



Original Article



# Portal Fibrotic Cord is Associated with Transjugular Intrahepatic Portosystemic Shunt Failure and Death in Cirrhotic Patients

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## Abstract

**Background and Aims:** Occlusive portal vein thrombosis (PVT) often causes portal hypertension-related complications in cirrhotic patients. Transjugular intrahepatic portosystemic shunt (TIPS) is an effective treatment for this difficult problem. However, the factors influencing TIPS success and overall survival in patients with occlusive PVT are unknown. This study investigated the factors influencing TIPS success and overall survival in cirrhotic patients with occlusive PVT. **Methods:** Cirrhotic patients with occlusive PVT were selected from a prospective database of consecutive patients treated with TIPS in Xijing Hospital between January 2015 and May 2021. Baseline characteristics, TIPS success rate, complications, and survival were collected, and the factors associated with the TIPS success rate and transplant-free survival were analyzed. **Results:** A total of 155 cirrhotic patients with occlusive PVT were enrolled. TIPS succeeded in 126 (81.29%) cases. The 1-year survival rate was 74%. Compared with those without, patients with portal fibrotic cord had a lower TIPS success rate (39.02% vs. 96.49%,  $p < 0.001$ ), shorter median overall survival (300 vs. 1,730 days,  $p < 0.001$ ) and more operation-related complications (12.20% vs. 1.75%,  $p < 0.01$ ). Logistic regression analysis found that portal fibrotic cord (odds ratio 0.024) was a risk factor for TIPS failure. Univariate and multivariate analysis showed that portal fibrotic cord was an independent predictor of death (hazard ratio 2.111; 95% CI: 1.094–4.071,  $p = 0.026$ ). **Conclusions:** Portal fibrotic cord increased the TIPS failure rate and is a risk factor for poor prognosis in cirrhotic patients.

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**Keywords:** Fibrotic cord; Occlusive portal vein thrombosis; Portal hypertension-related complications; Transjugular intrahepatic portosystemic shunt; Liver cirrhosis.

**Abbreviations:** CT, computed tomography; MELD, model for end-stage liver disease; MPV, main portal vein; PPG, portal pressure gradient; PVR-TIPS, portal vein recanalization-transjugular intrahepatic portosystemic shunt; PVT, portal vein thrombosis; SMV, superior mesenteric vein; SV, splenic vein; TIPS, Transjugular intrahepatic portosystemic shunt.

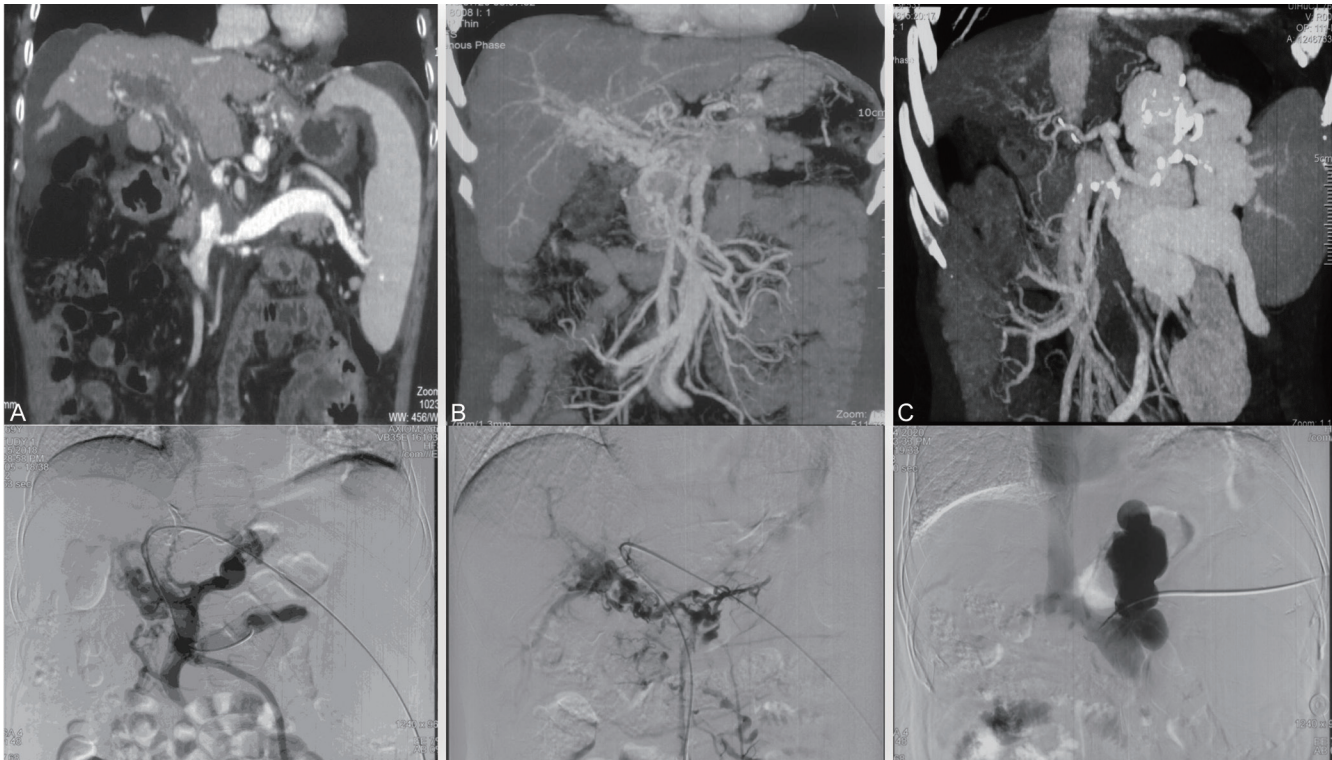
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## Introduction

