Int J Clin Exp Med 2017;10(2):3486-3493
www.ijcem.com /ISSN:1940-5901/IJCEM0043341

Original Article

Transjugular intrahepatic portosystemic shunt for chronic portal vein thrombosis and incidence of hepatic eeplopathy

Hongwei Zhao[1], Fuquan Liu[1], Zhendong Yue[1], Lei Wang[1], Zhenhua Fan[1], Yanna Liu[2], Jialiang Hui[2], Yi Xiang[2], Xiaolong Qi[2]

[1]*Department of Interventional Therapy, Beijing Shijitan Hospital, Capital Medical University, Beijing 100038, China;* [2]*Department of General Surgery, Nanfang Hospital, Southern Medical University, Guangzhou, China*

Received November 5, 2016; Accepted November 25, 2016; Epub February 15, 2017; Published February 28, 2017

Abstract: Objective: This study investigated the relationship between the incidence of hepatic encephalopathy (HE) after transjugular intrahepatic portosystemic shunt (TIPS) for chronic portal vein thrombosis (PVT) and the surgical procedures based on the anatomical classification of thrombosis. Methods: In the present retrospective study, 73 consecutive patients were diagnosed with chronic PVT and treated with TIPS with covered stent. Patients were enrolled between January 2012 and June 2015. The development of HE was assessed in the 1st, 3rd, and 12th months of their follow-up. A paired t-test was used to compare pre- and post-TIPS portal vein pressure. Results: Statistical differences were found between pre- and post-TIPS portal vein pressure intype I, II, III and IV patients (P<0.01). Minimal HE was mostly seen in type IV, IIa, and IIIa, respectively, at 1, 3, and 12 months, postoperatively. By contrast, the incidence of grade I HE was the highest in type IIa, IIIa, and IIb, respectively. Additionally, grade II HE occurred mostly in types IIb, IIa, and IIIb, respectively. Further, patients with type IIb and IIIb showed longer HE duration with a follow-up of 12 months. Conclusions: An appropriate anatomical classification of chronic PVT is essential for the application of TIPS clinically. The incidence of postoperative HE is higher in patients with simple thrombosis associated with the main portal veinor superior mesenteric vein.

Keywords: Hepatic cirrhosis, hepatic encephalopathy, transjugular intrahepatic portosystemic shunt, portal vein thrombosis, covered stent

Introduction

Portal vein thrombosis (PVT) is an obstructive deep vascular disease and one of the major complications of liver cirrhosis [1, 2]. It refers to thrombosis originating in the main portal vein or its intrahepatic branches, superior or inferior mesenteric veins, or splenic veins [3]. Patients with severe portal hypertension caused by PVT may manifest upper gastrointestinal hemorrhage and refractory ascites. However, PVT can be asymptomatic and most patients are not diagnosed until they exhibit symptoms of portal hypertension [4]. Until then, chronic thrombosis may occur to varying degrees and the efficacy of both surgical and medical treatment is limited. Transjugular intrahepatic porto-systemic shunt (TIPS) effectively decompresses the portal system by directly reconstructing portal vein flow and ameliorating the clinical manifestations of PVT [5, 6]. To the best of our knowedge, studies involving the incidence of hepatic encephalopathy (HE) and PVT prognosis after TIPS have rarely been published. This study aims to investigate the role of TIPS based on the anatomical classification of PVT and the incidence of HE postoperatively.

Methods

Patients

Between January 2011 and June 2015, a total of 73 PVT patients treated with TIPS in Beijing Shijitan Hospital were enrolled, accounting for 8.77% (73/832) of patients with cirrhosis and 14.26% (73/512) of TIPS-treated patients during the same period. The study includes 48 male and 25 female patients, aged between 36 and 72 years (average: 56.4±17.6), with a history of cirrhosis and portal hypertension for 3.2-

