Transjugular Intrahepatic Portosystemic Shunt for Portal Vein Cavernous Transformation: A Systematic Review and Single-Arm Meta-Analysis

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Keywords

Transjugular intrahepatic portosystemic shunt · Portal vein cavernous transformation · Systematic review · Single-arm meta-analysis

Abstract

Background: Transjugular intrahepatic portosystemic shunt (TIPS) is technically challenging in the treatment of portal vein cavernous transformation (PVCT), and there is no high-quality evidence regarding whether it is an option for patients with PVCT. We carried out a systematic review and meta-analysis to assess the feasibility and safety of TIPS for PVCT. **Methods:** Systematic search of PubMed, Chinese National Knowledge Infrastructure (CNKI) database, Cochrane Library, Embase, and Wanfang database through December 2021 for appropriate studies reporting efficacy and safety in patients with PVCT undergoing TIPS. The main outcome included the technical success rate, postoperative rebleeding rate, postoperative hepatic encephalopathy rate, stent pa-

tency rate, preoperative, and postoperative portal pressure. **Results:** Ten studies, including 292 patients were included. Our results showed that TIPS was technically successful in 82.97% (95% confidence interval [CI]: 77.14%–88.41%, $p = 0.297$) with low heterogeneity ($I^2 = 18.39\%$, $p = 0.279$). Postoperative rebleeding occurred in 9.56% (95% CI: 4.55%–16.77%, $p = 0.073$) with moderate heterogeneity ($I^2 = 46.45\%$, $p = 0.06$). Postoperative hepatic encephalopathy occurred in 18.55% (95% CI: 9.23%–27.05%, $p = 0.343$) with moderate heterogeneity ($I^2 = 48.62\%$, $p = 0.049$). Stent patency during follow-up was in 78.43% (95% CI: 70.74%–85.20%, $p = 0.805$) with low heterogeneity ($I^2 = 0\%$, $p = 0.654$). Postoperative portal pressure significantly reduced (WMD = 12.79 mm Hg, 95% CI: 12.09–13.48 mm Hg, $p < 0.00001$) with high heterogeneity ($I^2 = 61.4\%$, $p = 0.02$). Both Begg test and funnel plot showed that there was no significant publication bias. **Conclusions:** TIPS is feasible and safe in patients with PVCT and PVCT should not be considered an absolute contraindication to TIPS.

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Introduction

Portal vein cavernous transformation (PVCT) is characterized by long-term portal vein thrombosis (PVT), interconnected periportal and intrahepatic collateral veins, leading to portal hypertension [1, 2]. In addition, patients with PVCT usually have a history of cirrhosis or other liver diseases. PVCT increases the incidence of bleeding, refractory ascites, and hypersplenism. If left untreated, PVT and PVCT may lead to life-threatening mesenteric venous gangrene and other serious complications [3, 4]. However, there is no consensus regarding the application of interventional therapy in patients with PVCT, so the therapeutic option is rather limited and effective treatment is needed to be explored.

Transjugular intrahepatic portosystemic shunts (TIPSs) are an effective method in the management of portal hypertension, variceal bleeding, and refractory ascites [5, 6], with lower morbidity and mortality compared to surgical shunting. Recently, the Baveno VI consensus recommended that TIPS is an effective treatment of portal hypertension caused by various causes and TIPS can significantly decrease postoperative rebleeding rate and mortality [7]. TIPS is also considered as a safe and effective method in the treatment of PVT, when technically feasible, as it prevents the extension of thrombosis and lowers the risk of patients with PVCT. However, an evidence-based review concluded that PVCT is the main determinant of surgical failure [8], so TIPS for PVCT is still a challenge.

Previous studies reported that TIPS was a feasible, effective, and challenging treatment for patients with PVCT [9, 10]. These studies prompted us to investigate a safe and effective therapy that could improve the prognosis of patients with PVCT. Although some conclusions have been made, the safety and effect of TIPS have not been systematically reviewed. Therefore, we performed a meta-analysis to assess the existing evidence for the technical feasibility, safety, and efficacy of TIPS for patients with PVCT.