Portal vein thrombosis (PVT) in liver cirrhosis, especially occlusive PVT, often causes clinical complications, such as hematemesis, hematochezia, ascites, and intestinal ischemia.<sup>1,2</sup> Traditional medicine and endoscopic treatments are ineffective for the thrombus itself and its complications in cases with occlusive PVT.<sup>3–5</sup> Recent data have shown that portal vein recanalization-transjugular intrahepatic portosystemic shunt (PVR-TIPS) can reduce thrombus burden, restore portal vein blood flow, decrease portal pressure, enhance patient eligibility for liver transplantation, improve patient prognosis, and become an effective treatment for occlusive PVT.<sup>1,6–10</sup> However, even for experienced operators, TIPS for obstructive PVT is a difficult procedure. It is important to investigate the factors influencing TIPS success and patient survival.

The portal vein can be recanalized and TIPS can be performed successfully in patients with occlusive PVT but with a visible main portal vein structure. However, in patients without the original main portal vein structure, recanalization of the portal vein is difficult and TIPS often fails. We call complete PVT without a visible original main portal vein for portal fibrotic cord. Some have suggested that the portal fibrotic cord is a predictor of TIPS success and patient prognosis. To test that hypothesis, we selected chronic occlusive PVT patients with portal hypertension-related complications treated with TIPS between January 2015 and May 2021 from the database established by the Xijing Hospital of Air Force Military Medical University. The patients were divided into those with or without a portal fibrotic cord, and we analyzed the relationships between the two types of thrombi with liver function, TIPS success rate, incidence of complications, and survival. Of 155 cirrhotic patients with occlusive PVT who were enrolled, 41 (26.45%) had a portal fibrotic cord. Compared with patients without a portal fibrotic cord, patients with a portal fibrotic cord had worse liver function Model for End-Stage Liver Disease score, 13



**Fig. 1. Different degrees of portal vein thrombosis in cirrhosis.** (A) Occlusive portal vein thrombosis (PVT) with cavernous transformation without fibrotic cord. The main portal vein was filled with thrombus, but the original lumen structure was visible. There were many spongy collateral vessels around the portal veins. (B) Occlusive PVT with cavernous transformation and fibrotic cord. There were gross portal collaterals without a visible original main portal vein. (C) Occlusive PVT with fibrotic cord without cavernous transformation. The lumen structure of the original main portal vein was replaced by a fibrotic cord. Some portosystemic shunts were formed. Spiral enhanced computed tomography images with multiplanar reconstruction (upper). Digital subtraction angiography images (lower).

vs. 9,  $p < 0.001$ ; Child-Pugh Score, 9 vs. 7,  $p < 0.001$ ), lower operation success rate (39.02% vs. 96.49%,  $p < 0.001$ ), and shorter median overall survival (300 vs. 1,730 days,  $p < 0.001$ ). Univariate and multivariate analysis indicated that a portal fibrotic cord independently predicted TIPS failure and death in cirrhotic patients (hazard ratio 2.377; 95% CI: 1.154–4.892,  $p = 0.019$ ).

## Methods

### Study design

The selected cases were consecutive patients with chronic occlusive PVT with portal hypertension-related complications treated by TIPS between January 2015 and May 2021. The last selected patient was followed up for more than 6 months.

