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ORIGINAL ARTICLE

Safety and Efficacy of Transjugular Intrahepatic Portosystemic Shunt for Non-tumoral Cirrhotic Portal Vein Thrombosis Not Responding to Anticoagulation Therapy

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Abstract

Objectives To evaluate the feasibility, safety, and efficacy of add-on transjugular–intrahepatic–portosystemic shunt (TIPS) for portal vein recanalization (PVR) in cirrhotic patients with non-tumoral chronic portal vein thrombosis (PVT) after 6 months of monitored anticoagulation therapy (ACT).

Methods We conducted a retrospective search of the hospital database for patients who underwent TIPS for persistent PVT despite 6 months of ACT (January 2011 to August 2021). These patients were compared to control group (ACT group; no TIPS but continued on ACT). Post-TIPS periodic assessment was done to look for clinical outcome, PVR (using contrast-enhanced CT scan), and complications.

Results A total of 90 patients were analyzed. Thirty-six patients in TIPS group and 54 patients in ACT group. TIPS was successfully performed in all patients. TIPS group showed complete recanalization of portal vein in 77.8%, partial recanalization in 16.7%, and stable thrombus in 5.5% of the patients. TIPS thrombosis was seen in 3 patients, all underwent successful endovascular thrombolysis. Seven patients developed post-TIPS hepatic encephalopathy and were managed conservatively. In contrast, no patient in ACT group achieved PVR on 12-month follow-up. After propensity score matching, patients in TIPS group showed significantly lower incidence of variceal re-bleeding (22.2% vs. 77.8%, $p=0.03$) and refractory ascites (11.1% vs. 51.9%, $p<0.01$) with significantly better 12-month survival as compared to ACT group (88.9% vs. 69.4%, $p=0.04$).

Conclusion TIPS in cirrhotic patients with PVT result in superior recanalization rates, better control of ascites, and variceal re-bleeding resulting in better survival. TIPS may be considered a preferred therapy after anticoagulation failure.

Clinical Impact TIPS is associated with good technical and clinical success in patients of cirrhosis with PVT and should be considered in patients not responding to ACT.

Keywords Portal vein thrombosis · TIPS · Portal vein recanalization · Portal hypertension · Cirrhosis

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Introduction

Portal vein thrombosis (PVT) is seen in about 10–25% of cirrhosis patients [1]. Slow flow in portal vein and overall pro-thrombotic state in these patients hypothesized to be the main contributing factors [2, 3]. The natural history and clinical outcome of PVT are highly variable, dependent upon timing, size, extent, and degree of the thrombotic occlusion [4]. It is unclear whether PVT is the causal factor or the result of the severe liver disease; however, many studies showed that its prevalence is more in patients with advanced disease and is associated with poor outcomes [5]. In addition to worsening portal hypertension-related complications, progression of PVT into mesenteric vein may lead to life-threatening intestinal ischemia. PVT also associated with poor post-transplant outcomes and it might even contraindicate transplantation, especially when the thrombus extends to the spleno-mesenteric confluence [6]. Current clinical guidelines recommend anticoagulants like low molecular weight heparin or vitamin K antagonist anticoagulation in cirrhotic patients with symptomatic acute PVT, and data are sparse on management of asymptomatic and chronic PVT and need to be determined on a case-by-case basis [7]. Anticoagulant therapy had shown to be effective in PVT by several studies [8–11]. A recent meta-analysis showed that anticoagulation therapy (ACT) would result in higher rates of PVT recanalization compared to no treatment (71% vs. 42%, respectively; $p < 0.001$) [12]. LMWH had shown slightly better efficacy compared to warfarin. Lately there is growing interest on DOAC in PVT due to the advantage of no monitoring requirement [13–15]. Studies show that DOACs in PVT have similar efficacy and side effect profile compared to VKA [16]. Transjugular intrahepatic portosystemic shunt (TIPS) has historically been contraindicated in patients with PVT [17]. However, since the first reports in early 1990s [18], multiple studies have shown that TIPS can be successfully performed in patients with PVT. Now with the improvements in technique and expertise it is emerging as an indication [3, 19, 20]. The recent Baveno-VII guidelines also recommend TIPS placement in patients with PVT who fail to recanalize on anticoagulation, especially in patients listed for liver transplantation [19]. In addition to portal vein recanalization, TIPS would also reduce the portal pressures and in turn reduce the complications of portal hypertension. This retrospective study aims to evaluate technical feasibility of TIPS in PVT and compare portal vein recanalization rates and clinical outcomes of TIPS in 12-month follow-up, with a control group who were continued on anticoagulation.

