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REVIEW ARTICLE

Transjugular intrahepatic portosystemic shunt in the treatment of portal vein thrombosis: a critical review of literature

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Abstract Reports of successful transjugular intrahepatic portosystemic shunt (TIPS) surgery in patients with portal vein thrombosis (PVT) are considered anecdotal owing to the technical difficulty of the procedure and potential procedure-related complications. A literature review was undertaken to determine the feasibility and safety of TIPS in the treatment of PVT. All studies in which TIPS was attempted in patients with PVT were identified by searching through the PUBMED and MEDLINE databases. A total of 424 PVT patients undergoing TIPS were reported in 54 articles. The success rate of TIPS insertion was 67–100% in 19 case series. Further, 85 patients with portal cavernoma underwent successful TIPS insertions. Three therapeutic strategies of TIPS placement were used: (1) TIPS placement followed by portal vein recanalization via the shunt, (2) portal vein recanalization via percutaneous approaches followed by TIPS placement, and (3) TIPS insertion between a hepatic vein and a large collateral vessel without portal vein recanalization. Four approaches were used to access the portal vein: transjugular, transhepatic, transsplenic, and transmesenteric. Intra-abdominal hemorrhage secondary to hepatic capsule perforation was lethal in only three patients. No episode of pulmonary embolism was reported. Other procedure-related complications were reversible. The overall incidence of shunt dysfunction and hepatic encephalopathy was 8–33% and 0–50%, respectively. In conclusion, the reviewed studies uniformly support the feasibility and safety of TIPS for PVT even in the presence of portal cavernoma. Further, several major issues that remain unresolved are discussed.

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Keywords Transjugular intrahepatic portosystemic shunt · Portal vein thrombosis · Portal hypertension · Treatment

Abbreviations

AASLD	American Association for the Study of Liver Diseases
MPV	Main portal vein
PVT	Portal vein thrombosis
SMV	Superior mesenteric vein
TIPS	Transjugular intrahepatic portosystemic shunt

Introduction

Since the first transjugular intrahepatic portosystemic shunt (TIPS) surgery performed in a patient with continuous gastric variceal bleeding [1], the use of TIPS has progressively expanded [2]. The principal indications for TIPS include prevention of variceal rebleeding [3] and management of refractory ascites that requires repeated large-volume paracentesis [4]. On the basis of evidence from several recent case series [5, 6], the updated American Association for the Study of Liver Diseases (AASLD) practice guidelines on applications of TIPS recommend that TIPS surgery should be performed in patients with Budd–Chiari syndrome who fail to improve with anticoagulation [7]. More recently, particular attention has been paid to the early use of TIPS with covered stents as the first-line therapeutic modality in patients with acute variceal bleeding with Child-Pugh scores of class B or C [8]. However, because of the technical difficulty and potential procedure-related complications, TIPS surgery is still not widely recommended for the treatment of portal vein thrombosis (PVT) [2], and successful TIPS insertions in patients with PVT are regarded as anecdotal

reports [9]. The current practice guidelines and consensus on the management of PVT recommend that anticoagulation should be used in patients with acute PVT that is unrelated to cirrhosis [9, 10], given the relatively high recanalization rate reported in previous case series [11, 12]. However, the recommendation may be challenged by two recent studies. A prospective cohort study in Europe demonstrated that recanalization occurred in only one-third of patients receiving early anticoagulation for acute PVT [13]. In another large retrospective study conducted at the Mayo Clinic, the authors concluded that anticoagulation should be minimized in PVT patients with a history of gastrointestinal variceal bleeding [14]. Taken together, these findings suggest that the role of anticoagulation in the treatment of PVT is limited. Consequently, alternative therapies for PVT, including TIPS surgery, should be actively explored.

The theoretical benefit of TIPS for PVT is sizeable because TIPS can effectively smooth the portal vein by endovascular manipulation, and the TIPS-induced acceleration of the portal blood flow may prevent the recurrence and extension of thrombosis and its secondary complications [15, 16]; but only case reports or case series, rather than controlled studies on this topic, could be retrieved. Because of the limited data available, the comparative effectiveness of TIPS versus anticoagulation in the treatment of PVT could not be determined. In addition, a systematic review or meta-analysis was not feasible, given the heterogeneous patient population (with or without cirrhosis or malignancy), differing etiology of PVT, and the diverse indications for TIPS in the patients studied. Thus, the authors for the first time undertake a literature review to examine the feasibility and safety of TIPS in the treatment of PVT and to propose future research directions to address some issues that remain unresolved.

Methods

The PUBMED and MEDLINE (OVID) databases were searched for studies on TIPS. The reference lists of the included articles were also reviewed. The search items and eligibility criteria have been presented in "Appendix". The last search was performed on May 1, 2011. In this manner, 445 reports were retrieved. The initial eligibility assessment was performed via a review of the title and abstract of each publication. If a final decision was not reached after this review, the full text was considered.

Overview

Sixty-five full-text articles regarding the treatment of PVT by TIPS were identified. Eleven of these articles were non-English [17–27]. The remaining 54 English full-text articles in which a total of 424 patients with PVT underwent TIPS surgery were reviewed [28–81]. Of the 54 articles, 35 were case reports (<5 PVT-TIPS patients); and 19 were case series (≥5 PVT-TIPS patients) (Table 1, 2). The TIPS insertion success rate ranged from 67 to 100% in the 19 case series. Notably, TIPS surgery for PVT was found to have been feasible in many countries (Fig. 1). Of the 54 studies reviewed, 52% were performed in Europe, 30% in America, and 18% in Asia. Further, an increasing trend in the number of PVT patients undergoing TIPS surgery was identified (Fig. 2). This inspiring tendency is attributed to advances in TIPS techniques and a growing awareness that TIPS may represent an important alternative therapy for PVT, especially in patients with chronic PVT and symptomatic portal hypertension in whom anticoagulation or thrombolysis has failed or is contraindicated, or in whom percutaneous portal venous recanalization and thrombectomy to maintain portal venous patency have proven ineffective.