Table 1. Etiology, clinical presentation and Child-Pugh scores

	Number (n)	Percent (%)
Cause of Disease		
Hepatitis virus infection	59	80.82
Alcohol abuse	6	8.22
Hepatic vein obstruction	4	5.48
Biliary cirrhosis	3	4.11
Other causes	1	1.37
Clinical Presentation		
Vomiting	65	89.04
Melena	69	94.52
Ascites	32	43.84
Spider angioma	51	69.86
Liver palms	45	61.64
Dyspnea	48	65.75
Cyanosis	25	34.25
Acropachy	39	53.42
Child-Pugh Score		
Grade A	4	5.48
Grade B	46	63.01
Grade C	23	31.51

Table 2. Baseline characteristics of patients based on Zhao Classification

Type	Sex	Age (year)	Child-Pugh Score		
	Male:Female		A	B	C
I	10:4	50.4±10.9	1	5	8
IIa	7:2	46.2±13.1	0	8	1
IIb	6:3	52.9±17.3	0	6	3
IIc	4:3	59.1±12.8	0	6	1
IIIa	5:3	47.3±19.5	1	5	2
IIIb	6:4	48.2±14.8	1	6	3
IIIc	7:4	57.4±13.5	1	9	1
IV	3:2	59.0±21.2	0	1	4
Total	48:25	56.4±17.6	4	46	23

Type I: simple main portal vein thrombosis; Type II: main portal vein thrombosis associated with branch thrombosis; Type IIa: main portal vein thrombosis associated with intrahepatic thrombosis; Type IIb: main portal vein thrombosis associated with splenic vein thrombosis; Type IIc: main portal vein thrombosis associated with superior mesenteric vein thrombosis; Type III: simple portal venous thrombosis; Type IIIa: simple intrahepatic thrombosis; Type IIIb: simple splenic vein thrombosis; Type IIIc: simple superior mesenteric vein thrombosis; Type IV: mixed thrombosis (including cavernous transformation of the portal vein but normal intrahepatic branches; excluding complete cavernous transformation of the portal vein).

15.4 years (average: 8.9±5.8). The etiology and clinical presentations of liver cirrhosis and Child-Pugh score of our patients are summarized in **Table 1**. Fluency cover stents (Bard Inc, Germany) with a length of 60-120 mm and a diameter of 8 mm were implanted in all cases. A PVT anatomical classification (Zhao Classification) was established based on our previous clinical experience with diagnosis and treatment. The baseline characteristics of our study patients according to Zhao Classification are listed in **Table 2**.

Imaging

All the patients underwent abdominal CT scan, ultrasonography, and magnetic resonance imaging of portal vein (MRPV) prior to TIPS showing different sites of PVT (**Figure 1**).

TIPS

The procedure of TIPS is omitted here. Portal vein pressure was measured both before and after surgical bypass. Successful TIPS was defined as a 30% decline in portal vein pressure post-TIPS as well as the absence of abnormal venous varicosity under venography. The cover stents (φ 8 mm) were fully deployed during the procedure and the success rate was 100%.

In type I cases, the shunt was created only distal to the thrombus at the main portal vein. In type II patients, stents were placed at the normal lumen distal to the main portal vein thrombus through the intrahepatic branches. Shunts were established distal to the lesion of superior mesenteric vein as much as possible. Balloon angioplasty and thrombolysis were performed in case of splenic vein thrombosis. Among type III patients, shunts were created via normal intrahepatic branches of portal vein. The superior mesenteric vein thrombosis was managed with covered stent. Meanwhile, splenic vein thrombosis was treated with embolectomy, thrombolysis and balloon angioplasty. In type IV cases, stents were implanted through intrahepatic branches and deployed in normal branches distal to the main portal vein.

Follow-up

HE was evaluated according to the West-Haven Criteria in the 1st, 3rd, and 12th month of follow-up by two highly-ranked or associate chief physicians. Since there is an overlap between grade 0 and grade I according to the traditional

