



# Endovascular Management of Hepatic Encephalopathy

Hieu Le<sup>1,✉</sup> Siddhant Thukral<sup>2,✉</sup> A. Michael Devane<sup>3,✉</sup> Souheil Saddekni<sup>4,✉</sup> Rakesh K. Varma<sup>4,✉</sup>

<sup>1</sup>University of Alabama at Birmingham School of Medicine, Birmingham, Alabama, United States

<sup>2</sup>Department – School of Medicine, University of Missouri – Kansas City School of Medicine, Kansas City, Missouri, United States

<sup>3</sup>University of South Carolina School of Medicine Greenville, Prisma Health, Greenville, South Carolina, United States

<sup>4</sup>Department of Radiology, Division of Interventional Radiology, University of Alabama at Birmingham School of Medicine, Birmingham, Alabama, United States

**Address for correspondence** Rakesh K. Varma, MD, FSIR, Department of Radiology, Division of Interventional Radiology, University of Alabama at Birmingham School of Medicine, 619 19th Street South, NHB H623, Birmingham, AL 35249-6830, United States (e-mail: rvarma@uabmc.edu).

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## Abstract

### Keywords

- TIPS Reduction
- hepatic encephalopathy
- TIPS Occlusion
- spontaneous portosystemic shunt

Transjugular intrahepatic portosystemic shunt (TIPS) and spontaneous portosystemic shunts (SPSS) may lead to new or worsening hepatic encephalopathy (HE), especially in patients with chronic liver disease. Patients with medically refractory HE (rHE) may benefit from endovascular interventions. In this review, we briefly describe the post-TIPS and SPSS vascular anatomy, pathophysiology, classification, factors associated with HE, and the medical management of HE. In addition, we will discuss current endovascular techniques for HE management, their advantages, disadvantages, and review of the current literature.

## Introduction

Hepatic encephalopathy (HE) is a neuropsychiatric syndrome typically seen in patients with liver disease with or without portosystemic shunting.<sup>1</sup> Presentation of HE is comprised of symptoms including confusion, disorientation, abnormal sleep pattern, obtundation, and alterations to the quality of life.<sup>2</sup> While HE is seen in up to two-thirds of cirrhotic patients, the exact pathophysiology of HE is complex and yet to be fully understood.<sup>1-3</sup> Frequently reported factors in the development of HE include elevated serum ammonia, false neurotransmitters, astrocyte swelling, and oxidative stress.<sup>1</sup> Serum ammonia level is not predictive of HE in chronic liver disease and, therefore, is largely a clinical diagnosis. Ammonia level is an important marker in acute liver failure.<sup>4</sup> Medical and endovascular management of HE typically focuses on the reduction of

plasma ammonia levels; nevertheless, other factors may be deemed more important depending on the patient's clinical condition.<sup>5</sup>

The creation of a transjugular intrahepatic portosystemic shunt (TIPS) is a common inciting factor for developing HE. In a group of cirrhotic patients who primarily receive TIPS for management of decompensated portal hypertension, it is estimated that 5 to 35% will develop new or worsened HE following TIPS placement.<sup>2</sup> Although less common, HE can also be a complication of congenital or acquired SPSS.<sup>6</sup>

This review article describes the endovascular techniques for the management of treatment resistant HE secondary to post-TIPS creation and from SPSS. The advantages, disadvantages, and potential consequences of these techniques are reviewed, and we proposed an algorithm for optimal endovascular management. This study is approved by the institutional review board at our institution.

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## Clinical Presentation

Symptoms of HE vary between patients<sup>2,3</sup> ranging from those who experience an abrupt onset of HE symptoms (episodic HE) due to a precipitating event such as infection or gastrointestinal bleed to others who experience a gradual yet persistent onset of HE marked by chronic elevations in serum ammonia, unremitting electrophysiological abnormalities, and recurrent episodes of mental status dysfunction.<sup>7-10</sup>

► **Table 1** exhibits the West-Haven criterion, which is used to standardize HE severity objectively.<sup>10,11</sup> Other helpful psychometric tests for HE include the Reitan number connection test<sup>12</sup> and the psychometric encephalopathy score.<sup>13</sup>

Ammonia has been implicated<sup>2,14</sup> as the key molecule in the development of HE due to known toxic cellular effects and its well-documented association in cirrhotic patients.<sup>3</sup> Additional important factors that are also implicated include hyponatremia, inflammatory cytokines, manganese, reactive oxygen species, and benzodiazepines.<sup>3</sup> These compounds work to cause astrocyte swelling and dysfunction, which alters the blood-brain barrier and subsequently degrades neuronal function as defined as decreased acetylcholine activity, N-methyl-D-aspartate-glutamate hyperexcitability, and increased use of false neurotransmitters ultimately result in the classic symptoms of HE.