Materials and Methods

Patient Selection

A retrospective search of the hospital database was conducted for patients with cirrhosis who underwent TIPS for PVT not responding to 6-month ACT alone, from January 2011 to August 2021. The workflow of the study is shown in Fig. 1. Severity of PVT was graded as per the Sarin classification [21]. ACT was considered as failed, if it failed to recanalize the PV after 6 months of treatment or if the patient developed any of complications of PVT (variceal bleed, gross ascites, or mesenteric ischemia) during treatment. Patients who were continued on anticoagulants even after failed 6-month ACT during same time period were included as controls. Patients with incomplete data and who lost to follow-up in 12-month follow-up period were excluded. Patients with no visible intrahepatic portal radicals

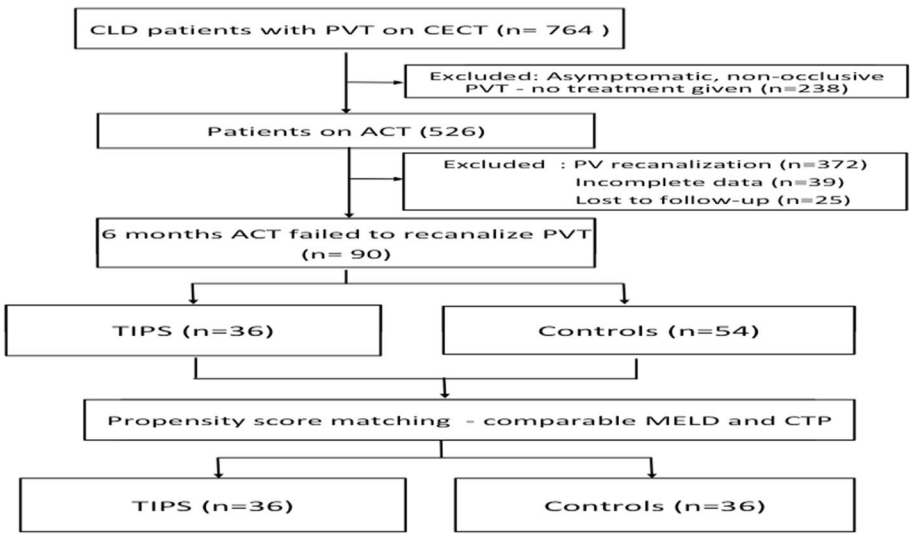

Fig. 1 Flowchart showing workflow of the study

on initial USG were also excluded as it is a necessary prerequisite for TIPS placement.

TIPS Procedure

TIPS was performed under general anesthesia and antibiotic prophylaxis. All these procedures were performed by a single, well-trained operator (A.M.). After securing the standard transjugular access and placing the sheath, right hepatic vein was cannulated from IVC using 5F MPA catheter and hydrophilic j-tip guidewire. The intrahepatic portal branch was punctured under ultrasound guidance, using a 0.038 in. trocar stylet of Rosch–Uchida transjugular liver access set (RUPS set, Cook Medical). After advancing the guidewire into portal system, recanalization was performed with balloon inflation and Urokinase injection. Urokinase was used in all TIPS patients. The dose was variable between 25,000 and 100,000 U based on extent of thrombus.

Once the liver parenchymal tract is dilated with balloon (8 mm or 10 mm), a self-expandable covered stent (Fluency Plus, BD) followed by a self-expandable uncovered stent (Wallstent, Boston Scientific) was deployed to drive the portal flow to the inferior vena cava. This allowed pressing the clots against the wall and maintain the portal vein patency. All patients received oral ACT with warfarin during 12-month post-TIPS follow-up period maintaining INR between 2 and 2.5. Pre-procedural images during TIPS and follow-up images of an example case are shown in Fig. 2.

Follow-up

Post-procedural portal vein recanalization was assessed on both Ultrasound and contrast-enhanced CT at 6 months and 12 months. Complete recanalization was defined as complete resolution of thrombus in follow-up imaging. Decrease in portal vein thrombus by $\geq 50\%$ was considered partial recanalization. Increase in thrombus by $\geq 50\%$ was considered progressive thrombosis. Along with these liver function tests, Child–Pugh and MELD scores were also documented at these intervals.

Diagnosis, Definitions, and End Points

Acute thrombus was defined as thrombus detected first time in previously patent PV, hyperdense thrombus on non-contrast CT, absent or limited collateral circulation, and PV