Therapeutic strategies

Three major therapeutic strategies of TIPS surgery are used for the treatment of PVT.

The first is to initially create a portosystemic shunt via a transjugular approach, and subsequently resolve portal venous occlusion via the shunt using a balloon catheter to dislodge thrombotic material or by using local thrombolysis [31, 63, 72, 80]. The major benefit of this strategy is that the creation of a portosystemic shunt provides a direct transjugular route for portal vein recanalization [31]. With this technique, the success rate of TIPS insertion can reach approximately 100%. However, not all patients with successful TIPS insertion achieve portal vein recanalization [63, 80]. This phenomenon is primarily due to the absence of adequate blood flow into the shunt as the occluded superior mesenteric vein (SMV) fails to be recanalized (Fig. 3). Therefore, the central issue with this technique is the identification of patients in whom portal vein recanalization will not be achieved and the avoidance of unnecessary TIPS insertions in such patients.

Luca et al. [80] for the first time concluded that thrombosis within a single vein, portal vein stenosis <25%, de novo diagnosis of PVT, and absence of gastroesophageal varices could independently predict a higher rate of portal vein recanalization after successful TIPS insertions. However, the clinical significance of these independent predictors is still a matter of discussion [82]. For example, in the aforementioned study, only 3% (2/70) of patients presented with portal cavernoma, and 44% (31/70) of patients presented with <50% of PVT. These inclusion

Table 1 Overview of case series

Authors ([ref.])	No. Pts	Period of enrollment	Age (years)	Sex (F/M)	Underlying diseases	Indications for TIPS	Child-Pugh A/B/C	Extension of PVT	No. CTPV	Degree of PVT	TIPS insertion success rate	Approach to access portal vein
Luca et al. ([80])	70	2003.1–2010.2	Mean ± SE (range): 55 ± 8 (34–70)	23/47	Liver cirrhosis	RVB (48); RA or refractory hydrothorax (18); PVT alone (4)	17/42/11	MPV (67); SMV (55); SV (18)	2	>50% (39); < 50% (31)	100% (70/70)	Transjugular
Han et al. ([78])	57	2001.12–2008.9	Mean ± SE: 51 ± 1.6	20/37	Liver cirrhosis	RVB (56); RA (1)	25/26/6	MPV (57); SMV (43); SV (45)	30	Partial[b] (35); complete (14); fibrotic cord (8)	75% (43/57)	Transjugular; transhepatic; transsplenic
Luo et al. ([79])	13	2006.4–2008.6	Mean (range): 48.9 (28–70)	5/8	Liver cirrhosis (8); no cirrhosis (5)	Variceal bleeding (7); abdominal pain and distension (6)	4/5/4	MPV (13); SMV (11); SV (4)	8	NA	100% (13/13)	Transjugular; transhepatic; transsplenic
Fanelli et al. ([77])	13	NA	Mean ± SD: 44.8 ± 13.5	4/9	MPN (7); PNH (1); oral contraceptives (1); hyperhomocysteinemia (2)	RVB (8); intestinal ischemia due to acute SMV thrombosis (2); high-risk varices in need of anticoagulation (2); RA(1)	NA	MPV (13); SMV (6); SV (4)	13	NA	77% (10/13)	Transjugular
Perarnau et al. ([76])	34	1990–2004	Mean ± SE: 55 ± 11	16/18	Liver cirrhosis: alcohol (17); hepatitis (12); other (5)	AVB (13); RVB (14); RA (5); others (2)	3/11/7 (13 unknown)	NA	19	Complete (34)	79% (29/34)	Transjugular
Liu et al. ([72])	26	NA	Range: (17–68)	NA	NA	Abdominal pain, fullness, anorexia	NA	NA	No	NA	100% (26/26)	Transjugular
Gazzera et al. ([67])	12	1992.3–2006.12	NA	N/A	Liver cirrhosis	NA	NA	NA	NA	Partial (12)	100% (12/12)	Transjugular
Semiz-Oysu et al. ([66])	10	NA	Mean (range): 39.6 (8–65)	2/8	NA	Gastrointestinal bleeding (6); gastrointestinal symptoms (3); ascites and thrombocytopenia (1)	NA	MPV (10); SMV (2); SV (2)	NA	Occlusive (10)	100% (10/10)	Transjugular; transhepatic; transsplenic
Bauer et al. ([63])	9	1999–2005.1	Median (range): 52 (26–61)	2/7	End-stage liver disease	To maintain portal vein patency alone (9); awaiting LT (8); unlisted LT (1)	NA	MPV (9); SMV (7); SV (4)	4	Partial (8); occluded (1)	100% (9/9)	Transjugular
Van Ha et al. ([61])	15	1995.12–2003.12	Mean (range): 53 (45–75)	2/13	Liver cirrhosis	Variceal bleeding (10); RA (4); refractory pleural effusion (1)	0/11/4	MPV (15); SMV (2)	4	Partial[b] (9); complete (4); unknown (2)	87% (13/15)	Transjugular; transhepatic
Senzolo et al. ([56])	28	1994.1–2005.6	Range: 17–65	8/20	Liver cirrhosis (13); protein C or S deficiency (2); PNH (1); infection (1); pancreatitis (1); sarcoidosis (1); increased factor VIII (1); factor V mutation (1); MPN (1); unknown (1)	Preoperative or awaiting LT (2); worsening ascites (1); variceal bleeding (15); RA (3); portal biliopathy (3); BCS (2); acute presentation of PVT (1)	NA	MPV (28); SMV (13); SV (8)	9	Partial (5); complete (23)	68% (19/28)	Transjugular