For all patients, we collected: (1) preoperative baseline data including case number, age, sex, clinical manifestations, routine blood tests, blood coagulation, blood glucose, liver and kidney function, abdominal B-mode ultrasound, and enhanced computed tomography (CT); (2) intraoperative data including operation method, success or not, reason for failure, intraoperative complications, portal pressure gradient (PPG) before and after stent implantation; and (3) postoperative data at follow-up visits were carried out at 1, 3, 6, and 12 months after TIPS and every 6 months thereafter. Blood biochemistry, liver and kidney function, main symptom improvement and duration of continuous improvement, stent patency, postoperative complications and patient survival were monitored. If the patients had any discomfort, they came back.

### Study population

The inclusion criteria were: (1) 18 to 75 years of age; (2) cirrhosis with portal hypertension-related complications refractory to medical and/or endoscopic treatment; (3) main portal vein occlusive thrombosis proven by at least one imaging examination (B-ultrasound, CT, magnetic resonance imaging, angiography); and (4) at least one postoperative follow-up. The exclusion criteria were: (1) malignant tumors including hepatocellular carcinoma or other diseases that shorten life expectancy; (2) Child-Pugh score  $> 12$ ; (3) common contraindications of TIPS such as heart failure NYHA grade  $\geq$  III, spontaneous bacterial peritonitis, and others; (4) HIV infection or AIDS-related diseases; and (5) liver transplantation.

### Diagnosis and definitions

Cirrhosis was diagnosed as documented by previous liver biopsy or a combination of usual clinical signs and biochemical parameters.<sup>11</sup> Occlusive PVT was defined as no blood flow in the main portal vein detected by colored Doppler ultrasonography and/or CT.<sup>12</sup> Portal fibrotic cord was defined as the original lumen of the original portal vein replaced by fibrotic cord and was not seen in the CT/B-ultrasound exam.<sup>5</sup> Cavernous transformation was defined as the formation of collateral vessels around the portal vein for hepatic blood flow (Fig. 1).<sup>13,14</sup> The enrolled patients presented with three conditions: occlusive PVT with cavernous transformation without fibrotic cord (Fig. 1A), occlusive PVT with cavernous transformation and fibrotic cord (Fig. 1B), and occlusive PVT with fibrotic cord without cavernous transformation (Fig. 1C).

### **TIPS procedure and technique**

Depending on the degree and extent of portal thrombosis, a four step PVR-TIPS treatment strategy was adopted. (1) Transjugular PVR-TIPS was performed via the internal jugular vein when the main portal vein was blocked but the lumens of the main portal vein and secondary branches were visible on CT. The main steps included puncture of the femoral artery by the Seldinger method. The superior mesenteric artery was selectively intubated for indirect portal vein angiography. In some cases, the intrahepatic portal vein branches were visible on indirect portal vein angiography because of blood flow to the liver through the cavernous transformation, which served as a marker for puncture. For patients whose intrahepatic portal vein branches were not visible on indirect angiography, the hepatic artery was labeled to help locate the portal vein for puncture. The internal jugular vein was punctured. A RUPS 100 puncture set (Cook, Chicago, IL, USA) was sent to the right hepatic vein. The pressure of the inferior vena cava and hepatic vein was measured. The portal vein was punctured from the right hepatic vein or inferior vena cava. A small amount of contrast agent was injected for confirmation. The guide wire was passed through the blocked portal vein to the distal end of the splenic vein or superior mesenteric vein. Direct portal vein angiography was performed, and the hard guide wire was exchanged. A transjugular liver access set was sent to the main portal vein through the liver parenchyma. Varicose veins were embolized, and portal vein pressure was measured before and after embolization. An 8 mm-diameter e-PTFE stent graft whose grafted segment covered the thrombus was implanted. If necessary, a second stent graft was added so it protruded from the hepatic vein by about 1 cm. The stent was expanded with a 6 mm-diameter balloon. Stent position and patency were confirmed by angiography. The PPG was measured. If necessary, the stent graft was expanded with an 8 mm-diameter balloon (Supplementary Fig. 1). (2) Transhepatic PVR-TIPS was performed when imaging showed no portal vein lumen structure but did show intrahepatic portal vein branches. The branches were punctured under the guidance of B-ultrasound, and the occluded main portal vein was recanalized with a guide wire and catheter, marking the portal vein with a guide wire to complete TIPS (Supplementary Fig. 2). (3) Trans-splenic PVR-TIPS was performed when the portal vein could not be recanalized through percutaneous transhepatic puncture or the PVT was accompanied by extensive splenic vein thrombosis. Branches of the splenic vein were punctured under the guidance of B-ultrasound to recanalize the portal vein (Supplementary Fig. 3). (4) Transcollateral TIPS was performed when the main portal vein could not be recanalized through the percutaneous transhepatic or percutaneous trans-splenic route, and TIPS could be completed through enlarged collateral vessels >6 mm in diameter (Supplementary Fig. 4).