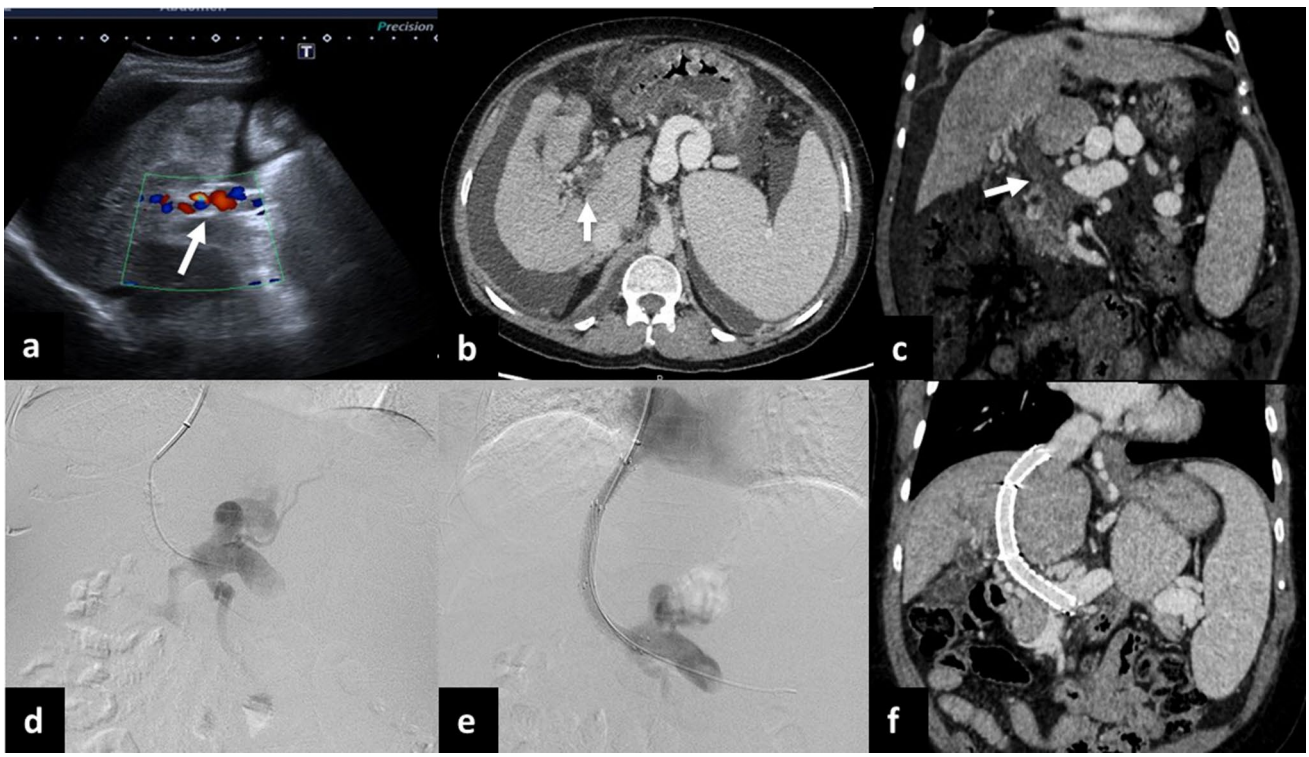

Fig. 2 Color Doppler image (**a**) showing no color flow in the portal vein and multiple prominent peri-portal collaterals (white arrow). Contrast-enhanced CT—axial image (**b**) and coronal image (**c**) showing hypodense thrombus (white arrow) in portal vein lumen reaching up to porto-mesenteric confluence. Digital subtraction angiogram image (**d**) showing non-opacification of portal vein with dilated left gastric and inferior mesenteric veins. TIPS stent venogram (**e**) shows normal wall-to-wall flow with no filling defects. Follow-up abdominal CT venous phase image (**f**) showing TIPS stent in full profile with wall-to-wall contrast opacification

expansion at the site of occlusion. A non-hyperdense thrombus, documented thrombus for more than 6 months or case with portal cavernoma were considered chronic thrombosis. ACT was considered as failed, if it failed to achieve partial or complete recanalization of PV after 6 months of treatment or if the patient developed any of complications of PVT (variceal bleed, gross ascites, or mesenteric ischemia) during treatment. In the absence of standard definition of "anticoagulation failure" in this context, we also included patients who developed variceal bleed or gross ascites during the course of ACT were also considered as "anticoagulation failure." Thrombosis was considered to be occlusive when blood flow within the PV was absent or thrombus involved more than 90% of the vessel. On follow-up imaging thrombus was defined using the following terminology: (a) Complete recanalization—complete resolution of thrombus. (b) Partial recanalization—decrease in portal vein thrombus by $\geq 50\%$. (c) Progressive thrombus—(i) Increase in thrombus by $\geq 50\%$ or (ii) extension of thrombus to unaffected segments of spleno-porto-mesenteric axis. Technical success of TIPS was defined as successful placement of TIPS stent. Hemodynamic success was defined as post-TIPS reduction in portal pressure gradient to below 12 mmHg or at least 50% reduction from pre-TIPS value. Clinical success of TIPS was defined as resolution of clinical indication (variceal bleed or ascites) for which the procedure was performed. Refractory ascites was defined as ascites that does not recede or that recurs shortly after therapeutic paracentesis, despite sodium restriction and diuretic treatment. The primary outcome was resolution of thrombus. The secondary outcomes include procedure-related complications, complications of portal hypertension, changes in laboratory parameters, and survival.

ACT Group

Patients with failed ACT who did not undergo TIPS in the same study period were included as control group. These patients continued to receive ACT in the follow-up period. These patients were followed up for 12 months for portal vein recanalization, complications of portal hypertension, and survival.

Statistical Analysis

Data are presented as frequencies, mean ± SD as appropriate. Qualitative variables were compared using the χ^2 test or Fisher's exact test, and quantitative variables were compared using Student's *t* test or Mann–Whitney *U* test. The propensity score matching between TIPS and ACT groups was adjusted for age, MELD score, PVT grade, and extent. Survival curves were calculated using Kaplan–Meier method and compared using log-rank test. Nonparametric Wilcoxon signed-rank test was used to compare paired before and after outcomes. Univariate Cox regression analysis was used to assess the influence of various laboratory values on patient survival outcomes. A p value < 0.05 was considered statistically significant. Statistical analysis was performed using SPSS 21.0.

