**Name of journal:** ***World Journal of*** ***Gastroenterology***

**Manuscript NO: 35553**

**Manuscript Type: ORIGINAL ARTICLE**

***Randomized Controlled Trial***

**Clinical outcome comparison between****transcatheter** **selective superior mesenteric artery urokinase infusion** **therapy and** **transjugular intrahepatic portosystemic shunt in** **patients with** **cirrhosis and acute** **portal vein thrombosis**

Jiang TT *et al*. Thrombolysis *vs* TIPSS in acute portal vein thrombosis of cirrhosis

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**Author contributions:** Jiang TT and Gao J designed the research; Jiang TT, Luo XP and Sun JM performed the research and participated in data acquisition and analysis; Jiang TT wrote the paper.

**Supported by** the National Natural Science Foundation of China, No. 81572888.

**Institutional review board statement:** The study was reviewed and approved by the ethics committee of the Second Affiliated Hospital of Chongqing Medical University (Number: 2012-076).

**Informed consent statement:** All study participants provided informed written consent prior to study enrollment.

**Conflict-of-interest statement:** None to declare.

**Data sharing statement:** None to declare.

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**Manuscript source:** Unsolicited manuscript

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**Received:** July 23, 2017

**Peer-review started:** July 25, 2017

**First decision:** August 30, 2017

**Revised:** September 10, 2017

**Accepted:** September 29, 2017

**Article in press:**

**Published online:**

**Abstract*****AIM***

To compare the outcomes of transcatheter superior mesenteric artery (SMA) urokinase infusion and transjugular intrahepatic portosystemic shunt (TIPS) for acute portal vein thrombosis (PVT) in cirrhosis.

***METHODS***

From January 2013 to December 2014, patients with liver cirrhosis and acute symptomatic PVT who met the inclusion criteria were randomly assigned to the SMA group or TIPS group. Two groups accepted transcatheter selective SMA urokinase infusion therapy or TIPS respectively. The total follow-up time was 24 months .The primary outcome measure was the change in portal vein patency status which was evaluated by angio-computed tomography or doppler ultrasound. Secondary outcomes were rebleeding and hepatic encephalopathy.

***RESULTS***

A total of 40 patients were enrolled, with 20 assigned to the SMA group and 20 assigned to the TIPS group. The symptoms of all patients in the two groups improved within 48 h .PVT was improved in 17 patients (85%) in SMA group and 14 patients (70%) in TIPS group. The main portal vein (MPV) thrombosis was significantly reduced in both groups (*P* < 0.001), but there was no significant difference between them (*P* = 0.304). In addition, in the SMA group, superior mesenteric vein (SMV) thrombosis and splenic vein (SV) thrombosis were significantly reduced (*P* = 0.048 and *P* = 0.02), but not occurred in TIPS group. At 6-month, 12-month, 24-month, in the SMA group and the TIPS group, the cumulative rates free of the first episode of rebleeding were 80%, 65%, and 45% *vs* 90%, 80%, and 60% (*P* = 0.320); the cumulative rates free of the first episode of hepatic encephalopathy rates were 85%, 80%, and 65% versus 50%, 40%, and 35% (*P* = 0.022).

***C******ONCLUSION***

Transcatheter selective SMA urokinase infusion and TIPS are safe and effective for acute symptomatic PVT in cirrhosis.

**Key words:** Cirrhosis; Portal vein thrombosis; Superior mesenteric artery; Urokinase; Transjugular intrahepatic portosystemic shunt

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**Core tip:** Transcatheter selective superior mesenteric artery urokinase infusion therapy and transjugular intrahepatic portosystemic shunt can both significantly reduced the acute portal vein thrombosis in cirrhosis, and there was no significant difference between them. Moreover, two treatment strategies did not result in serious adverse events such as bleeding.

Jiang TT, Luo XP, Sun JM, Gao J. Clinical outcome comparison between transcatheter selective superior mesenteric artery urokinase infusion therapy and transjugular intrahepatic portosystemic shunt in patients with cirrhosis and acute portal vein thrombosis.*World J Gastroenterol* 2017; In press

**INTRODUCTION**

Portal vein thrombosis (PVT) is defined as thrombosis occurring in the trunk of the portal vein or portal branches (the mesenteric or splenic veins)[1]. The prevalence of non-neoplastic PVT in liver cirrhosis ranges from 7.2% to 17%[2,3 4], and is higher at the decompensated or advanced stage[3,5], acute thrombosis can be severe and may lead to mesenteric ischemia and variceal bleeding. Recent studies have shown that acute PVT influences the outcomes of liver cirrhosis, including a worse survival time, and a significant increase in the risk of gastroesophageal variceal rebleeding[6-10].

