European Radiology (2019) 29:699–706
https://doi.org/10.1007/s00330-018-5645-2

VASCULAR-INTERVENTIONAL

Comparison of transjugular intrahepatic portosystemic shunt (TIPS) alone and combined with embolisation for the management of cardiofundal varices: a retrospective study

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Received: 31 January 2018 / Revised: 12 June 2018 / Accepted: 2 July 2018 / Published online: 23 July 2018

Abstract

Objectives To assess the efficacy of transjugular intrahepatic portosystemic shunt (TIPS) with and without adjunctive embolisation in managing cardiofundal varices bleeding.

Methods The retrospective study comprised 82 patients (54 men; mean age 53.9 years; mean Model of End-stage Liver Disease score 9.3) with cardiofundal varices bleeding who underwent TIPS creation from 2011 to 2015. Variceal rebleeding, the outflow tracts of varices, overt hepatic encephalopathy (HE) and post-procedure varices patency were assessed.

Results Gastrorenal shunt was present in 92.7% of patients ($n = 76$). Embolisation was performed in 67.1% of patients ($n = 55$). The 1- and 2-year variceal rebleeding rates in the TIPS combined with embolisation group were significantly lower than those in the TIPS alone group (3.8% and 13.4% vs 13.0% and 28.0%, respectively; $p = 0.041$). No significant differences between the two groups were found in the cardiofundal varices patency, overt HE or survival ($p > 0.05$).

Conclusions The results suggest that TIPS combined with embolisation can reduce the risk of variceal rebleeding for patients with cardiofundal varices.

Key Points

- *TIPS combined with embolisation reduces the risk of rebleeding in treating cardiofundal varices.*
- *TIPS combined with embolisation could not completely occlude cardiofundal varices.*
- *TIPS combined with embolisation could not prevent the development of hepatic encephalopathy.*

Keywords TIPSS · Gastric varix · Embolotherapy · Portal hypertension · Bleeding

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Abbreviations and acronyms

BRTO	Balloon-occluded retrograde transvenous obliteration
CECT	Contrast-enhanced computed tomography
GOV	Gastro-oesophageal varices
GVs	Gastric varices
HE	Hepatic encephalopathy
IGV	Isolated gastric varices
LGV	Left gastric vein
PGV	Posterior gastric vein
PSG	Portosystemic pressure gradient
SGV	Short gastric vein
TIPS	Transjugular intrahepatic portosystemic shunt

Introduction

Transjugular intrahepatic portosystemic shunt (TIPS) has been established as an effective treatment for variceal bleeding and

refractory ascites [1, 2]. The aim of TIPS is to decrease the portosystemic gradient (PSG) to a target threshold (usually 12 mmHg) and adjunctive embolisation of varices will be performed usually when haemodynamic success is not achieved [2–4]. However, recent studies demonstrated that TIPS combined with variceal embolisation could lower the rate of rebleeding compared with TIPS alone [5–7]. Hitherto, a consensus has not been reached on whether adjunctive embolisation is necessary during TIPS creation.

Cardiofundal varices are located in the fundus of the stomach, including gastro-oesophageal varices type 2 (GOV-2) and isolated gastric varices type 1 (IGV-1) [8, 9]. It has been reported that the mean PSG in patients with gastric variceal haemorrhage was lower than that in patients with oesophageal variceal haemorrhage, even less than 12 mmHg [10–12]. Thus, the necessity of concomitant embolisation of the collaterals feeding the GVs during the TIPS procedure is recognised and accepted worldwide [8, 13]. However, only two retrospective studies with small sample sizes have analysed the efficacy of TIPS with or without embolisation for gastric variceal bleeding [7, 14]. In those studies, all types of GVs were incorporated, and cardiofundal varices were in the minority. Therefore, the present retrospective study aims to compare TIPS combined with embolisation to TIPS alone in terms of cardiofundal variceal bleeding.

Material and methods

Patient population

Written informed consent for the procedure was obtained from each patient in this study. Between December 2011 and June 2015, 91 patients with bleeding from cardiofundal varices were admitted to the Department of Gastroenterology. The inclusion criteria were as follows: (1) diagnosis of liver cirrhosis through biopsy or typical cross-sectional imaging; (2) historical evidence of haemorrhage from the varices refractory to medical or endoscopic therapy; (3) the presence of GOV-2 or IGV-1 confirmed through gastroscopy and (4) a successful TIPS creation. Patients in whom the outcome could not be assessed (lost before 1 month of follow-up) were excluded from the study. Patients were classified according to whether they received the embolisation (TIPS combined with embolisation group) or not (TIPS alone group). Disposition of the patients is shown as a flow chart in Fig. 1.