Results

A total of 764 patients with cirrhosis diagnosed with non-tumoral PVT on contrast-enhanced CT abdomen over last 10 years (January 2011 to August 2021). Out of this, 238 patients had asymptomatic, non-occlusive thrombus. These patients were excluded from the analysis and they did not receive ACT. In remaining 526 patients, 372 (70.7%) showed complete recanalization with ACT, 39 patients had incomplete data, and 25 patients lost to follow-up. All these patients were also excluded. Remaining 90 patients were analyzed, of which 36 underwent TIPS after 6 months of ACT (TIPS group, cases) and 54 patients did not undergo TIPS and continued on ACT (ACT group, controls). Four patients, who were referred for TIPS showed complete non-visibility of intrahepatic portal radicals on ultrasound were denied TIPS placement as it is technically not feasible. These patients were included in ACT group. One patient had no intrahepatic portal radicals, but we could successfully place TIPS stent through a dominant portal collateral which had intrahepatic course.

TIPS vs. ACT Group: Baseline Characteristics

The baseline characteristics of TIPS group and ACT group are shown in Table 1. The mean age of TIPS group was 54.9 ± 8.1 years and of ACT group was 49.2 ± 6.2 ($p < 0.01$). NASH and Alcoholic liver diseases were the most common causes of cirrhosis in both the groups. In TIPS group, 27 patients had refractory ascites and 9 patients had variceal bleed as TIPS indication. Pre-procedural Child–Pugh Class A 16.6% (6/36), Class B 66.8% (24/36), and Class C 16.6% (6/36). In ACT group, 17 patients had variceal bleed and 37 patients had refractory ascites, and Child–Pugh Class distribution was as follows: Class A 20.4% (11/54), Class B 53.7% (29/54), and Class C 25.9% (14/54).

TIPS vs. ACT Group: PVT Characteristics

Portal vein thrombus in both groups was classified as per Sarin classification. In TIPS group, thrombus was seen: only in PV in 14 patients (38.9%), PV + SMV in 10 (27.8%), PV + SV in 5 (13.9%), and PV + SMV + SV in 7 patients (19.4%). Occlusive thrombus was seen in 12 (33.3%). Acute thrombus was seen in 5 (13.9%) and chronic thrombus was

Table 1 Baseline characteristics of participants

Characteristic	TIPS group	ACT group	*p*-value
Total number (*n*)	36	54	–
Age (years)	54.9 ± 8.1	49.2 ± 6.2	< 0.01
Sex ratio (M/F)	22/14	36/18	–
Cirrhosis etiology			
NASH	10 (36%)	16 (29.6%)	0.45
Alcohol related	9 (25%)	12 (22.2%)	
HBV	4 (11.12%)	6 (11.1%)	
HCV	3 (8.3%)	5 (9.3%)	
Autoimmune hepatitis	4 (11.12%)	8 (14.8%)	
NCPF	4 (11.2%)	3 (5.6%)	
Cryptogenic	2 (5.5%)	4 (7.4%)	
Child class			
A	6 (16.6%)	11 (20.4%)	0.23
B	24 (66.8%)	29 (53.7%)	
C	6 (16.6%)	14 (25.9%)	
MELD score (mean ± SD)	12.5 ± 3.3	13.3 ± 3.9	0.31
Portal vein thrombus classification (Sarin et al.)			
Grade of PVT			
1	4 (11.1%)	5 (9.3%)	0.12
2A	4 (11.1%)	10 (18.5%)	
2B	6 (16.7%)	6 (11.1%)	
3	22 (61.1%)	33 (61.1%)	
Extent			0.22
PV only	14 (38.9%)	21 (38.9%)	
PV + SMV only	10 (27.8%)	10 (18.5%)	
PV + SV only	5 (13.9%)	14 (25.9%)	
PV + SMV + SV	7 (19.4%)	9 (16.7%)	
Lumen occlusion			
Occlusive	12 (33.3%)	21 (38.9%)	
Non-occlusive	24 (66.7%)	33 (61.1%)	
Duration			
Acute	5 (13.9%)	0 (0%)	
Chronic	31 (86.1%)	54 (100%)	

ACT anticoagulant therapy, *MELD* Model for End-stage liver disease, *NASH* nonalcoholic steato-hepatitis, *PV* portal vein, *PVT* portal vein thrombosis, *SMV* superior mesenteric vein, *SV* splenic vein

seen in 31 patients (86.1%). Diagnosis of Acute PVT in 5 patients was made at the start of ACT. All of these patients had failed to achieve recanalization after at least 6 month of ACT. The median time between the PVT diagnosis and TIPS placement was 7.2 months.

In ACT group, thrombus was seen: only in PV in 21 patients (38.9%), PV + SMV in 10 (18.5%), PV + SV in 14 (25.9%), and PV + SMV + SV in 9 patients (16.7%). Occlusive thrombus was seen in 21 (38.9%). All patients in ACT group were of chronic PVT (100%). Seven patients in TIPS group and 5 patients in ACT group showed portal cavernoma formation. Comparison of PVT grades in both groups is depicted in Table 1.