Up to now, there has been no consensus on the treatment of liver cirrhosis with acute PVT in any guideline. Anticoagulation is usually used as a first-line treatment, and has been confirmed effective by some research[11,12], whereas systemic and local thrombolysis, per­cutaneous portal vein recanalization, and transjugular intrahepatic portosystemic shunt (TIPS) are often considered as second-line choices[13]. Recently, increasing endovascular selective catheterization thrombolytic therapy has been successfully implemented, which can be administered directly *via* percutaneous transhepatic or transjugular intrahepatic routes or indirectly *via* the SMA through the femoral or radical artery infusion of thrombolytic agents[14,15]. The aim of this study was to compare the clinical outcomes of transcatheter selective SMA urokinase infusion therapy and TIPS in patients with cirrhosis and acute PVT to evaluate their effectiveness and safety.

**MATERIALS AND METHODS**

***Patients***

From January 2013 to December 2014, all patients with cirrhosis and acute PVT in the Second Hospital of Chongqing Medical University were enrolled. All patients provided informed consent before admission. The ethics committee approved our research program. The inclusion criteria were as follows: (1) patients with liver cirrhosis; (2) clear thrombosis in the portal vein system as seen through Doppler ultrasound, angio-computed tomography (CTA), and/or angio-magnetic resonance imaging analyses (MRA); (3) acute thrombosis: onset within 1 week; (4) continued abdominal pain or abdominal distension. The exclusion criteria were as follows: (1) contraindications to anticoagulation therapy; (2) severe cardiac and lung disease; (3) previous TIPS or thrombolytic therapy; (4) PVT after liver transplantation; (5) malignant tumor; and (6) refused interventional therapy or follow-up.

***Preparation and*** ***status of*** ***PVT***

Before the study, clinical symptoms, physical examination, and laboratory examination were recorded. All patients had an endoscopy to check for varices prior to thrombolysis and band ligation would be used to prevent variceal bleeding in patients with varices.

Doppler ultrasound, CTA, and/or MRA were used to estimate thrombosis from the two aspects of position and severity. The PVT position was divided into the main portal vein (MPV), superior mesenteric vein (SMV), and splenic vein (SV). The PVT severity was divided into four levels: grade 0 (thrombus deficiency), grade I (MPV thrombus < 50% or only SMV and SV thrombus existed), grade II (MPV thrombus accounted for 50%-100%)，and grade III (complete blocking or cavernous transformation of the portal vein).

***Randomization***

By randomly generated numbers, patients who met the inclusion criteria were randomly allocated to the SMA group or the TIPS group.

***Intervention***

In the SMA group, we used the transfemoral approach for transcatheter selective SMA urokinase infusion therapy. (1) Transcatheter thrombolysis was completed as follows: the catheter was selected for the SMA and remained in place. Contrast agent was injected through the SMA catheter. The first impact volume was 500000 IU. After the completion of angiography, the indwelling SMA catheter was continuously pumped with urokinase, depending on the patient's weight (250000-500000 IU/2 ×/d, for a total of 15000 IU/kg/24 h). Thrombolysis time depended on the improvement of the patient’s clinical symptoms, a decrease in D-dimer, and imaging data; (2) anticoagulant therapy was completed as follows: patients were given subcutaneous heparin (2000 IU/2 ×/d) to maintain an international normalized ratio (INR) between 2 and 3. Patients were constantly monitored during thrombolytic therapy, including D-dimer, coagulation function, and routine blood tests. In addition, at intervals of 72 h and before removal of the catheter, angiography was re-performed. Superior mesenteric venography showed improvement of portal vein and SMV obstruction; CT-enhanced examination showed that the PVT had obviously absorbed (stale thrombus occupying < 50% after treatment); or with vascular recanalization, we can consider ending thrombolysis and removing the indwelling SMA catheter. After leaving the hospital, the patients continued taking oral warfarin for at least 3 mo.

In the TIPS group, TIPS was performed by two experienced physicians in accordance with standard procedures. Balloons expanded the oppilative passageway, and a covered stent was embedded into the passageway. Additional bare-metal stents were placed into other oppilative veins of the portal venous system. After the procedure, the patients were given hypodermic low-molecular-weight heparin to prevent acute thrombosis (6000 IU/3 ×/d, consecutive week). After discharge, all patients were treated with warfarin to achieve an INR of 2 to 3 for 6 mo.

***Follow-up***

All patients were followed up at 1, 3, 6, 12, 18, and 24 mo after the procedure. Physical examinations and laboratory testing (coagulation function, routine blood test) were performed in both groups at each arranged follow-up visit, and CTA or doppler ultrasound was performed at 6, 12, and 18 mo or whenever was clinically required (*e.g.,* for ascites, black stool, abdominal pain). During follow-up, no blind method was adopted for patients taking warfarin.

