or tumor thrombus involving superior mesenteric vein; (II) postoperative pathology suggestive of other malignant tumors such as cholangiocellular carcinoma or mixed HCC; (III) presence of local lymph node metastasis or distant metastasis; (IV) death of the patient in the perioperative period due to organ failure, hemorrhage, etc.; (V) loss of visitation within 1 year of

 

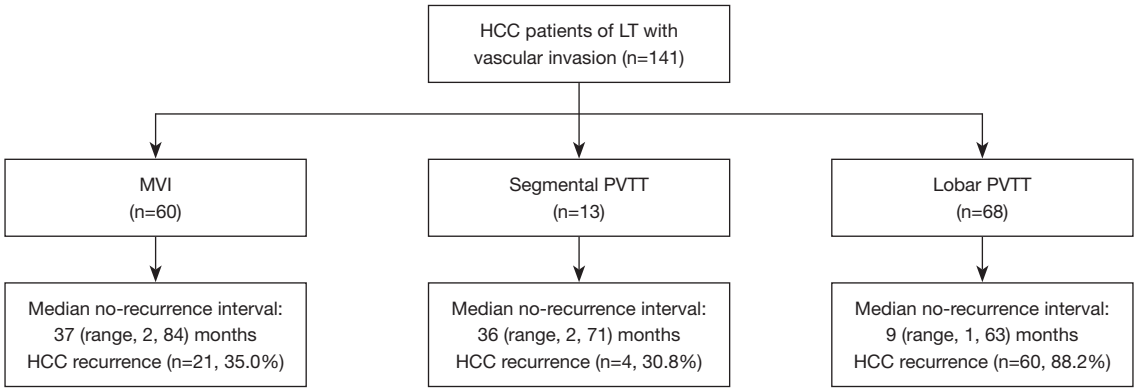


**Figure 1** Flow diagram of study patients. HCC, hepatocellular carcinoma; LT, liver transplantation; MVI, microvascular invasion; PVTT, portal vein tumor thrombus.

transplantation; and (VI) the case data were incomplete. Patients were fully informed of their condition and the possibility of recurrence before surgery and underwent LT with consent. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). This study was reviewed and approved by the Ethics Committee of the Institutional Review Board of Shulan (Hangzhou) Hospital (No. KY2024018), and informed consent was obtained from all the patients.

### *Diagnosis of PVTT*

All patients scheduled to undergo LT underwent computed tomography (CT), positron emission tomography (PET)-CT, magnetic resonance imaging (MRI), and blood tests to evaluate the recipient's hepatic vascularity and biliary tract and exclude extrahepatic lesions and distant metastases. Postoperative pathology confirms either microvascular invasion (MVI) or PVTT. We categorized PVTT into two types according to Cheng's (10) classification: (I) segmental PVTT: tumor thrombi involving segmental branches of the portal vein or above; and (II) lobar PVTT: tumor thrombi involving left and right branches or main portal vein (*Figure 2*).

### *Data collection and follow-up*

Preoperative baseline data and serological examinations were collected, including age, gender, HBV, Child-Pugh classification, alpha-fetoprotein (AFP) level, and pre-transplantation neoadjuvant therapy. The total tumor diameter, histological grade, and types of vascular invasion were based on postoperative pathology.

An interleukin-2 receptor blocker was administered on the day of surgery and the fourth day after surgery. Postoperative immunosuppressive therapy includes calcineurin inhibitors (cyclosporine or tacrolimus), mycophenolate mofetil (MMF), and steroids. Steroids were discontinued 1–2 months after surgery. Sirolimus was combined with tacrolimus for anti-rejection therapy 1 month after LT.

Patients were followed up by outpatient examination or telephone interview after discharge. Liver function, AFP level, and ultrasound were followed up monthly after LT. CT or MRI scans of the chest and abdomen were performed every 3 months for early detection of tumor recurrence. Once tumor recurrence was confirmed, local treatment included transarterial chemoembolization (TACE), radiofrequency ablation (RFA), and radioactive seed implantation, and systemic treatment was a tyrosine kinase inhibitor (TKI). The primary endpoints of this study were tumor recurrence and patient death. OS and recurrence-free survival (RFS) data were collected for all included patients.

