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ORIGINAL RESEARCH

Fully Covered Stent-TIPS for Advanced HCC Patients with Portal Vein Tumor Thrombus-Related Severe Symptomatic Portal Hypertension

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Purpose: Portal vein tumor thrombus (PVTT)–related severe symptomatic portal hypertension (SPH) leads to a poor prognosis in patients with advanced hepatocellular carcinoma (HCC). Traditional transjugular intrahepatic portosystemic shunt (TIPS) using covered plus bare stent can effectively relieve SPH, however, the bare segment is susceptible to obstruction due to PVTT invasion. This study aimed to evaluate the safety and efficacy of fully covered stent-TIPS (FCS-TIPS) for treatment of PVTT-related SPH in advanced HCC patients.

Patients and Methods: This retrospective study enrolled 25 patients with advanced HCC who underwent FCS-TIPS for PVTT-related severe SPH from June 2018 to January 2024. The evaluated outcomes included overall survival (OS), technical success rate, reduction in portal venous pressure gradient (PPG), stent patency rate, SPH control rate, liver function and complications.

Results: The technical success rate was 100% without perioperative deaths or severe procedure-related adverse events. The average PPG decreased by 13.4±4.6 mmHg. The overall symptom control rate of SPH was 96.0%. Variceal bleeding, ascites/hydrothorax, and enteropathy control rates were 100%, 95.0%, and 100%, respectively. Liver function showed mild improvement one month after TIPS. One patient (4.0%) experienced overt hepatic encephalopathy (OHE) and three (12.0%) patients developed shunt dysfunction during the follow-up period. None of the patients experienced shunt-induced extrahepatic metastasis. The median OS was 6.0 months and the cumulative survival rates at 3, 6, 12 months were 80.0%, 52.0% and 21.3%.

Conclusion: FCS-TIPS is safe and effective for treating PVTT-related severe SPH and can serve as a bridging therapy for advanced HCC.

Keywords: fully covered stent, transjugular intrahepatic portosystemic shunt, hepatocellular carcinoma, portal vein tumor thrombus, symptomatic portal hypertension

Introduction

Hepatocellular carcinoma (HCC) is the sixth most common cancer and the third leading cause of cancer-related deaths worldwide.[1] Portal vein tumor thrombosis (PVTT) is detected in approximately 10%–40% of HCC cases at diagnosis.[2] Portal vein involvement is a particularly severe complication of advanced HCC and can obstruct portal vein flow, thereby aggravating portal hypertension.[3,4] Severe PVTT is strongly associated with poor prognosis and can lead to symptomatic portal hypertension (SPH) complications, such as variceal bleeding, refractory ascites/hydrothorax and portal hypertensive enteropathy (PHE).[5] The SPH-related complications lead to a more conservative

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treatment strategy and the median survival time is only 2.7 months without aggressive intervention.[6] Although systemic therapy for HCC is advancing rapidly, a subset of advanced patients remain unable to tolerate it due to poor general condition, impaired liver function and severe complications associated with SPH.[7,8] Therefore, it is crucial to implement effective approach to alleviate SPH-related complications and create opportunities for further treatment. TIPS placement is envisioned to effectively relieve patients' symptoms and create the basis for further treatment.[9,10]

Transjugular intrahepatic portosystemic shunt (TIPS) is an effective treatment for reducing portal pressure.[11] Accumulating evidence suggests that TIPS is a palliative approach for advanced HCC patients with PVTT-related SPH, which is expected to reduce portal hypertension and improve the patient's general condition, serving as a bridging therapy for sequential systematic and locoregional treatment.[7,12–14] In traditional TIPS procedures, the covered segment of the stent is placed within the liver, while the bare segment is typically positioned in the portal vein.[15] The bare portion is generally intended to maintain blood flow within the stent, however, it is vulnerable to invasion by tumor thrombus in advanced HCC patients, which could increase the incidence of stent dysfunction.[16,17] Zhao et al tried to use covered stent-TIPS for HCC with PVTT, reporting that all 11 patients achieved relief from portal hypertension complications and the patency rate was 100%.[17] Therefore, this study aimed to evaluate the safety and efficacy of fully covered stent for advanced HCC patients with PVTT-related SPH.

Materials and Methods

Patients

This retrospective study was conducted in accordance with the Declaration of Helsinki of the World Medical Association. The Institutional Review Board approved this study and waived the requirement for informed consent from the patients. All patients signed informed consent for treatment. The main inclusion criteria were as follows: (1) age of 18–80 years; (2) met the diagnostic criteria for HCC with PVTT; (3) symptoms of SPH (variceal bleeding, refractory ascites/hydrothorax, with/without enteropathy); (4) East Coast Oncology Group (ECOG) score≤4; (5) patients unable to tolerate further treatment due to SPH; (6) received TIPS treatment. The main exclusion criteria were as follows: (1) absence of fully covered stent; (2) PVTT graded Vp1 and Vp2; (3) extrahepatic metastasis; (4) congestive heart failure, severe renal insufficiency, severe coagulopathy and hepatic arterial obstruction; (5) lack of baseline data. From June 2018 to January 2024, 132 advanced HCC patients with PVTT were retrospectively enrolled and 25 patients were included in this study based on the inclusion and exclusion criteria (Figure 1).

