Transjugular intrahepatic portosystemic shunt reduction for refractory hepatic encephalopathy: a case series

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ABSTRACT

Background: Transjugular intrahepatic portosystemic shunt (TIPS) is a therapeutic intervention for refractory ascites and variceal bleeding. However, the development of hepatic encephalopathy (HE) is a known complication. TIPS diameter can be reduced to decrease further HE episodes when refractory to pharmacotherapy. However, TIPS reduction for refractory hepatic encephalopathy (rHE) is poorly described. This case series identifies various characteristics and outcomes among this unique patient cohort.

Case Presentation: In this cohort of 8 patients, 63% were male, 75% were Caucasian, and 38% had alcohol-associated cirrhosis. Following TIPS reduction, the number of HE-related admissions (mean, median) decreased from 2.1 and 2 to 1.6 and 0.5 while the number of non-HE admissions following TIPS reduction increased from 0.6 and 0 to 1 and 0.5.

Conclusion: TIPS reduction reduced the number of hospitalizations for rHE but the total number of hospitalizations for all causes increased, demonstrating the high resource utilization for those with rHE following TIPS. Therefore, careful selection for initial TIPS placement remains a priority.

Keywords: Transjugular intrahepatic portosystemic shunt (TIPS), refractory ascites (RA), variceal bleed (VB), refractory hepatic encephalopathy (rHE), case report.

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Background

Due to the significant morbidity and mortality associated with variceal bleeding (VB), transjugular intrahepatic portosystemic shunt (TIPS) was created as salvage therapy in 1982 [1]. TIPS has since been employed in treating other complications of portal hypertension such as refractory ascites (RA) and hepatic hydrothorax [2]. However, hepatic encephalopathy (HE) can occur in up to one-third of cases. While post-TIPS HE can be managed with lactulose and polyethylene glycol with or without rifaximin, refractory HE (rHE) can occur and present a clinical conundrum.

Over the past 20 years, newer expandable-polytetrafluoroethylene stents in TIPS have reduced TIPS stenosis rates. Nonetheless, deleterious complications such as rHE remain a problem [3]. In these cases, a multi-disciplinary approach between interventional radiology and hepatology can occur to discuss TIPS reduction. There are no clear guidelines to assist providers regarding when revision is indicated, and this decision is principally made on clinical grounds and based on anecdotal experience.

While HE is a known and accepted complication of TIPS placement, it has been shown to increase healthcare costs, length of hospital stays, and mortality [4,5]. Due to both economic and patient burdens, research has been undergone to determine factors associated with post-TIPS HE. However, the research to date remains inconclusive [6]. Furthermore, there is a paucity of literature that looks at factors that determine outcomes in patients that have their TIPS reduced for rHE.

This case series aims to define the clinical characteristics and outcomes of this challenging population.

Case(s) Presentation

This case series was performed via retrospective chart review on eight patients who had their TIPS reduced for rHE from February 2011 to July 2021. Consent was waived in this study. All subjects had TIPS reduction for rHE. Demographic information was obtained for each patient to include their age, etiology of cirrhosis, initial indication for TIPS placement, number of admissions both for HE and non-HE reasons before and after TIPS reduction, and Model for End-Stage Liver disease (MELD) scores before and after TIPS reduction were recorded. Factors such as HE present prior to TIPS placement, pharmacologic

therapy for HE prior to TIPS placement, and whether patients had type 2 diabetes at the time of TIPS reduction were also gathered.

The demographic and indications for initial TIPS placement are shown in Table 1. The mean age of the cohort was 65 years, alcohol-associated cirrhosis was the most common etiology (38%), and RA was the most common reason for initial TIPS placement (75%). A description of the technique used for TIPS reduction was obtained for each patient (Table 2).

The mean MELD prior to TIPS placement was 15; the mean MELD at the time of TIPS reduction was 13. Half of the patients had documented HE prior to TIPS placement. Of this group, one patient was on lactulose, one patient was on lactulose and rifaximin, and two patients were not on any pharmacologic therapy prior to placement. Only one patient carried a diagnosis of covert HE through psychometric testing. At the time of TIPS reduction, 75% of the patients had a diagnosis of diabetes.