***Outcome measurements***

The primary outcome measure was the change in portal vein patency status, which was evaluated by CTA or doppler ultrasound. Secondary outcomes were rebleeding and hepatic encephalopathy. Changes in portal vein patency status were defined as follows: (1) recanalization, with complete disappearance or reconstruction of cavernous transformation; (2) improved, with recanalization, improvement from grade III or II to grade II or I, or disappearance of an SMV or SV thrombus; (3) stable; and (4) worsened, with worsening from grade I or II to grade II or III, progression of thrombus to cavernous transformation, or formation of a SMV or SV thrombus.

***Statistical analysis***

Statistical analysis was performed using the software SPSS version 19.0. All tests of significance were two-sided, and a *P* value < 0.05 was considered significant. A Student *t* test was used to compare the differences in continuous variables between the two groups. Bivariate associations between categorical variables were analyzed with the χ2 tests and Fisher exact test. Category ordinal variables, including Child-Pugh class and MPV thrombus severity, were analyzed with the Mann-Whitney *U* test. Survival analysis was performed by the Kaplan-Meier method and compared by log-rank test.

**RESULTS**

***Patients***

A total of 40 patients were in our study. Figure 1 shows the exclusion criteria. 20 patients were assigned to the SMA group, and the other 20 patients were assigned to the TIPS group. Between the two groups, the baseline characteristics (*i.e.,* age, sex, etiology, liver function, splenectomy, status of PVT) had no significant difference (Table 1). There were 29 (72.5%) men and 11 (27.5%) women. The mean patient age was 49.3 ± 11.0 years (range, 27-72 yr). There were 31 (77.5%) patients with cirrhosis caused by hepatitis B virus (HBV), 1 patient (2.5%) by hepatitis C virus (HCV), 6 patients (15%) by alcohol, 1 patient (2.5%) by an autoimmune disorder, and 1 patient (2.5%) had a cryptogenic etiology. The average Child-Pugh score was 8.98 ± 1.79, and the average MELD score was 8.56 ± 5.98. There was no significant difference between the two groups in the MPV status; SMV thrombosis and SV thrombosis were in 16 patients and 15 patients, respectively.

***Intervention and follow-up***

The technical success rate was 100% in both groups, and no fatal complications occurred.

In the SMA group, after treatment for 24 h, abdominal pain and abdominal distension were reduced by 80.0% (16/20), and 15.0% (3/20) patients had no re-aggravation of their symptoms. At 48 h after the start of treatment, all of the 20 patients had a definite improvement in symptoms, and no patient had abdominal pain, distention before the end of thrombolysis (SMA catheter withdrawal). The mean time of indwelling SMA catheter was 8.75 ± 2.31 d, and the average dose of urokinase was 3705000.0 ± 1437000.1 IU. Before removing the catheter, contrast studies showed that in 15 cases, PVT had completely disappeared; another 5 cases of PVT had been absorbed (compared with before treatment, residual thrombus was < 10%).

During the follow-up period, no patients died. Oral warfarin (1.5-3.0 mg/d) for at least 3 mo was administered to patients to achieve an INR of 2 to 3. One patient stopped using warfarin and was treated with vitamin K1 after discharge for 1 month; this patient has and INR of 9.27 and an APTT of 66.8s during follow-up. Two patients were diagnosed with malignant tumors.

In the TIPS group, after treatment for 24 h, abdominal pain and abdominal distension were reduced by 75.0% (15/20), and 15.0% (3/20) patients maintained the original symptoms. At 48 hours after the start of treatment, all of the 20 patients had a definite improvement in symptoms.

The average value of portal pressure decreased from 46.30 ± 11.50 mmHg to 32.30 ± 7.47 mmHg. The last ultrasound scan before discharge showed that PVT had completely disappeared in 14 cases, another 6 cases of PVT had been absorbed. During the follow-up period, one patient died of liver failure 14 months after treatment. Ten patients had gastrointestinal rebleeding. Six patients had hepatic encephalopathy. Shunt dysfunction occurred in eight patients, six of whom underwent stent recanalization. Three patients were diagnosed with hepatocellular carcinoma, and one patient was diagnosed with suspected liver cancer.