Diagnosis and Definitions

Advanced HCC was defined as the HCC combined with either vascular invasion or extrahepatic metastasis. PVTT was evaluated by computed tomography (CT) or magnetic resonance imaging (MRI). The degree of PVTT was based on Japan's Vp classification using the following five types: Vp0, absence of invasion of the portal vein; Vp1, invasion distal to the second order branches of the portal vein; Vp2, invasion of second order branches of the portal vein; Vp3, invasion of first order branches of the portal vein; Vp4, invasion of the main trunk of the portal vein and/or contra-lateral portal vein branch to the primarily involved lobe.[18]

Symptomatic portal hypertension complications were defined as those symptoms related to portal hypertension, including acute or repeated variceal bleeding failed to respond to conservative and endoscopic treatment, refractory ascites/hydrothorax, with/without enteropathy. These conditions are typically classified as further decompensated states through the Baveno VII consensus.[19] Refractory ascites/hydrothorax was defined as follows: (1) unresponsiveness to a limited sodium diet and intensive diuretic therapy; (2) diuretic intolerance; (3) rapid recurrence of ascites or hydrothorax after therapeutic puncture and drainage.[20] The enteropathy was defined as digestive symptoms, such as abdominal pain, diarrhea and poor appetite, accompanied by edema of small bowel or colon, particularly in the duodenum and ileocecum. Shunt-induced extrahepatic metastasis was defined as new-onset hematogenous metastasis after shunt opening of TIPS, which was diagnosed by systemic imaging.

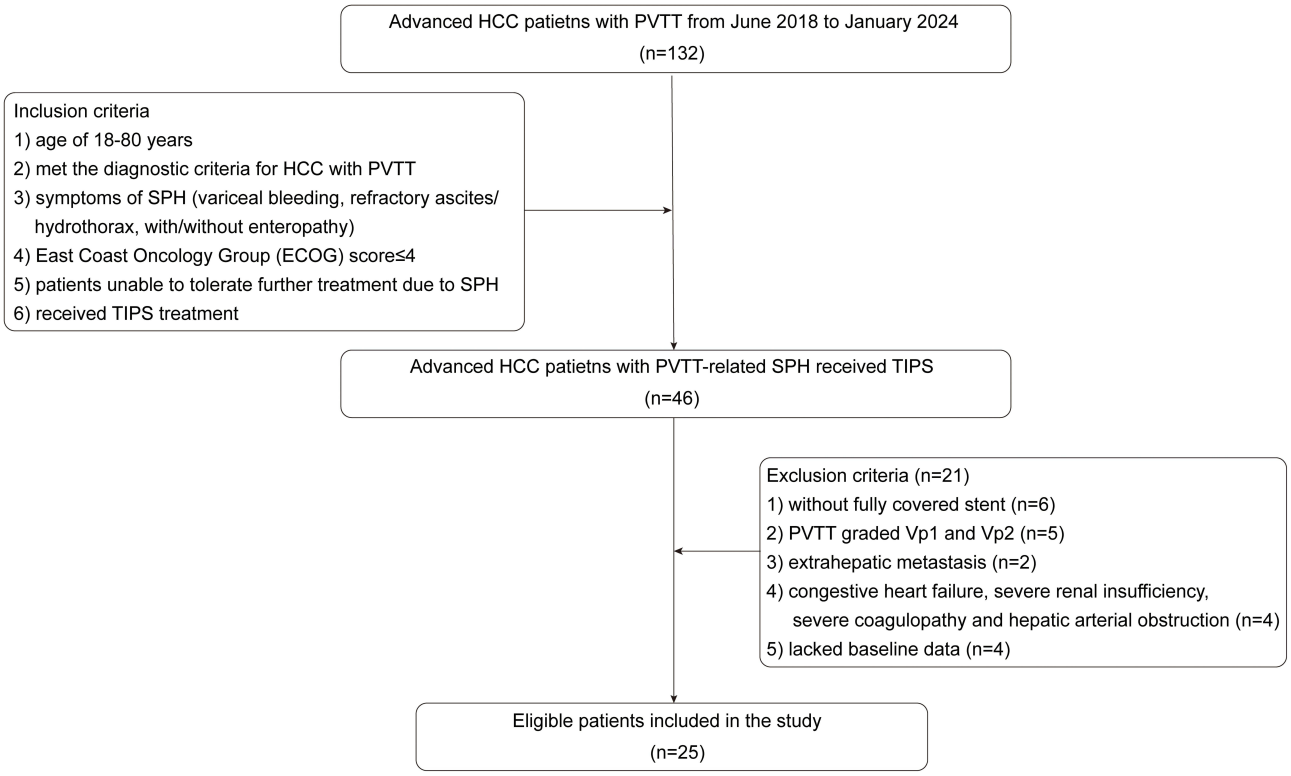

Figure 1 Patient flow diagram.
Abbreviations: HCC, hepatocellular carcinoma; PVTT, portal vein tumor thrombus; SPH, symptomatic portal hypertension; TIPS, transjugular intrahepatic portosystemic shunt.

