Clinical Analysis of hepatocellular carcinoma patients with segmental portal vein tumor thrombus after deceased donor liver transplantation: a long-term retrospective study

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Research Article

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Abstract

Background

Hepatocellular carcinoma (HCC) patients with portal vein tumor thrombus (PVTT) have conventionally been regarded as a contraindication for liver transplantation (LT). However, the outcomes of deceased donor liver transplantation (DDLT) in patients with segmental PVTT remain unknown. The aim of this study is to evaluate the feasibility and effectiveness of DDLT in the treatment of HCC with segmental PVTT.

Methods

We retrospectively analyzed 254 patients who underwent DDLT for HCC in our institution from January 2015 to November 2019. To assess the risks of PVTT, various clinicopathological variables were evaluated. Overall (OS) and recurrence-free survival (RFS) analyses based on different PVTT types were performed in HCC patients.

Results

Of the 254 patients, a total of 46 patients had PVTT, of whom 35 had lobar PVTT and 11 had segmental PVTT in second-order branches or below. Alpha-fetoprotein (AFP) level, tumor maximal diameter, histological grade, micro-vascular invasion (MVI), RFS, and OS were significantly different between the control and PVTT groups. Lobar PVTT was associated with unfavorable 5-year RFS and OS compared with MVI group (28.6% and 17.1%, respectively). Instead, no significant difference was observed between the segmental PVTT and MVI group in terms of 5-year RFS and OS (RFS: 36.4% vs. 40.4%, $p = 0.667$; OS: 54.5% vs. 45.1%, $p = 0.395$). Further subgroup analysis showed segmental PVTT with AFP levels ≤ 100 ng/ml presented significantly favorable RFS and OS rates than those with AFP level > 100 ng/ml ($p = 0.050$ and 0.035, respectively).

Conclusions

In summary, lobar PVTT in first-order branches remains a contraindication to DDLT. HCC patients with segmental PVTT and AFP level ≤ 100 ng/ml may be acceptable candidates for DDLT.

Background

Hepatocellular carcinoma (HCC) is the most common primary liver cancer, accounting for the third-highest cancer-associated deaths worldwide(1, 2). HCC invading into portal vein or branches is defined as portal vein tumor thrombus (PVTT), which has been reported in 44-62.2% of patients with HCC(3, 4). The

median survival of untreated patients with PVTT is usually less than 6 months(5). Therefore, PVTT is considered an unfavorable prognostic factor for HCC(6, 7).

Liver transplantation (LT) is the potentially curative treatment for HCC, as it has the advantage of removing not only the tumor but also the cirrhotic liver(8). To achieve optimal results, a strict selection of patients, such as Milan criteria and UCSF criteria, has been established(9, 10). Among the criteria, the selection variables mainly focus on tumor size and tumor number, which exclude approximately 50% of patients with advanced HCC(11). Thus, expanded selection criteria of LT for HCC patients are expected.

Macro-vascular invasion like PVTT has previously been considered a contraindication for LT due to the high incidence of recurrence and poor prognosis following LT(12, 13). However, PVTT can be divided into different types including the main trunk of the portal vein, left or right portal vein, and segmental branches of the portal vein(14). Previous literature mainly focused on PVTT in the main trunk of the portal vein(15), and the outcomes of LT in HCC patients with segmental PVTT remained unknown. In addition, several recent studies reported survival benefits of living donor liver transplantation (LDLT) in HCC patients with PVTT(16, 17). However, the outcomes of these patients after deceased donor liver transplantation (DDLT) remained unclear. Therefore, we conducted the present study to evaluate the feasibility and effectiveness of DDLT for HCC patients with segmental PVTT and explored the survival outcomes.

Methods

Study patients

Data of patients who underwent DDLT for HCC from January 2015 to December 2019 in Renji Hospital, School of Medicine, Shanghai Jiao Tong University (Shanghai, CN) were retrospectively reviewed. Adult patients diagnosed as HCC with or without PVTT who underwent DDLT were included in the present study (Fig. 1). The exclusion criteria were as follows: (1) pathological diagnosis of intrahepatic cholangiocarcinoma (ICC), combined HCC-ICC or other malignancies; (2) perioperative death due to infection, bleeding, organ failure, etc.; (3) loss of follow-up within 90 days after LT; (4) incomplete medical records. Finally, patients were divided into different groups according to PVTT status. This study was conducted in accordance with the Declaration of Helsinki and was approved by the institutional ethics committee of Renji Hospital, School of Medicine, Shanghai Jiao Tong University.

Diagnosis of PVTT

All patients with HCC who were scheduled for LT were evaluated preoperatively by blood tests, ultrasound, CT scan of the abdomen and chest, positron emission tomography (PET)-CT, and endoscopy to exclude extrahepatic lesions and distant metastasis. The diagnosis of PVTT was based on preoperative imaging examination and postoperative pathological confirmation. PVTT was classified into two types in our study: (1) a PVTT in the second-order branches of the portal vein or below was defined as segmental; (2)

a PVTT in the right or left portal vein was defined as lobar. Patients with tumor thrombus in the main trunk of the portal vein or superior mesenteric vein were excluded (Fig. 2).

Data collection and follow-up

Preoperative baseline data and serological examinations including age, gender, hepatitis B virus, AFP level, carcinoembryonic antigen 19-9 (CA19-9) level and pretransplant loco-regional therapy were collected. Data of cirrhosis, tumor number, satellite lesions, tumor maximal diameter, histological grade and MVI were based on postoperative pathology.