The healthy liver is effective in clearing intestinal compounds implicated in provoking HE. However, decreased hepatic function, as well as shunting (both iatrogenic and congenital/physiological), will negate the liver's ability to remove these substances, thereby causing harmful elevations in serum level.<sup>2</sup> The conversion rate from compensated to decompensated liver cirrhosis is between 5 and 7%.<sup>11,15</sup> Studies estimate that between 10 and 20% of patients with liver cirrhosis will develop SPSS due to portal hypertension.<sup>16</sup> The biological advantage conferred by the generation of SPSS is to help the body negate the effects of portal hypertension via shunts allowing blood to bypass the liver.<sup>16</sup> However, as portal pressures rise, the increasing amount of shunted blood will further contribute to liver disease and subsequent portal hypertension resulting in an enclosed cycle worsening complications.<sup>16</sup> Recent studies<sup>7,17</sup> reported that between 46 and 70% of patients with medically refractory hepatic encephalopathy (rHE) also have radiological evidence of large (diameter > 8 mm) SPSS.

**Table 1** West-Haven classification of hepatic encephalopathy

Grade	Criteria
1	Trivial lack of awareness, euphoria, shortened attention span, impaired performance of addition
2	Lethargy or apathy, minimal disorientation of time or place, subtle personality changes, inappropriate behavior
3	Somnolence to semi-stupor but responsive to verbal stimuli, confusion, gross disorientation
4	Coma (unresponsive to verbal or noxious stimuli)

## Medical Management of HE

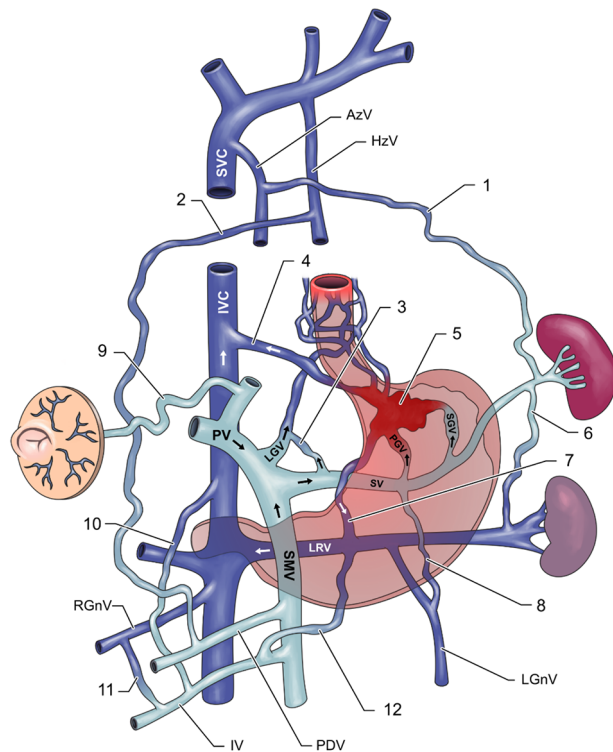
Most patients with HE (98%) will be successfully managed medically without the need for invasive intervention.<sup>2,5,18</sup> Treatment typically has two components: the induction phase and the maintenance of remission phase. Most cases of significant HE are precipitated by infection, gastrointestinal bleeding, or medications. The key to treat HE is to eliminate the precipitating factors. A diet low in animal protein and high in plant protein is recommended to prevent HE.<sup>19</sup> Additionally, first-line treatment for the management of HE includes the use of nonabsorbable disaccharides such as lactulose.<sup>20</sup> Lactulose is metabolized to lactic acid and acetic acid by gut bacteria, which effectively lowers intestinal pH, thereby reducing the survival of urease producing organisms and subsequently promoting the conversion of ammonia to the less systemically absorbed ammonium.<sup>20</sup> Additionally, lactulose acts as an osmotic agent that further promotes the fecal excretion of nitrogen.<sup>20-22</sup> The usual initial dose of lactulose is 25 mL (16.7 g) oral syrup every 1 to 2 hours until the patient has two soft bowel movements with subsequent dose adjusted to 15 to 45 mL (10–30 g) two to four times daily to have two to three soft bowel movements per day.<sup>20-22</sup>