TIPS procedure

Transarterial localizer-assisted TIPS (TALA-TIPS) was performed in this study. The Intrahepatic arterial localizer was initially predetermined on the sagittal image of preoperative contrast enhanced CT (CECT). It was then displayed on coronal and axial images. We used the GE workstation to conduct 3D reconstruction of the hepatic and portal veins (Figure 2). Hepatic arteriography and indirect portal venography were performed to evaluate the arterial patency and the puncture path of TIPS.

All procedures were performed under local infiltration anesthesia at the jugular and femoral levels with 2% lidocaine. The right femoral artery was punctured by Seldinger technology and the microcatheter was positioned at the predetermined intra-hepatic arterial site. The right internal jugular vein was cannulated with a 10F sheath and a 5F catheter was used to select the hepatic vein. The radiologist used a needle (RUPS-100, COOK Inc., USA) to puncture the portal vein branch guided by the arterial localizer. After pre-expanding the shunt, the severe esophageal and gastric varices were embolized by controllable coils (Interlock, Boston Scientific Inc., USA) and/or tissue glue (Beijing Compont Pharmaceutical Technology Co., Ltd., China). Then, the fully covered stent (Viabahn, W. L. Gore & Associates, USA, or Fluency, Bard Inc., USA) was placed. The stent must fully encompass the PVTT. Anatomically, its distal end should be positioned above the splenic vein opening. Functionally, the stent placement must ensure unimpeded blood flow from both the splenic vein and the superior mesenteric vein. The distance between the distal end of the stent and the PVTT (DST) was measured. Portal venous pressure gradient (PPG) was measured before and after shunt placement. PPG is defined as the difference between the portal venous pressure (PVP) and the central venous pressure (CVP), and CVP was measured at the right atrial level. Technical success was defined as the successful creation of a shunt between the hepatic and portal veins, along with a satisfactory reduction in PPG. All the patients received dietary education after TIPS, which is mainly ensuring regular bowel movements and adjusting protein intake based on the patient's stool condition. None of the patients in this study received anticoagulant therapies after TIPS procedure.

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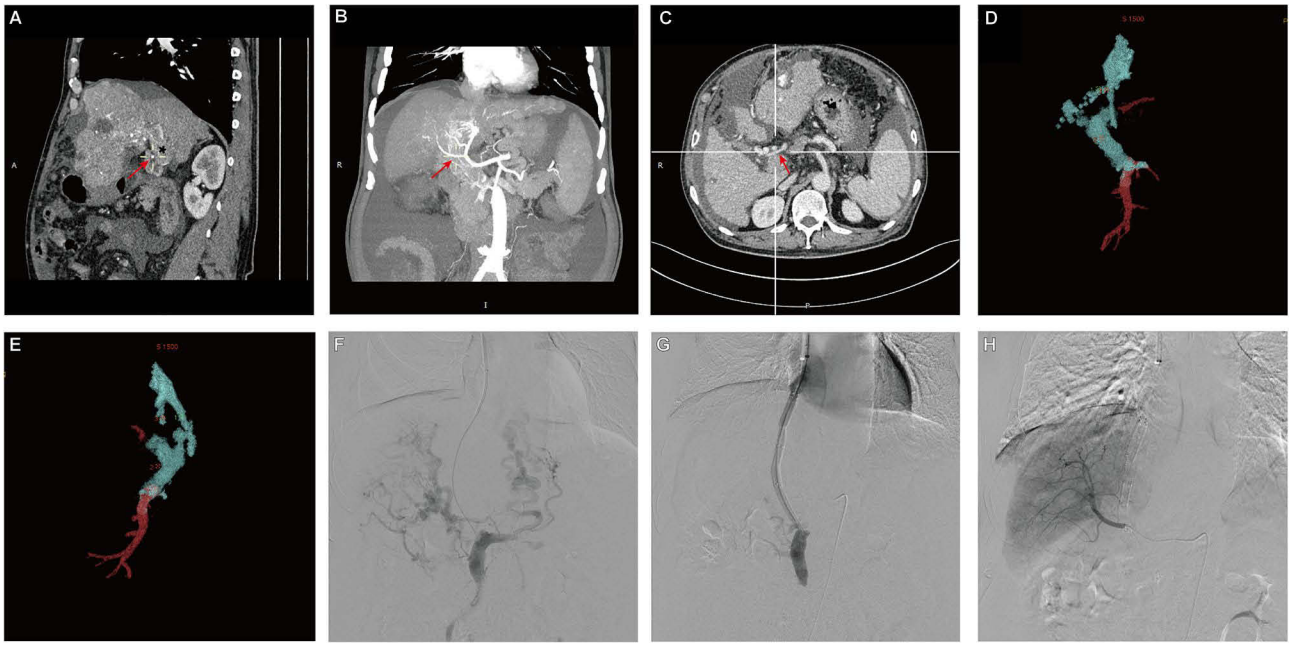