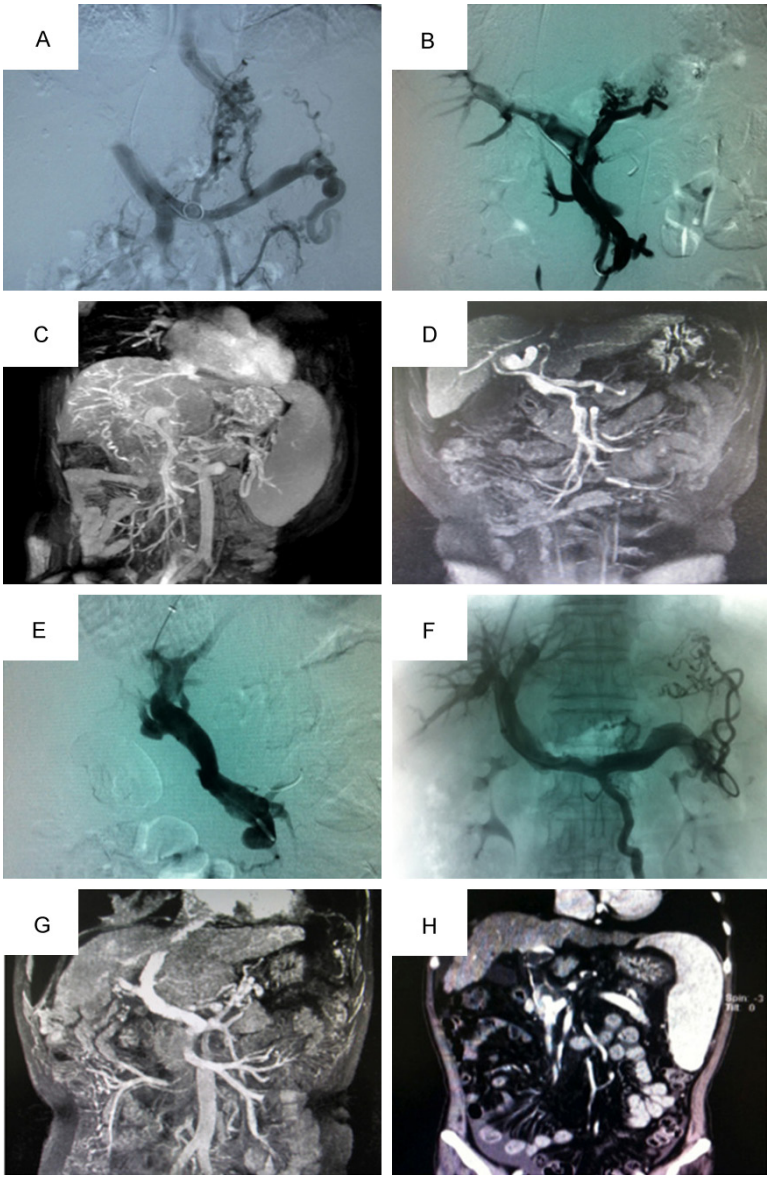

Figure 1. Imaging studies involving different PVT types. A: Angiography shows type I PVT (simple main portal vein thrombosis); B: Angiography shows type IIa PVT (main portal vein thrombosis associated with hepatic branch thrombosis); C: Coronal view of abdominal magnetic resonance shows type IIb PVT (main portal vein thrombosis associated with splenic thrombosis); D: Coronal view of abdominal magnetic resonance shows type IIc PVT (main portal vein thrombosis associated with superior mesenteric vein thrombosis); E: Angiology shows type IIIa PVT (simple intrahepatic thrombosis); F: Angiology shows type IIIb PVT (simple splenic vein thrombosis); G: Coronal view of abdominal magnetic resonance shows type IIIc PVT (simple superior mesenteric vein thrombosis); H: Coronal view of abdominal magnetic resonance shows type IV PVT mixed thrombosis).

HE grading system, we divided grade 0 HE into normal cognitive function and minimal hepatic encephalopathy (MHE). The MHE assessment was made by Number Connection Tests A (NCT-A), a test for visual concept and visual motor tracking. During the test, patients were required to connect the random numbers 1 to 25 in order. MHE was defined as a completion time exceeding 66 s.

Statistical analysis

All the analyses were performed with SPSS 19.0 (SPSS, Inc., Chicago, IL, USA). A paired t-test was used to compare pre- and post-TIPS portal vein pressure. Statistical significance was defined as $P<0.05$.