Antimicrobial therapy, comprised of drugs such as rifaximin, neomycin, and metronidazole, is also commonly used to promote a favorable gut microbiome that reduces the endogenous production of nitrogenous compounds.<sup>20</sup> Among antibiotics used, rifaximin (550 mg twice daily) is often preferred due to its low systemic absorption, broad-spectrum coverage, and proven clinical efficacy from large multicentered studies.<sup>20,23</sup> However, rifaximin should be used as an adjunct therapy to lactulose.<sup>20</sup> Oral neomycin and metronidazole are not routinely used due to major potential adverse effects of ototoxicity or nephrotoxicity and neurotoxicity, respectively.<sup>20</sup>

## Post-TIPS and SPSS Vascular Anatomy

During TIPS procedure, a communication is created between the portal vein and the hepatic vein. The result is shunting the portal circulation directly into the systemic circulation bypassing the liver, which will reduce the portosystemic gradient (PSG). However, this shunt can exacerbate HE.

SPSS can range from asymptomatic presentation to recurrent and rHE, ultimately culminating in progressive hepatic failure in cirrhotics. Commonly seen shunts in cirrhotics include splenorenal, gastrosplenic, and dilated paraumbilical veins. Broadly these can be divided into the ones draining into the superior vena cava (i.e., splenocoronary/pulmonary, splenoazygos, and pancreaticoduodenal/hemiazygos) and the ones draining into the inferior vena cava (i.e., gastrosplenic, gastrosplenic, gastro/splenogonadal, splenorenal, splenoadrenorenal, splenocaval, transsplenic and mesentericogonadal/renal/caval) (► **Fig. 1**).



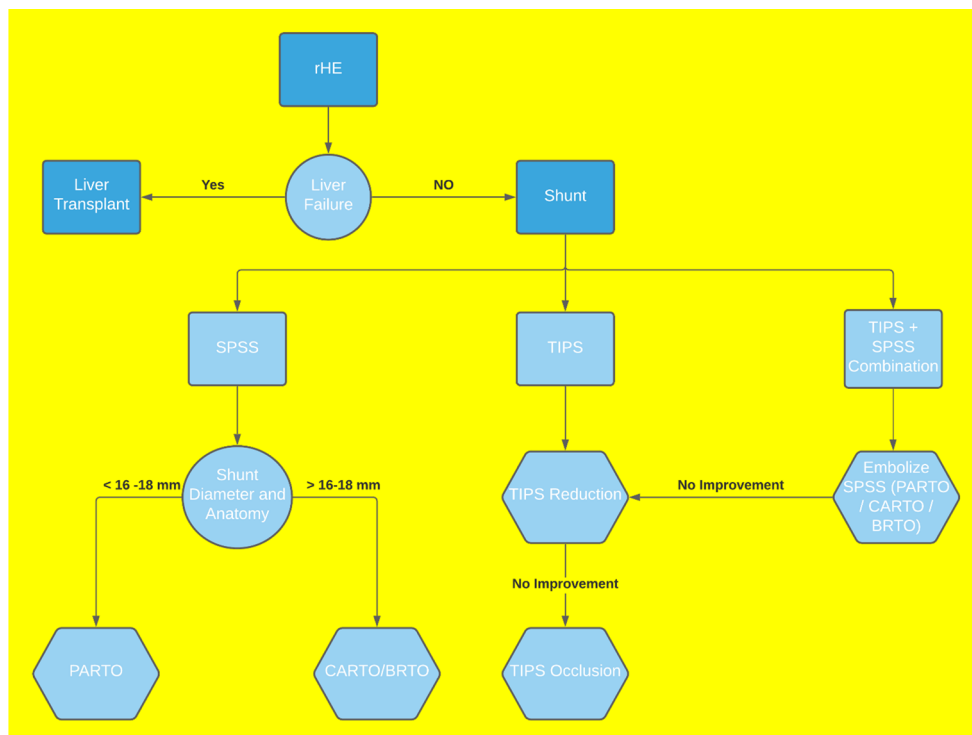
**Fig. 1** (1) Splenoazygos shunt, (2) pancreaticoduodenal/hemiazygos shunt, (3) splenocoronary shunt, (4) gastrocaval shunt, (5) gastric varices, (6) splenorenal shunt, (7) gastrosplenic shunt, (8) splenogonadal shunt, (9) dilated paraumbilical vein (caput medusae), (10) mesenteric-caval shunt, (11) mesenteric-gonadal shunt, and (12) mesenteric-renal shunt. AzV, azygos vein; HzV, hemiazygos vein; LGV, left gastric (or coronary) vein; LGnV, left gonadal vein; LRV, left renal vein; IVC, inferior vena cava; IV, ileocolic vein; PDV, pancreaticoduodenal vein; PGV, posterior gastric vein; PV, portal vein; RGnV, right gonadal vein; SCV, superior vena cava; SGV, short gastric veins; SMV, superior mesenteric vein; SV, splenic vein.