Figure 2 A 64-year-old male patient diagnosed as advanced HCC with Vp4 graded PVTT-related symptomatic portal hypertension underwent TIPS treatment for severe refractory ascites, and sequentially received systemic therapy of lenvatinib (8 mg/qd) and tislelizumab (200mg/q3w). (**A-C**) Intrahepatic arterial localizer (red arrow) on preoperative CECT. (**A**) Arterial localizer was initially predetermined ventral to the targeted portal vein entry site (asterisk). (**B-C**) Then, it was displayed on the coronal and axial images (red arrow). (**D, E**) The 3D reconstruction of portal vein, PVTT and hepatic vein on the anteroposterior (**D**) and lateral (**E**) images before TIPS procedure. The red color represented normal portal vein and its branches, and the blue color underneath represented PVTT and the blue color above represented hepatic veins. (**F**) Portal venography showed the main trunk of portal vein was blocked by tumor thrombus and cavernous transformation. The PPG was 31 mmHg before TIPS creation. (**G**) After TIPS creation, the blood flow within the stent was smooth, and the collateral circulation veins were significantly reduced. The PPG was 13 mmHg after TIPS creation. (**H**) Hepatic arteriography after TIPS was performed to ensure the arterial patency.

Sequential Therapy for HCC

Patients received sequential treatment after the TIPS procedure when SPH was controlled. Sequential treatment included optimal supportive therapy, molecular targeted agents, immunotherapy, radiation therapy and/or locoregional therapy, such as transarterial chemoembolization (TACE), hepatic artery infusion chemotherapy (HAIC) and radiofrequency ablation (RFA).

Follow-Up

Patients were followed up with laboratory tests every month after the TIPS procedure, such as blood count, liver function, coagulation function and alpha-fetoprotein (AFP). Abdominal CECT/MRI, chest CT and color Doppler ultrasonography (CDUS) were performed every two months. The endpoint of follow-up was death or July 3, 2024. Overall survival (OS) was calculated from the TIPS procedure to death or July 3, 2024. According to the West Haven criteria, hepatic encephalopathy (HE) was evaluated and divided into four grades. Grade 2 and above were defined as overt HE (OHE).[21] Shunt occlusion was considered as the following situations: (1) recurrent variceal bleeding; (2) recurrent ascites/hydrothorax or aggravation, excluding tumor and infection; (3) recurrent enteropathy; (4) maximum shunt-flow less than 50 cm/s or absence of flow within the shunt in CDUS.

Statistical Analysis

Continuous variables are presented as the mean ± SD or median. Categorical variables are expressed as percentage of the group (number of patients). Continuous variables were compared using *t*-test. Pearson's $\chi 2$ test was used to compare qualitative data. In the survival analysis, OS was evaluated by Kaplan–Meier curve and was compared by Log rank test between different groups. Statistical analysis was conducted using Stata/SE software (version 15.0). P value <0.05 was considered to be statistically significant.

Results

Patient Characteristics

This study enrolled 25 advanced HCC patients with PVTT-related SPH who underwent fully covered stent-TIPS. Among these patients, 20 (80.0%) were male and 5 (20.0%) were female. The average age was 62.3±11.2 years and 23 (92.0%) patients had hepatitis B virus infection. There were 6 patients (24.0%) with Child-Pugh class A, 14 patients (56.0%) with Child-Pugh class B, and 5 patients (20.0%) with Child-Pugh class C. All patients had advanced HCC and PVTT, along with severe SPH. There were 13 (52.0%) and 12 (48.0%) patients with PVTT of Vp3 and Vp4. Stratified by the BCLC system, 14 (56.0%) patients were BCLC stage C and 11 (44.0%) patients were BCLC stage D. The symptoms of SPH included variceal bleeding (7 cases, 28.0%), refractory ascites/hydrothorax (20 cases, 80.0%) and enteropathy (14 cases, 56.0%). More basic characteristics are shown in Table 1.

Table 1 Baseline Characteristics of Patients

Characteristics	Value
Sex, n (%)	
Male	20 (80.0)
Female	5 (20.0)
Age, years	62.3±11.2
Etiology of cirrhosis, n (%)	
HBV	23 (92.0)
HCV	1 (4.0)
Alcoholic	1 (4.0)
ECOG score	
1–2	14 (56.0)
3–4	11 (44.0)
Tumor number, n (%)	
Single	3 (12.0)
Multiple	18 (72.0)
Diffuse	4 (16.0)
Tumor diameter, n (%)	
<5cm	8 (32.0)
>5cm, ≤10cm	9 (36.0)
>10cm	8 (32.0)
BCLC grade, n (%)	
C	14 (56.0)
D	11 (44.0)
PVTT degree, n (%)	
Vp3	13 (52.0)
Vp4	12 (48.0)
Child-Pugh score	8.2±2.0
Child-Pugh class, n (%)	
A	6 (24.0)
B	14 (56.0)
C	5 (20.0)
MELD score	10.0±4.6
MELD class, n (%)	
<10	14 (56.0)
≥10	11 (44.0)
PLT (10^9/L)	114.6±70.1

(*Continued*)

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Table 1 (Continued).

Characteristics	Value
AST (U/L)	100.2±74.5
Creatine (μmol/L)	76.9±26.4
AFP, n (%)	
≤400 ng/mL	11 (44.0)
>400 ng/mL	14 (56.0)
Symptomatic portal hypertension, n (%)	
Variceal bleeding	7 (28.0)
Refractory ascites or hydrothorax	20 (80.0)
Enteropathy	14 (56.0)

Abbreviations: ECOG score, East Coast Oncology Group score; BCLC, Barcelona Clinic Liver Cancer; PVTT, portal vein tumor thrombus; MELD, Model for End-Stage Liver Disease; PLT, platelet; AST, aspartate aminotransferase; AFP, alpha-fetoprotein.