An interleukin 2 (IL-2) receptor blocker was administered on the day of the operation and the fourth postoperative day. Postoperative immunosuppressive treatment included a regimen consist of a calcineurin inhibitor (cyclosporine or tacrolimus), mycophenolate mofetil (MMF) and steroids. Steroids were withdrawn 1 month after surgery, and MMF was withdrawn 3 months after surgery. Sirolimus was used 3 months after LT combined with a low level of calcineurin inhibitor.

All patients were followed up using liver function, serum AFP level as well as ultrasound monthly during the first year and every 3 months thereafter. To allow early detection of recurrence, CT or MRI scan of the chest and abdomen were performed once every 6 months. When tumor recurrence was suspected, PET-CT was conducted. Adjuvant therapy including transarterial chemoembolization (TACE), radiofrequency ablation, sorafenib or lenvatinib were permitted once tumor recurrence was confirmed. The main endpoint of this study was recurrence of tumor and death of patients. Data of overall (OS) and recurrence-free survival (RFS) were collected for all included patients.

Statistical analysis

Continuous variables are presented as median with range and categorical variables are expressed as numbers with ratio. The correlations between PVTT category and clinicopathological characteristics were compared using $\chi 2$ or Fisher exact test for categorical variables and Student's t-test or Mann-Whitney U test for continuous variables. Survival curves were estimated using the Kaplan–Meier analysis and compared with the log-rank test. To evaluate association of MVI and segmental PVTT with recurrence-free survival and overall survival, Cox hazards proportional regression was performed. All statistical analyses were performed using SPSS (version 24.0). A *p*-value of <0.05 was considered statistically significant.

Results

Baseline characteristics

As shown in the flow chart (Fig. 1), 352 patients who underwent DDLT for HCC from January 2015 to December 2019 were screened for the study. 58 patients who were pathologically diagnosed as ICC, combined HCC-ICC, and other malignancies were excluded. Another 40 patients didn't meet the inclusion

criteria due to perioperative death, loss of follow-up, and incomplete medical records. Finally, a total of 254 patients were included in the present study.

The median age of included patients was 51 years (22–75 years), and 223 (87.8%) were male. The majority of patients (228, 89.8%) had HBV infection and 7 (2.8%) had HCV infection. The median preoperative AFP and CA19-9 levels were 35.4ng/ml (0.7-60500ng/ml) and 24.9u/ml (0.6-2492u/ml), respectively. 58 patients (22.8%) underwent pretransplant loco-regional therapy to control or reduce tumor burden. Through postoperative pathology, most patients had underlying cirrhosis (222, 87.4%). Multiple tumors were present in 107 patients (42.1%) and 24 of them had satellite lesions (9.4%). The median maximal tumor diameters were 4cm (0.3-24cm) and 83 patients (32.7%) had poorly differentiated tumor grade. MVI was present in 78 patients (30.7%) and PVTT was confirmed in 46 patients (18.1%). Further, lobar and segmental PVTT were observed in 35 and 11 patients, respectively. Finally, patients were categorized into control group (no MVI or PVTT, n = 156), MVI group (MVI only with no PVTT, n = 52), lobar PVTT group (n = 35), and segmental PVTT group (n = 11).

Comparisons of clinicopathological variables based on recurrence status were first performed (Table 1). Significant differences were observed in preoperative AFP level ($p < 0.001$), presence of cirrhosis ($p = 0.025$), tumor number ($p < 0.001$), satellite lesions ($p < 0.001$), maximal diameter ($p < 0.001$), histological grade ($p < 0.001$) and presence of MVI ($p < 0.001$) and PVTT ($p < 0.001$).

Table 1
Characteristics of patients receiving LT with HCC by recurrence status

Variable	Total (n = 254)	Non-recurrent (n = 142)	Recurrent (n = 112)	*p* value
Age, years	51(22–75)	53(22–75)	51(29–75)	0.082
Gender, male, n (%)	223(87.8)	125(88.0)	98(87.5)	0.898
HBV infection, n (%)	228(89.8)	131(92.3)	97(86.6)	0.140
HCV infection, n (%)	7(2.8)	3(2.1)	4(3.6)	0.703
AFP, ng/ml	35.4(0.7-60500)	15.5(0.7-55030)	119.4(1.1-60500)	< 0.001
CA19-9, u/ml	24.9(0.6–2492)	21.9(0.6-908.2)	28.4(0.6–2492)	0.215
Cirrhosis, present, n (%)	222(87.4)	130(91.5)	92(82.1)	0.025
Pretransplant treatment, present, n (%)	58(22.8)	27(19.0)	31(27.7)	0.102
Tumor number, multiple, n (%)	107(42.1)	45(31.7)	62(55.4)	< 0.001
Satellite lesions, present, n (%)	24(9.4)	4(2.8)	20(17.9)	< 0.001
Maximal diameter, cm	4(0.3–24)	3.5(0.3–15)	6(0.5–24)	< 0.001
Histological grade, poor differentiated, n (%)	83(32.7)	31(21.8)	52(46.4)	< 0.001
MVI, present (%)	78(30.7)	25(17.6)	53(47.3)	< 0.001
PVTT				< 0.001
No	208(81.9)	132(93.0)	76(67.9)	
Segmental	35(13.8)	6(4.2)	29(25.9)	
Lobar	11(4.3)	4(2.8)	7(6.3)	
Data are median (range) unless indicated otherwise.				
Acronyms: HBV, hepatitis B virus; HCV, hepatitis C virus; AFP, alpha-fetoprotein; CA19-9, carcinoembryonic antigen 19 – 9; MVI, micro-vascular invasion; PVTT, portal vein tumor thrombosis.				

Comparisons Between Mvi And Pvtt

The clinicopathological characteristics were compared between the MVI and PVTT groups (Table 2). A significant difference in the preoperative AFP level was observed between groups ($p = 0.001$). The maximal tumor diameter ($p < 0.001$) and poorly differentiated tumor grade ($p < 0.001$) differed from those of the control group, but not between the MVI and PVTT groups ($p = 0.069$ and 0.704, respectively). The presence of satellite lesions was significantly higher in the MVI group ($p < 0.001$).