Method

Literature Search

This study was carried out and reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [11] (PRISMA checklist available in online suppl. material; for all online suppl. material, see www.karger.com/doi/10.1159/000522313). Comprehensive research of databases was performed to collect the trails about TIPS in the

treatment of PVCT. Only randomized controlled trials, cases reports, cases series, retrospective studies, and single-arm studies were included. Language restriction was English and Chinese. We searched articles published up to December 2021, including PubMed, CNKI, Cochrane Library, Embase, and Wanfang database. The search strategy included following database subject headings and abstract words: “Transjugular intrahepatic portosystemic shunt” OR “TIPS” OR “interventional treatment,” “portal vein cavernous transformation” OR “cavernous transformation of the portal vein.” And reference lists from the resulting publications and reviews were searched.

Study Selection

All citations were assessed by two authors independently, and the other two authors checked the articles retrieved according to inclusion and exclusion criteria. Disagreement was settled by discussion and consensus. Study titles and abstracts were inspected firstly, and the full texts of potentially eligible studies were reviewed further by the same two authors. Studies were considered eligible if they met the criteria as follows: (1) design: randomized controlled trial, cases reports, cases series, retrospective studies, and single-arm studies; (2) participants: patients were diagnosed with PVCT; (3) patients underwent TIPS. The number of studies and reasons for exclusion were as follows: (1) valid data were unavailable or data not completed or inaccurate so that the study could not be analyzed; (2) relevant outcome indexes were not reported; (3) comments, reviews, abstracts, editorials, and thesis; and (4) duplicate publications.

Data Extraction

According to the inclusion and exclusion criteria, we read the full text, excluded the literature that does not accord with this research scheme, and record the reasons and quantity of exclusion. Finally, the selected literature was cross-checked by two researchers. The following items of information were extracted: the name of the first author, year of publication, baseline characteristics of patients, sample size, and other prognostic information or relevant information.

Risk Assessment

The Newcastle-Ottawa scale (NOS) scores were adopted to evaluate observational studies [12]. Studies with a mean score ≥ 5 were included. Quality assessment was conducted by two independent reviewers and in case of conflict, conflict was resolved by consensus. The methodological quality of case series and case reports was measured by the “Methodological quality and synthesis of case series and case reports” [13].

Statistical Analysis

We performed a Bayesian meta-analysis to measure the incidence rate of technical successful rate, postoperative rebleeding rate, postoperative hepatic encephalopathy rate, and stent patency rate. The hierarchical model was used for Bayesian meta-analysis and estimating pooled prevalence. Complete Bayesian analysis was conducted using Markov Chain Monte Carlo simulation of posterior distribution, and the results were based on 200,000 iterations after a burn-in period of 50,000 iterations. All the analyses were generated by Rstudio and R (4.0.2) using “xlsx” and “R2jags” and “mcmcplots” and “dplyr” and “forestplot” packages [14, 15]. In addition, the 95% highest posterior density and 95% credible inter-

Fig. 1. Flow diagram.

vals (CI) were computed. Then, as recommended in Bayesian inference, sensitivity analysis for the choice of the prior was performed choosing between plausible possibility [16] and excluding skeptical and enthusiastic priors. The double arccosine transformation was used to build the funnel plot [17]. Online supplementary material 1 shows model implementation in R language.

Changes between preoperative and postoperative portal pressure were assessed using mean difference and 95% CI. For these continuous data, we performed a random-effect model meta-analysis when significant heterogeneity was present.

To objectively evaluate the publication bias of the included literatures, the Begg test with $p < 0.05$ as the existence of publication bias was performed, the values larger than which were considered as no publication bias. Statistical heterogeneity between the studies in effect measures will be assessed by Mantel-Haenszel χ^2 test and the I^2 statistic. We considered possible explanations where substantial heterogeneity (I^2 statistic above 50%) was detected and

where applicable. In addition, if there was substantial heterogeneity ($I^2 \geq 50\%$), the trials were heterogeneous; meta-regression, subgroup analysis, and sensitivity analysis were selected to explore the source of the heterogeneity. Stata 16.0 was used to conduct a meta-regression to investigate potential sources of variability in prevalence reported between studies [18].