Results

Basic characteristics of patients post-TIPS

All the patients received TIPS successfully and were followed up for 0.5-18 months. One of the type I patients developed stress gastrointestinal bleeding and was treated with acid suppression therapy. Two cases presented with melena (50 mL each time) after TIPSondays7 and 16 post-TIPS, respectively. They were diagnosed with gastric variceal bleeding and portal hypertension-related gastric bleeding, respectively, under endoscopy. Although hemostasis was achieved by endoscopic procedures, one of the patients died of liver dysfunction 7 months post-TIPS. The other patient underwent liver transplantation 11 months after TIPS. One of the patients with type II died of liver dysfunction 8.5 months after TIPS. In addition, another patient received liver transplant 9 months post TIPS. One patient was lost to follow-up after 13 months. One of the patients with type III died of liver dysfunction 10 months after TIPS. Further, one patient underwent liver transplant 10 months post TIPS and another was lost to follow-up 7.5 months after TIPS. Among type IV cases, one patient died of severe ascites infection 1 month

Table 3. Incidence of HE 1 month after TIPS

Type	Grade 0		Grade I	Grade II	Grade III	Grade IV	Total
	N	M					
I	1	5 (35.7%)	4 (28.6%)	3 (21.4%)	1	0	14
IIa	2	1	4 (44.4%)	1	1	0	9
IIb	1	2	2	3 (33.3%)	1	0	9
IIc	4	1	2	0	0	0	7
IIIa	5	2	1	0	0	0	8
IIIb	1	3 (30%)	3 (30%)	3 (30%)	0	0	10
IIIc	5	3	2	1	0	0	11
IV	1	2 (40%)	1	1	0	0	5

Table 4. Incidence of HE 3 months after TIPS

Type	Grade 0		Grade I	Grade II	Grade III	Grade IV	Total
	N	M					
I	2	5	5	2	0	0	14
IIa	1	4 (44.4%)	2	2 (22.2%)	0	0	9
IIb	0	3	4 (44.4%)	2 (22.2%)	0	0	9
IIc	2	3 (42.9%)	2	0	0	0	7
IIIa	2	4 (50%)	2	0	0	0	8
IIIb	0	2	6 (60%)	2 (22.0%)	1	0	10
IIIc	3	3	3	2	0	0	11
IV	1	1	2 (40%)	1	0	0	5

Table 5. Incidence of HE 12 months after TIPS

Type	Grade 0		Grade I	Grade II	Grade III	Grade IV	Total
	N	M					
I	3	3	5 (35.7%)	2 (14.3%)	1	0	14
IIa	1	6 (66.7%)	1	1	0	0	9
IIb	0	2	4 (44.4%)	2 (22.2%)	1	0	9
IIc	2	4 (57.1%)	1	0	0	0	7
IIIa	4	2	2	0	0	0	8
IIIb	0	4 (40%)	3 (30%)	2 (20%)	1	0	10
IIIc	6	3	2	0	0	0	11
IV	0	1	2	1	0	0	4*

N: normal cognitive function, M: minimal hepatic encephalopathy, *one patient lost to follow up.

post TIPS; and another was lost to follow-up after 5.5 months.

Changes in portal vein pressure post-TIPS for different portal system thrombosis

Statistical differences between pre- and post-operative portal vein pressure were seen among type I, II, III and IV patients (32.0±7.2, 29.8±4.1, 32.4±4.3 and 32.2±2.8 versus 26.2±5.0, 23.2±4.3, 24.3±3.7 and 27.4±4.9, respectively; $P<0.01$).

Incidence of HE

As shown in **Table 3**, the incidence of MHE 1 month after TIPS was mainly seen in patients diagnosed with PVT type IV, I and IIIb. Meanwhile, grade I HE mainly occurred in patients involving type IIa, IIIb and IPVT. In addition, grade II HE was seen mainly in patients with type IIb, IIIb and I PVT. The incidence of MHE and HE 3 months after TIPS is summarized in **Table 4**. MHE was mainly detected in patients with type IIIa, IIa and IIc. Further, grade I HE mainly occurred in patients with type IIIa, IIb and IV whereas grade II HE was detected mainly in those with type IIa, IIb and IIIb. The incidence of MHE 12 months post-operatively was mainly seen in patients diagnosed with type IIa, IIc and IIIb. In addition, grade I HE was mainly reported in type IIb, I and IIIb cases. Furthermore, grade II HE was mostly reported in those with type IIb, IIIb and I, as shown in **Table 5**.