Table 2
Comparisons of patients receiving LT with HCC by MVI and PVTT status

Variable	Control (n = 156)	MVI (n = 52)	PVTT (n = 46)	*P* value
Age, years	53(29–74)	47(22–75)	51(34–66)	0.006
Gender, male, n (%)	133(85.3)	50(96.2)	40(87.0)	0.113
HBV infection, n (%)	146(93.6)	41(78.8)	41(89.1)	0.097
AFP, ng/ml	20.2(1.3-60500)	75.7(1.1-60500)	105.6(0.7-60500)	0.001
CA19-9, u/ml	23.6(0.6–2492)	35.9(0.6–278)	22.5(0.6-570.4)	0.479
Cirrhosis, present, n (%)	138(88.5)	42(80.8)	42(91.3)	0.238
Pretransplant treatment, present, n (%)	37(23.7)	10(19.2)	11(23.9)	0.786
Tumor number, multiple, n (%)	57(36.5)	26(50.0)	24(52.2)	0.073
Satellite lesions, present, n (%)	7(4.5)	14(26.9)	3(6.5)	< 0.001
Maximal diameter, cm	3.5(0.3–24)	4.8(1–17)	7.5(1–15)	< 0.001
Histological grade, poor differentiated, n (%)	36(23.1)	24(46.2)	23(50.0)	< 0.001
Recurrence, present, n (%)	45(28.8)	31(59.6)	36(78.3)	< 0.001
Recurrence interval, months	53(1–83)	26.5(1–80)	9(2–72)	< 0.001
Data are median (range) unless indicated otherwise.				
Acronyms: HBV, hepatitis B virus; AFP, alpha-fetoprotein; CA19-9, carcinoembryonic antigen 19 – 9; MVI, micro-vascular invasion; PVTT, portal vein tumor thrombosis.				

We further analyzed the postoperative survival outcomes among groups as shown in Fig. 3. During follow-up, tumor recurrence developed in 45 patients in the control group, 31 in the MVI group and 36 in the PVTT group. The 1-, 3- and 5-year RFS in the PVTT group was 39.1%, 21.7% and 21.7%, respectively, showing significant inferiority to the MVI group (67.3%, 40.4% and 40.4%, respectively, $p = 0.009$) and

control group (84.0%, 73.7% and 70.5%, respectively, $p < 0.001$). Death was observed in 34 patients in the control group, 29 in the MVI group and 30 in the PVTT group. The OS was also poorer in the PVTT group than the control group (80.4%, 37%, 34.8% vs. 93.6%, 82.1%, 79.5%, $p < 0.001$). However, no significant difference was observed in OS between PVTT group and MVI group (80.4%, 37%, 34.8% vs. 82.7%, 55.8%, 45.1%, $p = 0.276$).

Analysis Of Outcomes Based On Pvtt Location

Next, we performed comparisons by the level at which the PVTT was located. As shown in Table 3, preoperative AFP ($p = 0.415$), CA19-9 level ($p = 0.542$) and pretransplant treatment ($p = 0.100$) presented no difference between the lobar and segmental PVTT group. For tumor variables, neither tumor number ($p = 0.609$) nor maximal diameter (0.703) differed between groups. The recurrence rate was a little higher in the lobar PVTT group (82.9% vs. 63.6%), but no statistical significance was observed ($p = 0.220$). The recurrence interval was longer in the segmental PVTT group ($p = 0.049$).

Table 3
Comparisons of patients receiving LT with HCC by different PVTT location

Variable	Lobar (n = 35)	Segmental (n = 11)	*P* value
Age, years	51(34–66)	50(43–66)	0.648
Gender, male, n (%)	29(82.9)	11(100)	0.311
HBV infection, n (%)	31(88.6)	10(90.9)	1.000
AFP, ng/ml	105.7(1.1-60500)	76.4(0.7-60500)	0.415
CA19-9, u/ml	25.3(0.6-570.4)	18.5(1.6-173.7)	0.542
Cirrhosis, present, n (%)	31(88.6)	11(100)	0.559
Pretransplant treatment, present, n (%)	6(17.1)	5(45.5)	0.100
Tumor number, multiple, n (%)	19(54.3)	5(45.5)	0.609
Satellite lesions, present, n (%)	3(8.6)	0 (0.0)	1.000
Maximal diameter, cm	8(2–15)	7(1–12)	0.703
Histological grade, poor differentiated, n (%)	18(51.4)	5(45.5)	0.730
Recurrence, present, n (%)	29(82.9)	7(63.6)	0.220
Recurrence interval, months	8(2–72)	20(5–72)	0.049
Data are median (range) unless indicated otherwise.			
Acronyms: HBV, hepatitis B virus; AFP, alpha-fetoprotein; CA19-9, carcinoembryonic antigen 19 – 9.			

Next, we compared the RFS and OS by different PVTT status (Fig. 4). No significant difference in 5-year RFS was detected between the segmental PVTT group and the MVI group (36.4% vs. 40.4%, $p = 0.667$). However, the lobar PVTT group presented significantly worse RFS (17.1% vs. 40.4%, $p = 0.002$) compared with the MVI group. For OS, the segmental PVTT group showed somewhat better outcomes than both the MVI group and the lobar PVTT groups, though no statistical significance was attained ($p = 0.395$ and 0.077, respectively). The 1-, 3-, 5-year RFS and OS in the segmental PVTT group were 54.5%, 36.4%, 36.4% and 100%, 54.5%, 54.5%, respectively.