### *Statistical analysis*

SPSS 26.0 (IBM, Armonk, NY, USA) was used for all statistical analyses. Continuous variables were reported as the mean and standard deviation or as median and range and were compared using Student's *t*-test or Mann-Whitney *U* test when appropriate. Categorical variables were reported as numbers and percentages and were compared using the $\chi^2$ test or Fisher's exact test. Survival outcomes

 

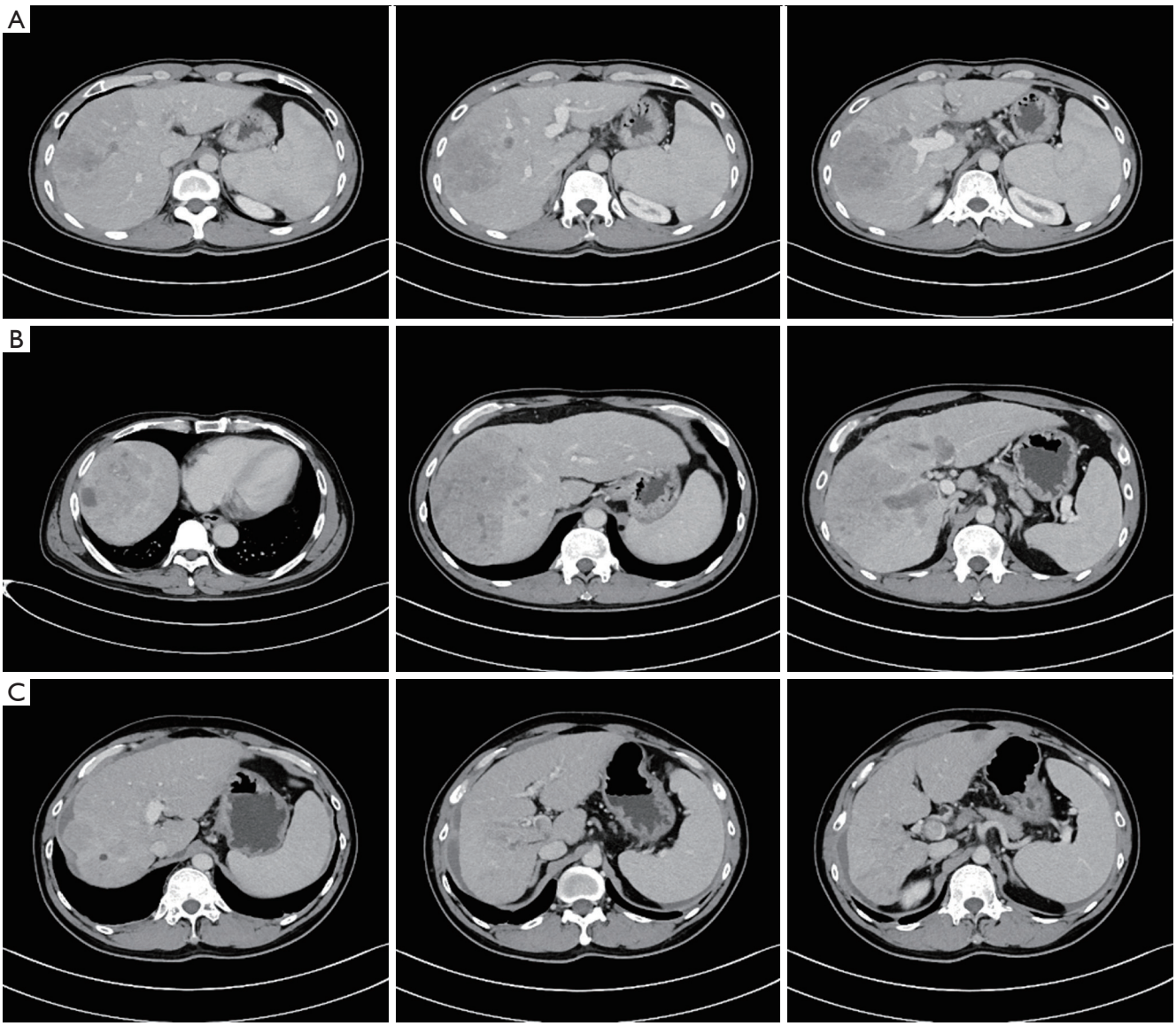


**Figure 2** Tumor thrombus in different portal vein locations. (A) A patient with tumor thrombus in the second branch of the portal vein; (B) a patient with tumor thrombus in the right and right portal vein; (C) a patient with tumor thrombus in the main trunk of the portal vein.

were assessed with Kaplan-Meier curves and log-rank tests, while predictors of OS and RFS were identified using multivariate Cox proportional hazards regression. A P value <0.05 was considered statistically significant.