## HE Management with Endovascular Techniques

Management for patients with rHE is complex with liver transplantation serving to be the ultimate therapy.<sup>22</sup> Patient selection for TIPS, therefore, is the most critical method for the prevention of rHE with the following being the most suggestive predictors for its development: age over 65, diabetes mellitus, previous HE (West-Haven Grade  $\geq 2$ ), Child-Turcotte-Pugh (CTP)  $> 10$ , and higher Model for End-Stage Liver Disease (MELD) score.<sup>24-27</sup> Patients who do not respond to medical management will require a more invasive approach. HE management with endovascular techniques can be subdivided based on the presence of TIPS, SPSS, or a combination of both (**►Fig. 2**). However, endovascular management does not provide clinical improvement in the setting of HE with liver failure, with liver transplantation to be the only option.

## TIPS Reduction/Occlusion

Endovascular therapies for the treatment of post-TIPS rHE focus on decreasing the shunting of intestinally derived toxins while increasing perfusion to hepatocytes<sup>2,22</sup> by reducing or occluding the lumen of the shunt. TIPS occlusion (**►Fig. 3**), while effective at reducing rHE, is associated with a high risk of variceal bleeding, ascites, pleural effusions, and hemodynamic changes with increased portal pressure and cardiac load secondary to increased pulmonary and systemic resistances due to acute splanchnic venous engorgement.<sup>7,28-30</sup> TIPS occlusion cannot be postoperatively titrated as compared with certain shunt reduction techniques;<sup>31</sup> hence, TIPS reduction is favored compared with occlusion.<sup>22</sup> Furthermore, the outcome of these treatments



**Fig. 2** Algorithm for endovascular management for treatment resistant hepatic encephalopathy.





**Fig. 3** Transjugular intrahepatic portosystemic shunt occlusion using an Amplatzer II plug in a case of refractory hepatic encephalopathy.

is difficult to predict, given the overall sicker population of patients that require them.<sup>7,22,28,29,31,32</sup> Thus, TIPS occlusion is reserved for patient with no improvement in HE after a TIPS reduction had been attempted. TIPS reduction preserves TIPS function, reducing exacerbation of portal hypertension while maintaining portal perfusion and hepatic detoxification from gut-derived nitrogenous compounds.<sup>33</sup> For these reasons, endovascular techniques have refined toward stent utilization for graded shunt reduction.<sup>22</sup> There is sparse data on the target PSG post-TIPS reduction. Sze et al published in their series of six patients who underwent TIPS reduction for medically refractory HE with the mean and median PSG increase by 8 mm Hg for a final gradient of 17 mm Hg (range: 10–20 mm Hg).<sup>34</sup>

Shunt reduction is typically successful in patients with HE with a published clinical success rate of up to 71%.<sup>22</sup> However, the results of Hauenstein et al concluded that TIPS reduction to treat HE demonstrated clinical success only in patients with preserved underlying liver functions as opposed to patients with acute liver failure.<sup>35</sup> Similarly, Schultheiss et al, in their series of 17 patients with median bilirubin at TIPS reduction of 2.6 mg/dL, demonstrated improvement of HE in 11 patients with no benefit of shunt reduction or occlusion in patients with acute liver failure.<sup>36</sup> Hence, TIPS reduction or occlusion for treating acute liver failure should be carefully evaluated as there may be no clinical improvement.