All patients had at least one covered stent used at the time of TIPS reduction. Stent specifics were also shown in Table 3 including the extent of TIPS reduction in millimeters (mm) and the subsequent increase in the portosystemic gradient (PSG). Half of the patients had either a Viabahn stent graft or a Viatorr stent graft. One patient had an Icast stent graft. Of the cohort, 75% of patients had at least two stents utilized with 25% of patients using the express non-covered stent (Table 2). The mean diameter of the TIPS before and after reduction was 8.5 mm and 5.4 mm, respectively. The mean PSG increased from 10.3 to 16.4 mmHg (Table 3).

Following TIPS reduction, the number of HE-related admissions (mean, median) decreased from 2.1 and 2 to 1.6 and 0.5. The number of non-HE admissions following TIPS reduction increased from 0.6 and 0 to 1 and 0.5. Of the non-HE-related admissions after TIPS reduction, one was for RA, and another was for new VB (Table 1). The other remaining admissions were for causes not related to complications of portal hypertension.

Discussion

Our data show a reduction in HE-related hospitalization following TIPS reduction, with an increase in the total number of non-HE-related hospitalizations. Our results show that patients who undergo TIPS reduction for rHE continue to require higher resource utilization.

While HE can improve after TIPS reduction, portal hypertension and its sequelae can worsen. This poses a clinical challenge. After TIPS reduction, one study found a recurrence of RA, which was similar to our study [7]. However, this study also found no recurrence of VB which is in contrast to the findings of our study as one patient did develop recurrent VB due to TIPS reduction.

A careful patient selection remains paramount. Studies have found that age itself is an independent predictor of

Table 1. *Demographic and clinical characteristics of the cohort.*

CASE	AGE	ETIOLOGY OF CIRRHOSIS/LIVER DISEASE	REASON FOR TIPS	# OF ADMISSIONS FOR HE PRIOR TO TIPS REDUCTION	# OF ADMISSIONS FOR HE AFTER TIPS REDUCTION	# OF ADMISSIONS FOR NON-HE PRIOR TO TIPS REDUCTION	# OF ADMISSIONS FOR NON-HE AFTER TIPS REDUCTION	MELD AT TIPS PLACEMENT	MELD AT TIPS REDUCTION
1	64	Alcohol	RA	1	1	3	0	18	13
2	66	Cryptogenic	RA and VB	3	0	0	0	18	17
3	60	Hepatitis C	RA	3	6	0	1	14	14
4	68	NASH, Alpha-1 antitrypsin deficiency	VB	4	1	0	1	13	9
5	69	Non-cirrhotic portal hypertension	RA	0	0	0	1	13	13
6	65	Alcohol	RA	0	0	1	0	16	10
7	65	NASH	VB	5	5	0	5	11	20
8	60	Hepatitis C, alcohol	RA	1	0	1	0	17	10

RA = refractory ascites; VB = variceal bleed.

Table 2. *Description of how TIPS was reduced for each patient.*

CASE	TECHNIQUE OF HOW TIPS WAS REDUCED?
1	Single stent dog bone technique using a balloon expandable Icast stent
2	Viabahn stent graft deployed within the Viatorr stent graft
3	Parallel placement of balloon expandable non-covered stent and Viatorr stent graft
4	Viabahn stent graft deployed within the Viatorr stent graft
5	Parallel placement of a self-expandable stent with a non-covered stent (express)
6	Double barrel stent mediated downsize using a self-expandable stent with a non-covered stent (express)
7	Viabahn stent graft deployed within the Viatorr stent graft
8	TIPS patent, but Viabahn stent deployed in constrained fashion

Table 3. *Characteristics of TIPS stent for cohort.*

CASE	INITIAL TIPS DILATED TO "X" MM	TIPS DIAMETER (MM) AFTER REDUCTION	PSG PRE-TIPS REDUCTION	PSG POST-TIPS REDUCTION
1	10	3	14	24
2	9	6	4	10
3	9	5	9	19
4	8	5	12	15
5	8	6	13	17
6	8	6	7	11
7	8	5	10	17
8	8	7	13	18