## Results

### *Baseline characteristics*

A total of 141 patients with pathologically confirmed HCC combined with vascular invasion were enrolled in this study and followed up until December 2023. The mean age was 51.4±11.0 years, and 134 (95.0%) patients were male. All patients were complicated with HBV, 113 (80.1%) patients with Child-Pugh classification A. The median AFP level was 102.1 (range, 0.8–60,500) ng/mL, and 55 (39.0%) patients had AFP >400 ng/mL. The median total tumor diameter was 9 (range, 1.1–29) cm, and 90 (63.8%) patients had a total tumor diameter >7 cm. Forty-eight (34.0%) patients were pathologically diagnosed with poor-differentiated.

 

**Table 1** Characteristics of patients by recurrence status

| Variables | Total (n=141) | Nonrecurrent (n=56) | Recurrent (n=85) | P value |
|---|---|---|---|---|
| Age (years) | 51.4±11.0 | 53.3±10.5 | 50.1±11.2 | 0.09 |
| Gender, male | 134 (95.0) | 56 (100.0) | 78 (91.8) | 0.042 |
| HBV infection | 141 (100.0) | 56 (100.0) | 85 (100.0) | NS |
| Child-Pugh classification | | | | 0.07 |
| A | 113 (80.1) | 49 (87.5) | 64 (75.3) | |
| B and C | 28 (19.9) | 7 (12.5) | 21 (24.7) | |
| AFP (ng/mL) | 102.1 [0.8–60,500] | 30.8 [0.8–20,500] | 348.9 [1.7–60,500] | 0.003 |
| AFP >400 ng/mL | 55 (39.0) | 13 (23.2) | 42 (49.4) | 0.002 |
| Pretransplant treatment, present | 68 (48.2) | 34 (60.7) | 34 (40.0) | 0.01 |
| Total tumor diameter (cm) | 9 [1.1–29] | 6.5 [1.1–23.9] | 10 [2–29] | <0.001 |
| Total tumor diameter >7 cm | 90 (63.8) | 22 (39.3) | 68 (80.0) | <0.001 |
| Histological grade, poor differentiated | 48 (34.0) | 11 (19.6) | 37 (43.5) | 0.001 |
| Vascular invasion | | | | <0.001 |
| MVI | 60 (42.6) | 39 (69.6) | 21 (24.7) | |
| Segmental PVTT | 13 (9.2) | 9 (16.1) | 4 (4.7) | |
| Lobar PVTT | 68 (48.2) | 8 (14.3) | 60 (70.6) | |

Data are expressed as n (%), mean ± standard deviation, or median [range]. HBV, hepatitis B virus; NS, no significant; AFP, alpha-fetoprotein; MVI, microvascular invasion; PVTT, portal vein tumor thrombus.

Sixty patients (42.6%) with MVI, 13 patients (9.2%) with segmental PVTT, and 68 patients (48.2%) with lobar PVTT.

Sixty-eight patients (48.2%) received neoadjuvant therapy before LT, including 34 (50.0%) patients with MVI, 8 (11.8%) patients with segmental PVTT, and 26 (38.2%) patients with lobar PVTT. Thirty-one (45.6%) patients were treated with TACE, 2 (2.9%) patients were treated with TKI, and 35 (51.5%) patients were treated combined with TACE and TKI. The modified Response Evaluation Criteria in Solid Tumors (m-RECIST) (11) was used to evaluate the efficacy of patients, including 7 (10.3%), 47 (69.1%), 6 (8.8%), and 8 (11.8%) patients who achieved complete response (CR), partial response (PR), stable disease (SD), and progressive disease (PD), with an objective response rate (ORR) value of 79.4%.

### *Comparisons between recurrence and no-recurrence*

We compared the clinicopathological variables based on the recurrence status of all patients (*Table 1*). Median AFP level (P=0.003), AFP level >400 ng/mL (P=0.002), pretransplant treatment (P=0.01), median total tumor diameter (P<0.001), total tumor diameter >7 cm (P<0.001), poor differentiated (P=0.001), types of vascular invasion (P<0.001) were statistically significant.

### *Comparison between different types of vascular invasion*

We compared the clinicopathological variables among the subgroups based on the three types of vascular invasion (*Table 2*). There were statistically significant differences between the MVI group and the segmental PVTT group only in median AFP level (P=0.01) and AFP level >400 ng/mL (P=0.002). While the MVI group and the lobar PVTT group had statistically significant differences in median AFP level (P<0.001), AFP level >400 ng/mL (P<0.001), pretransplant treatment (P=0.03), median total tumor diameter (P<0.001), total tumor diameter >7 cm (P<0.001), poor differentiated (P=0.03). There were significant differences between the segmental PVTT group and the lobar PVTT group in the median total tumor diameter (P=0.008) and total tumor diameter >7 cm (P=0.008).