Procedure

The TIPS procedure was performed using a previously described standard process [15]. A standard TIPS set (RUPS-100; Cook Medical) was used for TIPS creation in each patient. A portal venography was performed and a PSG was calculated. After the parenchymal tract was dilated using an 8 × 60-mm balloon catheter (Powerflex pro; Cordis), an expanded-polytetrafluoroethylene-covered stent (e-PTFE, Fluency; C.R. Bard, Inc.) was implanted. The completion shunt venography was re-performed and PSG was re-measured.

Embolisation of the GV was performed following TIPS creation at the discretion of the primary operators depending on the numbers and sizes of varices and the degree of angiographic filling following TIPS creation. Embolisation of afferent veins was necessarily performed for acute variceal bleeding. Selective catheterisation of the left, posterior or short gastric vein was performed using an angled catheter (Cobra; Terumo Medical Corporation). Subsequently, proximal embolisation was commonly performed using the materials according to the diameter of the afferent veins, such as a metallic coil (MReye; Cook Medical), alpha-cyanoacrylate (EC adhesive; Bai Yun Medical Adhesive Co.) and a vascular plug device (Amplatzer Vascular Plug; St. Jude Medical). Distal embolisation of submucosal components of gastric varices was not performed with a microcatheter. Finally, a portal venography was performed to assess the degree of embolisation. Low molecular weight heparin was prescribed for 3 days to prevent the development of an acute thrombus.

Imaging assessment

TIPS radiologic images or contrast-enhanced computed tomography (CECT) images were reviewed for the presence of fundal variceal outflow, including gastrorenal shunt, gastrocaval shunt, pericardial vein and azygous vein. CECT examinations were evaluated to assess the patency of the gastric fundal varices after TIPS creation. Variceal patency was defined as enhancement of tortuous vessels abutting into the submucosal structure of the stomach, whereas variceal occlusion was defined as the complete absence of contrast-filling varices [14].

Measured outcomes and definitions

The primary outcome was rebleeding from the varices after TIPS procedure. The secondary outcomes included stent dysfunction, cardiofundal varices patency, the incidence of overt hepatic encephalopathy (HE) and survival. Haemodynamic success refers to the post-TIPS reduction of PSG below an absolute value of 12 mmHg or a relative reduction of more than 20% [3]. Stent dysfunction was defined as stent stenosis or occlusion confirmed through contrast-enhanced CT, Doppler ultrasound or shunt venography. When performed, post-TIPS shunt venography was used as the gold-standard method to determine the stent status. The variceal rebleeding was identified by endoscopic examination. HE was assessed before and during the follow-up. Overt HE refers to the more severe HE grades (West Haven grades II–IV) [16].