Risk Of Segmental Pvtt With Recurrence-free Survival And Overall Survival

We further investigated association of MVI and PVTT with recurrence-free survival and overall survival as shown in Table 4. Compared to MVI group, segmental PVTT group (HR, 1.195, 95%CI, 0.525–2.717) showed no significantly higher risk of HCC recurrence in the Cox hazards proportional regression. After adjustments for clinicopathological variables, the primary findings remained consistent (aHR, 1.974, 95%CI, 0.728–5.355). For overall survival, the segmental PVTT group presented no higher risk than MVI group (aHR, 0.996, 95%CI, 0.328–3.025) in the final adjustment model as well.

Table 4
Association of MVI and segmental PVTT with recurrence-free survival and overall survival among patients with HCC who underwent DDLT

	MVI	Segmental PVTT	*p* value
Recurrence-free survival			
Event (%)	31 (59.6%)	7 (63.6%)	
HR (95% CI)	1.00 (reference)	1.195 (0.525, 2.717)	0.671
aHR (95% CI)[a]	1.00 (reference)	1.974 (0.728, 5.355)	0.182
Overall survival			
Event (%)	29 (55.8%)	5 (45.5%)	
HR (95% CI)	1.00 (reference)	0.666 (0.257, 1.728)	0.403
aHR (95% CI)[a]	1.00 (reference)	0.996 (0.328, 3.025)	0.995
HR calculated using Cox hazards proportional regression.			
[a]Calculated after adjustments for age, sex, hepatitis B virus infection, alpha-fetoprotein, carcinoembryonic antigen 19 – 9, liver cirrhosis, pretransplant treatment, tumor size and number, satellite lesion, and histological grade.			
Acronyms: MVI, micro-vascular invasion; PVTT, portal vein tumor thrombosis; HR, hazard ratio; CI, confidence interval; aHR, adjusted hazard ratio.			

Subgroup Analysis Of Segmental Pvtt

Further, we conducted subgroup analysis in segmental PVTT group by different tumor characteristics. As shown in Fig. 5, patients with AFP levels > 100 ng/ml presented significantly worse RFS (p = 0.050) and OS rates (p = 0.035) than those with AFP level ≤ 100 ng/ml. However, no long-term survival differences were detected based on maximal tumor diameter of 5cm (RFS, $p = 0.298$; OS, $p = 0.940$). Similarly, no RFS and OS benefits were observed in groups of single tumor lesion (RFS, $p = 0.658$; OS, $p = 0.502$) compared with multiple tumor lesions (Fig. 6).

Discussion

Advanced HCC combined with PVTT has been shown in 44-62.2% of HCC patients(4). According to the Barcelona Clinic Liver Cancer guideline, sorafenib is regarded as the only treatment option(18, 19), while surgical treatment including LT is a contraindication due to the increased risk of spread of cancer cells into bloodstream, resulting in negative outcomes. With aim to prolong survivals of patients with PVTT through LT, several recent studies have expanded the LDLT indications in these patients and reported acceptable results(20–22). However, the outcomes based on different PVTT types have few been reported. In addition, whether HCC with PVTT can be expanded in DDLT remains unknown as well. Therefore, we conducted the present study to determine whether HCC with different PVTT types is feasible for DDLT.

A total of 254 patients were included in the current study and divided into groups based on MVI and PVTT status. Tumor characteristics were first analyzed among groups. Unsurprisingly, patients in MVI and PVTT groups exhibited higher AFP level, multiple tumor numbers, more satellite lesions, larger tumor size and poorer histological grade than the control group. However, it is noted that these variables showed no difference between the MVI and PVTT groups. Generally, MVI is defined as cancer cells within vascular endothelium identified microscopically(23). Through the bloodstream, cancer cells expanded from micro-vessels into macro-vessels, then proceed to the branches of PV and later involve the first-order of PV and finally the main trunk(24). The flow of tumor cells rather than proliferation may explain the similarity of tumor characteristics between the MVI and PVTT groups. Further survival analysis showed that the RFS and OS rates of PVTT group were lower than that of MVI group and control group. The disappointing results seem consistent with previous studies of LT in HCC with PVTT(25, 26). Nevertheless, the level at which PVTT was located should not be ignored, which calls for more strict criteria and stratified study.

We further divided the patients based on segmental and lobar PVTT and compared the results. Preoperative AFP level, tumor numbers, maximal diameter and histological grade did not differ between groups. However, the lobar PVTT group presented significantly worse long-term outcomes compared with the MVI group, with the 5-year RFS and OS of only 17.1% and 28.6%. The unfavorable results may exclude lobar PVTT as indication for LT. On the contrary, no significant difference of RFS and OS were observed between the segmental PVTT group and MVI group, with somewhat better OS in patients with

segmental PVTT. Further Cox hazards proportional regression confirmed that the segmental PVTT group showed no significantly higher risk of recurrence or death compared with MVI group. Since HCC patients are expected to have 5-year survival rate of at least 50%(27), patients with segmental PVTT presenting 5-year OS of 54.5% should be considered as potential candidates for LT.

Preoperative AFP level has been accepted as one of the tumor biological indicators to predict tumor recurrence and select patients for LT(28, 29). Therefore, we further analyzed segmental PVTT group according to AFP cutoff of 100 ng/ml. It turns out that patients with AFP levels ≤ 100 ng/ml presented significantly favorable RFS and OS rates than those with AFP level > 100 ng/ml. Surprisingly, neither tumor diameter nor tumor number serves as predictors to further select patients with segmental PVTT. The results may suggest that tumor biological characteristics of AFP level plays more important role than morphological variables in tumor recurrence and prognosis(30, 31). Therefore, HCC patients with segmental PVTT and AFP level ≤ 100 ng/ml are acceptable for selecting criteria of LT.