Results

Studies Selection and Characteristics

The initial search yielded 274 records. After a comprehensive screening, 13 potentially eligible studies were identified. According to the inclusion criteria, 10 studies [19–28] (4 studies published in Chinese [20, 23, 27, 28])

Table 1. Characteristics of studies and patient populations

Study	Country/ region	Patients, n	Gender (male/ female)	Age, years	Main procedure	Etiology	Indication TIPS	Stent utilization	Vein thrombosis	NOS scores
Fanelli et al. [19]	Italy	13	9/4	44.8±13.5	TIPS	All patients have no cancer or liver cirrhosis	Recurrent bleeding: 8 Intestinal ischemia due to acute superior mesenteric vein thrombosis: 2 Refractory ascites: 1 Varices at high risk of bleeding need of anticoagulation therapy: 2	Covered stents: 10	Superior mesenteric vein: 3 Splenic vein: 1 Both splenic and mesenteric vein thrombosis: 3	–
Guo et al. [20]	China	21	13/8	48±11	TIPS	Liver cirrhosis: 17; non-liver cirrhosis: 4	Bleeding of esophageal and gastric varices: 21	Bare stents: 2 Cover stents: 4 Bare stents and cover stents: 13	NA	–
Jin et al. [28]	China	67	46/21	51.3±12.5	TIPS	Hepatitis B cirrhosis: 27; hepatitis C cirrhosis: 2; alcoholic cirrhosis: 7; autoimmune cirrhosis: 3; chronic myeloproliferative diseases: 2; pre thrombotic diseases: 6; cryptogenic cirrhosis: 20	Bleeding of esophageal and gastric varices (confirmed by gastroscopy): 67	A bare stent and a cover stent: 46 A bare stent: 1 Two bare stent and a cover stent: 9	NA	–
Li et al. [21] ^a	China	25	18/7	47.3±13.4	TIPS	Hepatitis B cirrhosis: 7; hepatitis C cirrhosis: 1; alcoholic cirrhosis: 7; myeloproliferative disease: 1; cryptogenic: 11	Patients had experienced at least one variceal bleeding episodes, but without serious cardiopulmonary diseases, hepatocellular carcinoma, or other malignancies	A bare stent and a cover stent	NA	7
Li et al. [23]	China	38	30/8	Range: 17–78	PTIPS	Decompensated liver cirrhosis: 29; thalassemia: 1; abnormal proliferation of bone marrow fibers: 1; chronic pancreatitis: 2; after liver transplantation: 1; abdominal trauma: 1; unknown etiology: 3	Recurrent bleeding: 24 Refractory ascites: 6 Recurrent bleeding and refractory ascites: 8	Bare stent and covered stent	Superior mesenteric vein: 12 Splenic vein: 4	–
Luo et al. [22]	China	15	11/4	29.1±8.0	TIPS	Noncirrhotic patients who had documented variceal bleeding secondary to chronic PVT and associated	Active gastrointestinal bleeding: 4 Had a history of variceal bleeding: 11	A covered stent: 8 Bare stents: 1 Covered stents: 2	Superior mesenteric vein: 6 Both splenic and mesenteric vein thrombosis: 3	–
Niu et al. [24]	China	76	45/31	52.3±14.7	TIPS	Hepatitis B cirrhosis: 54; hepatitis C cirrhosis: 5; alcoholic cirrhosis: 4; autoimmune cirrhosis: 2; cryptogenic cirrhosis: 11	Acute variceal bleeding: 4 Elective TIPS for recurrent variceal bleeding: 50 Refractory ascites: 9 Hepatic hydrothorax: 6 recurrent abdominal pain: 7	NA	NA	–
Qi et al. [25]	China	20	13/7	Range: 10–52	TIPS	All patients are noncirrhotic	Variceal rebleeding or refractory ascites The absence of malignancy before diagnosis of portal cavernoma	A bare stent: 5 Two bare stents: 2	Superior mesenteric vein: 1	–
Senzolo et al. [26] ^b	UK	9	NA	Range: 17–65	TIPS	NA	NA	NA	Superior mesenteric vein: 3 Splenic vein: 3	–
Shen et al. [27]	China	8	6/2	Range: 40–68	TIPS	NA	Bleeding of esophageal and gastric varices: 8	Bare stent and covered stent	NA	–

TIPS, transjugular intrahepatic portosystemic shunt; PTIPS, percutaneous transhepatic intrahepatic portosystemic shunt; NA, not available. ^a This trial reported a total of 51 patients (25 treated with TIPS and 26 treated with endoscopic variceal ligations and propranolol), and only patients treated with TIPS were included in our meta-analysis. ^b This trial reported a total of 28 patients with or without PVCT. Only 9 patients with PVCT were included in our meta-analysis.