### Controlled Expansion Endoprosthesis

Due to the high incidence of HE post-TIPS creation, many centers adopted under dilation of the stent graft to reduce the blood shunted through the liver and reduce the incidence of HE.<sup>37</sup> However, studies have shown that these stents grafts undergo passive dilation to their actual size, thus limiting the potential benefit of under dilation.<sup>37</sup> The Viatorr Controlled Expansion stents (VCX) (GORE and Associates, Flagstaff,

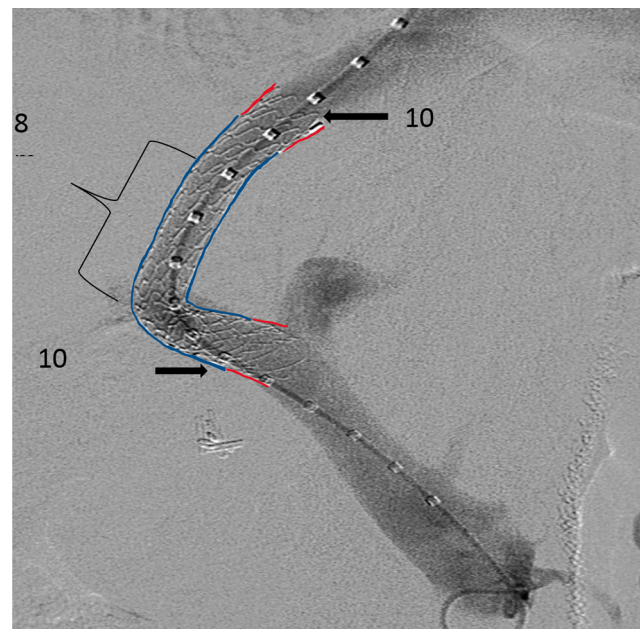
Arizona, United States) are newer generation stents with controlled expansion sleeve designed to optimize the diameter and prevent spontaneous expansion in under dilated Viatorr stents (►Fig. 4). Miraglia et al deployed TIPS VCX stents in 75 patients with 69 patients having their TIPS VCX stent dilated to 8 mm with a mean follow-up of 5.8 months. Their study concluded no passive dilation beyond the titrated diameter with clinical success of 88% and low HE rate of 6%.<sup>38</sup> Thus, patient needing TIPS with anticipated higher risk of developing HE might benefit from this technique for the initial stent placement. However, since the diameter cannot be reduced to less than 8 mm, this technique would be ineffective if the patient develops post-TIPS HE.

### Parallel Stent Graft Technique

TIPS reduction by the parallel placement of a self-expanding stent graft and balloon-expandable stent is frequently used to manage HE (►Fig. 5).<sup>33</sup> Parallel stent grafts allow for luminal adjustment of shunt diameter to manage the portosystemic pressure gradient to optimize TIPS configuration and flow.<sup>33</sup> Previous trials<sup>33</sup> have demonstrated clinical improvement in 62.5% of their patients and complete resolution of HE in 50% of their patients with the parallel stent graft technique.

### Sheath-Controlled Technique

While shunt reduction is effective, a common concern among interventionalists is stent migration during deployment.<sup>31,39–41</sup> The use of the sheath-controlled technique in which a constraining sheath is utilized during the deployment



**Fig. 4** Transjugular intrahepatic portosystemic shunt (TIPS) with Viatorr Controlled Expansion stents (VCX) in a 62-year-old woman with nonalcoholic steatohepatitis cirrhosis, refractory ascites, and grade I hepatic encephalopathy. 8–10 mm × 6 cm/2 cm VCX stent was expanded to 8 mm with portosystemic gradient reduction pre-TIPS—14 mm Hg to post-TIPS—6 mm Hg.



of polytetrafluoroethylene-covered balloon deployable stent allows for additional control during the procedure, minimized stent migration, and creation of an hourglass-shaped stent contour (►Fig. 6).<sup>39</sup> A study by Blue et al found a 100% technical success rate of shunt reduction, no stent migration during deployment, and all patients experienced improvement of HE utilizing the sheath-controlled technique.<sup>39</sup> The study concluded that the sheath-controlled technique is safe and effective and minimizes stent migration.