Our study has some potential limitations. Firstly, it is a retrospective study with an imbalance in the group population and a limited number of patients. Multicenter large-scale studies are needed to confirm the results. Secondly, detailed preoperative downstaging procedures including TACE or transarterial radioembolization (TARE) were unavailable in data collection, which may cause bias in results. In addition, PVTT below the second-order branches is difficult to be identified accurately in preoperative imaging. These patients require further exploration with more precise detection.

Conclusions

In conclusion, HCC patients with segmental PVTT may be acceptable candidates for DDLT. Low level of preoperative AFP level may provide better results in selecting patients with segmental PVTT. Future exploration in large-scale, prospective studies is required to develop more appropriate criteria of LT for HCC patients and provide a favorable prognosis.

Abbreviations

HCC
hepatocellular carcinoma
PVTT
portal vein tumor thrombus
LT
liver transplantation
DDLT
deceased donor liver transplantation
OS
overall survival
RFS

recurrence-free survival
AFP
alpha-fetoprotein
MVI
micro-vascular invasion

Declarations

Ethics approval and consent to participate

This study was performed according to the Declaration of Helsinki and approved by the local ethics committee of Renji Hospital, School of Medicine, Shanghai Jiao Tong University. Informed consent was obtained from all the patients for the use of their data for research purposes.

Consent for publication

Not applicable.

Availability of data and materials

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

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

MS and CC conducted the present study. MS and CS drafted the manuscript. SJ, HYS, HKH and NX collected clinical data. MS and SJ performed the statistical analyses. CS and JC participated in the study design and concept. YT and QX revised the manuscript. All authors read and approved the final manuscript.