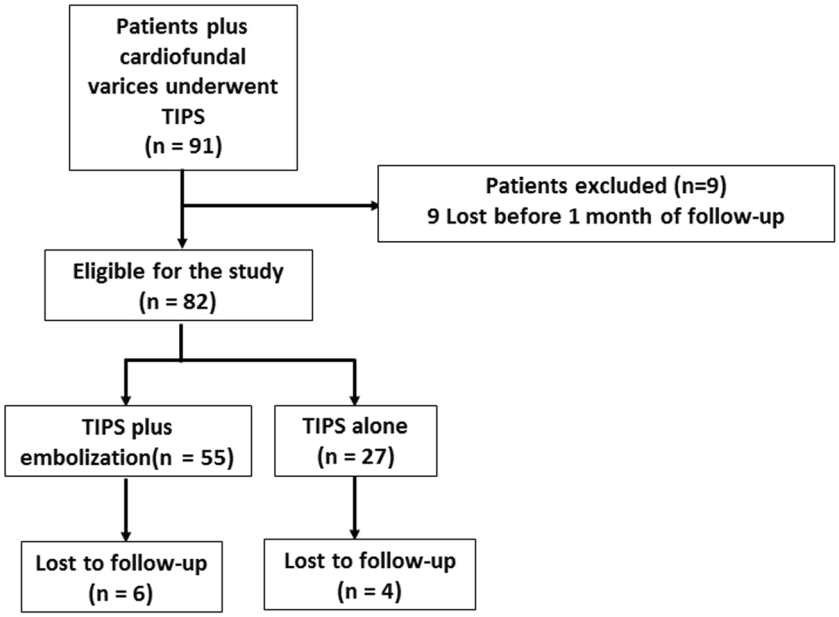


Fig. 1 Study flow chart

Statistical analysis

Data were presented as means ± standard deviations for quantitative variables and as absolute numbers for categorical variables. The study results were analysed using Pearson's χ^2 test, the Mann–Whitney *U* test and Student's *t* test. The cumulative probabilities were estimated using the Kaplan–Meier method and were compared with the log-rank test. All tests of significance were two-sided, and *p* values less than 0.05 were considered to indicate a significant difference. The data processing and statistical analyses were performed with SPSS (SPSS, version 24; IBM).

Results

Patient characteristics

Nine patients (lost before 1 month of follow-up) were excluded and 82 patients with cardiofundal varices were finally included. Fifty-five patients received adjunctive embolisation during TIPS creation and 27 patients underwent TIPS creation alone. Ten (12.2%) patients were lost to follow-up with a median follow-up time of 10.5 months (range 3–29 months). No significant differences were found between the two groups in the clinical characteristics ($p > 0.05$, Table 1).

TIPS procedure

The 8-mm e-PTFE-covered stent was used in four patients and the 10-mm covered stent was used in the other patients ($p = 0.595$). The average pre-TIPS PSG was 21.4 ± 6.5 mmHg and the post-TIPS PSG was 10.2 ± 3.4 mmHg. The haemodynamic success rate was 100%. In the TIPS combined with embolisation group, the metallic coil was used in 36 (65.5%) patients, alpha-cyanoacrylate combined with coil in 18 (32.7%) patients and a vascular plug in 1 (1.8%) patient. During the embolisation process, backflow of the alpha-cyanoacrylate was observed in three patients because of very proximal embolisation. Stent implantation was given in two patients because alpha-cyanoacrylate flowed from the afferent veins back to the intrahepatic shunt. Additionally, haemothorax or haemobilia was observed in one case each.

Variceal rebleeding

During the follow-up, 13 (15.9%) patients suffered recurrent haemorrhages from the varices rupture, including 6 (10.9%) patients from the TIPS combined with embolisation group (median rebleeding time of 21.5 months) and 7 (25.9%) patients from the TIPS alone group (median rebleeding time of 9 months) (Fig. 2). A total of 96.2% and 86.6% of the patients in the TIPS combined with embolisation group and 84.0% and 72.0% of the patients in the TIPS alone group were free from rebleeding at 12 and 24 months, respectively ($p = 0.041$, Fig. 3). The median time to recurrent bleeding was not reached.

Five patients of variceal rebleeding had evidence of shunt patency; three of these cases were from the TIPS combined with embolisation group and two cases were from the TIPS alone group, receiving medical treatments or cyanoacrylate injection.

Stent dysfunction

Stent dysfunction, which is a common complication of TIPS, occurred in nine patients. Of these patients, 4 (7.3%) patients

Table 1 Baseline characteristics of the patients

Variables	All TIPS	TIPS combined with embolisation	TIPS alone	*p* value
Age (years)*	53.9 ± 11.7	53.6 ± 11.5	54.5 ± 12.3	0.760
Male/female	54/28	35/20	19/8	0.546†
Gastric varices				0.072†
GOV-2	56	34	22	
IGV-1	26	21	5	
Aetiology				0.516†
Virus	49	34	15	
Alcohol	10	5	5	
Other	23	16	7	
Outflow tract of fundal varices				1.000†
Gastrorenal shunt	76	51	25	
Others	6	4	2	
Child–Pugh score*	7.3 ± 1.9	7.5 ± 2.1	6.9 ± 1.5	0.144
Child–Pugh class				0.350‡
A	35	21	14	
B	35	24	11	
C	12	10	2	
MELD score*	9.3 ± 3.9	9.5 ± 3.7	8.8 ± 4.4	0.439
Hepatic encephalopathy	2	2	0	1.000†
Ascites	41	31	10	0.100†
Portal vein thrombus	14	11	3	0.369†
Indication				0.547†
Acute varices bleeding	3	3	0	
Second prophylaxis	79	52	27	
Follow-up time*	21.9 ± 12.4	23.2 ± 12.6	20.0 ± 11.5	0.269
Lost to follow-up	10	6	4	0.723†