***Outcomes***

**Changes in PVT:** At the 6-mo follow-up, in the SMA group, 15 patients sustained recanalization, 4 improved, and 1 remained stable; no patient had a worsened condition. In the TIPS group, 12 patients maintained sustained recanalization, 4 improved, and 4 remained stable; no patient had a worsened condition (*P* = 0.239). At the 12-month follow-up, in the SMA group, compared with the 6-month follow-up, the patients' status of thrombus did not change. In the TIPS group, 13 patients achieved continuous recanalization, 2 were improved, 2 remained stable, and 3 patients worsened due to shunt dysfunction (*P* = 0.307). At the 24-month follow-up, 13 patients maintained sustained recanalization, 4 patients improved, 3 remained stable, and no one worsened in the SMA group. In the TIPS group, 11 patients sustained recanalization, 3 patients improved, 2 remained stable, and 4 worsened (one died of liver failure).For the thrombolytic result, there was no significant difference between the two groups (*P* = 0.304) (Table 2). One patient with MPV complete blocking and cavernous transformation (grade III), with severe abdominal pain and black stool, was treated by transcatheter SMA urokinase infusion therapy; the MPV achieved complete thrombosis, and 6 months later achieved sustained recanalization (Figure 2). In summary, the thrombus was significantly reduced in both groups (*P* < 0.001) (Tables 3 and 4) and it was patients with grade I and II PVT that benefitted the most. In addition, in the SMA group, SMV thrombosis and SV thrombosis were significantly reduced (*P* = 0.048, *P* = 0.02).

**Rebleeding:** A total of 11 patients in the SMA group and 8 patients in the TIPS group had rebleeding. In the SMA group, recurrent variceal bleeding occurred in seven patients; no explicit causation was found in the remaining four patients. In the TIPS group, gastrointestinal bleeding after shunt dysfunction occurred in four patients; no explicit causation was found in any of the four patients. The cumulative rates free of the first episode of rebleeding at months 6, 12, and 24 in the SMA group and in the TIPS group were 80%, 65%, and 45% *vs* 90%, 80%, and 60%, respectively (*P* = 0.320) (Figure 3A).

***Hepatic encephalopathy***

Hepatic encephalopathy occurred in 7 and 13 patients in the SMA group and the TIPS group, respectively. The cumulative rates free of the first episode of hepatic encephalopathy at months 6, 12, and 24 in the SMA group and in the TIPS group were 85%, 80%, and 65% *vs* 50%, 40%, and 35%, respectively (*P* = 0.022) (Figure 3B).

**DISCUSSION**

To date, the primary treatments for PVT include anticoagulation, thrombectomy, thrombolysis, and TIPS[16]. Although there is general agreement that anticoagulant therapy is needed for most symptomatic cases of PVT[17], there is no consensus on the treatment of liver cirrhosis with acute PVT. It was reported that simple anticoagulant therapy had a better curative effect on the patients with mild symptoms and limited scope of thrombus[18,19]. Compared to anticoagulation therapy, catheter-directed thrombolysis and TIPS are used infrequently, but their advantages are as follows: (1) can decrease the risk of rebleeding in cirrhosis patients with previous variceal bleeding; (2) increases the rate of portal vein recanalization; and (3) can also be used with patients with cavernous transformation of the portal vein (CTPV)[14,20-23].

In our study, acute PVT greatly improved after catheter-directed thrombolysis and TIPS, and there was no significant difference between the two groups. Evidence about the use of thrombolytics for the treatment of acute PVT in patients with cirrhosis is relatively rare; some studies showed that PVT disappearance occurs in 100% with no recurrence during follow-up [14]. Acute PVT in 70% of patients was improved after TIPS treatment, which is consistent with previous studies that PVT disappearance occurs in 57% to 100% of patients[22,24]. We consider that this is consistent with the view that a reduced portal vein flow velocity is the key risk factor of PVT formation[7, 14, 25]. Patients with concomitant cirrhosis have significantly slower portal vein flow rates than does the healthy population[14]. In addition, old thrombus often cannot be cleared completely, which aggravates local blood circulation disorder. Moreover, we observed that SMV thrombolysis and SV thrombolysis disappeared significantly in the SMA group, and no phenomenon occurred in the TIPS group. Previous reports showed that the treatment of acute PV-SMV thrombosis by the superior mesenteric artery catheter via the femoral artery was effective[14]. This method is simple, easy to operate, and very safe. Because the thrombolytic agent circulates into the branch of the intestinal vein, the treatment of mesenteric venous thrombosis is better. All in all, the acute PVT improved after SMA and TIPS; in addition, transcatheter selective SMA infusion therapy is better for the treatment of fresh thrombus in the mesentery.

Another problem that we are particularly concerned about is rebleeding. We observe that the rates of rebleeding are lower and the time to rebleeding is delayed in the TIPS group compared with the SMA group, although there is no significant difference between the two groups (*P* = 0.320). It has been confirmed that TIPS decreases the incidence of rebleeding as the second-line treatment for variceal hemorrhage[22,25]. In our study, a relatively low-dose infusion of urokinase, no simultaneous peripheral venous infusion, and close monitoring of blood coagulation (which may cause the incidence of rebleeding) kept complications relatively low.