Table 1 continued

Authors ([ref.])	No. Pts	Period of enrollment	Age (years)	Sex (F/M)	Underlying diseases	Indications for TIPS	Child-Pugh A/B/C	Extension of PVT	No. CTPV	Degree of PVT	TIPS insertion success rate	Approach to access portal vein
Wallace et al. ([55])	6	2000.8–2002.5	NA	NA	Malignancy (6)	Complications of portal hypertension	NA	MPV (6);	2	NA	100% (6/6)	Transjugular
Bilbao et al. ([52])	6	1998.5–2003.4	Mean (range): 52 (32–73)	1/5	MPN (2); pancreatic carcinoma (3); protein C deficiency (1)	Abdominal pain (4); variceal bleeding (2)	NA	MPV (6); RPV (3); LPV (3); SMV (6); SV (5);	2	Complete (2); unknown (4)	100% (6/6)	Transjugular; transhepatic; transsplenic; transileocolic
Jiang et al. ([53])	14	1998.12–2001.5	Mean ± SD: 53.6 ± 12.7	1/13	End-stage HCC	RA (3); variceal bleeding (1); variceal bleeding and ascites (10)	0/0/14	MPV (14); RPV (11); LPV (4)	5	Partial (6); complete (8)[d]	71% (10/14)	Transjugular
Ganger et al. ([39])	11	1992.1–1997.11	Range: 28–77	N/A	HCC and cirrhosis (1); MPN (2); PNH (1); protein S deficiency (1); granulomatous disease (1); HBV (1); cryptogenic (2)	Ascites (6); gastrointestinal bleeding (7);	1/4/4 (2 unknown)	NA	NA	NA	82% (9/11)	Transjugular; transhepatic
Stein et al. ([40])	12[a]	1996.7–1998.6	NA	NA	NA	AVB (5); portal vein recanalization failed (7)	NA	NA	NA	NA	100% (12/12)	Transjugular; transhepatic
Walser et al. ([37])	18[c]	1993–1997	NA	NA	Advanced liver disease or hepatoma	RVB or RA	NA	NA	NA	NA	67% (12/18)	Transjugular; transhepatic
Blum et al. ([31])	7	1990.1–1994.3	Range: 39–61	3/4	Liver cirrhosis	RVB (5); AVB (2)	0/2/5	MPV (7); SMV (2); SV (2)	No	Complete (7)	100% (7/7)	Transjugular
Radosevich et al. ([28])	10	1990.6–1992.2	Range: 43–74	0/10	Liver cirrhosis (9); hepatoma (1)	RVB (10)	1/2/7	NA	NA	Partial (3); complete (7)	70% (7/10)	Transjugular; transhepatic

AVB active variceal bleeding uncontrolled by medical or endoscopic therapy, *BCS* Budd–Chiari syndrome, *CTPV* cavernous transformation of portal vein, *HBV* hepatitis B virus, *HCC* hepatocellular carcinoma, *LPV* left portal vein, *LT* liver transplantation, *M* male, *MPN* myeloproliferative neoplasm, *MPV* main portal vein, *NA* not available, *PNH* paroxysmal nocturnal hemoglobinuria, *PVT* portal vein thrombosis, *RA* refractory ascites that requires frequent large-volume paracentesis, *RPV* right portal vein, *RVB* recurrent variceal bleeding uncontrolled by medical or endoscopic therapy, *SD* standard deviation, *SE* standard error, *SMV* superior mesenteric vein, *SV* splenic vein, *TIPS* transjugular intrahepatic portoysystemic shunt

[a] A total of 21 patients were observed in the study by Stein et al., but nine of them received only portal vein reconstruction without TIPS. So 12 patients were recorded in this table

[b] Partial portal vein occlusion refers to > 50% of lumen occupancy

[c] A total of 20 patients were observed in the study by Walser et al., but two of them received only primary embolotherapy without TIPS. So 18 patients were recorded in this table

[d] The number of patients with complete and partial portal vein occlusion in the abstract is 8 and 6, respectively; but the number of patients with complete and partial portal vein occlusion in the table is 10 and 4, respectively

Table 2 Overview of case series

Authors ([Ref.])	Procedure-related complications	Shunt dysfunction	Encephalopathy	Survival
Luca et al. ([80])	Stent migration into the MPV (1)	1-, 2-year cumulative rate 38%, 85% for bare stents 21%, 29% for covered stents	1-, 2-year cumulative rate 27%, 32%	TIPS success group: 1-, 2-year cumulative survival rate: 89 and 81%
Han et al. (78)	Hepatic capsule perforation (2) 1 died of intraperitoneal bleeding 1 was rescued Bile duct puncture (1)	1-, 2-year cumulative rate 21%, 32% for bare stents.	1-, 2-year cumulative rate: 25%, 27%	TIPS success group: 1-, 5-year cumulative survival rate: 86%, 77% TIPS failure group: 1-, 5-year cumulative survival rate: 78%, 62%
Luo et al. ([79])	Intraperitoneal bleeding and death (1) Hematoma beneath the hepatic capsule (reversible) (1)	15% (2/13)	8% (1/13)	TIPS success group: Survival rate: 92% (12/13)
Fanelli et al. ([77])	Intraperitoneal bleeding (reversible) (1)	30% (3/10)	20% (2/10)	TIPS success group: Survival rate: 70% (7/10). 1 died of sepsis (6.3 months); 1 of ischemic stroke; 1 of neoplasm (9.3 months) TIPS failure group: Survival rate: 100% (3/3)
Perarnau et al. ([76])	Early thrombosis (3) Hemobilia (1) Digestive bleeding (1)	28% (8/29)	1-, 2-year cumulative rate: 27%, 27%	TIPS success group: 1-, 2-, 4-year cumulative survival rate: 80%, 72%, 55% TIPS failure group: NA
Liu et al. ([72])	No	12% (3/26)	0% (0/26)	TIPS success group: Survival rate: 96% (25/26) 1 died of abdominal abscess and MOF
Gazzera et al. ([67])	NA	NA	NA	NA
Semiz-Oysu et al. ([66])	NA	NA	NA	TIPS success group: Survival rate: 60% (6/10) 1 died of continued bleeding (8 days) 1 of HRS and sepsis (28 days); 1 of intraperitoneal bleeding (3 days); 1 of intractable gastrointestinal bleeding (3 months)
Bauer et al. ([63])	No	11% (1/9)	0% (0/9)	TIPS success group: Survival rate: 78% (7/9) 1 died of renal failure and sepsis (44 months); 1 of massive variceal bleeding without portal vein recanalization (42 months)
Van Ha et al. ([61])	Hematoma in the neck (1)	8% (1/13)	8% (1/13)	TIPS success group: survival rate: 85% (11/13) 2 died of MOF (7, 20 days) TIPS failure group: 1 died of variceal bleeding (12 days); 1 lost to follow-up