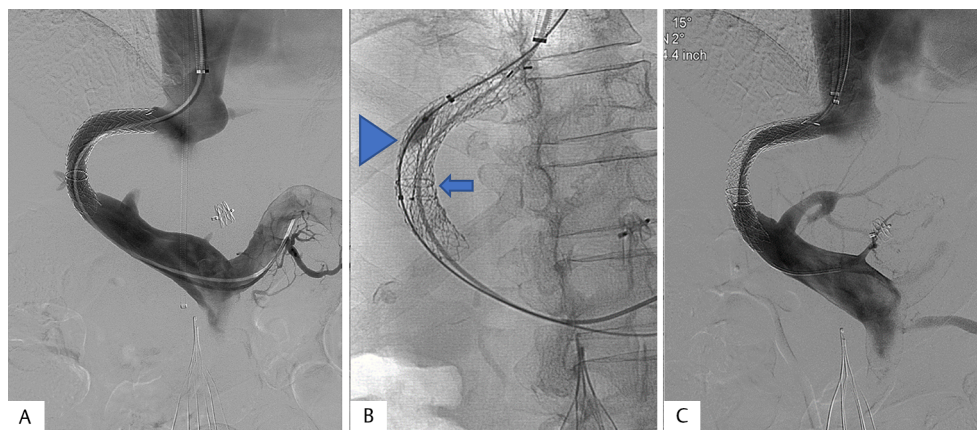
### Hourglass-Shaped Technique

A balloon-expandable polytetrafluoroethylene stent-graft is also utilized to achieve shunt reduction for rHE by tying the midportion with an absorbable polyglactin suture and inflated within the TIPS stent graft to create an hourglass shape. By dilating both ends or middle portion of the shunt, the PSG can be increase or decrease, respectively,

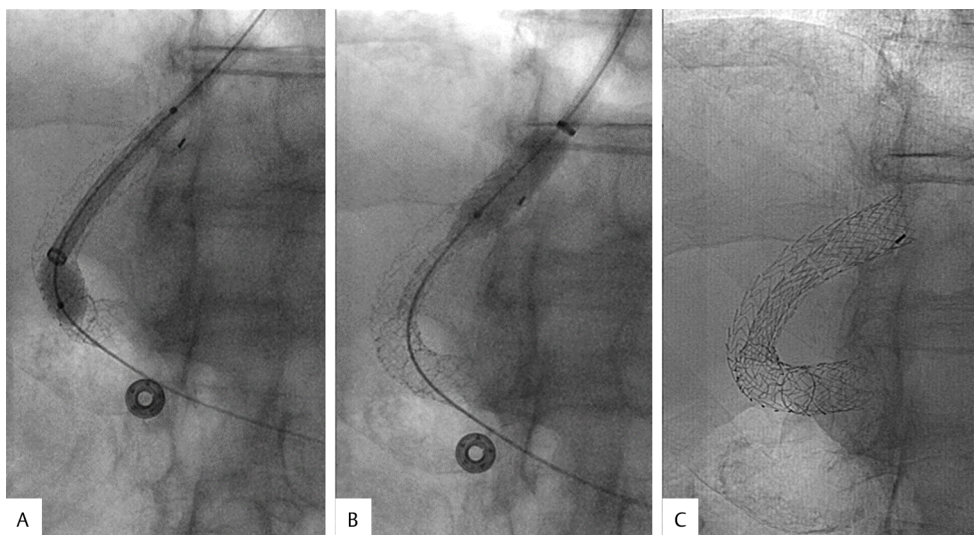
according to the patient's clinical condition.<sup>42</sup> In a series with 12 patients by Fanelli et al, there was a 100% technical success rate and 50% clinical success with a mean follow-up period of 73.9 weeks.<sup>42</sup> This technique has the advantage to further dilate the stent should the sequelae of portal hypertension reoccur and less expensive than other procedures as it only utilizes one stent.<sup>42</sup> The main disadvantage to this technique is higher incidence of hepatic or portal vein stenosis<sup>43</sup> and lack of data on long-term patency.