 

**Table 2** Comparisons of patients by MVI and PVTT status

| Variables | MVI (n=60) | Segmental (n=13) | Lobar (n=68) | P value (MVI *vs.* segmental) | P value (MVI *vs.* lobar) | P value (segmental *vs.* lobar) |
|---|---|---|---|---|---|---|
| Age (years) | 52.8±10.4 | 52.5±11.1 | 49.8±11.4 | 0.93 | 0.13 | 0.43 |
| Gender, male | 58 (96.7) | 13 (100.0) | 63 (92.6) | 0.50 | 0.44 | 0.58 |
| HBV infection | 60 (100.0) | 13 (100.0) | 68 (100.0) | NS | NS | NS |
| AFP (ng/mL) | 23.3 [1.3–20,000] | 436.8 [1.7–48,000] | 563.6 [0.8–60,500] | 0.01 | <0.001 | 0.67 |
| AFP >400 ng/mL | 9 (15.0) | 7 (53.8) | 39 (57.4) | 0.002 | <0.001 | 0.81 |
| Pretransplant treatment, present | 34 (56.7) | 8 (61.5) | 26 (38.2) | 0.74 | 0.03 | 0.11 |
| Total tumor diameter (cm) | 7.3 [2–28.7] | 7 [3.8–22.6] | 11.3 [1.1–29] | 0.75 | <0.001 | 0.008 |
| Total tumor diameter >7 cm | 29 (48.3) | 6 (46.2) | 55 (80.9) | 0.88 | <0.001 | 0.008 |
| Histological grade, poor differentiated | 16 (26.7) | 4 (30.8) | 28 (41.2) | 0.50 | 0.03 | 0.53 |
| Recurrence, present | 21 (35.0) | 4 (30.8) | 60 (88.2) | >0.99 | <0.001 | <0.001 |
| No-recurrence interval (months) | 37 [2–84] | 36 [2–71] | 9 [1–63] | 0.79 | <0.001 | <0.001 |

Data are expressed as n (%), mean ± standard deviation, median [range]. MVI, microvascular invasion; PVTT, portal vein tumor thrombus; HBV, hepatitis B virus; NS, no significant; AFP, alpha-fetoprotein.

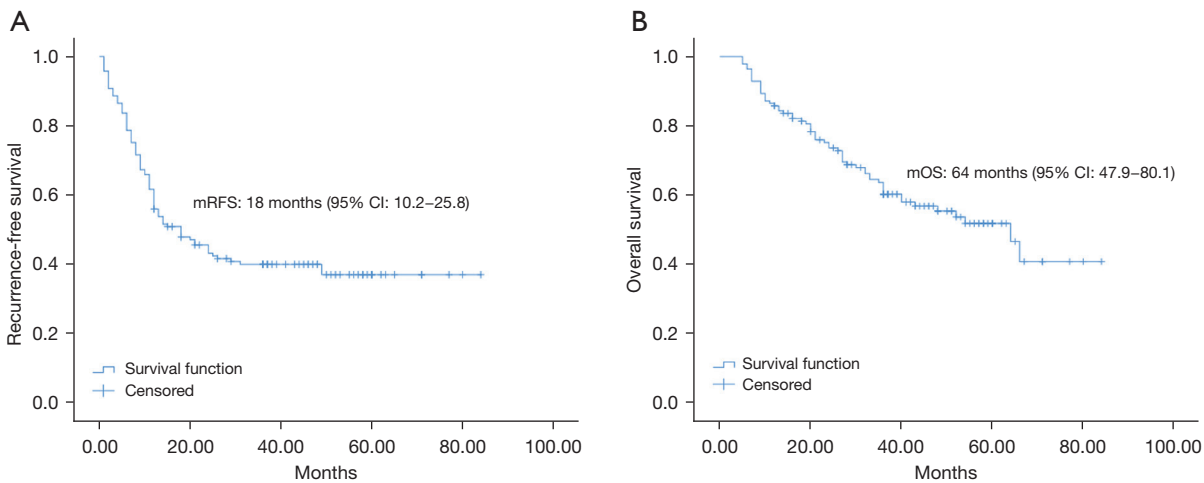


**Figure 3** Kaplan-Meier survival curve for RFS and OS. (A) mRFS and (B) mOS of the 141 patients who underwent DDLT to treat HCC with vascular invasion. mRFS, median recurrence-free survival; CI, confidence interval; mOS, median overall survival; DDLT, deceased donor liver transplantation; HCC, hepatocellular carcinoma; RFS, recurrence-free survival; OS, overall survival.