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Figures

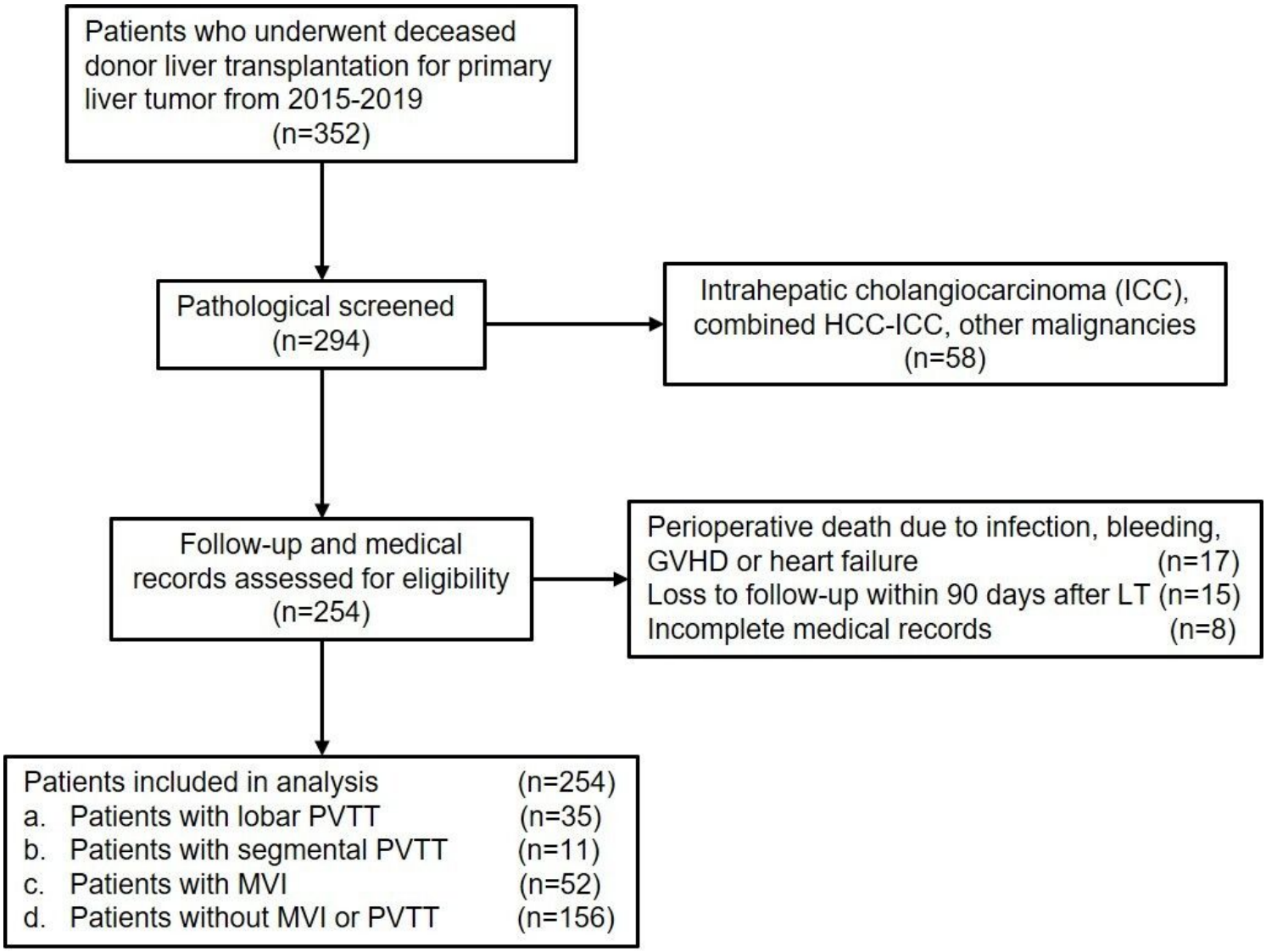


Figure 1

Study flow diagram

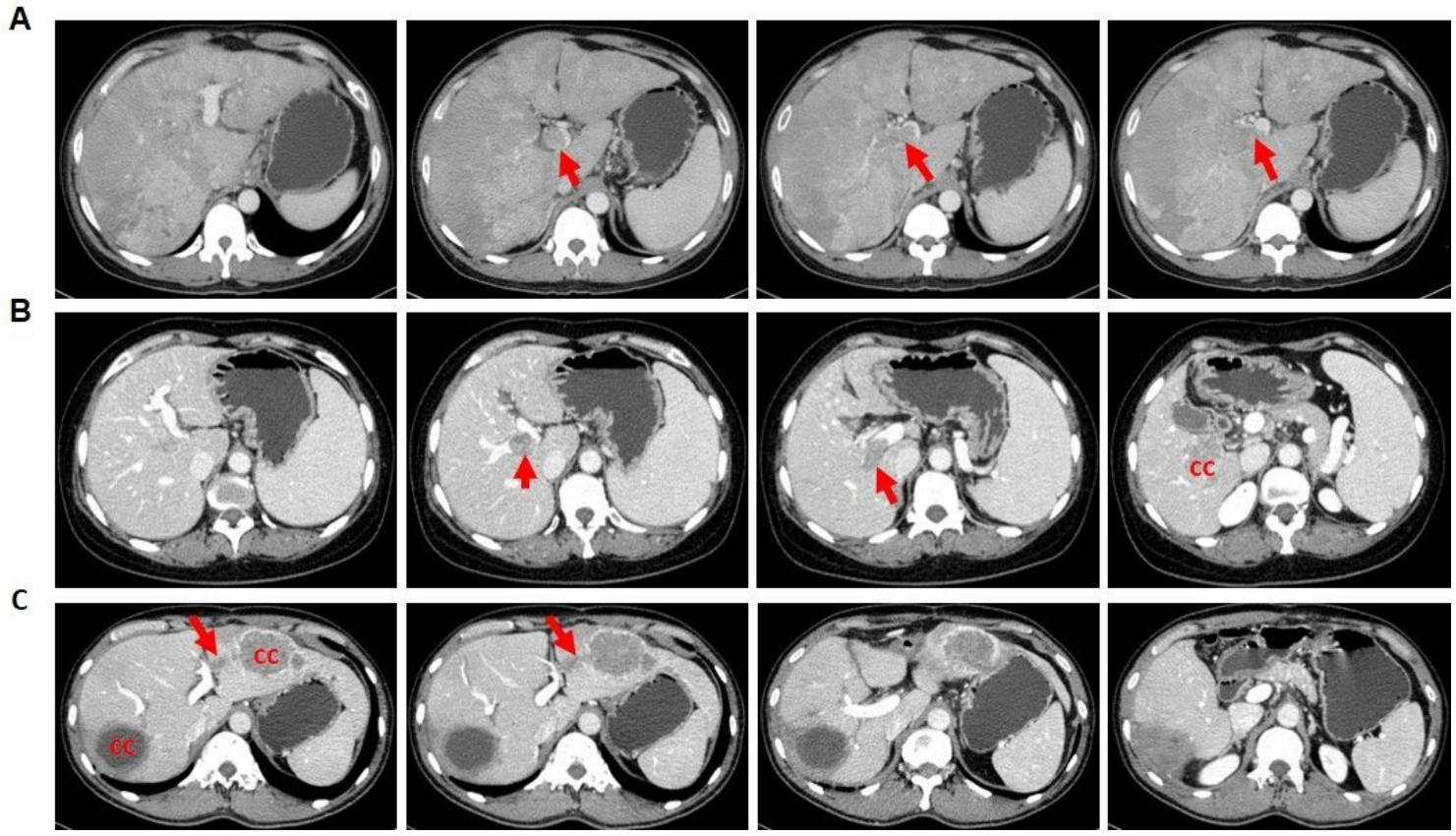
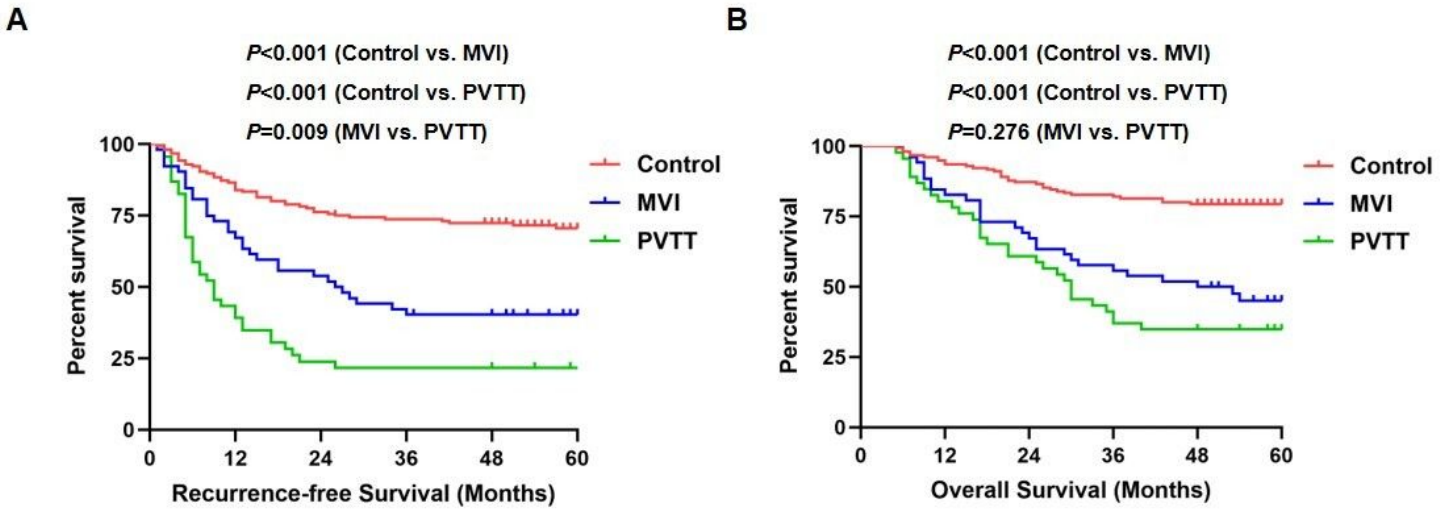