Table 2 TIPS indications, success rates, recanalization rates, and complications

Indication of TIPS	
Refractory ascites	27/36 (75%)
Variceal bleed	9/36 (25%)
Success rates	
Technical success*	36/36 (100%)
Hemodynamic success¶	36/36 (100%)
Clinical success$^{\Omega}$	
Refractory ascites	24/27 (88.9%)
Variceal bleed	7/9 (77.8%)
Portal vein recanalization rates	
Complete recanalization	28/36 (77.8%)
Partial recanalization	6/36 (16.7%)
Stable thrombus	2/36 (5.5%)
Complications	
Early complications	1/36 (2.7%)
Acute stent thrombosis	2/36 (5.4%)
Bleeding	
Late complications	
Stent thrombosis (partial)	2/36 (5.5%)
Overt hepatic encephalopathy	7/36 (19.4%)

*Technical success**—successful placement of TIPS stent; *Hemodynamic success*¶—post-TIPS reduction in portal pressure gradient to below 12 mmHg or at least 50% reduction from pre-TIPS value; *Clinical success*$^{\Omega}$—resolution of clinical indication (variceal bleed or ascites) for which the procedure was performed

Recanalization Rates

Out of 36 patients, 28 patients (77.8%) showed complete recanalization of PV and 6 patients (16.7%) showed partial recanalization on follow-up. Two patients (5.5%) with partial PV thrombosis showed no significant difference in thrombus size and extent on follow-up. PVT with SMV involvement significantly reduced the complete recanalization rates compared to PVT without SMV involvement (58.8% vs. 89.5%, $p = 0.03$). All acute PVT cases ($n = 5$) showed complete recanalization with TIPS. All cases of partial recanalization or stable thrombus were of chronic PVT. Grade of thrombosis in portal vein and splenic vein involvement shown to be poor predictors of portal vein recanalization ($p = 0.31$ and 0.27, respectively). TIPS success rates, post-procedure recanalization rates, and complications are shown in Table 2.

None of the patients in ACT group showed portal vein recanalization on follow-up. In these patients, despite further 6 months of ACT, there was no partial or complete PVR and most had stable thrombus.

Technical and Clinical Success Rates

TIPS stent was successfully placed in all 36 attempted cases with 100% technical success rate. In TIPS group, 2 of 9 patients (22.2%) suffered episodes of variceal bleed, while 3 of 27 patients (11.1%) suffered refractory ascites requiring paracentesis in 12-month post-TIPS follow-up. In ACT group, 11 out of 17 patients (64.7%) showed variceal re-bleeding in the follow-up period. 17 out of 37 patients (45.9%) suffered persistent refractory ascites requiring paracentesis on follow-up. There was significant difference between TIPS and ACT groups in rates of variceal re-bleeding (22.2% vs. 64.7%, respectively, $p=0.04$) and refractory ascites (11.1% vs. 45.9%, respectively, $p=0.02$).

Hemodynamic Changes

There was significant difference ($p<0.001$) between pre-procedure portosystemic pressure gradient (29.8 ± 6.9 mmHg) as compared to post-procedure values (9.8 ± 4.4 mmHg). Target post-TIPS pressure gradient was achieved in all patients (100% hemodynamic success). Pressure gradients of patients in ACT group were not obtained.

Complications

In TIPS group, total 3 patients (8.2%) showed in-stent thrombosis in follow-up period. One patient developed complete stent thrombosis on day 2 of the procedure. Two other patients developed partial stent thrombosis during 12-month follow-up which were managed with endovascular thrombolysis. Seven patients (19.4%) experienced episodes of overt hepatic encephalopathy in the follow-up period which were managed conservatively. In patients developing HE, mean post-TIPS pressure gradient was 8.1 ± 3.1 mm vs. 11.5 ± 2.7 mm in non-HE group. However, it was not statistically significant ($p=0.18$). Post-TIPS 12-month portal vein patency rate was 91.6% (33 of 36). No anticoagulation-related bleeding complications were seen in ACT group.

Survival

12-month survival rate in TIPS group was 88.9%. Four patients died in the follow-up period. The causes of mortality were uncontrolled massive variceal bleed (day 2 of TIPS), acute renal failure (7 months), acute liver failure (8 months), and septic shock secondary to portal biliopathy related cholangitis (9 months), respectively. Although all these patients had relatively high MELD scores compared to rest of the patients (mean, 16.2 vs. 12.1), the difference was not statistically significant in predicting 12 month mortality ($p=0.12$). No statistically significant change noted in serum albumin, bilirubin, creatinine, PT/INR, and MELD scores following TIPS at 6-month or 12-month follow-up from baseline (Table 3). These parameters found to be poor predictors of 12 months mortality on univariate analysis. The difference in survival rates was not significant between TIPS and ACT groups (88.9% vs. 74.1%, respectively, $p=0.09$).

In ACT group, 14 patients (25.9% mortality) died in 12-month follow-up period. Out of 14, 7 patients died due to uncontrollable variceal bleed, 5 patients due to acute liver failure, and 2 patients died due to sepsis-related multi-organ failure.

TIPS Group vs. ACT Group After Propensity Score Matching

After propensity score matching for MELD and Child–Pugh score, 36 patients in TIPS group were compared with 36 patients in ACT group. All patients in ACT group showed stable thrombus in 12-month follow-up, whereas all TIPS group patients showed complete recanalization. There was significant difference between TIPS group and ACT group in rates of variceal re-bleeding (22.2% vs. 77.8%, respectively, $p=0.03$) and refractory ascites (11.1% vs. 51.9%, respectively, $p<0.01$). These comparisons are shown in bar chart in Fig. 3. Survival rates were better in TIPS group compared to ACT group (88.9% vs. 69.4%, $p=0.04$). These outcome comparisons are depicted in Table 4. Kaplan–Meier curves comparing survival in both groups are shown in Fig. 4.