In the TIPS group, the patency rate in 24 mo was consistent with previous studies using covered stents[27]. TIPS is related to an increased risk of hepatic encephalopathy[22,23]. Our study showed that occurrences of hepatic encephalopathy in the TIPS group were markedly higher than in the SMA group, and 50% of patients with hepatic encephalopathy, which is caused by the portosystemic shunting, had this occurrence within of months after TIPS treatment, whereas patients in the SMA group had hepatic encephalopathy caused by deterioration of liver function.

There are some limitations to our study. First, the lack of a large sample of participants is the major limitation, and further large-scale studies are needed. Second, ours was not a double-blind study, because patients in our study needed to be closely followed up for blood clotting, and to detect complications that may be life-threatening.

In conclusion, transcatheter SMA infusion therapy and TIPS are both safe and effective treatments for patients with cirrhosis and acute PVT,particularly for grade I and II PVT ,and transcatheter SMA urokinase infusion therapy is more ideal for the treatment of fresh thrombus in the mesentery.

**ARTICLE HIGHLIGHTS**

***Research background***

Acute portal vein thrombosis is a common complication of cirrhosis and would lead to adverse prognosis. Increasing endovascular selective catheterization thrombolytic therapy and transjugular intrahepatic portosystemic shunt has been successfully implemented which brings new opportunities for the treatment of acute portal vein thrombosis (PVT).

***Research motivation***

The aim of this study was to compare the clinical outcomes of transcatheter

selective superior mesenteric artery (SMA) urokinase infusion therapy and transjugular intrahepatic portosystemic shunt (TIPS) in patients with cirrhosis and acute PVT to evaluate their effectiveness and safety which can confirm the effectiveness of two treatments for acute PVT.

***Research objectives***

Evaluate effectiveness and safety of transcatheter selective SMA urokinase infusion therapy and TIPS in patients with cirrhosis and acute PVT to provide theoretical support for the implementation of new therapies.

***Research methods***

They made a randomized controlled trial, and the total follow-up time was 24 mo. The outcome measure was the change in portal vein patency status rate of rebleeding and hepatic encephalopathy.

***Research results***

Two treatments can quickly relieve symptoms within 48 hours .The main portal vein thrombosis was significantly reduced in both groups and there was no significant difference between them. No fatal complications occurred.

***Research conclusions***

Transcatheter SMA infusion therapy and TIPS are both safe and effective treatments for patients with cirrhosis and acute PVT, particularly for grade I and II PVT, and transcatheter SMA urokinase infusion therapy is more ideal for the treatment of fresh thrombus in the mesentery.

***Research perspectives***

Further large-scale studies are needed. It is better to have a separate anticoagulant group as a control.

**REFERENCES**

1 **Primignani M**. Portal vein thrombosis, revisited. *Dig Liver Dis* 2010; **42**: 163-170 [PMID: 19766546 DOI: 10.1016/j.dld.2009.08.003]

2 **Violi F**, Corazza RG, Caldwell SH, Perticone F, Gatta A, Angelico M, Farcomeni A, Masotti M, Napoleone L, Vestri A, Raparelli V, Basili S; PRO-LIVER Collaborators. Portal vein thrombosis relevance on liver cirrhosis: Italian Venous Thrombotic Events Registry. *Intern Emerg Med* 2016; **11**: 1059-1066 [PMID: 27026379 DOI: 10.1007/]

3 **Stine JG**, Shah PM, Cornella SL, Rudnick SR, Ghabril MS, Stukenborg GJ, Northup PG. Portal vein thrombosis, mortality and hepatic decompensation in patients with cirrhosis: A meta-analysis. *World J Hepatol* 2015; **7**: 2774-2780 [PMID: 26644821 DOI: 10.4254/wjh.v7.i27.2774]

4 **Aman**N, Gul H, Roghani IS, Afridi Z. Frequency of portal vein thrombosis in cirrhosis on ultrasound. *J Med Sci* 2015; **23**: 11-13

5 **Turon** F, Baiges A, Garcia-Criado A, Nuñez I, Gilabert R, Bru C, Hernández-Gea V. Portal Vein Thrombosis in Patients with Cirrhosis. Incidence and Factors Associated with Its Development. *J Hepatol* 2016; **64**: S260 [DOI: 10.1016/S0168-8278(16)00290-7]

6 **Qi X**, Li H, Liu X, Yao H, Han G, Hu F, Shao L, Guo X. Novel insights into the development of portal vein thrombosis in cirrhosis patients. *Expert Rev Gastroenterol Hepatol* 2015; **9**: 1421-1432 [PMID: 26325361 DOI: 10.1586/17474124.2015.1083856]