### Self-Expanding Stents Technique

The use of self-expanding stents has been documented for the achievement of SPSS reduction. Haskal and Middlebrook<sup>44</sup> reported on a wall stent that was constrained with a 3-0 silk suture to create an hourglass shape. This led to a reduction in portosystemic shunting similar to that utilized by a balloon-expandable stent.<sup>39,44</sup> Madoff et al



**Fig. 5** A 67-year-old woman with alcoholic cirrhosis and refractory hepatic encephalopathy. (A) S/P transjugular intrahepatic portosystemic shunt (TIPS) placement for variceal bleeding from alcoholic cirrhosis. (B) A self-expandable stent graft and a balloon-expandable stent in a parallel configuration, giving an hourglass-shape to the TIPS shunt, thereby reducing the diameter. (C) Digital subtraction angiography portogram S/P TIPS shunt reduction with portosystemic gradient increase from 2 to 5 mm Hg.



**Fig. 6** A 53-year-old woman with alcoholic cirrhosis with refractory hepatic encephalopathy. (A) The stent is buttressed by the sheath during balloon retraction followed by the (B) proximal portion of the stent being angioplastied to complete the hourglass shape and the (C) central portion to the stent dilated up to 5 mm.

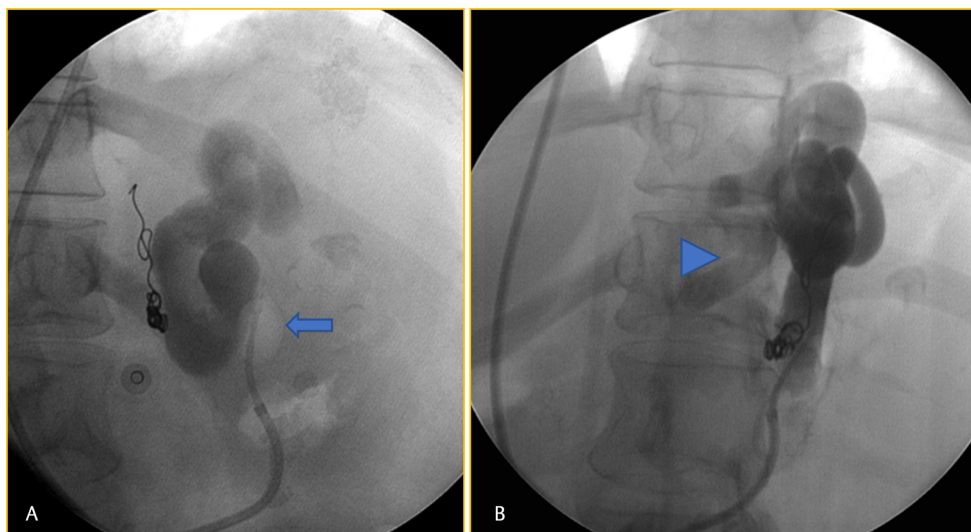
evaluated the feasibility of suture constrained endograft for the management of TIPS-related HE.<sup>45</sup> Their study reported a 100% technical success rate with a mean increase of PSG of 196% or 8.3 to 17.6 mm Hg following reduction. However, the diameter of suture contained stents cannot be titrated once deployed as compared with the sheath-assisted controlled stent graft technique.

### Spontaneous Portosystemic Shunt Occlusion

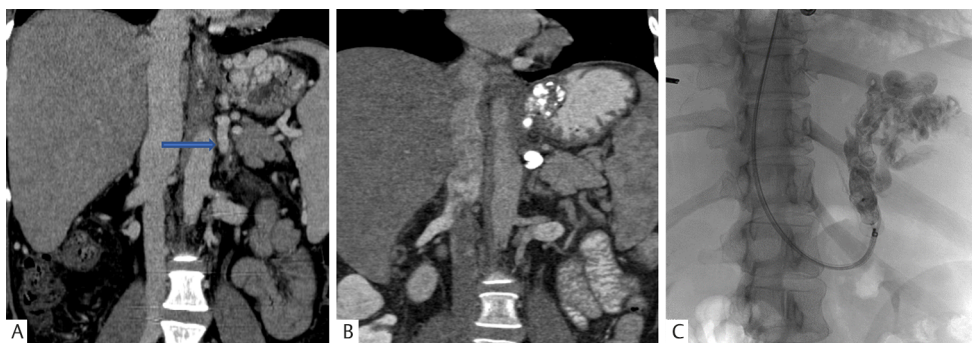
Endovascular therapies for the treatment of HE due to SPSS focus on occluding the lumen of the shunt. A systematic review and meta-analysis of studies by Patil et al concluded that SPSS occlusion or embolization was safe, with minimal complications in patients with good liver function. Patients with a CTP score > 11,<sup>18</sup> MELD  $\geq$  15, and/or baseline presence of hepatocellular carcinoma<sup>46</sup> were unlikely to benefit from shunt occlusion due to very high mortality and recurrent or persistent HE. These patients would need evaluation and enlist for liver transplantation.