The puncture tract of the liver or spleen was embolized by coils combined with tissue glue. TIPS success criteria were establishing a shunt between the hepatic vein or inferior vena cava and the branch of the portal vein or collateral vessels and observing fluent bloodflow in the stent shunt with PPG reduced to <12 mmHg<sup>15</sup> or by at least 25% compared with baseline.<sup>16</sup>

### **Anticoagulants**

If the patient did not have an underlying disease that involved a hypercoagulable state and the covered segment of the stent covered the thrombus, no anticoagulation treatment was needed. Otherwise, low molecular weight heparin or warfarin was used for anticoagulation. Patients with

underlying diseases with a hypercoagulable state should receive long-term anticoagulation after the operation. Patients in whom the covered segment of the stent did not cover the thrombus should receive anticoagulation until the thrombus disappears completely.

### **Statistical analysis**

Quantitative variables were reported as medians and range. Qualitative variables were reported as absolute and relative frequencies. Nonparametric tests were used to compare median values, and the chi-square test was used to compare frequencies or proportions. Multivariate logistic regression analysis was performed to investigate the factors influencing TIPS success. For overall survival, we used the Kaplan-Meier method and compared the results with log-rank testing. Multivariate Cox proportional hazards models were used to identify independent predictors of overall survival. All tests were two-sided, and *p*-values of <0.05 was considered statistically significant. SPSS (version 25, IBM Corp., Armonk, NY, USA) was used for data analysis.

## **Results**

### **Patient characteristics**

From January 2015 to May 2021, there were 1,794 TIPS cases because of portal hypertension-related complications, 738 with PVT, 239 with complete PVT, 159 with complete PVT in cirrhosis. Four cases were excluded, one because of age >75 and three because of liver transplantation. A group of 155 cases with complete PVT accompanied by portal hypertension-related complications and treated with TIPS were included in the study (Fig. 2). Of these patients, 148 were treated with TIPS for recurrent variceal bleeding after drug and endoscopic therapy, and seven were treated with TIPS for refractory ascites. The shortest follow-up time was 1 month, the longest was 78 months, and one case was lost to follow-up. Ninety patients were men and 65 were women. The youngest was 29 years of age, the oldest was 73, and the median age was 52 years. Hepatitis B virus infection was the most common etiology of cirrhosis (101/155, 65.16%). Other etiologies were present in 34.84% of patients (54/155). The median model for end-stage liver disease (MELD) score was 10 (6–26). The median Child-Pugh score was 8 (5–12). Child-Pugh A, B, and C was seen in 33, 97, and 25 cases, respectively. Eighty-one patients (52.26%) had undergone splenectomy. Portal cavernous transformation was found in 127 cases (81.94%), and portal fibrotic cord was found in 41 cases (26.45%). In Eighty-three cases (53.55%), thrombosis involved the main portal vein (MPV) and superior mesenteric vein (SMV), in two cases (1.29%) thrombosis involved the MPV and splenic vein (SV), and in 18 cases (11.61%) thrombosis involved the MPV, SMV, and SV. There were 24 cases (15.49%) with transjugular PVR-TIPS, 107 (69.03%) with transhepatic PVR-TIPS, 18 (11.61%) with trans-splenic PVR-TIPS, and six (3.87%) with transcollateral TIPS. The patient characteristics are shown in Table 1.

### **Portal fibrotic cord increases the incidence of TIPS failure and operation-related complications**

TIPS succeeded in 126 of 155 cirrhotic patients with complete PVT. The overall success rate was 81.29%. To evaluate the risk factors of TIPS failure, logistic regression analysis was performed, and the results indicated that portal fibrotic cord was a risk factor for TIPS failure (Table 2). Patients were divided into two groups, 41 with portal fibrotic cord and 114 without portal fibrotic cord. There were no significant differ-