Unless otherwise indicated, data are the number of patients

TIPS transjugular intrahepatic portosystemic shunt, *GOV-2* gastro-oesophageal varices-2, *IGV-1* isolated gastric varices-1, *MELD* Model of End-stage Liver Disease, *GV* gastric varices

*Data are means ± standard deviation

† χ^2 test

‡ Mann–Whitney *U* test

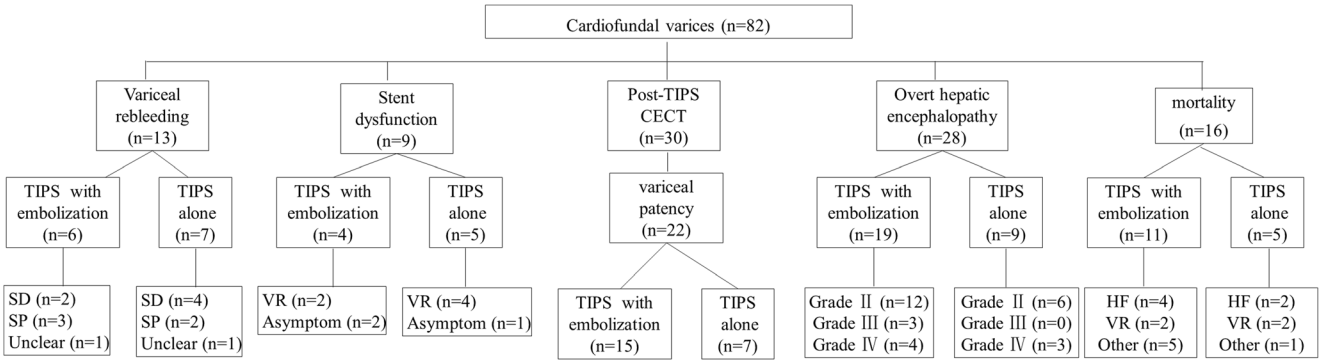
were from the TIPS combined with embolisation group and 5 (18.5%) patients were from the TIPS alone group ($p = 0.126$, Fig. 2). Six patients experienced GVs rebleeding; two cases were from the TIPS combined with embolisation group and four cases were from the TIPS alone group. Shunt patency was restored with TIPS revision in seven patients.

Imaging assessment

Seventy-six (92.7%) patients' dominant gastric fundal varices outflow tracts were gastrorenal shunt, 4 (4.9%) gastrocaval shunt and 1 (1.2%) each was azygous vein or ascending lumbar vein. During the follow-up, 30 (36.6%) patients had CECT images at a median of 8 months (range 0–32 months). Of these 30 patients, eight were from the TIPS alone group and the others were from the TIPS combined with embolisation group (Fig. 2). The rate of cardiofundal varices patency was not significantly different between the two groups (68.2% vs 87.5%, $p = 0.391$, Fig. 4).

Hepatic encephalopathy

During follow-up, 28 (34.1%) patients experienced overt HE; 18 (64.3%) cases were categorised as West Haven grade II, 3 (10.7%) West Haven grade III and 7 (25.0%) West Haven grade IV (Fig. 2). The 12- and 24-month probability of overt HE was 29.4% and 37.4%, respectively, in the TIPS combined with embolisation group and 33.9% and 33.9%, respectively, in the TIPS alone group ($p = 0.746$, Fig. 5). No significant difference in the classification of overt HE was found between the two groups ($p = 0.507$).



Note. TIPS, transjugular intrahepatic portosystemic shunt; CECT, contrast enhanced computed tomography; SD, stent dysfunction; SP, stent patency; VR, variceal rebleeding; HF, hepatic failure.

Fig. 2 Distribution of outcomes between the two groups

Survival

Sixteen (19.5%) patients died during follow-up. Additionally, one patient underwent liver transplantation after 41 months. The transplant-free survival rates after 12 and 24 months were 94.5% and 82.3%, respectively, for the patients who underwent TIPS creation with embolisation and 84.7% and 84.7%, respectively, for the patients who received TIPS alone ($p = 0.759$, Fig. 6). The causes of death included hepatic failure (37.5%), rebleeding (25%), hepatocellular carcinoma (12.5%), hepatic encephalopathy (12.5%), multiple organ failure (6.25%) and unknown causes (6.25%) (Fig. 2).