TIPS Procedure

All 25 patients achieved technical success of TALA-TIPS with fully covered stent. There were 24 (96.0%) and 1 (4.0%) patients using Viabahn stent and Fluency stent, respectively. To reduce the occurrence of HE, small diameter stents were used and there were 3 (12.0%), 9 (36.0%) and 13 (52.0%) using 6 mm, 7 mm and 8 mm fully covered stents, respectively. The stent length was selected based on the anatomy and PVTT length. Eight patients required two stents, while the remaining patients were treated with one single stent. The average total stent length was 11.3±3.1 cm. All cases got complete coverage of the PVTT and the distance between the distal end of the stent and the PVTT was 26.2 mm (range, 4.1 mm-59.7 mm). For patients with severe gastric and esophageal varices, 3 (12.0%) patients were embolized with coils and 10 (40.0%) patients were treated with coils plus tissue glue. PPG significantly decreased from 29.5 ±6.2 mmHg before TIPS to 16.0±5.1 mmHg after TIPS (t=14.52, $p<0.001$) and the average reduction was 13.4 ±4.6 mmHg. After the TIPS procedure, 24 patients (96.0%) received locoregional therapy, 11 patients (44.0%) received molecular targeted agents, 5 patients (20.0%) received immunotherapy and 4 patients (16.0%) received radiation therapy when SPH was well controlled (Table 2). By the end of the follow-up period, none of the patients had extrahepatic metastasis.

Table 2 Characteristics of TIPS Procedure

Characteristics	Value
Cover stent, n (%)	
Viabahn	24 (96.0)
Fluency	1 (4.0)
Stent diameter, n (%)	
6mm	3 (12.0)
7mm	9 (36.0)
8mm	13 (52.0)
Total stent length, (cm)	11.3±3.1
Distance between the distal end of stent and PVTT (DST, mm, range)	26.2 (4.1–59.7)
Coronary vein embolization, n (%)	
Coil	3 (12.0)
Coil + tissue glue	10 (40.0%)
No	12 (48.0%)

(*Continued*)

Table 2 (Continued).

Characteristics	Value
PPG, (mmHg)	
Pre-TIPS	29.5±6.2
Post-TIPS	16.0±5.1
Reducing	13.4±4.6
Post-TIPS treatment, n (%)	
Locoregional therapy[a]	24 (96.0)
Targeted therapy	11 (44.0)
Immunotherapy	5 (20.0)
Radiation therapy	4 (16.0)

Notes: a, Locoregional therapy included transarterial chemoembolization (TACE), hepatic artery infusion chemotherapy (HAIC) and radiofrequency ablation (RFA).
Abbreviations: PPG, portal pressure gradient; TIPS, transjugular intrahepatic portosystemic shunt.

Symptom Control and TIPS-Related Complications

A total of 96.0% (24/25) of patients experienced complete or partial remission of symptoms. All 7 patients with variceal bleeding were effectively controlled and no rebleeding was observed during follow-up. Complete or partial remission was achieved in 80.0% (16/20) and 15.0% (3/20) of the patients with refractory ascites or hydrothorax, respectively. Only 5.0% (1/20) of patients with refractory ascites had no remission, which was attributed to thrombosis within the stent. A total of 92.9% (13/14) and 7.1% (1/14) of patients with enteropathy achieved either complete or partial remission, respectively (Table 3).

Table 3 Symptoms Control Rate, TIPS-Related Complications and Survival Rate

Characteristics	Value
Variceal bleeding, n (%)	7
Control	7 (100)
Rebleeding	0 (0)
Refractory ascites/hydrothorax, n (%)	20
Complete remission	16 (80.0)
Partial remission	3 (15.0)
No remission	1 (5.0)
Enteropathy, n (%)	14
Complete remission	13 (92.9)
Partial remission	1 (7.1)
No remission	0
TIPS-related complications, n (%)	
Hepatic encephalopathy	2 (8.0)
I / II	1 (4.0) / 1 (4.0)
Shunt dysfunction, n (%)	3 (12.0)
Shunt thrombosis	1 (4.0)
Tumor progression	2 (8.0)
Abnormal liver function impairment	1 (4.0)
Overall survival rates (mo)	
3	80.0%
6	52.0%
12	21.3%

Abbreviation: TIPS, transjugular intrahepatic portosystemic shunt.

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Table 4 Liver Function Before TIPS and One Month After TIPS

Child-Pugh	Grade A	Grade B	Grade C
Pre-TIPS	6 (24.0%)	14 (56.0%)	5 (20.0%)
Post-TIPS	6 (24.0%)	17 (68.0%)	2 (8%)

Abbreviation: TIPS, transjugular intrahepatic portosystemic shunt.