Figure 2

Tumor thrombus in different portal vein location. (A) A patient with tumor thrombus in the main trunk of portal vein. (B) A patient with tumor thrombus in the right portal vein. (C) A patient with tumor thrombus in the second branch of portal vein. CC, cancer center

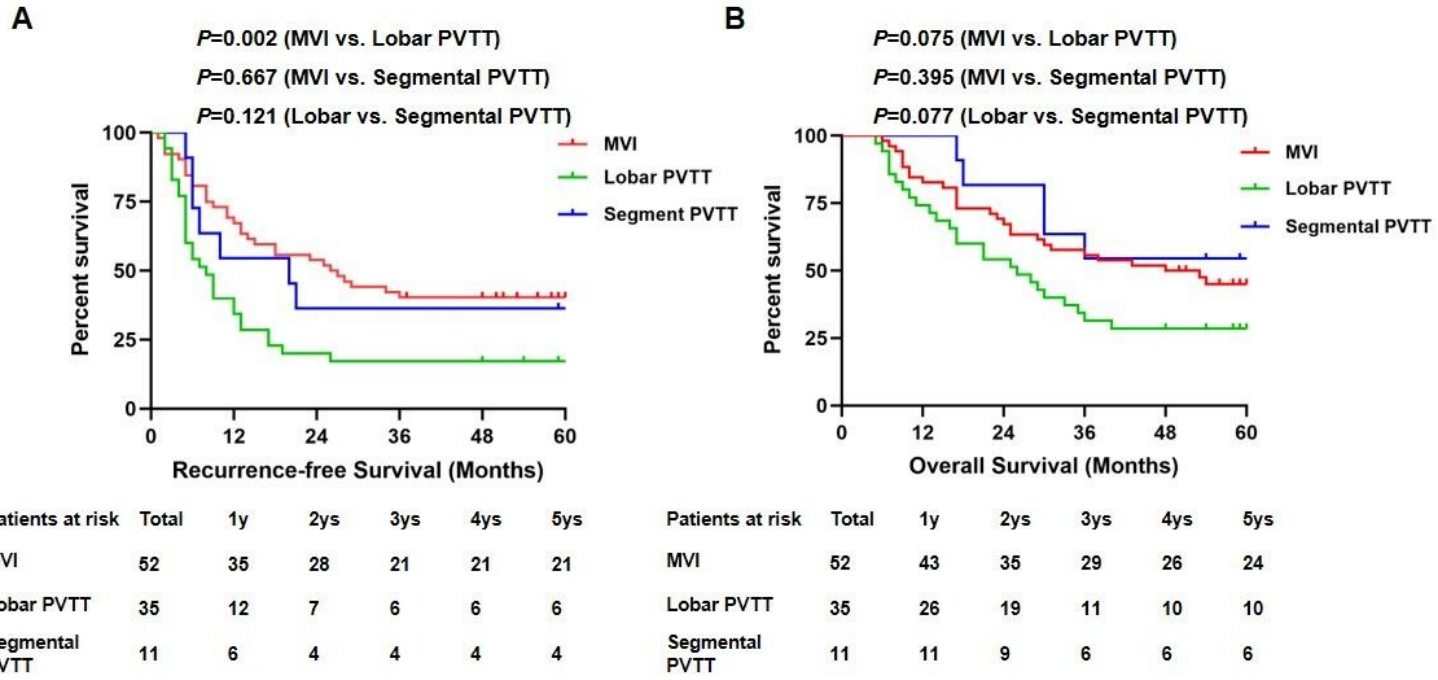


Patients at risk	Total	1y	2ys	3ys	4ys	5ys
Control	156	131	119	114	112	110
MVI	52	35	28	21	21	21
PVTT	46	18	11	10	10	10

Patients at risk	Total	1y	2ys	3ys	4ys	5ys
Control	156	146	136	128	124	124
MVI	52	43	35	29	26	24
PVTT	46	37	28	17	16	16

Figure 3

Recurrence-free survivals (A) and overall survivals (B) comparison among control, MVI and PVTT group.



Patients at risk	Total	1y	2ys	3ys	4ys	5ys
MVI	52	35	28	21	21	21
Lobar PVTT	35	12	7	6	6	6
Segmental PVTT	11	6	4	4	4	4

Patients at risk	Total	1y	2ys	3ys	4ys	5ys
MVI	52	43	35	29	26	24
Lobar PVTT	35	26	19	11	10	10
Segmental PVTT	11	11	9	6	6	6

Figure 4

Recurrence-free survivals (C) and overall survivals (D) comparison among MVI, lobar and segmental PVTT group.