Discussion

PVT is common clinically, with a prevalence ranging from 10% to 25% [7]. Usually, it is associated with hepatic tumor, pancreatitis, and surgical procedures. Approximately, 10% of patients with liver cirrhosis experience PVT [8]. China has a high incidence of hepatitis B virus infection, and hepatitis B cirrhosis is the leading cause of PVT, accounting for 57.07% of all cases. Cirrhosis is also associated with alcoholic hepatitis and hepatitis C infection. Other types including primary biliary cirrhosis, and hepatitis B associated with alcoholic hepatitis cirrhosis, autoimmune hepatitis cirrhosis, and drug-induced cirrhosis are rarely seen. In patients with liver cirrhosis, flow interruption in portal system with or without

increases blood flow, and the vasodilatation dysfunction increases the pressure in portal vein as well as its branches leading to splenomegaly, ascites, upper gastrointestinal hemorrhage, HE, and hepatorenal syndrome. Ascites accounts for 30% to 50% while upper gastrointestinal hemorrhage constitutes nearly 20%.

Thrombosis is classified into acute and chronic types according to the traditional criteria [9]. They share the same etiology as well as therapeutic mechanisms including thrombolysis or prevention of clot formation to ameliorate the symptoms, and portal vein recanalization to restore the venous blood flow. However, acute thrombosis is mainly managed via anti-coagulation, thrombolysis and mechanical removal in portal vein recanalization. Most of these patients show effective disease control following appropriate surgical intervention. However, it should be noted that patients may have developed chronic thrombosis before PVT diagnosis. Thus, the efficacy of anti-coagulation and thrombolysis is limited. Recanalization is a routine procedure due to limited surgical advantage [10]. Therefore, interventional techniques may have a promising role in the treatment of PVT [11-14]. PVT patients undergoing interventional therapy are divided into two types: acute or subacute thrombosis (usually within half a month) and chronic thrombosis. In the former type, anti-coagulation and indirect thrombolysis yield satisfactory results in most of the cases, and are excluded from the present study. Only a few were switched to TIPS treatment. Chronic thrombosis is divided into complete, partial and organized types. This study comprises 7 cases (9.59%) of complete thrombosis, 41 cases (56.16%) of partial thrombosis, 8 (6.85%) cases of organized thrombosis and 13 cases (17.81%) of mixed thrombosis. However, the small sample size failed to yield adequate statistical power. It is well recognized that it is necessary to rebuild portal vein shunts with TIPS for chronic PVT patients [15-17]. The benefits of TIPS are as follows: 1. The intrahepatic communication between hepatic and portal veins decreases the risk of bleeding during thrombolysis. 2. Portal vein puncture facilitates direct thrombolysis using balloon catheter, thrombus fragmentation device, and shaping catheter or catheter sheath, followed by re-vascularisation. Furthermore, catheter insertion at the site of thrombus leads to thrombolysis. 3. In patients with severe cirrhosis, intrahepatic portal vein occlusion and portal hypertension, the portosystemic shunt carries blood to the liver and decreases the reflux pressure of gastrointestinal and splenic veins. Complete PVT, the most complicated type of PVT, was once considered a contradiction for surgery and intervention therapy. However, recent advances in intervention techniques and materials suggest that. TIPS is the most preferred and also the most complex choice. The key to successful TIPS is to ensure patency at the distal end of the portal vein (splenic or mesenteric vein) and create a shunting channel. If necessary, percutaneous transhepatic puncture can be used to localize the lumen and branches of the portal vein. Extreme precautions and patience are needed for technical success.