7 **Qi X**, Dai J, Yang M, Ren W, Jia J, Guo X. Association between Portal Vein Thrombosis and Survival in Non-Liver-Transplant Patients with Liver Cirrhosis: A Systematic Review of the Literature. *Gastroenterol Res Pract* 2015; **2015**: 480842 [PMID: 25810714 DOI: 10.1155/2015/480842]

8 **Qi X**, Dai J, Jia J, Ren W, Yang M, Li H, Fan D, Guo X. Association between portal vein thrombosis and survival of liver transplant recipients: a systematic review and meta-analysis of observational studies. *J Gastrointestin Liver Dis* 2015; **24**: 51-59, 4 p following 59 [PMID: 25822434 DOI: 10.15403/jgld.2014.1121.qix]

9 **Qi X**, Su C, Ren W, Yang M, Jia J, Dai J, Xu W, Guo X. Association between portal vein thrombosis and risk of bleeding in liver cirrhosis: A systematic review of the literature. *Clin Res Hepatol Gastroenterol* 2015; **39**: 683-691 [PMID: 25956490 DOI: 10.1016/j.clinre.2015.02.012]

10 **Zang L**, Sun Z, Li W, Liu X. [Meta-analysis of risk factors of gastroesophageal varices rebleeding after therapeutic endoscopy]. *Zhonghua Gan Zang Bing Za Zhi* 2015; **23**: 275-280 [PMID: 26133819 DOI: 10.3760/cma.j.issn.1007-3418.2015.04.009]

11 **Loffredo L**, Pastori D, Farcomeni A, Violi F. Effects of Anticoagulants in Patients With Cirrhosis and Portal Vein Thrombosis: A Systematic Review and Meta-analysis. *Gastroenterology* 2017; **153**: 480-487.e1 [PMID: 28479379 DOI: 10.1053/j.gastro.2017.04.042]

12 **Tonon**M, Piano S, Sacerdoti D, Dalla Valle F, Grbec M, Spiezia L, AngeliP. Efficacy and safety of treatment of acute nonmalignant portal vein thrombosis with subcutaneous fondaparinux in patients with cirrhosis and marked thrombocytopenia. *Hepatology* 2015; **62**: 591A [DOI: 10.1016/j.dld.2015.12.066]

13 **Tsochatzis EA**, Senzolo M, Germani G, Gatt A, Burroughs AK. Systematic review: portal vein thrombosis in cirrhosis. *Aliment Pharmacol Ther* 2010; **31**: 366-374 [PMID: 19863496 DOI: 10.1111/j.1365-2036.2009.04182.x]

14 **Wang MQ**, Guo LP, Lin HY, Liu FY, Duan F, Wang ZJ. Transradial approach for transcatheter selective superior mesenteric artery urokinase infusion therapy in patients with acute extensive portal and superior mesenteric vein thrombosis. *Cardiovasc Intervent Radiol* 2010; **33**: 80-89 [PMID: 20033163 DOI: 10.1007/s00270-009-9777-2]

15 **Wang MQ**, Liu FY, Duan F, Wang ZJ, Song P, Fan QS. Acute symptomatic mesenteric venous thrombosis: treatment by catheter-directed thrombolysis with transjugular intrahepatic route. *Abdom Imaging* 2011; **36**: 390-398 [PMID: 20652243 DOI: 10.1007/s00261-010-9637-1]

16 **Sharma AM**, Zhu D, Henry Z. Portal vein thrombosis: When to treat and how? *Vasc Med* 2016; **21**: 61-69 [PMID: 26584887 DOI: 10.1177/1358863X15611224]

17 **European Association for the Study of the Liver.** Electronic address: easloffice@easloffice.eu. EASL Clinical Practice Guidelines: Vascular diseases of the liver. *J Hepatol* 2016; **64**: 179-202 [PMID: 26516032 DOI: 10.1016/j.jhep.2015.07.040]

18 **Harnik IG**, Brandt LJ. Mesenteric venous thrombosis. *Vasc Med* 2010; **15**: 407-418 [PMID: 20926500 DOI: 10.1177/1358863X10379673]

19 **Bergqvist D**, Svensson PJ. Treatment of mesenteric vein thrombosis. *Semin Vasc Surg* 2010; **23**: 65-68 [PMID: 20298951 DOI: 10.1053/j.semvascsurg.2009.12.008]

20 **Liu K**, Li WD, Du XL, Li CL, Li XQ. Comparison of Systemic Thrombolysis Versus Indirect Thrombolysis via the Superior Mesenteric Artery in Patients with Acute Portal Vein Thrombosis. *Ann Vasc Surg* 2017; **39**: 264-269 [PMID: 27671456 DOI: 10.1016/j.avsg.2016.06.029]