Table 2. Quality assessment of case series and case reports

Description	Ascertainment			Causality		Reporting	
	Selection	2. Was the exposure adequately ascertained?	3. Was the outcome adequately ascertained?	4. Were other alternative causes that may explain the observation ruled out?	5. Was there a challenge/rechallenge phenomenon?	6. Was there a dose-response effect?	7. Was follow-up long enough for outcomes to occur?
	1. Does the patient(s) represent(s) the whole experience of the investigator (center) or is the selection method unclear to the extent that other patients with similar presentation may not have been reported?						8. Is the case(s) described with sufficient details to allow other investigators to replicate the research or to allow practitioners make inferences related to their own practice?
Fanelli et al. [19]	U	Y	Y	N	Y	N	Y
Guo et al. [20]	U	Y	Y	Y	Y	N	Y
Jin et al. [28]	U	Y	Y	Y	Y	N	Y
Li et al. [23]	Y	Y	Y	Y	Y	N	Y
Luo et al. [22]	U	Y	Y	Y	Y	N	Y
Niu et al. [24]	U	Y	Y	Y	Y	N	Y
Qi et al. [25]	U	Y	Y	Y	Y	N	Y
Senzolo et al. [26]	U	Y	Y	N	Y	N	Y
Shen et al. [27]	U	Y	Y	N	Y	N	Y

Y, yes; U, unclear; N, no.

and 6 studies published in English [19, 21, 22, 24–26]) were included in our meta-analysis. Figure 1 displays the selection algorithm and numbers of included and excluded studies.

Overall, our meta-analysis included 10 studies that reported TIPS or percutaneous transhepatic intrahepatic portosystemic shunt (PTIPS) in the treatment of PVCT. The sample size ranged from 8 to 76, reaching a total of 292 cases. Nine studies provided data on the indication of TIPS, 8 studies provided data on the etiology, and 6 provided data regarding the vein thrombosis. The main study characteristics of included studies are shown in Table 1 and the quality assessment of case series and case reports are shown in Table 2.

Meta-Analysis Results

Successful Rate

All included studies reported the technically successful rate. The pooled successful rate was 79.64% (95% CI: 67.28%–89.33%) and significant heterogeneity can be identified ($I^2 = 68.67\%$, $p = 0.06$). Moreover, we performed a sensitivity analysis to explore the potential source of heterogeneity. When Qi's [25] study was excluded, we found that there is a low heterogeneity ($I^2 = 18.39\%$, $p = 0.279$) between included studies and the pooled successful rate was 82.97% (95% CI: 77.14%–88.41%; Fig. 2). Both Begg test ($p = 0.325$) and funnel plot (Fig. 3) showed that there was no significant publication bias.

Postoperative Rebleeding Rate

Nine included studies [19–25, 27, 28] reported the postoperative rebleeding rate. The pooled postoperative rebleeding rate was 9.56% (95% CI: 4.55%–16.77%; Fig. 4) with moderate heterogeneity ($I^2 = 46.45\%$, $p = 0.06$).

Incidence of Postoperative Hepatic Encephalopathy

Nine included studies [19–25, 27, 28] reported the postoperative hepatic encephalopathy rate. The pooled postoperative hepatic encephalopathy rate was 18.55% (95% CI: 9.32%–27.05%; Fig. 5) with no significant heterogeneity ($I^2 = 48.62\%$, $p = 0.049$).

Stent Patency Rate during Follow-Up

Eight included studies [19–23, 25, 27, 28] reported the stent patency rate. The pooled stent patency rate was 78.43% (95% CI: 70.43%–85.20%; Fig. 6) with moderate heterogeneity ($I^2 = 0\%$, $p = 0.654$).

Fig. 2. A forest plot showing the success rate of TIPS on PVCT.

Fig. 3. A funnel plot showing the publication bias.