Table 3 Blood parameters before the TIPS and on follow-up

Parameter	Pre-TIPS value	Follow-up	
		6 months	1 year
MELD score (mean ± SD)	12.5 ± 3.3	13.2 ± 2.2 ($p=0.1$)	13.4 ± 2.1 ($p=0.3$)
Serum albumin (g/dl) (mean ± SD)	2.8 ± 0.4	2.9 ± 0.3 ($p=0.2$)	2.9 ± 0.4 ($p=0.2$)
Serum creatinine (mg/dl) (mean ± SD)	0.8 ± 0.3	0.9 ± 0.3 ($p=0.8$)	0.8 ± 0.2 ($p=0.7$)
Bilirubin (mg/dl) (mean ± SD)	1.8 ± 1.1	1.7 ± 0.8 ($p=0.2$)	2 ± 0.7 ($p=0.2$)
INR (mean ± SD)	1.9 ± 0.2	2.4 ± 0.2 ($p=0.3$)	2.6 ± 0.3 ($p=0.3$)

INR international normalized ratio, *MELD* model for end-stage liver disease

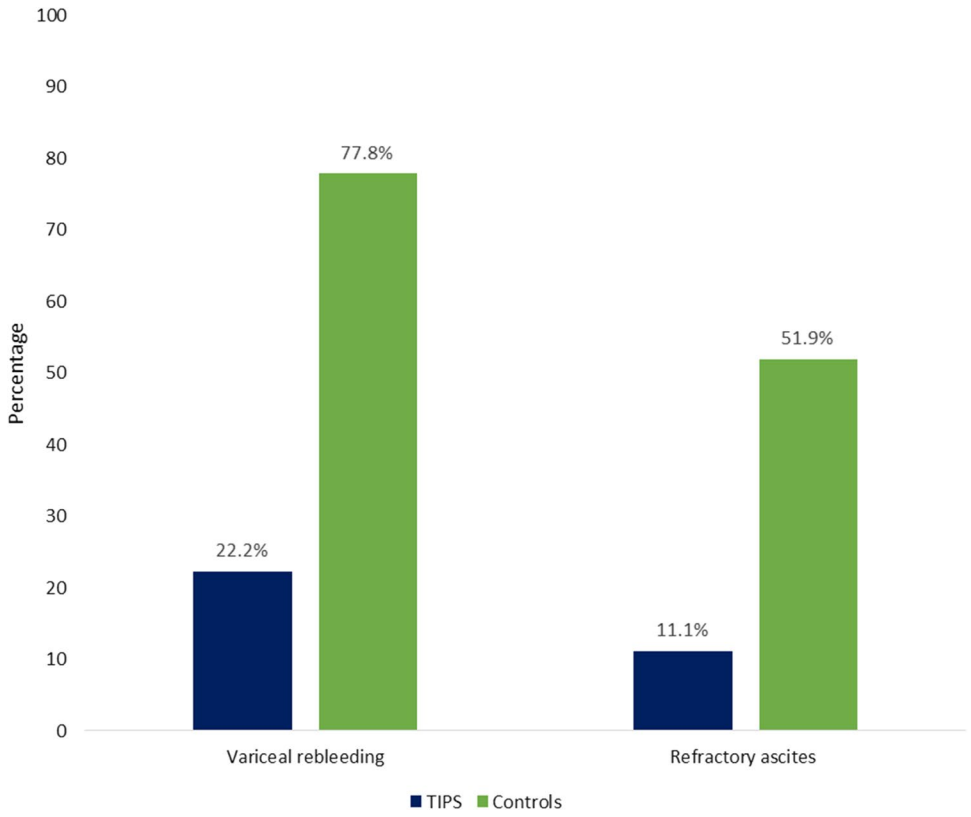

Fig. 3 Bar diagram showing comparison of variceal re-bleeding and refractory ascites rates between TIPS and control groups after propensity score matching

Table 4 TIPS vs. control group after propensity score matching

Parameter	TIPS group ($n=36$)	ACT group ($n=36$)	p
Age	54.9 ± 8.1	52.2 ± 6.2	0.12
CTP score	8.6 ± 1.2	8.2 ± 0.8	0.10
MELD score	13.2 ± 2.1	13.4 ± 1.9	0.67
Complications of PVT			
Variceal bleed	9	9	–
Ascites	27	27	
Outcomes			
PV recanalization rates	100%	0%	< 0.01
Clinical failure			
Variceal re-bleed	2/9 (22.2%)	7/9 (77.8%)	0.03
Persistent refractory ascites	3/27 (11.1%)	14/27 (51.9%)	< 0.01
Survival	32/36 (88.9%)	25/36 (69.4%)	0.04

CTP score Child–Turcotte–Pugh score, *MELD* model for end-stage liver disease, *PV* portal vein, *PVT* portal vein thrombosis

Discussion

Our study showed that TIPS is a viable therapeutic option in patients with PVT after failed ACT and showed excellent technical success rate (36/36, 100%) and very good recanalization rates (34/36, 94.4%). TIPS also showed good clinical success rate in controlling portal hypertension-related complications like variceal bleed and refractory ascites in these patients (77.8% and 88.9%, respectively). After propensity score matching with ACT group, patients in TIPS group showed significantly lower incidence of variceal re-bleeding (22.2% vs. 77.8%, $p=0.03$) and refractory ascites (11.1% vs. 51.9%, $p<0.01$). Survival rates were better in TIPS group compared to ACT group (88.9% vs. 69.4%, $p=0.04$).