Table 2 continued

Authors ([Ref.])	Procedure-related complications	Shunt dysfunction	Encephalopathy	Survival
Senzolo et al. (56)	Capsular perforation without sequelae (10)	32% (6/19)	5% (1/19)	TIPS success group: Survival rate: 95% (18/19) 1 died of bleeding TIPS failure group: Survival rate: 78% (7/9) 1 died of RVB; 1 died of underlying hematological diseases
	Extrahepatic portal vein laceration (cured by covered stent) (1)			
	Biliary punctures without sequelae (3)			
Wallace et al. ([55])	NA	NA	NA	NA
Bilbao et al. ([52])	No	50% (3/6)	0% (0/6)	TIPS success group: Survival rate: 83% (5/6) 1 died of tumor progression (10 months)
Jiang et al. ([53])	Needle puncture through the liver and into the peritoneum cavity without sequelae (2)	20% (2/10)	50% (5/10)	TIPS success group: Mean survival time: 132.3 days 5 died of dyscrasia or liver failure TIPS failure group: Mean survival time: 34 days
Ganger et al. ([39])	Laceration of liver and capsule (died) (1)	33% (3/9)	NA	TIPS success group: Survival rate: 78% (7/9) 1 died of MOF (0.5 month), 1 died of TIPS complications
	Laceration of IVC (reversible) (1)			TIPS failure group: NA
Stein et al. ([40])	Minor subcapsular bleeding (1)	2/12 (17%)	NA	NA
	Biliary leak from intrahepatic duct (1)			
Walser et al. ([37])	No	9 shunt revisions (up to 5 per patient)	NA	TIPS success group: NA TIPS failure group: Alive for a mean interval of 14 months
Blum et al. ([31])	No	14% (1/7)	0% (0/7)	TIPS success group: Survival rate: 86% (6/7); 1 died of progressive liver failure with sepsis (1 month)
Radosevich et al. ([28])	No	29% (2/7)	0% (0/7)	TIPS success group: Survival rate: 71% (5/7) 1 died of hepatoma (1 day), 1 of progressive liver failure (2 months) TIPS failure group: 2 alive; 1 lost to follow-up

HRS hepatorenal syndrome, *IVC* inferior vena cava, *MOF* multiple organ failure, *MPV* main portal vein, *NA* not available, *RVB* recurrent variceal bleeding, *TIPS* transjugular intrahepatic portoysystemic shunt

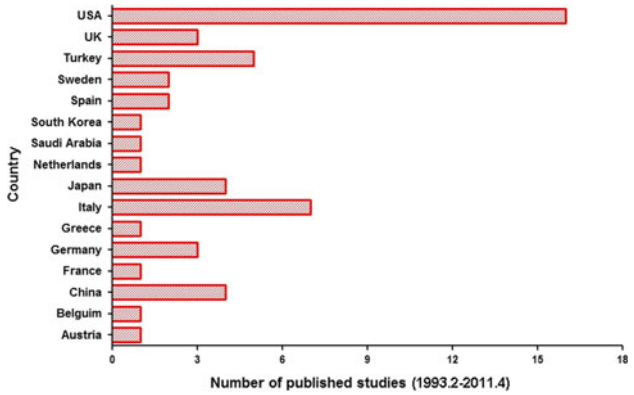

Fig. 1 Number of published articles according to the country where the studies were performed. These articles were published between February 1993 and April 2011

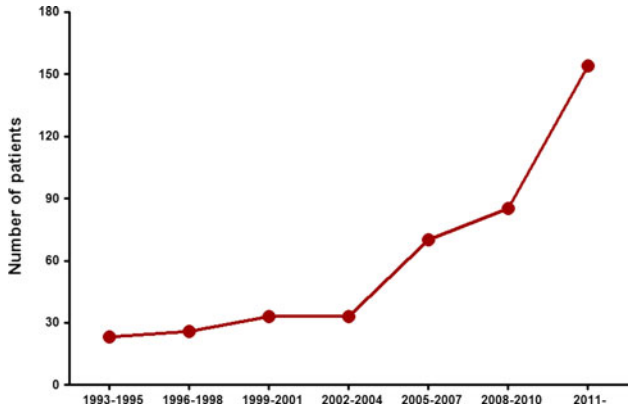

Fig. 2 Number of PVT-TIPS patients according to publication date

biases increase the rates of TIPS success and portal vein recanalization, thereby lowering the clinical significance of predictors for portal recanalization after TIPS placement. Accordingly, further studies are necessary to accurately identify patients in whom portal vein recanalization cannot be achieved.

