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Original Article

Transjugular Intrahepatic Portosystemic Shunt Reduction for Medically Refractory Hepatic Encephalopathy

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Abstract

Objective Transjugular intrahepatic portosystemic shunt (TIPS) is an established intervention for symptomatic portal hypertension, with many patients experiencing hepatic encephalopathy (HE) as an undesirable side effect. For medically refractory HE, TIPS reduction can decrease the burden of neurotoxic metabolites. This study aimed to evaluate the efficacy of TIPS reduction for the treatment of medically refractory post-TIPS HE.

Methods A retrospective search using an institutional database yielded 45 patients who underwent TIPS reduction between 2011 and 2021. Four patients were excluded due to lack of post-TIPS HE, and 41 patients in total were included. The primary endpoint was improvement of HE after TIPS reduction as measured by the West Haven scores. Secondary endpoints included postreduction recurrence of ascites or gastrointestinal bleeding, procedural complications, and 30-day mortality.

Results TIPS reduction was performed in all 41 patients with a 30-day mortality rate of 9.8%. No deaths were attributable to the procedure itself. Twenty-seven patients (65.9%) had improvement in HE and 10 patients (24.4%) proceeded to TIPS occlusion due to refractory HE. The average pre- and postreduction West Haven grades were 2.9 ± 0.5 and 1.9 ± 1.2 ($p < 0.001$), respectively. One patient (2.4%) had spontaneous TIPS thrombosis after reduction and developed arterial gastrointestinal bleeding, 15 patients (36.6%) experienced recurrent ascites, and there were no cases of variceal hemorrhage.

Conclusions In this population, TIPS reduction improved medically refractory HE in 65.9% of patients with a 36.6% risk of recurrent ascites, no cases of variceal hemorrhage, and 9.8% 30-day mortality.

Keywords

- Transjugular intrahepatic portosystemic shunt
- Hepatic encephalopathy
- TIPS reduction

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Introduction

Transjugular intrahepatic portosystemic shunt (TIPS) is an established, nonsurgical intervention for symptomatic portal hypertension. Common indications include refractory ascites, variceal hemorrhage, Budd–Chiari syndrome, and portal decompression prior to abdominal operation.[1,2]

The primary adverse outcome following TIPS creation is hepatic encephalopathy (HE), which occurs in 25 to 45% of patients.[3] HE presents with symptoms ranging from covert to overt. The West Haven criteria (WHC) are a set of clinical descriptors frequently used to grade the severity of HE. According to the WHC, covert HE is grade 0 to I, where 0 is a normal state of consciousness and I indicates subtle changes in behavior with minor changes in level of consciousness. Overt HE is described by WHC grades II to IV. Grade II is characterized by lethargy, disorientation for time, or personality changes, and a grade III refers to somnolence/semi-stupor, gross disorientation, and confusion. Grade IV is defined by coma and total unresponsiveness.[4]

The pathophysiology underlying post-TIPS HE involves the urea cycle and the gut–liver–brain axis. Under normal circumstances, the liver plays a key role in the detoxification of ammonia and other byproducts of metabolism from the gastrointestinal (GI) tract. In patients with TIPS, blood is shunted away from the hepatic parenchyma and the clearance of toxic metabolites is reduced (►**Fig. 1A**). The accumulation of these neurotoxic metabolites then contributes to the development of HE. Medical management of HE utilizes agents like lactulose and rifaximin, which increase excretion or reduce production of metabolites in the GI tract.[5] When medical management of HE fails, reduction or occlusion of the TIPS may be required.

TIPS reduction is an accepted method of controlling medically refractory post-TIPS HE, which decreases the diameter of the shunt and redirects blood flow through the hepatic parenchyma. Reduction can be accomplished through various means, most of which involve deploying a smaller-caliber stent within the existing TIPS (►**Fig. 1B**).[6–8] One major concern with TIPS reduction or occlusion is the potential for recurrence of ascites or GI bleeding, but data regarding the frequency of these complications are limited. Smaller studies have demonstrated conflicting results, with some indicating no relevant postreduction recurrence of refractory ascites or variceal bleeding, and others showing a minimal risk of variceal bleeding and relatively high recurrence rate of refractory ascites.[9–11] The goal of this study was to describe a single-center experience treating medically refractory HE with TIPS reduction and to quantify the recurrence of GI bleeding and ascites after TIPS reduction.