Our results are comparable to previous studies which evaluated the feasibility and technical success of TIPS in

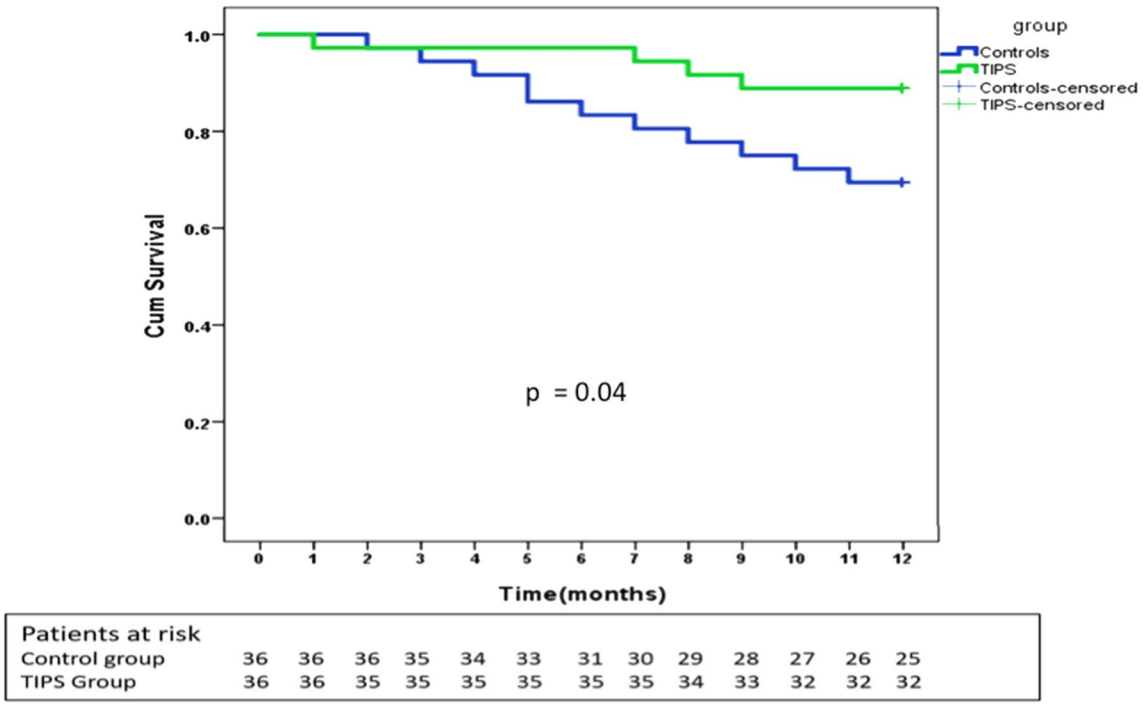

Fig. 4 Kaplan–Meier survival curves of TIPS and control groups after propensity score weighting demonstrates statistical trend toward improved survival in the TIPS group ($p = 0.04$)

PVT. Most of the previous studies are retrospective in nature with portal hypertension-related complications like variceal bleed and ascites being the most common indications for TIPS. Transplant candidates with PVT were second most common indication as portal vein recanalization is associated with better post-transplant outcomes. In a retrospective study by Bauer et al. [22] ($n = 9$) showed 100% technical success rate and 85.7% portal vein patency rate with TIPS in patients with PVT on transplant list. Four of these patients had cavernoma formation on pre-procedure imaging. Early retrospective studies [23–25] reported a variable technical success rate of 75–100% based on whether an additional trans-hepatic and trans-splenic routes were employed. Chen et al. [26] demonstrated 77.7% technical success using percutaneous trans-hepatic balloon-assisted TIPS placement in patients with chronic totally occlusive PVT and symptomatic portal hypertension. An RCT by Luo et al. [27] compared efficacy of TIPS and endoscopic band ligation plus propranolol in prevention of recurrent esophageal variceal bleeding in patients with advanced cirrhosis with PVT. In this trial TIPS group showed higher probability of remaining free of recurrent variceal bleeding (77.8% vs. 42.9%, $p = 0.002$) and higher PV recanalization rates (64.9% vs. 19.4%). Similar findings were reported by another RCT by Lv et al. [28]. Rosenqvist et al. [29] performed trans-hepatic thrombolysis followed by TIPS placement in patients with PVT. They had reported 100% technical success in acute thrombosis and 50% success in chronic PVT with this technique. TIPS placement by Lakhoo and Gaba [30] had resulted in complete resolution in 58%, partial clot reduction in 33%, and stable clot in 8% of the patients with no cases of clot progression. Qi et al. [31] found that a successful TIPS in these patients not only reduces re-bleeding rates but also significantly improves survival, when compared to failed cases ($p < 0.04$). Serum albumin found to be the only independent predictor of survival in both of these groups. Zhao et al. [32] evaluated the relationship between survival and vascular patency immediately after TIPS. The overall survival time of patients with completely patent PV was significantly better compared to survival in incomplete patent PV immediately after TIPS (57.1 ± 0.8 vs. 39.1 ± 2.6 months, respectively, $p < 0.001$). In an RCT, Wang et al. [33] had concluded that post-TIPS anticoagulants may not be necessary as portal vein recanalization rates, stent dysfunction, re-bleeding rates, and survival were similar in patient with and without ACT. Thornburg et al. [34] reported 98% technical success and 92% portal vein patency rate in transplant candidates at a median follow-up of 19.2 months. Out of 24 patients who underwent transplantation, 23 patients (96%) received an end-to-end portal vein anastomosis and there were no cases post-transplant PVT recurrence. Klinger et al. [35] had performed TIPS in 17 patients with acute non-cirrhotic, non-malignant PVT, where there is persistent hemodynamically significant PVT (PSPG > 12 mmHg) after transjugular