The second strategy is to recanalize the thrombosed portal vein via percutaneous approaches followed by TIPS placement [28, 37, 40, 52, 53, 56, 61, 78, 79]. Not all of these procedures are followed with TIPS insertions because the thrombosed portal trunk may not be successfully recanalized. Thus, unnecessary TIPS placements can be avoided. The TIPS insertion failure rate is higher in studies reporting this strategy, because a higher proportion of the included patients presented with completely occluded or obliterated main portal vein (MPV) and portal cavernoma, thereby increasing the technical difficulty. Therefore, it appears to be very necessary to identify potential patients in whom TIPS cannot be successfully placed.

To date, predictions of TIPS technical failure have been conducted in only two studies [56, 78]. Senzolo et al. demonstrated that the absence of a visible patent intrahepatic portal branch was the only risk factor for technical failure in a univariate analysis [56]. But several limitations influenced the result. First, only transjugular approaches were employed in this study. If percutaneous transhepatic approaches had been employed, some cases of technical failures might have been successful [28]. Second, this study indicated that the degree (partial or complete occlusion) and age of the PVT were not significantly associated with technical failure; but the age of thrombus was unknown in

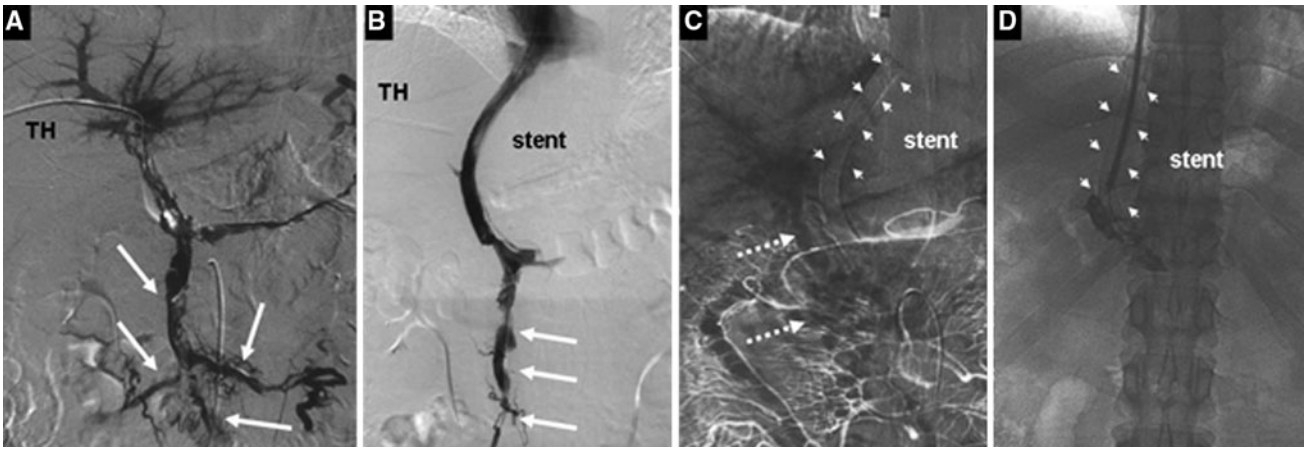

Fig. 3 Unnecessary stent-placement in a patient with extensive thrombosis within the SMV branches. Direct portography via a percutaneous transhepatic approach showed diffuse thrombosis within the portal venous system (*panel A*). After a stent was successfully created, there was still diffuse thrombosis within the SMV branches (*panel B*). One month later, color Doppler ultrasonography revealed that the shunt was completely occluded. Indirect portography showed no blood flow through the shunt and the development of cavernous vessels (*panel C*). An attempt to recanalize the thrombosed shunt failed (*panel D*). *Thick arrows* indicate extensive thrombosis within the SMV, *thin arrows* indicate stent, *dashed arrows* indicate numerous collateral vessels. *TH* transhepatic approach

36% of patients (10/28). In addition, TIPS placement was successful in all patients with partial PVT, and all patients in the TIPS failure group presented with total PVT. Contrarily, our team concluded that the degree of PVT was an independent predictor of TIPS technical failure in a multivariate analysis [78]. Further, TIPS procedures were recommended in patients with partially or completely occluded MPV, but not in those with obliterated MPV or fibrotic cord. This limited experience should be further confirmed in larger studies.

The third strategy is to create a TIPS between a hepatic vein and a large collateral vessel, with no need of recanalization of the thrombosed portal vein [30, 38, 51, 56, 64, 69, 78] (Table 3). This novel strategy provides an additional opportunity to divert blood from the liver and subsequently result in portal decompression in cases where a completely occluded or fibrotic portal vein cannot be recanalized. However, a large-caliber target collateral vessel that can fulfill the role of the occluded or fibrotic portal vein and be used as a stent is an essential prerequisite for this strategy. In addition, although no severe procedure-related complications occurred in these reports, precise pre-TIPS assessment of portal venous anatomy and post-TIPS surveillance are a must when undertaking this technique, and these might be not possible in all patients.

Figure 4 shows an algorithm used at our center to facilitate the TIPS procedure in the presence of PVT.

Approaches to access the portal vein in the presence of PVT

Four approaches are used to access the target portal vein and to further facilitate recanalization of the thrombosed portal vein (Fig. 5). These include a transjugular approach, a transhepatic approach [28, 30, 37, 39, 40, 49, 50, 52, 57, 61, 66, 70, 78], a transsplenic approach [52, 64, 69, 78], and a transmesenteric approach [34, 35, 52, 60] in order of increasing operative risk and technical difficulty.