21 **Qi X**, Han G, Fan D. The preferable treatment for cirrhotic portal vein thrombosis: anticoagulation or transjugular intrahepatic portosystemic shunt? *Hepatology* 2010; **51**: 713-714 [PMID: 20104582 DOI: 10.1002/hep.23217]

22 **Han G**, Qi X, He C, Yin Z, Wang J, Xia J, Yang Z, Bai M, Meng X, Niu J, Wu K, Fan D. Transjugular intrahepatic portosystemic shunt for portal vein thrombosis with symptomatic portal hypertension in liver cirrhosis. *J Hepatol* 2011; **54**: 78-88 [PMID: 20932597 DOI: 10.1016/j.jhep.2010.06.029]

23 **Luca A**, Miraglia R, Caruso S, Milazzo M, Sapere C, Maruzzelli L, Vizzini G, Tuzzolino F, Gridelli B, Bosch J. Short- and long-term effects of the transjugular intrahepatic portosystemic shunt on portal vein thrombosis in patients with cirrhosis. *Gut* 2011; **60**: 846-852 [PMID: 21357252 DOI: 10.1136/gut.2010.228023]

24 **D'Avola D**, Bilbao JI, Zozaya G, Pardo F, Rotellar F, Iñarrairaegui M, Quiroga J, Sangro B, Herrero JI. Efficacy of transjugular intrahepatic portosystemic shunt to prevent total portal vein thrombosis in cirrhotic patients awaiting for liver transplantation. *Transplant Proc* 2012; **44**: 2603-2605 [PMID: 23146469 DOI: 10.1016/j.transproceed.2012.09.050]

25 **Stine JG**, Wang J, Shah PM, Argo CK, Intagliata N, Uflacker A, Caldwell SH, Northup PG. Decreased portal vein velocity is predictive of the development of portal vein thrombosis: A matched case-control study. *Liver Int* 2017; Epub ahead of print [PMID: 28632958 DOI: 10.1111/liv.13500]

26 **Qi X**, He C, Guo W, Yin Z, Wang J, Wang Z, Niu J, Bai M, Yang Z, Fan D, Han G. Transjugular intrahepatic portosystemic shunt for portal vein thrombosis with variceal bleeding in liver cirrhosis: outcomes and predictors in a prospective cohort study. *Liver Int* 2016; **36**: 667-676 [PMID: 26235541 DOI: 10.1111/liv.12929]

27 **Perarnau JM**, Le Gouge A, Nicolas C, d'Alteroche L, Borentain P, Saliba F, Minello A, Anty R, Chagneau-Derrode C, Bernard PH, Abergel A, Ollivier-Hourmand I, Gournay J, Ayoub J, Gaborit C, Rusch E, Giraudeau B; STIC-TIPS group. Covered vs. uncovered stents for transjugular intrahepatic portosystemic shunt: a randomized controlled trial. *J Hepatol* 2014; **60**: 962-968 [PMID: 24480619 DOI: 10.1016/j.jhep.2014.01.015]

**P-Reviewer:** Memeo R, Tripathi D **S-Editor:** Qi Y **L-Editor: E-Editor:**

**Specialty type:** Gastroenterology and hepatology

**Country of origin:** China

**Peer-review report classification**

Grade A (Excellent): 0

Grade B (Very good): B

Grade C (Good): C

Grade D (Fair): 0

Grade E (Poor): 0

**Figure 1** **Study flow and inclusion criteria of two groups.** PVT: Portal vein thrombosis; TIPS: Transjugular intrahepatic portosystemic shunt; SMA: Superior mesenteric artery.

Liver cirrhosis with acute PVT (n=57)

Excluded(n=17)

1. contraindications to anticoagulation therapy(n=4)

2. previous TIPS or thrombolytic therapy(n=3)

3. malignant tumor(n=10)

TIPS group(n=20)

Lost to follow up(n=0)

Died(n=1)

Lost to follow up(n=0)

Died (n=0)

SMA group(n=20)

Allocation

Follow up

Randomized (n=40)

Enrollment



**Figure 2** **Contrast images by angio-computed tomography before and after transcatheter selective** **superior mesenteric artery urokinase infusion therapy in a patient.** A: A patient with MPV complete blocking and cavernous transformation (grade III) before urokinase infusion; B: 6 mo after urokinase infusion, MPV achieved sustained recanalization, but there is still cavernous transformation.