Discussion

The present study was conducted to access the efficacy of TIPS combined with embolisation and TIPS alone in the cardiofundal varices bleeding. The results obtained suggested that TIPS combined with embolisation significantly lowered the rebleeding rate, but could not prevent the overt HE and the varices patency as compared with TIPS alone.

Recurrent variceal bleeding was lower in the TIPS combined with embolisation group than that in the TIPS alone group, a result which differs from previous studies [7, 14]. First, this inconsistency may be due to the different objectives as the previous studies incorporated all types of GVs.

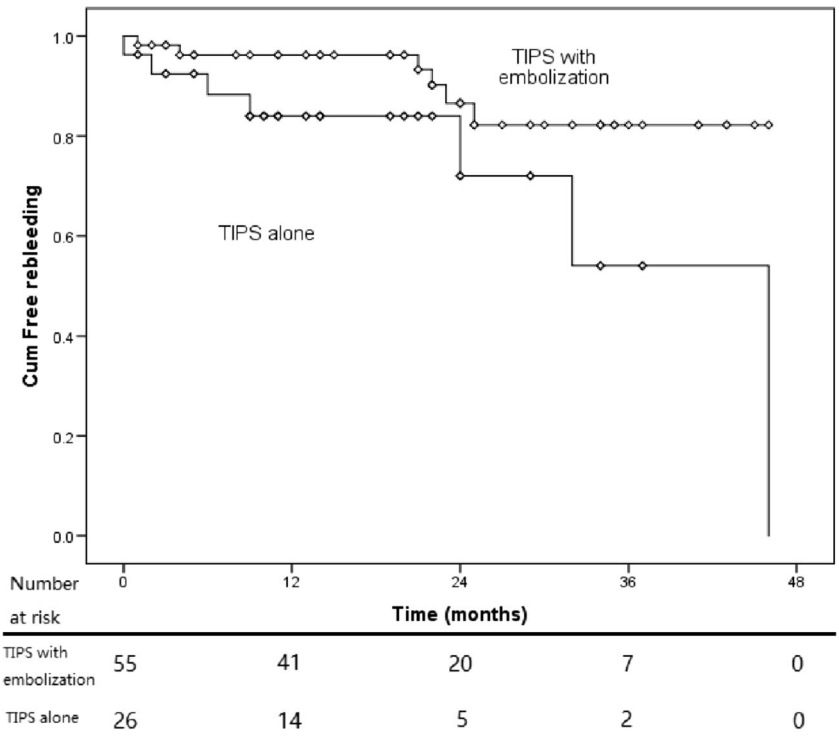


Fig. 3 Kaplan–Meier analysis of cumulative free of rebleeding among the 55 patients in the TIPS combined with embolisation group and the 27 patients in the TIPS alone group. There were no significant differences between the two groups (log-rank test, $p = 0.041$). TIPS transjugular intrahepatic portosystemic shunt

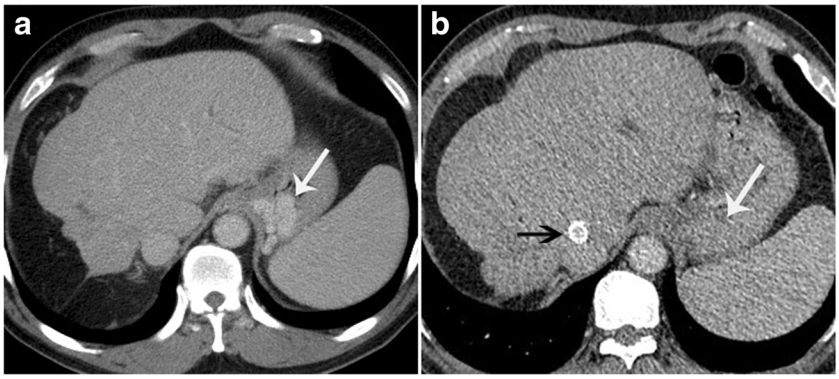


Fig. 4 Images from a 61-year-old man with IGV-1. Pre-TIPS axial enhanced CT image (**a**) demonstrates submucosal components of GV (white arrow) in gastric fundus. The patient underwent TIPS creation and coil embolisation on the LGV and PGV, with PSG reduction from 19 to 9 mmHg. Variceal occlusion (white arrow) is evident on axial enhanced CT scan (**b**) performed 418 days after TIPS creation; black arrow designates patent shunt