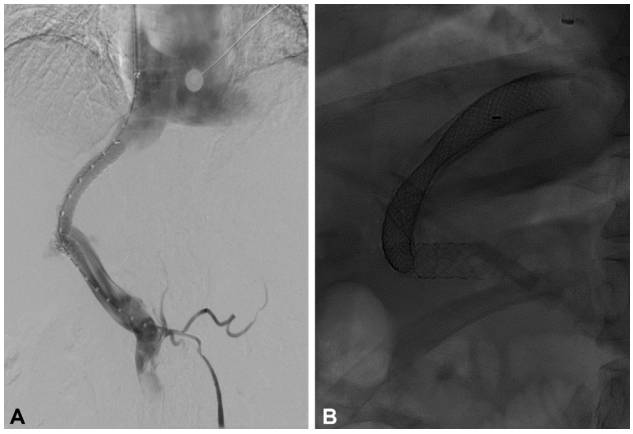

Fig. 1 (**A**) Transjugular intrahepatic portosystemic shunt (TIPS) visualized prior to reduction. (**B**) Post-TIPS reduction by the constrained Wallstent method.

Materials and Methods

Study Design

This retrospective study was conducted at a single university medical center, was approved by the institutional review board, and was HIPAA (Health Insurance Portability and Accountability ACT) compliant. Forty-five patients who underwent TIPS reduction between 2011 and 2021 were identified using an institutional radiological database, and 41 patients who required TIPS reduction due to medically refractory HE were included in this study.

Patient Population

Demographic, clinical, and serologic data were gathered for each patient by chart review. All patients included in this study had new-onset or worsened HE after TIPS creation and initially underwent medical management. Patients were considered candidates for TIPS reduction only after failure of medical therapies to control symptoms of HE.

TIPS Reduction Procedure

TIPS reduction was accomplished by a variety of methods, including suture-constrained Wallstents (Boston Scientific), under-dilated VBX stent grafts (Gore Medical), and simultaneous parallel placement of self-expandable and balloon-expandable stent grafts within the original TIPS.

Outcomes

The primary endpoint was improvement of HE after TIPS reduction as measured by the West Haven scores. This was accomplished by retrospective examination of pre- and postreduction clinical encounter notes and application of the WHC. Secondary endpoints included recurrence of GI bleeding or ascites requiring paracentesis after TIPS reduction, procedural complications, and 30-day mortality. Any occurrence of GI bleeding or ascites before or after TIPS reduction was recorded for each patient to assess for the re-development of symptomatic portal hypertension. Procedural complications were classified according to the Society of Interventional Radiology (SIR) adverse event criteria.

Statistical Analysis

Statistical analyses were performed using Microsoft Excel (Microsoft Corporation). A one-tailed *t*-test was used to evaluate the significance of pre- and postreduction West Haven scores. Normally distributed variables were reported

using mean and standard deviation, while non-normal variables were reported using median and range. Two-sided p-values ≤ 0.05 were considered statistically significant.

Results

Patient Characteristics

The mean patient age at initial TIPS creation was 62.5 years. Males accounted for 63.4% of the patient population and females accounted for 36.6% of the patients. Nine patients (22.0%) had a history of HE prior to TIPS. After TIPS creation, all patients had HE, which was refractory to medical management with lactulose, rifaximin, zinc, or a combination of these medications. All clinical data and patient characteristics prior to the TIPS reduction procedure are shown in ►**Table 1**.

Outcomes of TIPS Reduction

TIPS reduction was technically successful in all 41 patients at a median time of 103 days with a range of 7 to 1,785 days after initial TIPS creation. Thirty-day mortality was 9.8%, and no deaths were attributable to the TIPS reduction procedure itself. Following the procedure, 27 patients (65.9%) had improvement in HE symptoms and 10 patients (24.4%) proceeded to TIPS occlusion due to refractory HE. West Haven scores decreased from 2.9 ± 0.5 to 1.9 ± 1.2 after TIPS reduction ($p < 0.001$). One patient (2.4%) had spontaneous TIPS thrombosis after the reduction procedure and developed arterial GI bleeding requiring embolization; this was classified as a moderate adverse event according to the SIR adverse event criteria. There were no other procedural complications. Fifteen patients (36.6%) had recurrent ascites requiring paracentesis after TIPS reduction and there were no cases of variceal bleeding. Outcomes of TIPS reduction are shown in ►**Table 2**.