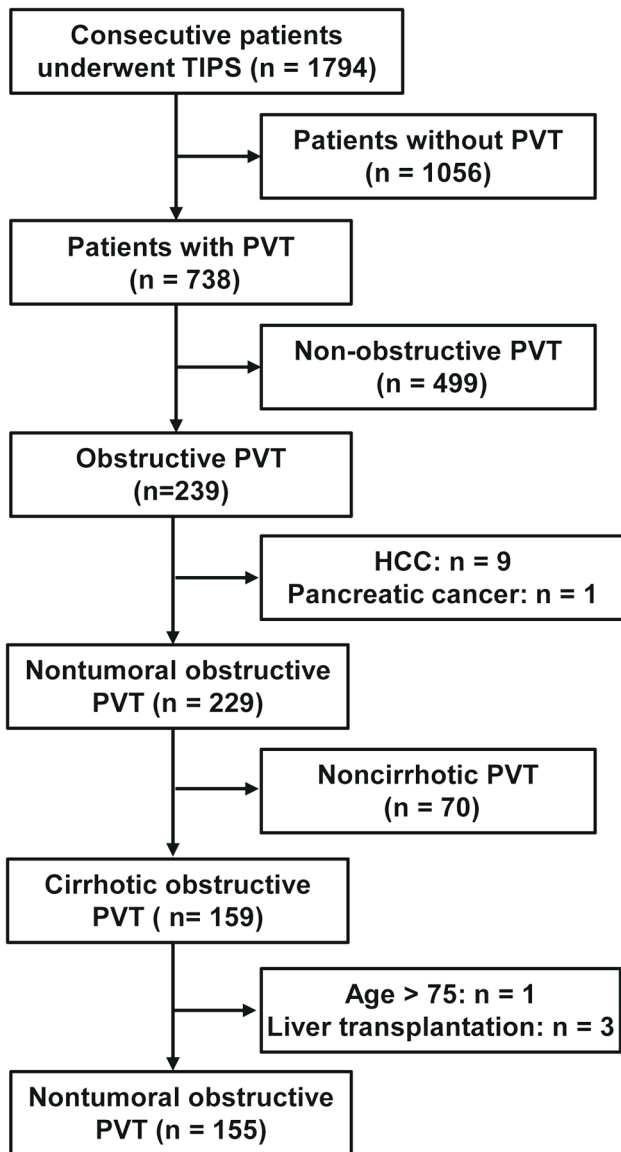


Fig. 2. Flowchart of patient selection.

ences in age, sex, etiology of liver cirrhosis, or incidence of portal cavernous transformation in the two groups. Compared with those without portal fibrotic cord, patients with portal fibrotic cord had a higher rate of splenectomy history (65.85% vs. 47.37%,  $p < 0.05$ ), worse liver function (MELD, 13 vs. 9,  $p < 0.001$ ; Child-Pugh Score, 9 vs. 7,  $p < 0.001$ ), lower TIPS success rate (39.02% vs. 96.49%,  $p < 0.001$ ), and higher incidence of operation-related complications, especially abdominal bleeding (12.20% vs. 1.75%,  $p < 0.01$ ; Table 3). A total of 95.12% of patients (39/41) with portal fibrotic cord required percutaneous transhepatic or percutaneous trans-splenic puncture, while 80.70% of patients without portal fibrotic cord (92/114) underwent transhepatic/splenic/collateral TIPS.

Operation-related complications included abdominal bleeding, subcutaneous hematoma, and ectopic embolism. Seven patients suffered from abdominal bleeding, which was stopped by blood transfusion in six. One patient had splenic vein injury and was treated with splenectomy. Com-

Table 1. Baseline characteristics (n=155)

Parameter	Value
Median (range) or absolute (percentage)	
Median age (years)	52 (29–73)
Sex	
Male	90 (58.06%)
Female	65 (41.94%)
Etiology	
HBV	101 (65.16%)
Other	54 (34.84%)
Manifestations	
Refractory variceal bleeding	148 (95.48%)
Refractory ascites	7 (4.52%)
Liver function scores	
MELD	10 (6–26)
Child-Pugh	8 (5–12)
Child-Pugh class A/B/C	33/97/25
Splenectomy	
Yes	81 (52.26%)
No	74 (47.74%)
Portal cavernous transformation	
Yes	127 (81.94%)
No	28 (18.06%)
Portal fibrotic cord	
Yes	41 (26.45%)
No	114 (73.55%)
Extent of thrombosis	
MPV	52 (33.55%)
MPV+SMV	83 (53.55%)
MPV+SV	2 (1.29%)
MPV+SMV+SV	18 (11.61%)
TIPS success	
Yes	126 (81.29%)
No	29 (18.71%)
TIPS Access	
Transjugular	24 (15.49%)
Transhepatic	107 (69.03%)
Trans-splenic	18 (11.61%)
Transcollateral	6 (3.87%)

HBV, hepatitis B virus; MELD, model for end-stage liver disease; MPV, main portal vein; SMV: superior mesenteric vein; SV, splenic vein; TIPS, transjugular intrahepatic portosystemic shunt.

pared with those without, patients with portal fibrotic cord had more abdominal bleeding (12.20% vs. 1.75%,  $p < 0.01$ ). Three cases of subcutaneous hematoma occurred at the puncture site of the internal jugular vein or femoral artery,