According to international guidelines, PVT refers to thrombosis of the main portal vein and its intrahepatic branches. Simple thrombosis of mesenteric vein and splenic vein thrombosis are considered as two different entities internationally .However, in China, under clinical conditions, simple mesenteric or splenic thrombosis presenting with chronic abdominal pain and ascites without anomalous portal vein is not rare. TIPS is performed following failure of medical and surgical interventions .Therefore, in the present study, a new PVT classification “Zhao Classification” is proposed based on our clinical experience.

Anomalous shunting pathway (stenosis and occlusion) and HE are common complications of TIPS. Drug-covered stent has largely increased the shunt patency. The neurological mechanism of HE, however, remains to be investigated [18]. HE is diagnosed by a series of nervous system disorders after excluding other encephalopathies. In addition, psychological disorders and cognitive dysfunction also are complications of liver cirrhosis. They primarily include personality changes, HE, and result in hepatic coma. However, the current classification of HE does not include neurocognitive disorders. HE-related neurological impairment includes normal and disease phenotypes, and is further classified as normal, mild and phenotype based on psychological and neurophysiological testing. Although widely used for HE, West Haven Criteria are obviously avoided in the assessment of consciousness in early and end-stage. Glasgow Coma Scale is

used for HE coma sub-classification while Clinical Hepatic Encephalopathy Staging Scale (CHESS) is adopted in mental state assessment. Although CHESS is easy to use, it fails to definitively distinguish coma from non-comatose status. According to the West Haven Criteria, grade 0, including normal cognition and mild HE, is defined as the absence of clinical signs of phenotype HE. However, grading ambulatory HE patients simply based on clinical symptoms remains difficult because few specific physical signs are apparent in grades 0 or I cases. The grade 0 subtypes include normal and mild types, which is debatable. MHE, including paroxysmal or persistent HE, refers to the anomalous changes in intelligence, nervous system and mental status in patients with chronic liver disease, without recognizable clinical symptoms of HE or biochemical changes. However, these patients are otherwise diagnosed according to precise intellectual or electrophysiological tests. The ability to operate and respond to emergency is impaired in MHE patients, and therefore, unless promptly treated, MHE develops into clinical HE, with a morbidity rate as high as 50%. In patients with MHE without evident clinical symptoms and biochemical abnormalities, psychometric tests or neurophysiological variables are needed for diagnosis.

Studies involving HE (especially MHE) focus on patients with cirrhosis, with limited emphasis on other severe liver diseases, for example, hepatocellular carcinoma, toxic hepatopathy, and patients after portosystemic shunt and liver transplantation. The poor understanding of the specificity of HE after TIPS and misdiagnosis of cirrhosis may result in patient mismanagement. Therefore, additional studies are needed to investigate HE induced by special primary disease [19].

Esophageal hemorrhage and gastric variceal hemorrhage are traditionally treated with surgical procedures including portacaval bypass, renal-splenic venous shunt and intestinal shunt. However, the incidence of HE postoperatively is high and the procedure is rarely indicated .Conversely, TIPS is considered an effective treatment for esophageal and gastric variceal hemorrhage and refractory ascites induced by PVT. It is minimally invasive with a wide range of indications and effective outcomes. It can also be conducted in patients with massive hemorrhage as long as the blood pressure remains stable. Decompression of portal vein is facilitated by a bypass created between intrahepatic and hepatic veins. However, blood in the portal vein, partly or entirely, entering the systemic circulation without detoxication of liver, may result in the development of HE. Studies suggest that factors contributing to HE after TIPS include, but are not limited to, preoperative liver function, stent diameter, and vena coronaria ventriculi embolism. Thus, the incidence of HE is decreased if the foregoing factors are treated appropriately. However, the occurrence, outcome, therapy and prognosis of post-TIPS HE in patients with different types of PVT has yet to be established.