Changes of Preoperative and Postoperative Portal Pressure

Six included studies [19, 20, 22, 23, 25, 28] reported the differences between preoperative and postoperative portal pressure. Preoperative portal pressure ranged from 22.9 to 28.09 mm Hg with a mean preoperative portal pressure of 25.30 mm Hg. The postoperative portal pressure significantly reduced (WMD = 12.79 mm Hg, 95% CI: 12.09–13.48 mm Hg; Fig. 7) with significant heterogeneity ($I^2 = 61.4\%$), so a random-effect model was performed.

Survival Rate

Seven included studies [21–25, 27, 28] reported the survival rate in follow-up. All those studies reached a total survival rate of 80%. Jin et al. [28] reported the 1- and 2-year survival rates are 94.3% and 83.2%, respectively, and Niu et al. [24] reported the 1- and 2-year survival rates are 93.7% and 83%, respectively, indicating patients with PVCT underwent TIPS can reach a favorite clinical effect. The main outcomes are shown in Table 3.

Meta-Regression and Subgroup Analysis

Nine studies reported the male/female ratio; all studies reported the main procedure, publication year, and countries/region; and six studies reported that all the patients with or without cirrhosis, so all those factors were taken into account to perform a meta-regression. Unfortunately, we found that successful rate (online suppl. Table S1), postoperative hepatic encephalopathy rate (online suppl. Table S2), postoperative rebleeding rate (online suppl. Table S3), and stent patency rate (online suppl. Table S4) were not significantly associated with male/female ratio, main procedure, countries/region, publication year, and cirrhosis. We found that changes between preoperative and postoperative portal pressure is weakly associated with publication year [$\exp(b) = 0.72$, 95% CI: 0.54–0.95] and cirrhosis [$\exp(b) = 0.96$, 95% CI: 0.009–0.99] (online suppl. Table S5). However, the weak association should be identified by further studies.

Cirrhosis, technical differences, study design, and country/region were taken into account to perform a subgroup analysis (online suppl. Table S6). We found that it is not yet appropriate to draw final conclusions about the impact of technical differences, study design, and coun-

Fig. 4. A forest plot showing the postoperative rebleeding rate of TIPS on PVCT.

Fig. 5. A forest plot showing the postoperative hepatic encephalopathy rate of TIPS on PVCT.

Fig. 6. A forest plot showing the stent patency rate of TIPS on PVCT.

Fig. 7. A forest plot showing the changes of preoperative and postoperative portal pressure of TIPS on PVCT.

Table 3. Characteristics and main outcomes

Study	Follow-up, months	Survival rate	Successful case	Post-operative rebleeding rate	Incidence of postoperative hepatic encephalopathy	Stent patency rate	Pre-operative portal pressure, mm Hg	Post-operative portal pressure, mm Hg
Fanelli et al. [19]	Mean 17.4±14.7 (range: 3.3–40.1)	NA	10/13	1/10	2/10	7/10	22.9±6	8±2.7
Guo et al. [20]	Range: 3–24	NA	19/21	3/19	2/19	13/19	23.5±4.6	11.4±4.9
Jin et al. [28]	Mean: 23.91±12.35	1 year: 94.3% 2 years: 83.2%	56/67	7/56	15/56	46/56	28.09±7.28	17.53±6.12
Li et al. [21]	Mean: 21 (range: 1–47)	85.7%	21/25	1/21	3/21	19/21	NA	NA
Li et al. [23]	Mean: 26.7±10.4 (range: 3.0–74.0)	80.6%	36/38	2/36	4/36	26/36	25.2±2.9	13.2±1.3
Luo et al. [22]	Median follow-up time was 45.2	80	11/15	4/11	3/11	9/11	25.8±5.7	9.5±4.2
Niu et al. [24]	Mean: 45.9±23.6	1 year: 93.7% 2 years: 83.0%	59/76	1/59	20/59	NA	NA	NA
Qi et al. [25]	Median follow-up time was 19.9 (range, 3.9–96)	90%	7/20	1/7	0/7	5/7	26.3±1.1	12.4±1.1
Senzolo et al. [26]	Median follow-up time was 19.9 (range, 3.9–96)	94.7%	6/9	NA	NA	NA	NA	NA
Shen et al. [27]	At least 12	NA	7/8	1/7	0/7	6/7	NA	NA

NA, not available.

try/region on successful rate, postoperative hepatic encephalopathy rate, postoperative rebleeding rate, stent patency rate, and changes between preoperative and postoperative portal pressure, because only one study used PTIPS and only two studies were from non-China areas. Besides, a subgroup analysis of with or without cirrhosis may reduce I^2 statistics value on changes between preoperative and postoperative portal pressure, stent patency rate during follow-up, and postoperative rebleeding rate. However, heterogeneity of incidence of postoperative hepatic encephalopathy and successful rate cannot be explained completely by cirrhosis, so further studies are needed to explore the heterogeneity.