### *Analysis of outcomes based on types of vascular invasion*

We analyzed survival outcomes for all patients (*Figure 3*) and in three subgroups (*Figure 4*). Among 141 patients, the median RFS was 18 months [95% confidence interval (CI): 10.2–25.8], and the median OS was 64 months (95% CI: 47.9–80.1), the 1-, 2-, and 3-year RFS and OS were 61.7%, 41.1%, 34.8%, and 86.5%, 68.1%, 53.2%. A total of 60 patients (42.6%) died during the follow-up. The causes of death were tumor recurrence in 56 cases (93.3%), liver graft failure in 2 cases (3.3%), gastrointestinal bleeding in 1 case (1.7%), and myocardial infarction in 1 case (1.7%). The lobar PVTT group had the shortest median no-recurrence time 9 (range, 1–63) months, followed by the

 

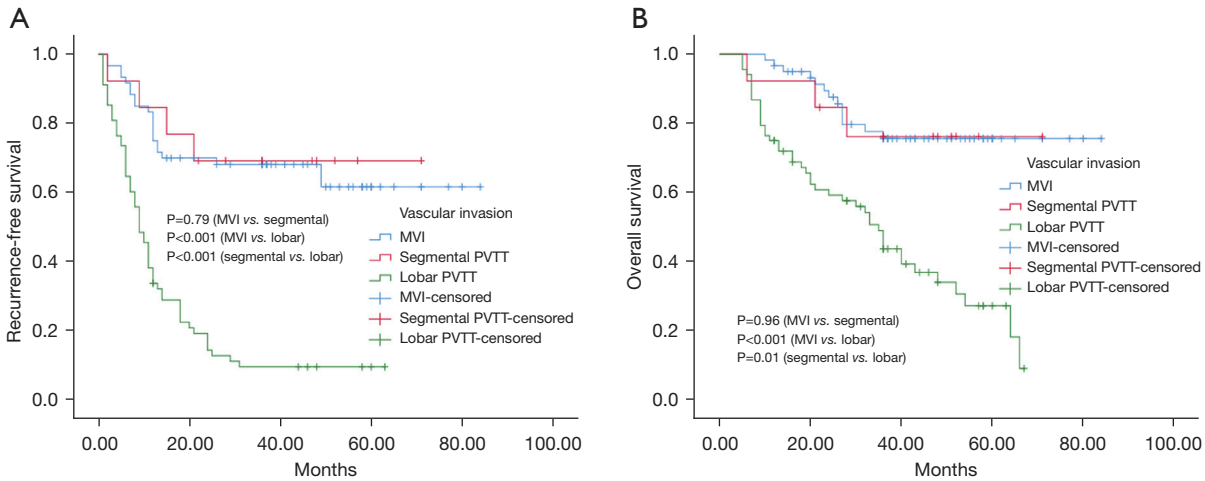


**Figure 4** RFSs (A) and OSs (B) comparison among MVI, segmental PVTT, and lobar PVTT. RFS, recurrence-free survival; OS, overall survival; MVI, microvascular invasion; PVTT, portal vein tumor thrombus.

**Table 3** Univariate and multivariate analysis of prognosis factors for RFS in patients who underwent LT

| Variables | Univariate analysis | | | Multivariate analysis | | |
|---|---|---|---|---|---|---|
| | HR | 95% CI | P value | HR | 95% CI | P value |
| Preoperative AFP level (≤400 *vs.* >400 ng/mL) | 2.146 | 1.398–3.293 | <0.001 | N/A | N/A | N/A |
| Child-Pugh classification (A *vs.* B and C) | 1.805 | 1.1–2.961 | 0.01 | 1.925 | 1.134–3.269 | 0.01 |
| Pretransplant treatment (presence *vs.* absence) | 1.627 | 1.052–2.516 | 0.02 | N/A | N/A | N/A |
| Total tumor diameter (≤7 *vs.* >7 cm) | 3.521 | 2.063–6.011 | <0.001 | 2.510 | 1.436–4.386 | 0.001 |
| Histological grade (well and moderate *vs.* poor) | 2.034 | 1.323–3.128 | 0.001 | 1.897 | 1.205–2.985 | 0.006 |
| Vascular invasion | | | | | | |
| MVI | Reference | | | Reference | | |
| Segmental PVTT | 0.867 | 0.298–2.527 | 0.79 | N/A | N/A | N/A |
| Lobar PVTT | 4.711 | 2.831–7.839 | <0.001 | 3.304 | 1.899–5.751 | <0.001 |

RFS, recurrence-free survival; LT, liver transplantation; HR, hazard ratio; CI, confidence interval; AFP, alpha-fetoprotein; N/A, not applicable; MVI, microvascular invasion; PVTT, portal vein tumor thrombus.