mortality in this population [8,9], with a generally accepted consensus that the risk for mortality increases over 65 years old. In our cohort, 63% of the patients were found to be 65 years or older at the time of TIPS placement and reduction. There is no absolute contraindication that the elderly should not receive TIPS, but caution should be used in this demographic. Additionally, diabetes has been found to be an independent risk factor for post-TIPS HE, which is an important criterion to look at given the ongoing prevalence of non-alcoholic steatohepatitis (NASH) cirrhosis in the United States population [10]. In our cohort, 75% of patients had diabetes, which may have put them at increased risk of developing post-TIPS HE and other complications. The exact mechanism of how diabetes helps promote the development of HE is not well understood, but some hypotheses to date have included intestinal bacterial overgrowth, bacterial translocation, increased glutaminase activity, and impaired gut motility resulting in constipation [11].

The MELD score was initially developed to assess for 90-day mortality after TIPS placement. While no clear consensus exists, data previously has shown that patients with MELD >18 should not undergo TIPS placement as the 3-month survival is significantly lower in this population [12]. Our cohort had a mean MELD score of 15 at the time of TIPS placement, which indicates an overall appropriate patient selection. Interestingly, MELD improved after TIPS reduction from a mean of 15 to a mean of 13.

Identifying HE prior to TIPS placement remains a priority. Ideally, patients with a history of HE should not have TIPS placed. There is literature that supports that it is okay to create TIPS in patients with covert HE if there is a large portosystemic shunt that is embolized at the same time as TIPS placement [13]. However, this is not common practice and theoretically would increase the risk of re-introducing the initial portal hypertension complication such as ascites or VB. One patient had a history of covert HE, but they did not have any shunts embolized at the time of TIPS placement. Additionally, one other patient had active HE at the time of TIPS placement. A risk-benefit discussion for RA was the reason the TIPS was ultimately pursued.

Stent characteristics and portal pressures are other important characteristics when deciding to place and reduce TIPS. It is becoming standard practice to place covered stents in lieu of bare metal stents given their theoretically decreased risk of HE [3]. All patients in this study received a stent graft as described in Table 2. While stent grafts have less risk of TIPS dysfunction and post-TIPS HE, the question of optimal stent diameter remains up for debate in the literature. One retrospective case-controlled study showed that a dilation of 8 mm stents was shown to decrease the risk of post-TIPS HE without causing an increased risk of VB, TIPS dysfunction, or death [14]. In our cohort, 38% of patients had a TIPS diameter greater than 8 mm when TIPS was placed, but all were reduced to less than 8 mm.

Our study has several limitations including having a small sample size, lack of a control group, and

being retrospective. Furthermore, admissions were only accounted for if occurring at our institution. Additionally, TIPS revision was performed by various interventional radiology staff which could affect results to some degree.

Conclusion

The literature regarding outcomes and characteristics in patients that undergo TIPS reduction for rHE is sparse. Our study shows that TIPS reduction reduces rates of admission for HE but increases the risk of admissions for causes not related to HE which demonstrates the high resource utilization and challenges in this unique population. Until future larger prospective studies are performed, careful patient selection considering various characteristics mentioned in this study remains a priority.

What is new?

TIPS reduction for rHE is described in the literature, but the characteristics and outcomes in this population are not well-known. This case series aimed to look at several characteristics and outcomes among eight patients who had TIPS reduction for rHE. To our knowledge, this is the first study to look in detail at various characteristics and outcomes in this population.

List of Abbreviations

HE	Hepatic encephalopathy
MELD	Model for end-stage liver disease
NASH	Non-alcoholic steatohepatitis
PSG	Portosystemic gradient
RA	Refractory ascites
rHE	Refractory hepatic encephalopathy
TIPS	Transjugular intrahepatic portosystemic shunt
VB	variceal bleeding.

Conflict of interest

The authors declare no conflicts of interest regarding the publication of this article.

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Consent for publication

Informed consent was waived as this was a retrospective study.

Ethical approval

Ethical approval was not indicated at our institution to publish an anonymous case series.

Consent of patient

Consent was waived as this was a retrospective chart review.

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Summary of the case

1	**Patient (gender, age)**	n/a
2	**Final diagnosis**	n/a, rHE
3	**Symptoms**	Confusion, insomnia
4	**Medications**	n/a
5	**Clinical procedure**	TIPS reduction
6	**Specialty**	Hepatology