Discussion

In our study, ten studies, including 292 patients with PVCT were included. Pooled results demonstrated that TIPS is feasible in most patients with PVCT and TIPS could be a choice for those who with PVCT uncontrolled by conventional therapy such as nonselective β -blocker, endoscopic variceal ligation [29], and vasoactive drugs (somatostatin or its analog, octreotide; vasopressin or its analog, terlipressin) [30].

A recent study by Lomax and colleagues [9] concluded that PVCT should not be considered an absolute contraindication to TIPS, although the presence of PTCV is as-

sociated with a significantly high failure rate (high-quality evidence) and PVCT was previously considered as a contraindication to TIPS because of its postoperative adverse events and technical difficulty [31, 32]. Besides, the experiences from TIPS in the treatment of PVCT are exceedingly limited due to low incidence of PVCT, and only a few cases were reported. Specifically, it is tough to create an intrahepatic shunt at the same time as avoiding damage to surrounding cavernous vein [33]. In other words, the most important and challenging step of TIPS is the shunt creation, which establishes a channel between the hepatic vein and the portal vein, but PVCT complicates the vascular condition, leading to the difficulties of TIPS. Even previous studies concluded that TIPS is exceedingly feasible for PVT recanalization [34], PVCT is still the main determinant of the technical success because portal vein and its branches are gradually thrombosed or occluded in this setting. In patients with portal vein occluded completely, when TIPS was performed, the blood could not be drawn back, so it was difficult to judge whether the shunt creation was successful. In this setting, ultrasound-guided percutaneous transhepatic or percutaneous transsplenic approach is also helpful to find an appropriate puncture target [35, 36].

According to previous studies, percutaneous transhepatic or transsplenic approach could be feasible in finding an appropriate site for TIPS creation [37–40], making surgery much easier during treatment of PVCT. In our meta-analysis, only one included a study by Li et al. [23] reported that PTIPS was used, achieving a low postoperative rebleeding rate (2/36) and acceptable successful rate (36/38). However, further trials are needed to verify the safety and efficacy of PTIPS and other possible approaches.

To our knowledge, the feasibility of TIPS placement has been reported to be beneficial in patients with cirrhosis and PVT [26, 41–43]. Compared to surgery, TIPS is a technique with relatively lower invasiveness, which can be performed in vulnerable patient groups, reducing the postoperative portal pressure. Besides, a recent meta-analysis by Rodrigues et al. [8] involving 392 patients, in which all patients had PVT (17% with PVCT), concluded that TIPS was technically successful in 95% and portal vein recanalization rate at 12 months is 79%. Although Rodrigues et al. [8] had made some conclusions, there is no specific data regarding the TIPS for PVCT. Our results show that TIPS implantation can be successful in most cases (82.97%, 95% CI: 77.14%–88.41%). Something should be noticed that one of our included studies by Qi et al. [25] reported a low success rate of 35% and it is sen-

sitive to our pooled result. In Qi's [25] study, this difference can be explained by the fact that the main portal vein was occluded and became fibrotic cord in most patients (19/20), indicating that occluded main portal vein makes TIPS creation more difficult. This finding was consistent with previous studies by Wils et al. [44] and Han et al. [45].