**Table 2. Logistic regression analysis of factors associated with TIPS failure**

Variable	p-value	OR		95% CI
Age >52 years	0.870	1.101	0.348	3.486
Sex (male)	0.558	0.704	0.218	2.276
Etiology (HBV)	0.281	0.495	0.138	1.779
Splenectomy	0.412	0.586	0.163	2.102
MELD score >10	0.575	1.688	0.271	10.524
Child-Pugh score >8)	0.524	0.561	0.094	3.327
Fibrotic cord	< 0.001	0.024	0.006	0.093
Extent of thrombosis (MPV)	0.493	0.645	0.184	2.262

CI, confidence interval; HBV, hepatitis B virus; MELD, model for end-stage liver disease; OR, odds ratio.

all of which absorbed and disappeared 2 to 4 weeks after the operation. Five cases with tissue glue to embolize varicose veins had ectopic pulmonary embolism. However, because of the small size embolization particles and small embolization range, the patients had no obvious clinical symptoms. Only anticoagulant therapy was administered. Complications not associated with the operation included fever, liver damage, hepatic encephalopathy, and stent dysfunction. Thirteen

patients had fever (8.39%). One with acute varicose bleeding had fever because of lung infection, which induced liver failure, and the patient died 13 days after TIPS. The others recovered from fever after antibiotic treatment. Thirty-nine patients (25.16%) suffered from liver function injury, most of whom showed increased bilirubin after TIPS. Hepatic encephalopathy after TIPS occurred in 38 cases (30.16%), 22 had no recurrence after the removal of inducements and drug

**Table 3. Clinical features stratified by presence of portal fibrotic cord**

Parameter	Fibrotic cord	Nonfibrotic cord
Median (range) or absolute (percentage)	n=41	n=114
Median age (years)	51 (36-73)	53 (29-72)
Sex male/female	26/15 (63.41/36.59%)	64/50 (56.14/43.86%)
Etiology HBV/others	27/14 (65.85/34.15%)	74/40 (64.91/35.09%)
Liver function scores		
MELD	13 (6-26)	9 (6-26)***
Child-Pugh	9 (5-12)	7 (5-11)***
Splenectomy	27 (65.85%)	54 (47.37%)*
Extent of thrombosis		
MPV	12 (29.27%)	40 (35.09%)
MPV+SMV	24 (58.54%)	59 (51.75%)
MPV+SV	0 (0.00%)	2 (1.75%)
MPV+SMV+SV	5 (12.19%)	13 (11.41%)
Cavernous transformation	34 (82.93%)	93 (81.58%)
TIPS success	16 (39.02%)	110 (96.49%)***
TIPS access		**
Transjugular	2 (4.88%)	22 (19.30%)
Transhepatic/splenic/collateral	39 (95.12%)	92 (80.70%)
Operation-related abdominal hemorrhage	5 (12.20%)	2 (1.75%)**
Symptom improvement	21 (51.22%)	111 (97.37%)***
Encephalopathy after TIPS	4/16 (25.00%)	34/110 (30.91%)
Shunt dysfunction	6/16 (37.50%)	22/110 (20.00%)
Overall survival at 12 months	32%	86%***
Median overall survival (days)	300	1,730***

\*p<0.05; \*\*p<0.01; \*\*\*p<0.001. HBV, hepatitis B virus; MELD, model for end-stage liver disease; MPV, main portal vein; SMV, superior mesenteric vein; SV, splenic vein; TIPS, transjugular intrahepatic portosystemic shunt.

**Table 4. Complications**

Complications	Frequency, n (%)
Operation-related complications	
Abdominal hemorrhage	7/155 (4.52%)
Subcutaneous hematoma	3/126 (2.38%)
Ectopic embolism	5/126 (3.97%)
Nonoperation-related complications	
Fever	13/155 (8.39%)
Liver function damage	39/155 (25.16%)
All encephalopathy after TIPS	38/126 (30.16%)
Refractory encephalopathy	16/126 (12.70%)
Shunt dysfunction	28/126 (22.22%)

TIPS, transjugular intrahepatic portosystemic shunt.

treatment, 16 (12.70%) had refractory encephalopathy, and symptoms improved in seven after a TIPS flow restriction operation. Twenty-eight patients (22.22%) developed TIPS stent dysfunction. In terms of nonoperation-related complications, there were no significant differences between patients with and without portal fibrotic cord (Table 4).