thrombolysis. The reported technical success of TIPS was 94.1% and 2-year portal vein patency rate was 88.2% in these patients. Jiang et al. [36] compared the outcomes of transcatheter superior mesenteric artery (SMA) urokinase infusion and transjugular intrahepatic portosystemic shunt (TIPS) for acute PVT in cirrhosis. They found that thrombosis was significantly reduced in both groups ($p < 0.001$), and there was no significant difference between them ($p = 0.304$). Lv et al. [37] prospectively evaluated an individualized management algorithm to treat PVT in cirrhosis using no treatment, anticoagulation, and TIPS based on liver disease stage and degree and extent of thrombus. This approach achieved 81.3% partial or complete recanalization rates with low portal hypertension-related complications.

In our study the patient who developed shunt block on day 2 had a history of splenectomy 2 years back. Splenectomy might have resulted in reduced portal flow and contributed to the shunt thrombosis as suggested by Dong et al. [38].

A recent meta-analysis of 13 studies by Rodrigues et al. [39] showed the cumulative TIPS technical success rate of 95%, 1-year recanalization rate of 79%, 1-year shunt patency rates of 84%, and 1-year survival rate of 89%. Cavernoma formation, thrombosis of superior mesenteric vein, and use of uncovered stents were associated with poor recanalization. Another recent meta-analysis by Valentin et al. [40] also showed similar results. Davis et al. [41] conducted a meta-analysis comparing TIPS and anticoagulation in PVT. They found that both groups had high rates of recanalization; however, patients with anticoagulation showed better survival rates which was not seen in TIPS group. Based on this they have suggested that benefits of anticoagulation extend beyond recanalization and it may potentially modify the course of chronic liver disease.

In patients where portal vein cannulation is difficult via transjugular route, trans-hepatic, trans-splenic routes, and even trans-superior and -inferior mesenteric vein routes were described in the literature [42, 43]. Thrombolysis through SMA access followed by TIPS was also described for higher recanalization rates [44]. However, we did not employ these alternate methods.

In this study, TIPS is only considered as second-line therapy once PVT failed to recanalize after ACT. As almost 70% cirrhotic patients overall have PVT recanalization after ACT, these patients might have improved control of ascites and bleed. However, these patients were excluded from analysis in our study. TIPS indication was mainly refractory ascites and variceal bleeding as TIPS for PVT progression was not indicated in routine practice. We agree that there might be some bias in patient selection as this was a retrospective analysis as in the ACT group there were 17 patients with refractory ascites. Many patients despite having standard indication for TIPS like refractory ascites still do not received TIPS due to high cost of the procedure. Small sample size and relatively shorter follow-up period were other major limitations of our study. Due to retrospective nature, the study was more reflective of a real-world scenario and there was less homogeneity among patients in cirrhosis grade and other treatments of portal hypertension received in the follow-up period. Future prospective studies are needed to overcome these limitations and validate the results.

Conclusion

TIPS has very good technical success rate in patients of PVT with failed ACT. TIPS had resulted in better 12-month portal vein recanalization rates, decreased portal hypertension-related complications, and better survival compared to controls who were continued on ACT. Therefore, in patients with cirrhosis with PVT where ACT is ineffective, TIPS may be considered as second-line therapy. Patients who already developed symptoms of PVT, TIPS may be considered as first-line therapy for quicker portal vein recanalization and to prevent further progression of thrombus. Further randomized trials are needed with larger sample size to better define the roles of TIPS and anticoagulation in PVT.

Author's contribution AM contributed to conceptualization, methodology, reviewing, editing, and finalizing the manuscript. UKM contributed to data curation, data analysis, and preparation of 1st draft of the manuscript. AJ contributed to Patient enrolling, clinical management and methodology, data analysis, and finalizing the manuscript. AC contributed to patient enrolling, clinical management, and data analysis. YP contributed to imaging evaluation of patients and reviewing the manuscript. SKS contributed to supervising the research and reviewing and editing to reach the final version of manuscript.

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Declarations

Conflict of interest The authors declare that they have no conflicts of interest.

Consent for publication For this type of study, consent for publication is not required.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the Institutional and/or the National Research Committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

Informed consent This study has obtained IRB approval from (indicate the relevant board) and the need for informed consent was waived.

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