Although a transjugular approach is safer and easier than the other three approaches, it is difficult to target a landing site in cases in which the portal vein branch is poorly visualized or in which puncture of hepatic vascular anatomy is difficult. In comparison, a transhepatic approach can provide a short and more direct access to the intrahepatic portal vein branch, a better angle for endovascular manipulations, and an easier handle for probing a thrombus. Indeed, a transjugular approach in combination with a transhepatic approach can significantly increase the portal vein recanalization rate over that achievable by using a transjugular approach alone; further, the combination does not lead to bleeding complications as the tract is embolized with a gelatin sponge [28]. However, the potential risk of bleeding from the puncture tract should be fully recognized, and emergency surgery should be adopted in a timely manner if uncontrollable intraperitoneal bleeding occurs. If puncture of the intrahepatic portal vein branch is impossible via a transhepatic approach, a transsplenic or transmesenteric approach to access the portal vein can be attempted. A patent splenic vein and additional minilaparotomy are required for the transsplenic and transmesenteric approach, respectively.

TIPS in the presence of portal cavernoma

The development of PVT is a dynamic process, ranging from recent thrombus to portal cavernoma [83]. Portal cavernoma, also known as cavernous transformation of the portal vein, refers to the formation of numerous hepatopedal collateral vessels in the liver hilum as an important compensatory mechanism for PVT [84]. At the stage of portal cavernoma, the primary therapeutic goals are to prevent and treat complications of portal hypertension and portal biliopathy [10]. Accordingly, TIPS, by decreasing portal pressure, seems to be a theoretically effective therapeutic tool in patients with either repeated variceal bleeding or refractory biliary complications. However, in the case of a portal cavernoma, portal vein puncture becomes more difficult owing to the complex anatomy, and TIPS is often contraindicated [85].

In the studies reviewed, at least 85 patients with portal cavernoma underwent successful TIPS insertions [28, 30, 33, 34, 36, 38, 40, 42, 43, 46, 51–53, 55–58, 61, 63, 64, 69, 76–80]. Two studies revealed that the rates of technical success were not significantly different between patients with and without portal cavernoma (6/9 vs. 13/19 and 3/4 vs. 10/11) [56, 61]. These results suggest that portal cavernoma should not be a contraindication for TIPS. A careful pre-operative evaluation of the portal venous system should be conducted to determine the best puncture route and to avoid the surrounding cavernous lesions [43]. In addition, as recanalization of a completely occluded or obliterated MPV is nearly impossible, TIPS insertion in a large collateral vessel, if present, can be attempted.

TIPS in candidates for liver transplantation

PVT occurs frequently in patients with advanced liver disease awaiting liver transplantations [86–88]. This poses a formidable challenge to liver transplantation because of the associated operative complexity, postoperative complications, and perioperative mortality [87–90]. Despite advances in surgical techniques, some patients with end-stage liver disease and concomitant extensive PVT are still precluded from the transplant list [91, 92]. At some centers,

Table 3 Overview of stent placement in collateral vein

Authors ([Ref.])	Age	Sex	Underlying Disease	Indications for TIPS	Extension of PVT	Age of PVT	Degree of PVT	Shunt creation	Shunt patency	Outcome
Han et al. ([78])	44	M	Cirrhosis	RVB	MPV, SMV	Chronic	Occluded	From HV to CV	Patent	Alive (5 years)
Wils et al. ([69])	45	M	Cirrhosis	RVB	N/A	Chronic	Occluded	From HV to CV	Patent	Alive (4 years)
	51	M	Ulcerative colitis; abdominal abscess	Awaiting LT; splenomegaly	N/A	Chronic	Occluded	From HV to CV	Patent	Died of ARDS (5 days)
	60	F	Myelofibrosis	RVB	MPV, SV, SMV	Chronic	Occluded	From HV to CV	Patent	Died of RVB (4 days)
	41	M	Idiopathic	RVB	N/A	Chronic	Occluded	From HV to CV	Patent	Alive (3 months)
Tuite et al. ([64])	37	M	Hypercoagulability	AVB	MPV, SMV, IMV, SV	>10 years	Complete	From HV to CV	Stenosis (3 weeks); (stent/dilation)	Died of acute promyelocytic leukemia (5 months)
Senzolo et al. ([56])	N/A	N/A	Cirrhosis	N/A	MPV	Chronic	Occlusive	From HV to CV	Patent	Died of bleeding from unknown source (2 days)
Brountzos et al. ([51])	72	F	Cirrhosis	RA	MPV, LPV	Chronic	Occluded	From HV to CV	Patent	Alive (16 months)
Yamagami et al. ([38])	65	F	Cirrhosis splenectomy	RVB	MPV, SMV (SV ligation)	Chronic	Occluded	From HV to CV	Patent	Alive (6 months)
Bezzi et al. ([30])	55	M	Cirrhosis; HCC	RVB	MPV	Chronic	Occluded	From HV to RGV	Patent	Alive (3 months)

NA not available, *M* male, *F* female, *RVB* recurrent variceal bleeding uncontrolled by medical or endoscopic therapy, *AVB* active variceal bleeding uncontrolled by medical or endoscopic therapy, *RA* refractory ascites requiring frequent large-volume paracentesis, *LT* liver transplantation, *MPV* main portal vein, *LPV* left portal vein, *RPV* right portal vein, *SMV* superior mesenteric vein, *IMV* inferior mesenteric vein, *SV* splenic vein, *HV* hepatic vein, *CV* collateral vein, *RGV* right gastric vein, *ARDS* acute respiratory distress syndrome, *HCC* hepatocellular carcinoma