No severe procedure-related complications such as bleeding, ectopic embolization or bile duct injury occurred. Only one person had OHE and the symptoms improved through medical treatment. A total of 3 (12.0%) patients experienced shunt dysfunction during the follow-up period. One patient developed in-stent thrombosis due to hepatic arterioportal fistula (HAPF). Two patients experienced HCC progression with stent invasion by PVTT. One had a DST of 4.7 mm and survived for 1 month after TIPS, and the other had a DST of 17 mm and survived for 3 months after TIPS. Although portal flow decreased in some patients after TIPS, only one patient (4.0%) experienced abnormal liver function impairment, which was alleviated through medical therapy (Table 3). Liver function classified by Child–Pugh was improved in 1 month after TIPS compared with pre-TIPS (Table 4).

Survival Analysis

During follow-up, 88.0% (22/25) patients died of tumor progression, and the median OS was 6.0 (95% CI: 5.0–10.8) months (Figure 3). The cumulative survival rates at 3, 6, 12 months were 80.0%, 52.0% and 21.3%. As shown in Figure 4, neither the stent diameter nor MELD score had a significant impact on survival. In contrast, the OS of patients with PVTT graded Vp3 was significantly better than that of patients with Vp4 (p=0.029, HR=0.348 [95% CI: 0.14–0.90]). The OS of patients with a DST<30 mm was significantly worse than that of patients with a DST≥30 mm (p=0.039, HR=2.639 [95% CI: 1.05–6.64]). The optimal cut-off value of the DST was calculated by x-tile software. The OS of patients with AFP levels ≤400 ng/mL was significantly better than that of patients with AFP levels >400 ng/mL (p=0.043, HR=0.358 [95% CI: 0.13–0.97]). The OS of patients with ECOG of 1–2 was significantly better than that of patients with ECOG of 3–4 (p<0.001, HR=0.044 [95% CI: 0.01–0.16]). Univariate analysis showed that patients with longer stent length had significantly worse OS (p=0.048, HR=1.188 [95% CI: 1.001–1.411], Table S1).

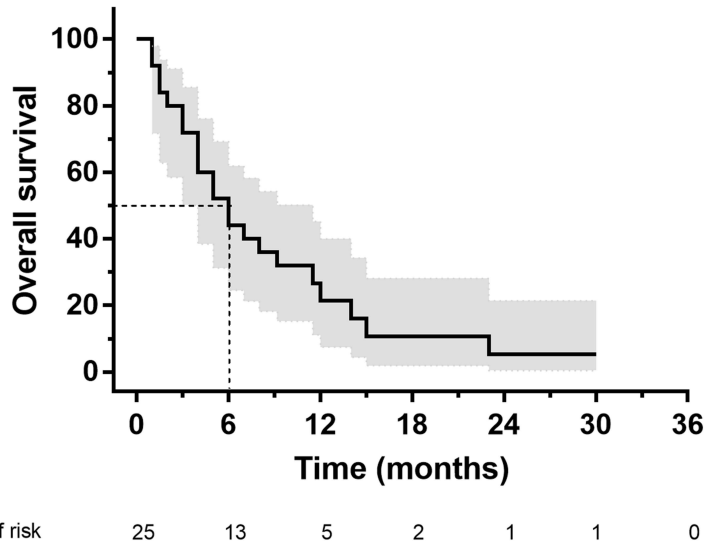

Figure 3 Kaplan-Meier analysis of overall survival.