segmental PVTT group 36 (range, 2–71) months and the MVI group 37 (range, 2–84) months. The recurrence rate was also higher in the lobar PVTT group (MVI *vs.* segmental: 35.0% *vs.* 30.8%, P>0.99), (MVI *vs.* lobar: 35.0% *vs.* 88.2%, P<0.001), (segmental *vs.* lobar: 30.8% *vs.* 88.2%, P<0.001). The 1-, 2-, and 3-year RFS rates were 38.2%, 18.2%, and 9.1% in the lobar PVTT group, 83.3%, 66.7%, and 65.5% in the MVI group, and 84.6%, 66.7%, and 58.3% in the segmental PVTT group. The 1-, 2-, and 3-year OS rates were 75.0%, 59.4%, and 45.9% in the lobar PVTT group, 98.3%, 87.3%, and 76.0% in the MVI group, and 92.3%, 83.3%, and 75.0% in the segmental PVTT group.

### *Univariate and multivariate Cox regression analyses of RFS and OS*

Cox regression was used for univariate and multivariate analyses to explore the independent risk factors affecting RFS and OS (*Tables 3,4*). Multivariate analysis revealed that Child-Pugh classification (B and C) [hazard ratio (HR): 1.925; 95% CI: 1.134–3.269; P=0.01], total tumor diameter >7 cm (HR: 2.510; 95% CI: 1.436–4.386; P=0.001), poor

 

**Table 4** Univariate and multivariate analysis of prognosis factors for OS in patients who underwent LT

| Variables | Univariate analysis | | | Multivariate analysis | | |
|---|---|---|---|---|---|---|
| | HR | 95% CI | P value | HR | 95% CI | P value |
| Preoperative AFP level (≤400 *vs.* >400 ng/mL) | 1.878 | 1.130–3.121 | 0.01 | N/A | N/A | N/A |
| Child-Pugh classification (A *vs.* B and C) | 2.087 | 1.171–3.720 | 0.01 | 2.284 | 1.241–4.202 | 0.008 |
| Pretransplant treatment (presence *vs.* absence) | 1.597 | 0.951–2.681 | 0.07 | N/A | N/A | N/A |
| Total tumor diameter (≤7 *vs.* >7 cm) | 3.369 | 1.744–6.508 | <0.001 | 2.578 | 1.282–5.181 | 0.008 |
| Histological grade (well and moderate *vs.* poor) | 1.884 | 1.130–3.141 | 0.01 | N/A | N/A | N/A |
| Vascular invasion | | | | | | |
| MVI | Reference | | | Reference | | |
| Segmental PVTT | 1.077 | 0.307–3.782 | 0.90 | N/A | N/A | N/A |
| Lobar PVTT | 4.125 | 2.216–7.676 | <0.001 | 3.150 | 1.608–6.173 | 0.001 |

OS, overall survival; LT, liver transplantation; HR, hazard ratio; CI, confidence interval; AFP, alpha-fetoprotein; N/A, not applicable; MVI, microvascular invasion; PVTT, portal vein tumor thrombus.

**Table 5** Characteristics of segmental PVTT by recurrence status

| Variables | Nonrecurrent (n=9) | Recurrent (n=4) | P value |
|---|---|---|---|
| Age (years) | 53.4±13.3 | 50.5±3.7 | 0.67 |
| Gender, male | 9 (100.0) | 4 (100.0) | NS |
| HBV infection | 9 (100.0) | 4 (100.0) | NS |
| Child-Pugh classification | | | 0.64 |
| A | 6 (66.7) | 3 (75.0) | |
| B and C | 3 (33.3) | 1 (25.0) | |
| AFP (ng/mL) | 436.8 [0.8–20,500] | 974.5 [26.2–48,000] | 0.87 |
| AFP >400 ng/mL | 5 (55.6) | 2 (50.0) | 0.65 |
| Pretransplant treatment, present | 6 (66.7) | 2 (50.0) | 0.51 |
| Total tumor diameter (cm) | 7 [3.8–9.6] | 9.5 [6–22.6] | 0.24 |
| Total tumor diameter >7 cm | 4 (44.4) | 2 (50.0) | 0.65 |
| Histological grade, poor differentiated | 1 (11.1) | 3 (75.0) | 0.052 |

Data are expressed as n (%), mean ± standard deviation, or median [range]. PVTT, portal vein tumor thrombus; NS, no significant; HBV, hepatitis B virus; AFP, alpha-fetoprotein.

differentiated (HR: 1.897; 95% CI: 1.205–2.985; P=0.006), lobar PVTT (HR: 3.304; 95% CI: 1.899–5.751; P<0.001) were independent risk factors for RFS. However, Child-Pugh classification (B and C) (HR: 2.284; 95% CI: 1.241–4.202; P=0.008), total tumor diameter >7 cm (HR: 2.578; 95% CI: 1.282–5.181; P=0.008) and lobar PVTT (HR: 3.150; 95% CI: 1.608–6.173; P=0.001) were independent risk factors for OS.