**Portal fibrotic cord independently predicts death in cirrhotic patients**

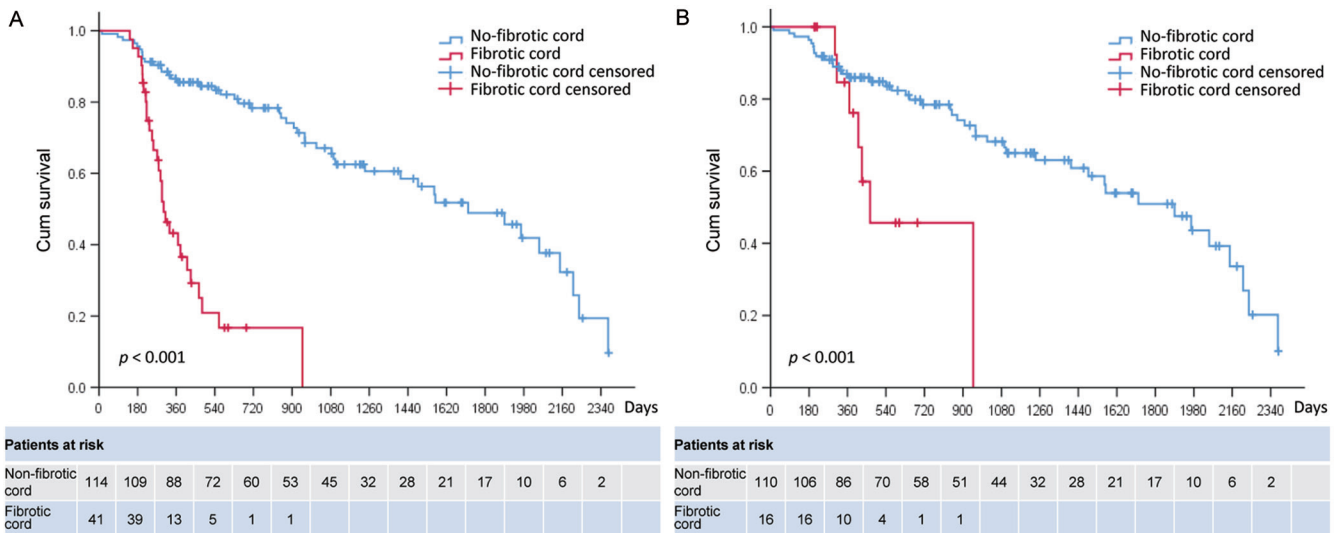
The 1-year survival rate and median survival were only 32% and 300 days, respectively, in patients with portal fibrotic cord, compared with 86% and 1,730 days in patients without portal fibrotic cord. Kaplan-Meier survival curve analysis showed that the overall survival of patients with portal fibrotic cord was significantly lower than that of patients without portal fibrotic cord, despite the overall population or the population with successful TIPS (Fig. 3). The result indicated that portal fibrotic cord was closely related to the survival of cirrhotic patients. Analysis of factors related to survival by the Cox regression model showed that a MELD score of >10,

fibrotic cord, and TIPS failure were independent predictors of death in cirrhotic patients (Table 5).

**Discussion**

Occlusive PVT with portal hypertension-related complications is a difficult clinical problem. For thrombosis itself, the effectiveness of anticoagulants is poor, and for portal hypertension complications caused by thrombosis, drug, and endoscopic treatments are ineffective. Liver transplantation is fraught with difficulties.<sup>3-5</sup> TIPS has brought new light for such cases, but its success rate does not reach 100% even for experienced operators, and factors that can affect TIPS success and patient survival have not been determined. This study confirmed that portal fibrotic cord was an independent predictor of TIPS failure and death in cirrhotic patients at a single center with continuing follow-up for up to 6 years.

Some previous studies reported that portal vein cavernous transformation affected the TIPS success rate. In a study by Perarnau *et al.*,<sup>17</sup> among 34 cirrhotic patients with occlu-



**Fig. 3. Kaplan-Meier curves of overall survival in all patients and TIPS success cohorts.** (A) Kaplan-Meier curves show that the overall survival of patients with portal fibrotic cord (red line) was lower than that of patients without portal fibrotic cord (blue line). (B) Kaplan-Meier curves show that patients with portal fibrotic cord (red line) had lower survival without transplantation after TIPS than those without portal fibrotic cord (blue line). Statistical analysis by log-rank test. TIPS, transjugular intrahepatic portosystemic shunt.

**Table 5. Univariate and multivariate Cox regression analysis of predictors of survival**

Variable	Univariate analysis			Multivariate analysis		
	HR	95% CI	p-value	HR	95% CI	p-value
Age >52 years	0.915	0.581 1.443	0.703			
Sex (Male)	1.297	0.818 2.055	0.268			
Etiology (HBV)	1.287	0.788 2.101	0.313			
Splenectomy	1.117	0.712 1.753	0.629			
MELD score >10	5.335	3.148 9.042	<0.001	3.550	1.826 6.900	<0.001
Child-Pugh score >8)	3.930	2.452 6.300	<0.001	1.524	0.788 2.950	0.211
Fibrotic cord	7.416	4.213 13.055	<0.001	2.377	1.154 4.892	0.019
TIPS failure	8.173	4.768 14.011	<0.001	5.236	2.735 10.024	<0.001