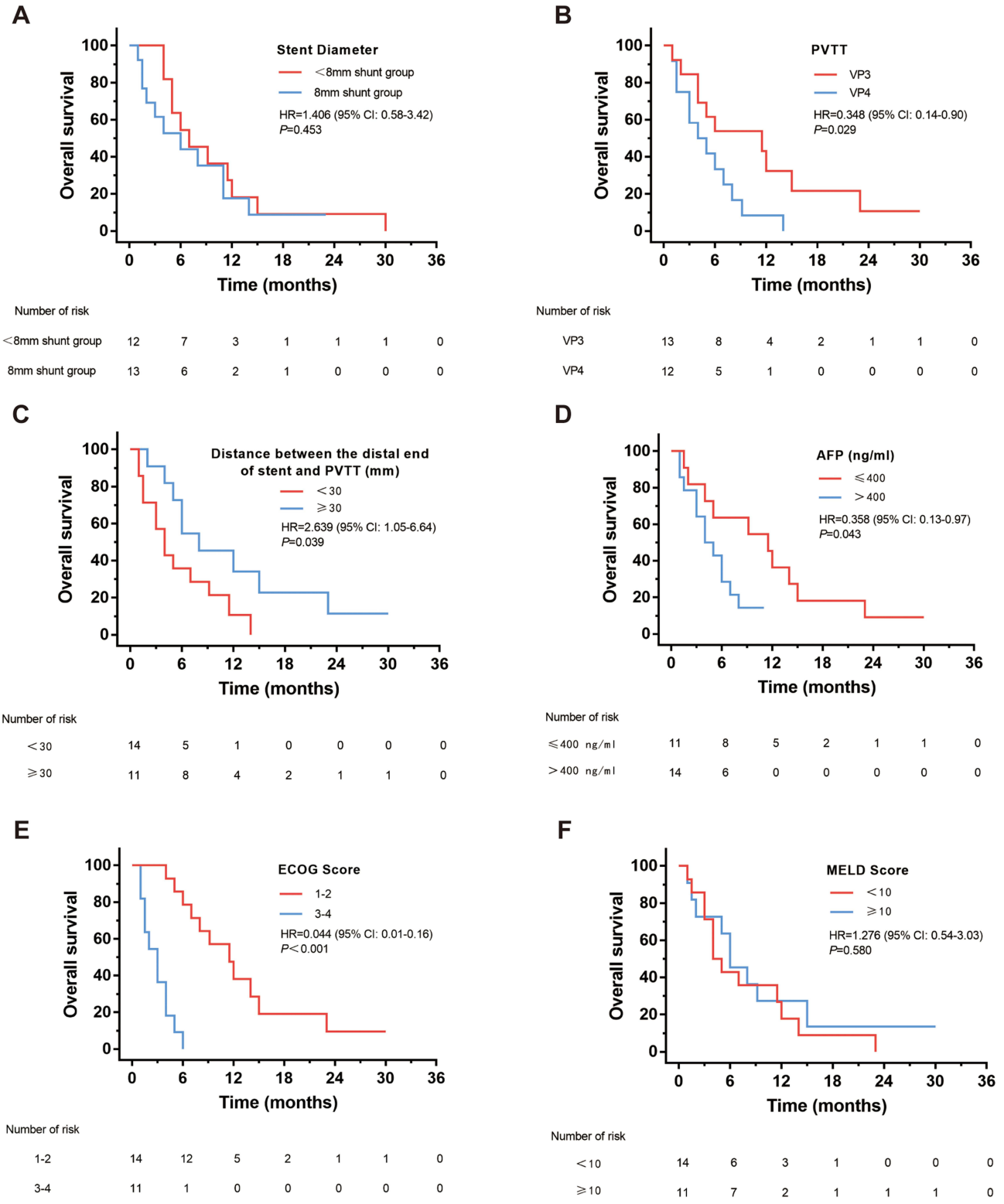

Figure 4 Log rank test for different stratification factors. (**A**) Stent diameter; (**B**) PVTT grade; (**C**) Distance between the distal end of stent and PVTT (DST); (**D**) AFP level; (**E**) ECOG score; (**F**) MELD score.

Discussion

When combined with PVTT-related SPH, the treatment options for most patients with advanced HCC are limited by complications of portal hypertension, leading to poor survival.[22] However, the consensus or guidelines on the

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management of PVTT-related SPH in patients with advanced HCC remains unclear. TIPS is a minimally invasive therapy that creates a shunt between portal and systematic circulation and can effectively treat complications of portal hypertension.[23] Traditional TIPS typically employs the "covered plus bare" stent configuration to ensure adequate blood flow within the stent.[24] The dedicated TIPS stent, such as Viatorr stent, also has a 2 cm bare segment, which may be susceptible to invasion by tumor thrombus. Herein, we explored the safety and efficacy of fully covered stent-TIPS (FCS-TIPS) for treating PVTT-related SPH in advanced HCC patients.

The median OS of this study was 6.0 months, which was higher than the reported outcomes without aggressive intervention (2.7 months).[6,25] A single-center retrospective study by Gao et al reported a median OS of 9.6 months in patients treated with TIPS combined with molecular target agents and immunotherapy.[7] The discrepancy might be attributed to worse hepatic function, heavier tumor burden, more advanced stage of PVTT and more severe SPH in our study. Although treatment options for HCC have rapidly developed, especially systemic therapy, terminal patients with PVTT-related SPH may still be unable to tolerate any therapies. Rescue TIPS can decrease portal pressure and relieve SPH, creating an opportunity for these patients to receive further sequential therapy.[7]

Standard TIPS uses the combination of covered and bare stents, which can reduce stent restenosis and maintain blood flow within the stent in non-neoplastic portal hypertension. However, for portal hypertension caused by PVTT, the bare segment of the stent may be unsuitable because it can lead to shunt occlusion due to tumor ingrowth into the mesh of the stent. Fully covered stent could be a better choice. It can partially prevent thrombus invasion into the stent and ensure its patency. A previous study had shown that covered stents for HCC patients with main trunk PVTT were effective and clinically feasible.[17] Shunt occlusion occurred at least once after TIPS creation in three (12.0%) patients in our study, which was better than that report by Liu et al[14] and Han et al.[26] This demonstrates that fully covered stent does not increase the rate of shunt dysfunction compared to the conventional covered-plus-bare stent combination. To some extent, the heparin-coated surface of Viabahn stent also contributes to stent patency.[27] The average PPG reduction was 13.4±4.6 mmHg, which was consistent with the findings reported by Liu et al[13] and Gao et al.[7] Meanwhile, the overall incidence of HE was 8.0%, which was lower than that reports by Gao et al[7] and Liu et al.[14] This may be attributed to the small stent diameter and the effective dietary education after TIPS. In our study, the distance between the distal end of the stent and PVTT (DST) also significantly influenced overall survival. Patients with a longer DST had better survival; however, the distal end of the stent should be carefully positioned to avoid disrupting blood flow of splenic vein.