**Figure 3 Superior mesenteric artery group and in the transjugular intrahepatic portosystemic shunt group.** A: Cumulative rate free of the first episode of rebleeding in superior mesenteric artery (SMA) group and in transjugular intrahepatic portosystemic shunt (TIPS) group (*P* = 0.320 by log-rank test); B: Cumulative rate free of the first episode of hepatic encephalopathy in SMA group and in TIPS group (*P* = 0.022 by log-rank test).

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| **Table 1 Baseline characteristics of the study population** |
| **Characteristic** | **SMA group (*n* = 20)** | **TIPS group (*n* = 20)** | ***P* value** |
| Age (yr)1 | 48.4 ± 13.2 | 50.1 ± 8.6 | 0.632 |
| Male sex | 14 | 15 | 1.0003 |
| Etiology |  |  | 0.1563 |
| HBV | 14 | 17 |  |
| HCV | 0 | 1 |  |
| Alcohol | 5 | 1 |  |
| Autoimmune | 0 | 1 |  |
|  Cryptogenic | 1 | 0 |  |
| Child-Pugh class |  |  | 0.0652 |
| A | 6 | 1 |  |
| B | 8 | 9 |  |
| C | 6 | 10 |  |
| Child-Pugh score1 | 8.6 ± 1.7 | 9.4 ± 1.8 | 0.135 |
| MELD score1 | 8.0 ± 6.9 | 9.1 ± 5.1 | 0.582 |
| Splenectomy | 6 | 3 | 0.4513 |
| Past Esophageal or gastric varices | 13 | 18 | 0.1273 |
| Past Gastrointestinal bleeding | 12 | 18 | 0.0653 |
| MPV thrombus |  |  | 0.9382 |
| Grade I | 6 | 7 |  |
| Grade II | 13 | 11 |  |
| Grade III | 1 | 2 |  |
| SMV thrombus | 11 | 5 | 0.1053 |
| SV thrombus | 8 | 7 | 1.0003 |

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| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| 1Data are mean plus or minus standard deviation; 2Determined with Mann-Whitney *U* test;3Determined with Fisher exact test. Data are numbers of patients. MELD: Model for end-stage liver disease; MPV: Main portal vein; SMV: Superior mesenteric vein, SV: Splenic vein.

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| **Table 2 Comparison of**  **portal vein thrombosis changes between**  **superior mesenteric artery group and**  **transjugular intrahepatic portosystemic shunt group** |
|  | **SMA group ( *n* = 20)** | **TIPS group (*n* = 20)** |  |  |  |
| **Time (mo)** | **6**  | **12**  | **24** | **6**  | **12**  | **24** | ***P* value** |
| Recanalization | 15 | 15 | 13 | 12 | 13 | 11 | *P* = 0.239 (6 mo) |
|  Improved | 4 | 4 | 4 | 4 | 2 | 3 | *P* = 0.307 (12 mo) |
|  Stable | 1 | 1 | 3 | 4 | 2 | 2 | *P* = 0.304 (24 mo) |
|  Worse | 0 | 0 | 0 | 0 | 3 | 4 |  |

Data are numbers of patients. Determined with Mann-Whitney *U* test. TIPS: Transjugular intrahepatic portosystemic shunt; SMA: Superior mesenteric artery.

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| **Table 3 Changes in**  **portal vein thrombosis before and after urokinase infusion in**  **superior mesenteric artery group** |

|  |  |  |  |
| --- | --- | --- | --- |
|  | **Before** | **After** | ***P* value** |
| MPV thrombus |  |  | *P* < 0.001 |
| Grade 0 | 0 | 13 |  |
| Grade I | 6 | 4 |  |
| Grade II | 13 | 3 |  |
| Grade III | 1 | 0 |  |
| SMV thrombus | 11 | 4 | 0.0481 |
| SV thrombus | 8 | 1 | 0.021 |

1Determined with Fisher exact test. *P* value is a comparison at 24-month follow-up.Data are numbers of patients. Determined with Mann-Whitney *U* test.

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| **Table 4 Changes in**  **portal vein thrombosis before and after**  **transjugular intrahepatic portosystemic shunt in**  **transjugular intrahepatic portosystemic shunt group** |

|  |  |  |  |
| --- | --- | --- | --- |
|  | **Before** | **After**  | ***P* value** |
| MPV thrombus |  |  | *P* < 0.001 |
| Grade 0 | 0 | 11 |  |
| Grade I | 7 | 3 |  |
| Grade II | 11 | 2 |  |
| Grade III | 2 | 4 |  |
| SMV thrombus | 5 | 7 | 0.7311 |
| SV thrombus | 7 | 3 | 0.2731 |

1Determined with Fisher exact test. *P* value are a comparison at 24-month follow-up. Data are numbers of patients. Determined with Mann-Whitney *U* test. SMA: Superior mesenteric artery; MPV: Main portal vein. |