The stent patency rate is another important issue that should be noticed. When TIPS was performed, shunts patency can be achieved, and the expansion of thrombus can be avoided [46]. According to the study involving 392 PVT cases by Rodrigues et al. [8], shunt patency at 12 months was 84% (95% CI: 76%–90%). Similarly, the stent patency rate during the follow-up in our meta-analysis was 78.43% (95% CI: 70.43%–85.20%). After TIPS, anticoagulation may prevent thrombus extension and maintain PTV canalization [47, 48]. However, among included studies, all patients received intraoperative anticoagulation, but data regarding postoperative anticoagulation were not reported. Interestingly, Wang et al. [49] thought that it is widely accepted that post-TIPS anticoagulation does not correlate with the stent patency, but Rodrigues et al. [8] thought that utilization of post-TIPS anticoagulation was associated with a higher patency rate. Besides, the patency of bare stent and covered stent is different and covered stent is generally considered as a technology with much more advantage for shunts patency [50–53]. There are still some controversies about the utilization of post-TIPS anticoagulation in preventing thrombus extension and stent restenosis.

Considering the safety, postoperative hepatic encephalopathy rate and postoperative rebleeding rates are 18.55% (95% CI: 9.32%–27.05%) and 9.56% (95% CI: 4.55%–16.77%), respectively. Besides, according to the postoperative hepatic encephalopathy rate and postoperative rebleeding rate, we concluded that TIPS creation was generally safe, suggesting that TIPS is a feasible and effective procedure in the treatment of PVCT. In included studies, data regarding survival rate is limited (only 5 included studies reported survival rate), so it is not yet appropriate to draw final conclusions about survival rate. However, in an interventional catheter room, clinicians still need to be cautious, because the complex interconnected periportal or intrahepatic collateral veins add the difficulty of surgery.

Meta-regression and subgroup analysis were performed to find the resource of heterogeneity. We found that cirrhosis is a study-level factor that has weak association with our results. Francoz et al. [54] reported that PVCT may often be accompanied by cirrhosis. Besides, the prognosis and clinical outcome are different between

patients with or without PVCT [55]. Shen et al. [56] found that liver stiffness significantly increased in PVCT patients with cirrhosis. Previous studies found that liver stiffness is closely related to the prognosis of patients with cirrhosis [57, 58], so we thought that the association between our results and cirrhosis can be explained by aforementioned studies. However, although the various factors can lead to PVCT, the etiology is not clear. Further studies are needed to verify this finding.

In this meta-analysis, Bayesian meta-analysis was performed. Compared to the frequentist meta-analysis, Bayesian meta-analysis provides more accurate estimates for small samples because this method takes into account possible bias, reaching more accurate estimates for small samples.

Similar to any meta-analyses, our study has some limitations. Firstly, single-arm studies and controlled studies were included in this meta-analysis, so the pooled results and final conclusions should be treated with cautions. Secondly, four included studies published in Chinese. For doctors outside of China, there will be some difficulties to understand these studies because of language. However, all Chinese studies are published in top Chinese journals and these results are also crucial for this meta-analysis. Thirdly, surgical experience and hospital cost should be taken into account in further studies. Fourthly, after meta-regression and subgroup analysis, we found that changes between preoperative and postoperative portal pressure are weakly associated with publication year and cirrhosis. We also found that cirrhosis may have an impact on changes between preoperative and postoperative portal pressure, stent patency rate during follow-up, and postoperative rebleeding rate, but these findings should be identified by further studies because of the small sample size. Because of these limitations, we call for future trials to include prospective, multicenter, randomized, blind design to verify our results.

Conclusion

In conclusion, our meta-analysis demonstrated that TIPS reduced the incidence of variceal rebleeding, and TIPS achieved ideal efficacy and safety in the treatment of PVCT, so PVCT should not be considered as an absolute contraindication of TIPS. What is more, although TIPS is still technically challenging, it remains an option for patients with PVCT.

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Statement of Ethics

The article does not contain any studies with human participants or animals performed by any of the authors. Therefore, the paper is exempt from further Ethical Committee approval.

Conflict of Interest Statement

None of the authors have identified any conflicts of interest and financial disclosures.

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Author Contributions

Conceptualization: Jingxin Yan and Lushun Zhang; validation: Yaxuan Wang, Meilin Zhu, Jingxin Yan, and Lushun Zhang; writing – original draft preparation: Jingxin Yan, Manjun Deng, Yaxuan Wang, Meilin Zhu, Ting Li; writing – review and editing: Haiyang Hu, Zhenwu Lei, Yaxuan Wang, Yingxing Guo, Lushun Zhang; software: Jingxin Yan and Manjun Deng.

Data Availability Statement

All data were derived from previously published studies, so the data availability statement is not required.

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