Another concern with TIPS creation in patients with HCC is the risk of extrahepatic metastasis, particularly in those with PVTT. A recent study reported that lung metastasis occurred in 2.4% of patients, 3.9–32.9 months after TIPS creation.[28] In a systematic review, Zhao et al also showed a lower rate of lung metastasis (1%) in 280 patients with HCC who underwent TIPS creation.[29] Previous studies indicated that the incidence of extrahepatic metastasis in HCC patients after TIPS was relatively low, and there was no evidence suggesting that TIPS creation increased the risk of extrahepatic metastasis. On the other hand, the most crucial treatments for advanced HCC combined with PVTT-related SPH are portal pressure reduction and anti-primary tumor therapy. Lung oligometastasis appears to have minimal impact on overall survival and can be managed with sequential systemic therapy and ablation after TIPS.

Currently, the commonly used diameters of TIPS-dedicated stents are typically either 8 or 10 mm.[30] In theory, wider shunt may lead to better portal pressure reduction and stent patency, but it also may result in high incidence of HE and worse liver function. A previous study had shown that TIPS with an 8 mm covered stent had a similar shunt effect compared to a 10 mm covered stent; however, the incidence of HE was significantly reduced with an 8 mm stent (27% vs 43%).[31] A recent meta-analysis also indicated that the rate of post-TIPS HE was significantly higher in the 8 mm stent group than in the 6–7 mm stent group, while there were no discernible differences in PPG reduction, variceal rebleeding, shunt dysfunction and 1-year overall survival.[32] In our study, there were no significant differences in overall survival between the <8 mm and 8 mm stent groups and the PPG reduction was similar between both groups (14.0±3.9 vs 12.9 ±5.3 mmHg, p=0.572). The overall symptom control rate of SPH was 96.0%, which was also similar to previous studies.[7,14] Compared to variceal bleeding and ascites, portal hypertensive gastropathy and enteropathy are easily overlooked. The symptoms of PHE are often atypical and can present as abdominal pain, diarrhea, and poor appetite, which affect the general condition of patients and subsequent therapy.[33] TIPS can alleviate portal hypertension and is one

of the most effective options for treating PHE.[34,35] It can also serve as rescue therapy in patients with severe PHE bleeding. In this study, all patients with enteropathy achieved either complete or partial remission in this study.

PVTT can cause stenosis or occlusion of the portal vein, making it challenging to puncture the portal branch in some cases. However, the technical success rate in this study was 100%, which is higher than previous reports.[7,14,36] This is partly due to the assistance of the hepatic arterial localizer and the 3D reconstruction of CECT before the TIPS procedure. For patients with PVTT, it is possible that there would be no blood return even if the puncture needle successfully entered the portal vein. Before the portal vein puncture, we performed indirect portography and positioned the tip of the microcatheter at the predetermined intra-hepatic arterial site based on CECT. We then used the microcatheter to precisely locate targeted portal vein entry site. This technique improved the success rate of TIPS procedure.

Rescue TIPS can effectively and rapidly downstage tumors by controlling complications of esophageal variceal bleeding and refractory peritoneal effusion. This improves the patient's general condition and liver function,[10] creating opportunities for advanced HCC patients to undergo further sequential anti-tumor treatments. For advanced HCC, systemic therapies such as sorafenib, lenvatinib or atezolizumab-bevacizumab are recommended as the first-line treatments.[37] CARES-310 indicated that camrelizumab plus rivoceranib showed a statistically significant and clinically meaningful benefit in progression-free survival (PFS, 5.6 months vs 3.7 months) and overall survival (22.1 months vs 15.2 months) compared with sorafenib for patients with unresectable hepatocellular carcinoma.[38] CHANCE001[39] and CHANCE2201[40] respectively showed that TACE plus immune checkpoint inhibitors (ICIs) and molecular target treatment (MTT) could significantly improve PFS, OS and objective response rate (ORR) compared to either TACE or systemic monotherapy alone, which also demonstrated an acceptable safety profile. Radiotherapy plus ICIs and MTT also provided favorable treatment responses and survival outcomes, along with manageable adverse events (AEs) in HCC patients with PVTT.[41,42]

This study has some limitations. First, this was a retrospective single-center study and there might be selection bias. Second, this was a single-arm study and we could not compare the outcomes of TIPS plus sequential therapy versus traditional therapy for advanced HCC patients with PVTT-related SPH. Third, the study did not provide a comparison with TIPS using dedicated stent-grafts. Prospective comparative trials were required to determine which stents are most suitable Fourth, only 25 patients were included in this study, and a larger number of cases are necessary for survival analysis in future research.

Conclusion

In conclusion, FCS-TIPS significantly reduced portal pressure and relieved SPH, and did not affect stent patency or increase the risk of extrahepatic metastasis, serving as a bridging therapy for advanced HCC patients with PVTT-related severe SPH. Further studies are needed to determine which type of stent is most suitable for PVTT-related SPH, as well as to identify the patients who would benefit from TIPS treatment.

Ethics Approval and Informed Consent

This study was approved by the Institutional Review Board and Ethics Committee of Peking University First Hospital. To preserve patient privacy and data confidentiality, patient data have been de-identified before analysis. All analyses in this retrospective study were performed based on the data from anonymized patients. Since the study was a retrospective study, the need for informed consent was waived, and all methods were performed in accordance with the Declaration of Helsinki.

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Disclosure

The authors report no conflicts of interest in this work.

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