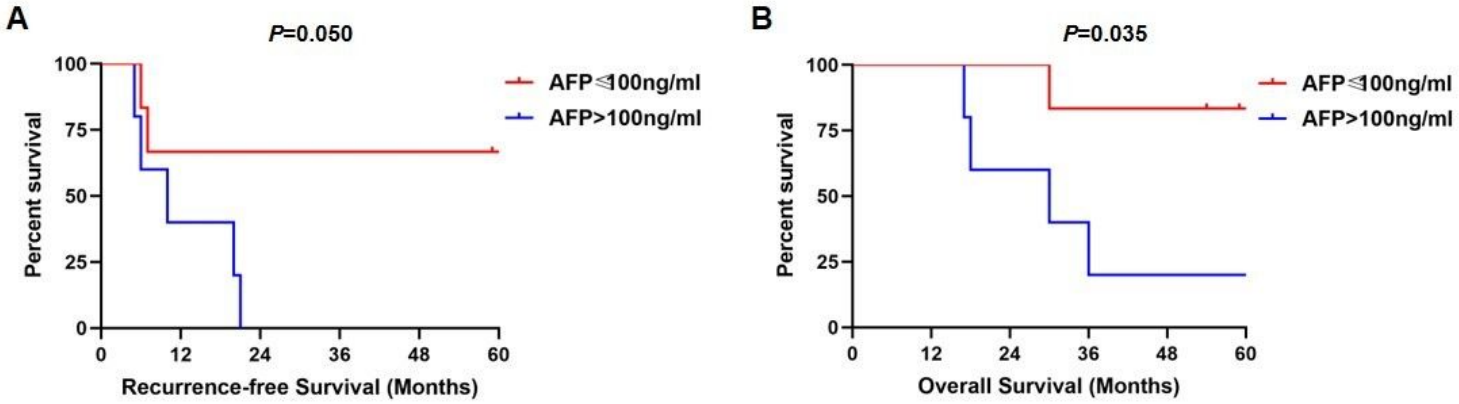


Figure 5

Recurrence-free survivals (A) and overall survivals (B) comparison in subgroup analysis of patients with segmental PVTT based on AFP level of 100 ng/ml.

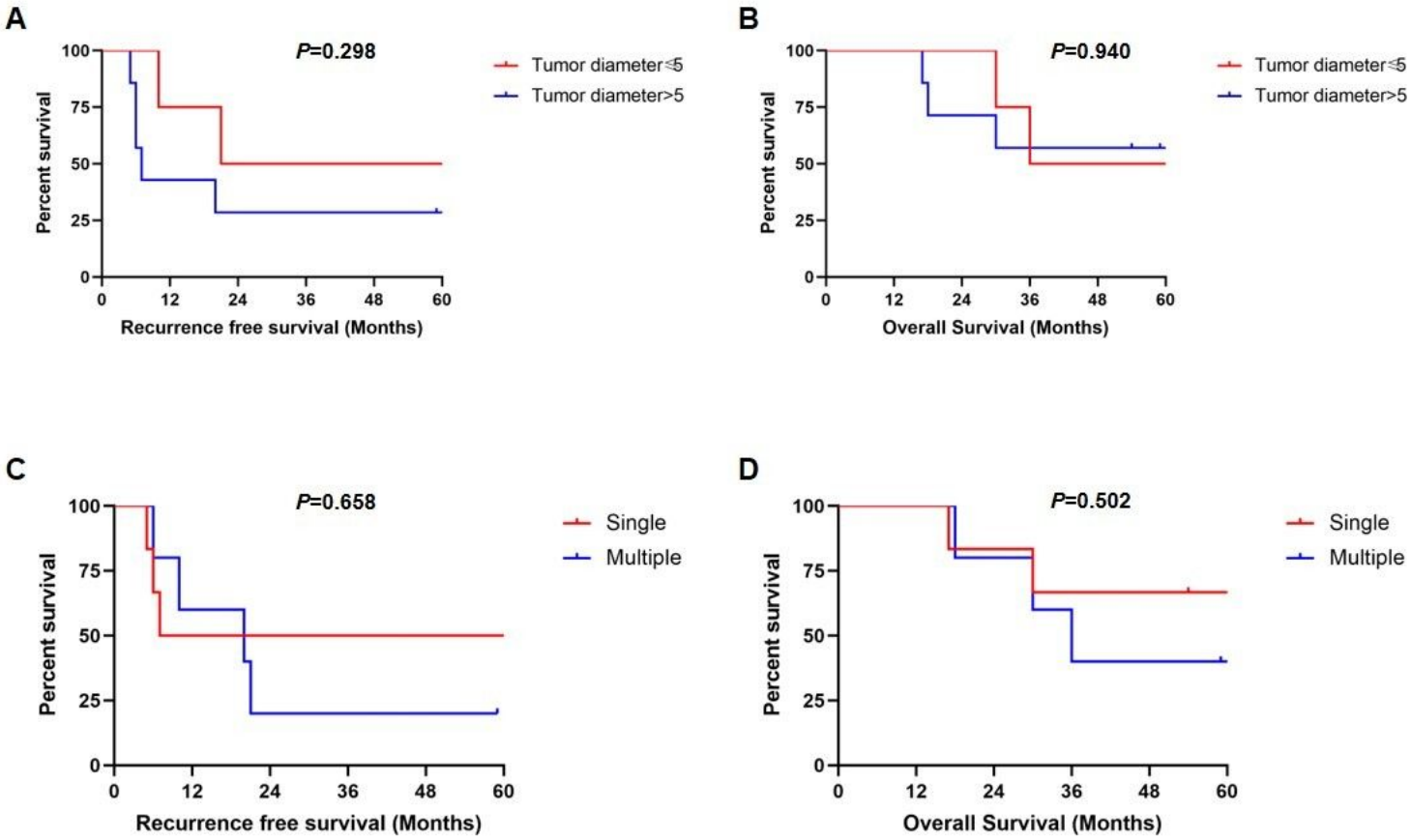


Figure 6

Recurrence-free survivals and overall survivals comparisons in subgroup analysis of patients with segmental PVTT based on maximal tumor diameter of 5 cm (A&B) and tumor numbers (C&D).