CI, confidence interval; HBV, hepatitis B virus; HR, hazard ratio; MELD, model for end-stage liver disease; TIPS, transjugular intrahepatic portosystemic shunt.

sive PVT, the TIPS success rate was 63% in 19 patients with cavernous transformation and 100% in 15 patients without cavernous transformation. However, other studies reported that the TIPS success rate was 100% in occlusive PVT with portal cavernous transformation.<sup>8,9,18</sup> In our study, the TIPS success rates in patients with a nonfibrotic cord with portal cavernous transformation (96.77%, 90/93) and in those without portal cavernous transformation (97.06%, 33/34) were not different. However, the TIPS success rate in patients with fibrotic cord was only 39.02% (16/41). Cavernous transformation has also been designated as one of the most serious types of PVT in Baveno VII, the latest consensus in portal hypertension.<sup>19</sup> This point is worth discussing. Cavernous transformation is a pathological form, not a degree, of portal thrombosis. The concept of cavernous transformation was first described in the 1960s.<sup>13</sup> Cavernous transformation of the portal vein refers to a compensatory pathological performance of collateral circulation blood vessels around the portal vein with cross sections that look like sponge gill holes because of portal hypertension and increased blood flow resistance. It is essentially a compensatory change. In addition to the degree of obstruction of the main portal vein, cavernous transformation is also related to portal pressure, intrahepatic resistance, and portosystemic shunts. When portal pressure increases, cavernous transformation may occur even if the main portal vein is not obstructed (Supplementary Fig. 5). There was no cavernous transformation when enlarged portosystemic shunts occurred even if the main portal vein was blocked (Fig. 1C). So it may not be appropriate to consider cavernous transformation as portal thrombosis. Cavernous transformation itself has little impact on the TIPS operation and success rate. The only relevant factor is cavernous transformation accompanied by fibrotic cord. After the portal vein develops a fibrotic cord, its lumen structure can no longer be identified on imaging, which greatly increases the difficulty and risk of the operation.

The influence of portal vein thrombosis on the course of liver cirrhosis and patient survival has been a controversial issue.<sup>20</sup> A previous study suggested that both cirrhotic and noncirrhotic PVT lengthened the time required for endoscopic ligation to eradicate varicose veins compared with patients without thrombosis.<sup>3</sup> PVT was an independent predictor for failure to control bleeding in cirrhotic patients with varicose bleeding, liver function damage, and short-term death.<sup>21–24</sup> Other studies have found the opposite. The main reason for the inconsistent conclusions of these studies was the heterogeneity of liver diseases and thrombus degree among the selected cases. They did not divide the different degrees and

scopes of thrombus. Previous studies at our center and at others have showed that mural or partial PVT did not affect cirrhotic patient prognosis, but occlusive PVT increased the incidence of other decompensated events and reduced long-term transplant-free survival in cirrhotic patients and liver transplantation patient survival rates at 1 year.<sup>25–28</sup> This study found that portal fibrotic cord was a prognostic factor for cirrhotic patient death, consistent with our previous conclusions. In addition, we found that patients with portal fibrotic cord had worse liver function, which also supported the conclusion it increased mortality. Most patients with portal fibrotic cord had an enlarged portosystemic shunt (Fig. 1C). A recent study found that cirrhotic patients with enlarged portosystemic shunts had worse liver function and higher mortality,<sup>29</sup> also consistent with our findings. Although the causal relationship was unclear among those with fibrotic cord instead of the original portal vein, liver function deterioration, and enlarged portal shunts, it did not affect our conclusions.

TIPS, especially for occlusive PVT, remains one of the most difficult peripheral interventional operations and is not widely available in China, Europe, or the USA. Considering the different levels of technical skill in each center, it is difficult to carry out multicenter research on TIPS treatment for occlusive PVT. This study, although only involving a single center, had the largest sample size of occlusive thrombosis cases ever, and the data were prospectively collected. We have preliminarily confirmed that patients with portal fibrotic cord have worse liver function, a higher TIPS failure rate, and higher mortality. Such patients can be relatively excluded from TIPS.

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None to declare.

### Conflict of interest

The authors have no conflict of interests related to this publication.

### Author contributions

Designed the study (JT), performed TIPS operations (JT, CH,

XY, KL, WJ), preserved clinical imaging data (JN), collected clinical data (NH, JX, YZ, XL, YM, YX, XG), wrote the manuscript (JT).

### Ethical statement

This was a single-center retrospective cohort study approved by the Medical Ethics Committee of the First Affiliated Hospital of Air Force Medical University (approval number: KY20212129-C-1).

### Data sharing statement

The raw data supporting the conclusions of this article will be made available by the authors.

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