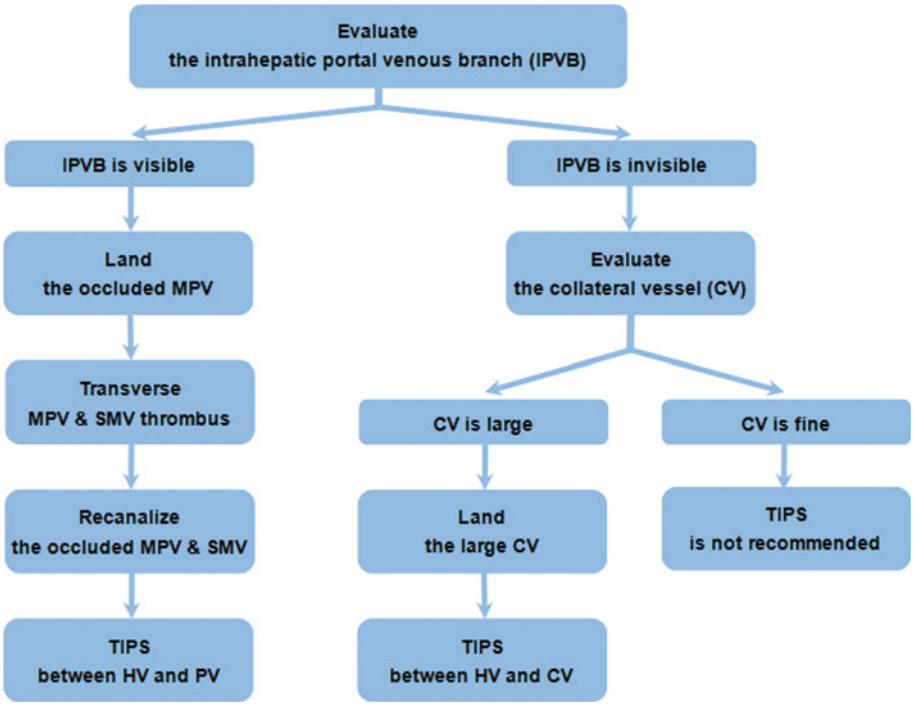

Fig. 4 Algorithm to facilitate TIPS procedures in the treatment of portal vein thrombosis. A large collateral vessel is defined as one that can fulfill the role of the occluded or fibrotic portal vein and be used as a stent. *HV* hepatic vein, *MPV* main portal vein, *PV* portal vein, *SMV* superior mesenteric vein, *TIPS* transjugular intrahepatic portosystemic shunt

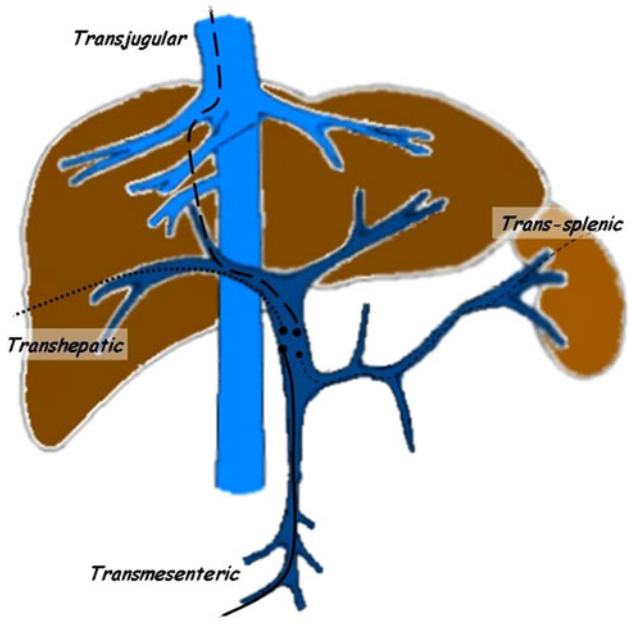

Fig. 5 Schematic of the four approaches to access the intrahepatic portal vein branch

TIPS insertion to maintain portal vein patency is indicated for candidates for liver transplantation without any severe complications of portal hypertension (i.e., variceal bleeding and refractory ascites) [47, 63, 71, 73].

However, the extension of a stent distally into the extrahepatic MPV or the SMV can potentially jeopardize the transplant surgery [93]. Thus, whether or not TIPS stents should be extended into the SMV is debatable [94]. Stent placement primarily depends on the extension and degree of the thrombus and on whether the thrombus within the SMV could disappear if the stent was not placed into the SMV. First, if the residual SMV thrombus is slim and blood flow from the SMV into the shunt is present, the thrombus will naturally disappear after successful TIPS creation. This is primarily due to the so-called scouring effect from the persistent portal vein inflow [95]. In this case, the extension of a stent into the SMV is unnecessary. Second, if the SMV thrombus is enormous and there is little or no blood flow from the SMV into the shunt, another stent should be placed into the SMV to maintain shunt patency. In this case, the transplant surgery does become more complicated. On the one hand, if the stent were not extended to the SMV, shunt patency might be compromised. On the other hand, SMV thrombosis will greatly preclude the possibility of liver transplantation. Third, in the presence of diffuse thrombosis within the SMV branches, stent extension into the SMV is unnecessary primarily because of the absence of adequate blood flow into the shunt.

Complications of TIPS in the treatment of PVT

Procedure-related complications

Portal vein puncture and percutaneous mechanical manipulation are more dangerous in patients with PVT than in

patients with normal portal venous systems. Laceration of the portal vein or liver capsule appears to be more frequent in the former patients. However, a retrospective study revealed a similar incidence of intraperitoneal hemorrhage (0% in group with PVT versus 1% in group without PVT, $p = 1.00$) [76]. In addition, it is important to note that intra-abdominal hemorrhage secondary to hepatic capsule perforation was lethal in three patients [39, 78, 79], as the risk of this complication was not fully recognized. These fatalities suggest that careful postoperative surveillance and timely surgical repair should be actively performed.

The most risky procedural complication that hepatologists and radiologists are concerned about is the potential risk of fatal pulmonary embolism after a portocaval shunt is successfully established, because a residual thrombus within the portal venous system may drift into the pulmonary circulation through the shunt [78, 80]. It should be noted that no episode of clinically evident pulmonary embolism has been reported in the literature yet. This is probably because the thrombus reduces in size with swift blood flow and pulmonary microembolism does not result in any clinical event. Certainly, further studies are needed to assess the possibility of pulmonary embolization after TIPS by pulmonary imaging and to explore the necessity of anticoagulant therapy for the prevention of such adverse events.