Gastro-oesophageal varices type 1, the most common GV subtype, is considered as a continuation of oesophageal varices, sharing similar vascular anatomy and response to treatments [13]. The common dominant feeders of cardiofundal varices are the posterior gastric vein (PGV) or the short gastric vein (SGV) [17, 18]. These veins, which are located distant from the TIPS compared with the left gastric vein (LGV), may maintain the preferential blood flow through spontaneous portosystemic shunt after TIPS creation [19, 20]. Second, a possible explanation for this discrepancy may be the MELD score because this score is positively correlated with the rebleeding risk [21]. The MELD scores reported in the previous studies were obviously higher than that in present study (15.5 and 13.5 vs 9.7).

The majority of cardiofundal varices showed consistent patency despite TIPS creation and concurrent embolisation of afferent vessels, which was in accordance with the results of a previous study [14]. We speculated that it might be caused by the mechanism and location of embolisation as the metallic coil was only used in most patients to embolise the proximity of the feeders. Balloon-occluded retrograde transvenous obliteration (BRTO) has been introduced as an alternative procedure for the treatment of GVs with large gastrorenal shunt [22–24]. This approach is desirable as it could directly eliminate the submucosal parts of GVs. However, it is questionable whether variceal patency is a significant clinical outcome for TIPS creation. Because size of varices was directly related to the risk of bleeding. The patients should remain free of

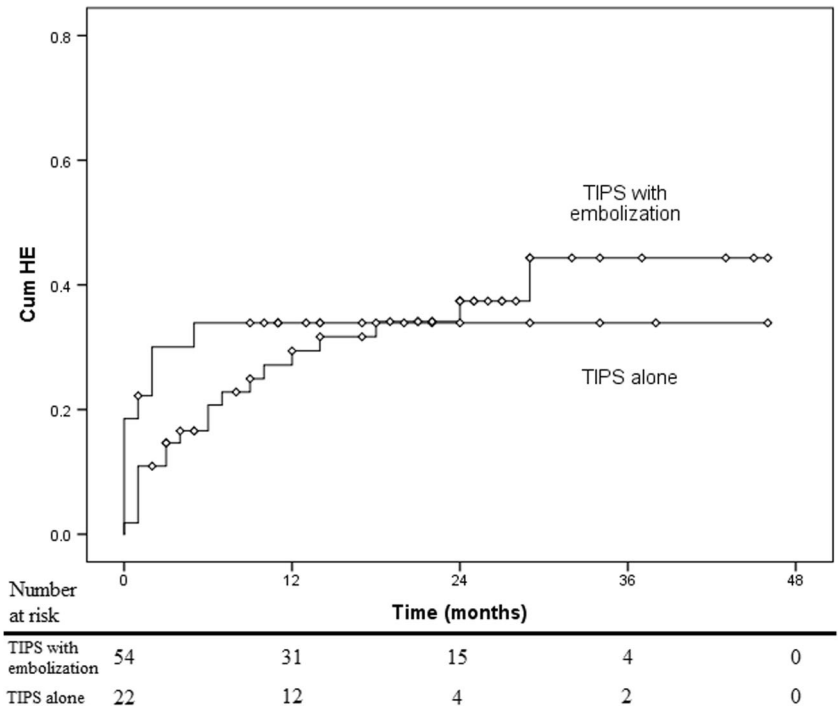


Fig. 5 Kaplan–Meier analysis of cumulative HE among the 55 patients in the TIPS with embolisation group and the 27 patients in the TIPS alone group. There were no significant differences between the two groups (log-rank test, $p = 0.746$). TIPS transjugular intrahepatic portosystemic shunt, HE hepatic encephalopathy