### *Analysis of segmental PVTT*

We analyzed patients with segmental PVTT based on recurrence (*Table 5*). The recurrence group had a slightly higher median AFP level and median total tumor diameter but did not reach statistical significance (P=0.87, P=0.24). However, we found that poorly differentiated patients had a higher risk of recurrence (well and moderate *vs.* poor:

 

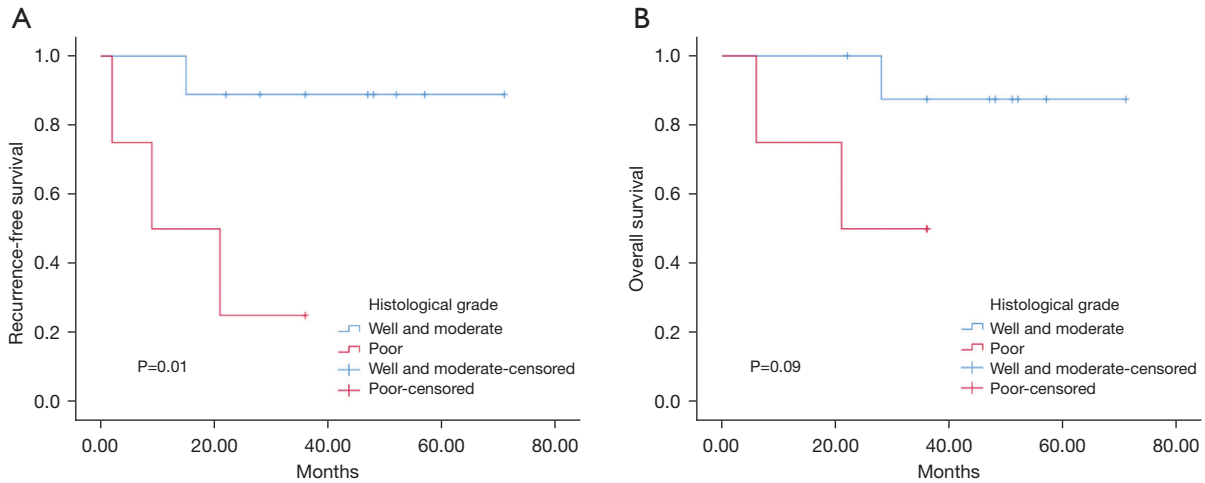


**Figure 5** RFSs (A) and OSs (B) comparison in subgroup analysis of patients with segmental PVTT based on histological grade. RFS, recurrence-free survival; OS, overall survival; PVTT, portal vein tumor thrombus.

75.0% *vs.* 11.1%, P=0.052). We analyzed RFS and OS based on histological grade. Patients with well and moderate differentiation had higher rates of RFS (P=0.01) and OS (P=0.09) than patients with poor differentiation (*Figure 5*).

## Discussion

MC is the cornerstone of LT, and although appropriately expanding the criteria can also lead to a good prognosis, the incidence of MVI increases with an increase in tumor size (12,13). Even within the MC, Lei *et al.* (14) found that patients with MVI had a significantly higher 5-year recurrence rate (78.5% *vs.* 58.4%, P<0.001) and a significantly lower OS rate (46.9% *vs.* 70.9%, P<0.001) than patients without MVI. MVI is defined as microscopically visible cancer cell infiltration in the vascular space lined by vascular endothelial cells, whose incidence is positively correlated with tumor size and is considered an independent and substantial predictor of recurrence (13,15,16).

Once PVTT forms, treatment becomes more difficult and risky, and if not effectively controlled, it can progress rapidly with the advancement of vascular invasion. One study found that the median time for a tumor thrombus in the second branch of the portal vein to develop into the first branch, and from the first branch to the main portal vein, was 8.2 and 11.5 days, respectively (17). However, the prognosis for patients with different types of PVTT is different. Shi *et al.* (18) divided PVTT into types Ⅰ–Ⅳ according to Cheng's classification, and their 1-year OS rates were 54.8%, 36.4%, 25.9%, and 11.1%. Similarly, different therapeutic strategies affect the prognosis of PVTT. One study analyzed 627 HCC patients with PVTT and compared hepatectomy, TACE, and sorafenib, finding that the prognosis after hepatectomy was significantly longer than that of TACE and sorafenib (19). Hence, it is necessary to develop a personalized treatment strategy for PVTT through multidisciplinary diagnosis and treatment (20).