Other procedure-related complications are often reversible, including migration of a stent in the MPV, hemobilia, biliary leak from an intrahepatic duct, and hematoma in the neck [40, 61, 76, 80].

Shunt dysfunction

The overall incidence of shunt dysfunction ranged from 8 to 33% for bare stents in 13 case series [28, 31, 39, 40, 52, 53, 56, 61, 63, 72, 76, 77, 79]. 1- and 2-year cumulative rates of shunt dysfunction were reported in two case series [78, 80], but were significantly different between the two (38% vs. 21% at one postoperative year; 85% vs. 32% at two postoperative years) [78, 80]. The relatively higher rate of shunt dysfunction in the study by Luca et al. [80] might be due to the fact that anticoagulation was not used, given the possibility of anticoagulant-related hemorrhagic complications. However, no episode of such complications was observed in our study although all patients received anticoagulation after TIPS insertions. Further studies might be necessary to explore the risk-to-benefit ratio of anticoagulation for the prevention of shunt dysfunction in PVT-TIPS patients.

Compared to bare stents, covered stent-grafts can significantly improve TIPS patency [96]. Luca et al. reported that the rate of shunt dysfunction was significantly lower in patients receiving covered stents than those receiving bare stents (21% vs. 38% at one postoperative year, 29% vs. 85% at two postoperative years, $p < 0.001$) [80]. This finding indicates that covered stents should be recommended in cirrhotic patients with PVT.

Given that coagulation disorders are frequently observed in cirrhotic patients with PVT [97, 98], these patients might have a substantially higher risk of venous thromboembolism than those without PVT. Accordingly, the incidence of shunt thrombosis is expected to be higher in these patients than in those without PVT. However, Perarnau et al. [76] reported that the incidence of shunt stenosis in cirrhotic patients with PVT was similar to that in patients without PVT (28% vs. 35%, $p = 0.57$). This finding suggests that the presence of PVT does not increase the rate of shunt dysfunction in cirrhotic patients undergoing TIPS surgery.

Hepatic encephalopathy

The overall incidence of hepatic encephalopathy ranged from 0% to 50% in 10 case series [28, 31, 52, 53, 56, 61, 63, 72, 77, 79]. Nearly all episodes of hepatic encephalopathy occurred with the first postoperative year. The 1- and 2-year cumulative rates of hepatic encephalopathy were 25–27% and 27–32%, respectively in three case series [76, 78, 80]. In addition, the probability of de novo hepatic encephalopathy after TIPS was not significantly different between the patients with and without PVT (25% vs. 21% at 6 postoperative months, 27% vs. 24% at one postoperative year, 27% vs. 29% at two postoperative years, $p = 0.42$) [76].

Conclusions and future directions

The reviewed studies uniformly support the feasibility and safety of TIPS in the treatment of PVT, if indicated. However, the common limitations of these studies are obvious, including the retrospective nature, the absence of comparative effectiveness, the heterogeneous population, and the potential publication bias against negative studies. Thus, several future directions are further implied in this review. First, although a high rate of portal vein recanalization has been reported in PVT-TIPS patients, the long-term outcomes of such patients remain unknown. The clinical effectiveness and survival benefits of TIPS in the treatment of PVT should be further explored in prospective cohort studies. Second, TIPS has been recommended as the second-line therapeutic modality or rescue therapy for severe complications of portal hypertension in cirrhotic patients without PVT. However, given that PVT negatively influences the prognosis of cirrhotic patients, future studies should explore whether TIPS can be used as the first-line therapeutic modality in the setting of PVT. To date, only one randomized controlled trial to compare TIPS with endoscopic treatment combined with non-selective blockers and anticoagulants for the prevention of variceal rebleeding in cirrhotic patients with PVT has been

registered with ClinicalTrials.gov (NCT01326949). In the future, more prospective controlled studies should be performed to compare the outcomes of TIPS with those of conservative therapy in patients with PVT. Third, although an algorithm to facilitate TIPS procedures has been developed, it should not be widely used until more practical experience is available. Further studies should focus on evaluating the benefits and drawbacks of the various TIPS techniques, especially those associated with the transsplenic and transmesenteric approaches.

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Conflict of interest None.

Appendix

Search items

("Portal venous" (all fields) or "portal vein" (all fields)) and "thrombosis" (all fields) or "thrombus" (all fields) or "thrombi" (all fields) or "thrombin" (all fields) or "thrombosed" (all fields) or "thrombotic" (all fields) or "occlusion" (all fields) or "occlusive" (all fields) or "occluded" (all fields) or "obstruction" (all fields) or "obstructed" (all fields) or "stenosis" (All Fields) or "stenotic" (all fields) or "embolization" (all fields) or "embolisation" (all fields) or "embolism" (all fields) or "emboli" (all fields)) and ("transjugular intrahepatic portosystemic shunt" (all fields) or "TIPSS" (all fields)).

Eligibility criteria

Inclusion criteria

1. All case reports, case series, cohort studies, and controlled studies were included, regardless of the retrospective or prospective nature of the study.
2. No publication date restrictions were imposed.
3. The participants were diagnosed with PVT; they included children and adults with or without underlying liver cirrhosis and with or without malignancy.
4. The participants underwent TIPS procedures, and each case result was included in the study regardless of technical failure or success.

Exclusion criteria

1. Reviews or comments on the treatment of PVT or the applications of TIPS were excluded.
2. Abstracts and non-English language full-text articles were excluded.
3. The objectives of the study were assessed in animals.
4. Portal vein obstruction caused by external constriction.
5. Thrombosis occurred within the portal vein as a complication of stent stenosis or hepatic vein outflow obstruction.
6. Portal vein recanalization was achieved using the percutaneous approach alone.

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