In the present study, patients diagnosed with type I developed HE (including MHE) in 15 days after TIPS, and most of them were graded 0, I and II. Further, the incidence of HE in patients with type IIb and IIIb was relatively high during the 3th and 12th months postoperatively, and the duration was longer especially in HE grades I and II. Moreover, we found that the incidence of HE was low in type IIb and IIIb patients, who developed splenic thrombosis. A possible reason maybe that the intestinally derived toxic compounds bypassed the liver and entered the systemic circulation, resulting in neurological dys function. Endogenous, ammonia synthesis occurs via protein catabolism while exogenous ammonia is derived from the breakdown of nitrogenous substance in the intestine. Ninety percent of the exogenous ammonia diffuses from the blood vessel of gastrointestinal mucosa and is produced by bacterial ureases. Most of the exogenous ammonia enters from the right hemicolon while only a small portion is generated in the small intestine. The superior mesenteric vein drains the blood from small intestine, right hemicolon and pancreatic head and the splenic vein carries blood from the left hemicolon, mainly from spleen and pancreas tail and even inferior mesenteric vein. Thus, exogenous ammonia is mainly absorbed from superior mesenteric vein, and is carried to the liver through the blood, where it is converted into urea in the ornithine cycle. Urea subsequently is cleared from the body. However, exogenous ammonia is barely produced in the splenic vein or its tributaries. We demonstrated that the levels of blood ammonia in the superior mesenteric vein were much higher than in the splenic vein, and the left and right main branches of portal vein, where ammonia was

higher than in the inferior vena cava. Similar results were obtained in the serum assay (blood ammonia, endotoxin) of patients without PVT following TIPS. The gradient of ammonia and endotoxin levels decreased in a statistically significant manner along the superior mesenteric, portal, splenic and peripheral veins. In the present study, the accumulation of exogenous ammonia resulted in a rapid increase of blood ammonia in the systemic circulation as the superior mesenteric venous ammonia levels were twice that of the splenic vein and vena cava. Further, the pathogenic mechanism of HE is complex and the decreased clearance of blood ammonia in HE is attributed to the diminished hepatic flow and impaired liver function, which are associated with not only the shunt volume but also the shunt substance. Liver dysfunction is more likely to manifest when high levels of factors such as insulin and glucagon are shunted from the liver [20].

In conclusion, diagnosis of chronic PVT based on "Zhao Classification" facilitates clinical practice. The TIPS intervention in patients with different types of chronic PVT results in partial recanalization of the portal veins. However, the use of covered stents increases the incidence of postoperative HE due to the entry of blood flow in the shunting vessel into the vena cava, especially in patients with superior mesenteric vein thrombosis, with a higher incidence of HE grade I-III 1 year after TIPS and longer disease duration. We suggest creation of shunts with a small diameter (4-6 mm) based on TIPS to lower the incidence of HE postoperatively in these patients. Multi-center studies with larger sample sizes are needed to improve the diagnosis and treatment of chronic PVT and minimize postoperative complications.

Acknowledgements

This work was supported by grants awarded byNational Natural Science Foundation of China (81600510).

Disclosure of conflict of interest

None.

Address correspondence to: Dr. Fuquan Liu, Department of Interventional Therapy, Beijing Shijitan Hospital, Capital Medical University, 10 Tieyi Road, Yangfangdian, Beijing 100038, China. Tel: 010-63925588; Fax: 010-63925588; E-mail: hongweizhao2014@163.com