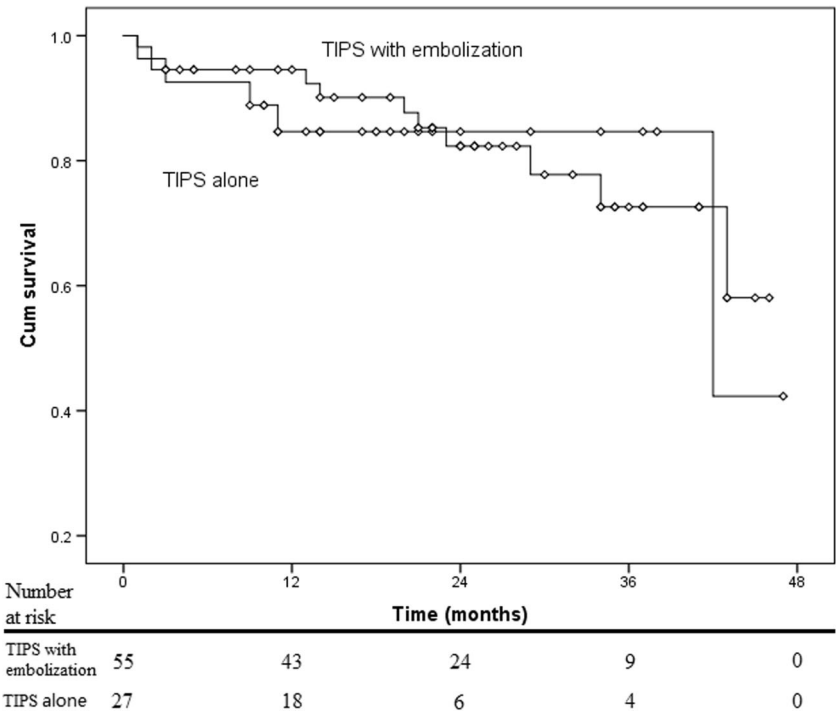


Fig. 6 Kaplan–Meier analysis of cumulative survival among the 55 patients in the TIPS combined with embolisation group and the 27 patients in the TIPS alone group. There were no significant differences between the two groups (log-rank test, $p = 0.759$). TIPS transjugular intrahepatic portosystemic shunt

variceal rebleeding if the varices became smaller and the PSG became lower after TIPS combined with embolisation.

At the same time, there is no significant difference in overt HE between the two groups. In contrast, Shi et al [25] reported that TIPS with adjunctive embolisation using cyanoacrylate decreased the HE incidence as compared with TIPS alone. The degree of embolisation may explain this discrepancy. The efficacy of liquid embolic material appears to be superior to that of metallic coils [26, 27]. Moreover, a probable explanation may be the use of stents with different diameters. A recent study suggested that the stent diameter is a risk factor for the incidence of HE [28]. A smaller stent was implanted in the TIPS combined with embolisation group in the previous study, whereas a 10-mm-diameter stent was implanted in most patients in this study.

The use of adjunctive embolisation during the TIPS process is generally safe and well tolerated [29, 30]. The primary advantage of embolisation after stent implantation is the ability to assess the response of angiographic collateral vessel filling after TIPS creation. However, a patent shunt represents a channel for misplaced embolisation of embolic material. In this study, stent implantation was performed in two patients because of alpha-cyanoacrylate migration. Distal embolisation with a microcatheter could be helpful in the prevention of ectopic embolism.

The present study had several important limitations. First, this study represents the non-randomized, retrospective experience of a single institution. Second, embolisation was specifically performed at the discretion of the operators. Thus, the numbers of patients in the two cohorts were disproportionate. Third, the Fluency stent was implanted in all patients instead of the Viatorr stent. The Viatorr stent is superior to the Fluency during the TIPS creation [31]. However, it was not available in our country until 2016. Several recent studies suggested that TIPS using the Fluency stent is also effective in treating complications of portal hypertension [28, 32]. Finally, CECT examination was not performed in all cases after TIPS creation because it was not necessary during the follow-up.

In conclusion, TIPS combined with concurrent embolisation might be more effective than TIPS alone in reducing the risk of variceal rebleeding, despite not exerting a great influence on varices occlusion and overt HE incidence.

Funding This study has received funding by the Beijing Hope Run Special Fund of Cancer Foundation of China (Grant No. LC2015A01 to X.L.).

Compliance with Ethical Standards

Guarantor The scientific guarantor of this publication is Xiao Li.

Conflict of Interest The authors of this manuscript declare no relationships with any companies whose products or services may be related to the subject matter of the article.

Statistics and Biometry No complex statistical methods were necessary for this paper.

Informed Consent Written informed consent was obtained from all subjects (patients) in this study.

Ethical Approval Institutional review board approval was obtained.

Methodology
- retrospective
- observational
- performed at one institution

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