Table 1 Patient characteristics prior to TIPS reduction

Variable	Outcome
Age at TIPS creation (y)	62.5 ± 8.4
Sex	
Male	26 (63.4)
Female	15 (36.6)
Primary TIPS indication	
Refractory ascites	25 (61.0)
Varices/variceal bleeding	7 (17.1)
Preoperative for abdominal operation	7 (17.1)
Other	2 (4.9)
Liver disease etiology	
Non-alcoholic steatohepatitis	23 (56.1)
Hepatitis C virus	7 (17.1)
Alcohol	5 (12.2)
Cryptogenic cirrhosis	1 (2.4)
Other	5 (12.2)
History of hepatic encephalopathy prior to TIPS	9 (22.0)
Pre-TIPS MELD-Na	14.7 ± 3.8
Post-TIPS hepatic encephalopathy	41 (100.0)
Medications utilized for post-TIPS hepatic encephalopathy	
Rifaximin	41 (100.0)
Lactulose	40 (97.6)
Zinc	28 (68.3)
Post-TIPS West Haven score	2.9 ± 0.5
Post-TIPS MELD-Na	17.1 ± 4.8

Abbreviations: MELD-Na, model for end-stage liver disease-sodium; TIPS, transjugular intrahepatic portosystemic shunt.

Table 2 Outcomes of TIPS reduction

Variable	Outcome
Technical success	41 (100.0)
Postreduction West Haven score	1.9 ± 1.2
Ascites requiring paracentesis	15 (36.6)
Primary TIPS indication	
Ascites	13 (31.7)
Hydrothorax	2 (4.9)
Recurrent variceal bleeding	0 (0.0)
Procedural complications	1 (2.4)
Postreduction MELD-Na	17.3 ± 4.5
TIPS occlusion due to refractory hepatic encephalopathy	10 (24.4)

Abbreviations: MELD-Na, model for end-stage liver disease-sodium; TIPS, transjugular intrahepatic portosystemic shunt.

Discussion

TIPS is an established intervention for portal hypertension that carries a 25 to 45% risk of HE. Only about 3 to 7% of post-TIPS HE cases can be managed medically with lactulose, rifaximin, and zinc sulfate; the majority of cases require modifications to the shunt or liver transplantation for management of persistent HE symptoms.[7]

The primary objective of this study was to determine if TIPS reduction improved symptoms of HE as measured by the WHC. In this population, TIPS reduction led to a decrease in West Haven scores from 2.9 ± 0.5 in the preprocedural period to 1.9 ± 1.2 postprocedure. A similar, single-center study by Schindler et al classified their patients as responders and nonresponders, based on whether patients yielded a single point of West Haven improvement after TIPS reduction. Their study found a 55% response and 45% nonresponse to TIPS reduction, which are comparable to the findings of this study.[9]

Few studies have examined rates of TIPS occlusion after TIPS reduction for refractory HE. Kochar et al followed nine patients who underwent TIPS reduction for management of HE. Three of these patients found an improvement after

initial TIPS reduction, but six patients proceeded to TIPS occlusion.[11] Similarly, patients in our study whose HE did not improve after TIPS reduction underwent a TIPS occlusion.

Although TIPS reduction has a role in managing post-TIPS HE, there are several limitations associated with this procedure. This study examined the recurrence of ascites and variceal bleeding, as well as procedural complications. After TIPS reduction, 15 patients (36.6%) in this cohort re-developed ascites requiring paracentesis, of whom 13 (31.7) had a primary TIPS indication of ascites and 2 (4.9) for hydrothorax. Since 25 of the patients in this cohort initially underwent TIPS creation due to refractory ascites, this represents a relatively high recurrence rate, although it is comparable to the findings of other studies. A study conducted by Sarwar et al studied a sample size of 11 patients with post-TIPS refractory HE. Of the 12 patients in this study who were in the variceal bleeding group, none experienced variceal hemorrhage after TIPS reduction and only one experienced hematemesis after the reduction.[10]

This study is limited in its retrospective chart review design. The retrospective nature of the study limited our ability to perform a more in-depth analysis of our sample. Next, the grading of the HE events was conducted retrospectively, which could have induced bias in the grading of the events. Given the number of other studies that examined TIPS reduction for medically refractory HE with smaller populations, a meta-analysis of all studies including ours could be useful to make more accurate and generalizable conclusions for our patients. Future prospective studies could utilize a standardized real-time grading method for HE events and could compare the efficacy of the different reduction methods for HE management.

Funding
None.

Conflict of Interest
None declared.

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