Recently, Hong Kong scholars compared LT and hepatectomy for HCC with PVTT and found that the 3-year OS rate and RFS rate were higher in LT (OS: 69.2% *vs.* 25.1%, P=0.007, RFS: 64% *vs.* 10.4%, P<0.001) (7). Similarly, Lee *et al.* (21) reported the effect of different PVTT types on the prognosis of LT, but this result was based on a small sample size (n=11). Yang *et al.* (22) discovered that HCC patients with PVTT who had neoadjuvant therapy before LT and had a good response to treatment had a much higher 3-year RFS (72.0%) and OS (90.9%) rate than patients who had a bad response after LT.

Patients with HCC who have both HBV and severe cirrhosis, as well as insufficient liver reserve function, are unable to undergo hepatectomy. Although LT is the only way to cure tumors combined with severe cirrhosis, we found that patients with recurrence showed poor tumor histology and biological behavior, and the proportion of lobar PVTT in patients with recurrence was extremely high (70.6%). The lobar PVTT group had higher levels of AFP, larger tumors, and a higher proportion of poorly differentiated tumors compared to the other two groups. This indicates that the tumor's histologic and biological characteristics deteriorate with increasing tumor size and

 

worsening portal vein invasion. This is one reason why the lobar PVTT group has a higher rate of tumor recurrence. Specifically, the 1-, 2-, and 3-year RFS and OS in the lobar PVTT group were 38.2%, 18.2%, and 9.1%, and 75.0%, 59.4%, and 45.9%. These unfavorable factors indicate that lobar PVTT should be considered a contraindication to LT.

When we compared the MVI group to the segmental PVTT group, we were surprised to find that although the AFP level increased substantially with the advancement of vascular invasion, there was no significant difference in the tumor recurrence rate. The tumor recurrence rates between the MVI and segmental PVTT groups were 35.0% and 30.8%, respectively; the difference was not statistically significant (P>0.99). Both groups showed high 1-, 2-, and 3-year RFS rates (MVI and segmental: 83.3%, 66.7%, 65.5%, and 84.6%, 66.7%, 58.3%) and OS rates (MVI and segmental: 98.3%, 87.3%, 76.0%, and 92.3%, 83.3%, 75.0%). Our study is very close to the research results of Choi *et al.* (23) while patients with MVI had similar 3-year RFS rates (MVI and segmental: 72.6% and 63.9%) and OS rates (MVI and segmental: 69.7% and 60.3%) compared with segmental PVTT. This provides a basis for LT in the treatment of vascular invasion.

However, assessing segmental PVTT with preoperative radiology is quite difficult. Recent research has utilized a variety of imaging techniques and developed predictive models to improve the detection of benign and malignant portal venous emboli (24-29). In the future, patients can benefit from LT by increasing the detection rate and accuracy of segmental PVTT through imaging technology enhancement. Therefore, we believe that carefully selected patients with segmental PVTT should be potential candidates for LT.

Multivariate analysis showed that Child-Pugh classification, total tumor diameter, poor differentiated, and lobar PVTT were major risk factors for RFS and OS. However, in the survival analysis of segmental PVTT, the RFS rate (P=0.01) and OS rate (P=0.09) were higher in the well and moderately differentiated group. Nevertheless, we can diagnose HCC when we consider the patient's medical history and the characteristic imaging results. Doctors seldom conduct a needle biopsy before surgery to confirm the diagnosis. Therefore, more research is required to identify methods for screening patients with favorable tumor histology and biological behavior for LT. Recent research suggests that tumor biomarkers, such as AFP, and the response to neoadjuvant therapy can indirectly show biological and histological features of the tumor (3,30). Further study is needed to determine whether combining AFP levels and selecting patients with a good response to neoadjuvant therapy for LT can improve the prognosis of PVTT patients.

This study's limitations include the absence of an analysis of the curative effect of neoadjuvant therapy before transplantation and its potential impact on prognosis, which may result in a bias. Moreover, because this is a retrospective study, there is an imbalance in the patient population, so further study with more cases is needed.

## Conclusions

In conclusion, lobar PVTT has a poor prognosis and should be considered as a contraindication for LT, but segmental PVTT may be acceptable. Long-term and large-scale clinical data analysis is needed in the future to determine whether neoadjuvant therapy can screen eligible patients with segmental PVTT for LT.

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## Footnote

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*Ethical Statement:* The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki

 

(as revised in 2013). This study was reviewed and approved by the Ethics Committee of the Institutional Review Board of Shulan (Hangzhou) Hospital (No. KY2024018), and informed consent was obtained from all the patients.



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