References

[1] Basit SA, Stone CD and Gish R. Portal vein thrombosis. Clin Liver Dis 2015; 19: 199-221.
[2] Tang W, Wang Y, Zhao X, Wang X, Zhang T, Ou X, Shou W, You H and Jia J. Procoagulant imbalance aggravated with falling liver function reserve, but not associated with the presence of portal vein thrombosis in cirrhosis. Eur J Gastroenterol Hepatol 2015; 27: 672-678.
[3] Bagheri Lankarani K, Homayon K, Motevalli D, Heidari ST, Alavian SM and Malek-Hosseini SA. Risk factors for portal vein thrombosis in patients with cirrhosis awaiting liver transplantation in Shiraz, Iran. Hepat Mon 2015; 15: e26407.
[4] Rossle M, Bausch B and Klinger C. Therapy algorithm for portal vein thrombosis in liver cirrhosis: The internist's point of view. Viszeralmedizin 2014; 30: 401-408.
[5] Qi X, Han G, He C, Yin Z, Zhang H, Wang J, Xia J, Cai H, Yang Z, Bai M, Wu K and Fan D. Transjugular intrahepatic portosystemic shunt may be superior to conservative therapy for variceal rebleeding in cirrhotic patients with non-tumoral portal vein thrombosis: a hypothesis. Med Sci Monit 2012; 18: Hy37-41.
[6] Qi X, Li Z, Huang J, Zhu Y, Liu H, Zhou F, Liu C, Xiao C, Dong J, Zhao Y, Xu M, Xing S, Xu W and Yang C. Virtual portal pressure gradient from anatomic CT angiography. Gut 2015; 64: 1004-1005.
[7] Raja K, Jacob M and Asthana S. Portal vein thrombosis in cirrhosis. J Clin Exp Hepatol 2014; 4: 320-331.
[8] Dai J, Qi X, Peng Y, Hou Y, Chen J, Li H and Guo X. Association between D-dimer level and portal venous system thrombosis in liver cirrhosis: a retrospective observational study. Int J Clin Exp Med 2015; 8: 15296-15301.
[9] Chen CY and Liao KM. The incidence of deep vein thrombosis in Asian patients with chronic obstructive pulmonary disease. Medicine (Baltimore) 2015; 94: e1741.
[10] Kallini JR, Gabr A, Kulik L, Ganger D, Lewandowski R, Thornburg B and Salem R. Noncirrhotic complete obliterative portal vein thrombosis: Novel management using transsplenic transjugular intrahepatic portosystemic shunt with portal vein recanalization. Hepatology 2016; 63: 1387-1390.
[11] Senzolo M, M Sartori T, Rossetto V, Burra P, Cillo U, Boccagni P, Gasparini D, Miotto D, Simioni P, Tsochatzis E and A Burroughs K. Prospective evaluation of anticoagulation and transjugular intrahepatic portosystemic shunt for the management of portal vein thrombosis in cirrhosis. Liver Int 2012; 32: 919-927.

[12] Plessier A, Rautou PE and Valla DC. Management of hepatic vascular diseases. J Hepatol 2012; 56 Suppl 1: S25-38.
[13] Qi X, Zhang X, Li Z, Hui J, Xiang Y, Chen J, Zhao J, Li J, Qi FZ and Xu Y. HVPG signature: A prognostic and predictive tool in hepatocellular carcinoma. Oncotarget 2016; 7: 62789-62796.
[14] Luo X, Wang Z, Tsauo J, Zhou B, Zhang H and Li X. Advanced Cirrhosis Combined with Portal Vein Thrombosis: A randomized trial of TIPS versus endoscopic band ligation plus propranolol for the prevention of recurrent esophageal variceal bleeding. Radiology 2015; 276: 286-293.
[15] Luca A, Miraglia R, Caruso S, Milazzo M, Sapere C, Maruzzelli L, Vizzini G, Tuzzolino F, Gridelli B and 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.
[16] Abdel-Razik A, Mousa N, Elhelaly R and Tawfik A. De-novo portal vein thrombosis in liver cirrhosis: risk factors and correlation with the Model for End-stage Liver Disease scoring system. Eur J Gastroenterol Hepatol 2015; 27: 585-592.
[17] Perarnau JM, Baju A, D'Alteroche L, Viguier J and Ayoub J. Feasibility and long-term evolution of TIPS in cirrhotic patients with portal thrombosis. Eur J Gastroenterol Hepatol 2010; 22: 1093-1098.
[18] Kim HK, Kim YJ, Chung WJ, Kim SS, Shim JJ, Choi MS, Kim DY, Jun DW, Um SH, Park SJ, Woo HY, Jung YK, Baik SK, Kim MY, Park SY, Lee JM and Kim YS. Clinical outcomes of transjugular intrahepatic portosystemic shunt for portal hypertension: Korean multicenter real-practice data. Clin Mol Hepatol 2014; 20: 18-27.
[19] Ahuja NK, Ally WA and Caldwell SH. Direct acting inhibitors of ammoniagenesis: a role in post-TIPS encephalopathy? Ann Hepatol 2014; 13: 179-186.
[20] Amodio P. Hepatic encephalopathy: historical remarks. J Clin Exp Hepatol 2015; 5: S4-6.