Balloon-occluded retrograde transvenous obliteration (BRTO) was one of the initially practiced minimally invasive endovascular methods for the occlusion of gastric vein (GV) and shunts that contribute to rHE (**►Fig. 7**).<sup>47</sup> Studies by Bessari and Lightfoot as well as Koito et al<sup>30,48</sup> have shown a 79 to 100% technical success rate of BRTO. However, the major drawbacks were balloon rupture (~8.7% of cases), embolization of sclerosant to the systemic circulation,<sup>49</sup> and prolonged catheter indwelling times ranging from 4 to 20 hours.<sup>50,51</sup>

Several modifications to BRTO have been performed to improve patient safety and technical concerns. In contrast to BRTO, plug-assisted retrograde transvenous obliteration (PARTO) utilizes a permanent occlusive device such as Amplatzer vascular plug to occlude varices, thereby reducing procedure time and risk of sclerosant embolization<sup>50</sup> (**►Fig. 8**). In addition, there is no balloon catheter indwelling times and no added risk of balloon rupture. Previous studies<sup>49,50</sup> have demonstrated equivalent, if not greater treatment efficacy, in treatment of GV with PARTO as compared with BRTO. However, the plugs are currently only available



**Fig. 7** Balloon-occluded retrograde transvenous obliteration: A 47-year-old woman with nonalcoholic steatohepatitis and Grade II hepatic encephalopathy. (A) Sclerosant mixture (1cc Lipiodol: 2cc STS: 3cc air) injected into the varices after coil embolization of the collateral vein, balloon (air filled, arrow). (B) Oblique view with opacification of the afferent vein (arrowhead), the end point to injection.



**Fig. 8** Plug-assisted retrograde transvenous obliteration (PARTO): A 68-year-old male with hepatic encephalopathy. (A) Pre-PARTO coronal computed tomography (CT) demonstrating a contrast enhanced gastroduodenal shunt (arrow), (B) post-PARTO coronal CT and (C) fluoroscopic image showing lipiodol retention into the shunt and the Amplatzer vascular plug at the outflow. The typical ratio of the emulsion is 1:2:2 of lipiodol: sodium tetradecyl sulfate: air.



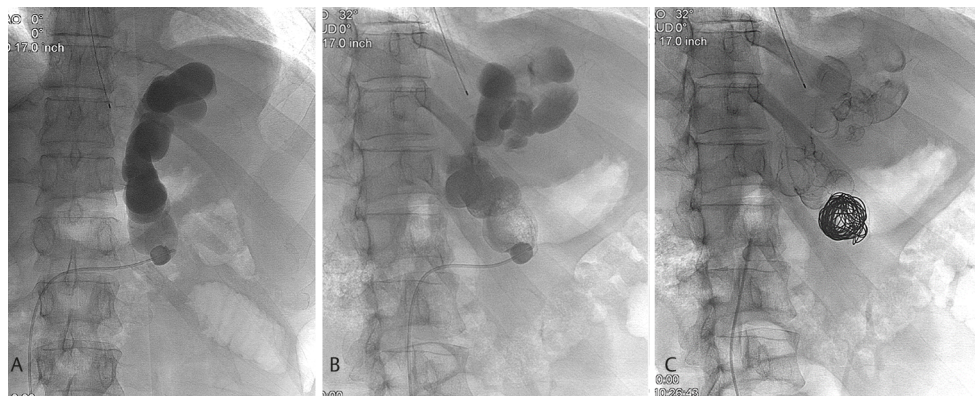
up to 22 mm diameter, restricting treatable shunt size to 16 to 18 mm. Technical limitations of PARTO include tortuous and angulated shunts limiting sheath advancement for plug deployment. In such scenarios, coil-assisted retrograde transvenous obliteration (CARTO) serves as an alternative method for shunt occlusion. CARTO is a modified technique that uses coils and Gelfoam slurry to achieve shunt occlusion in situations where shunt size, shunt angle, or vessel tortuosity is not conducive for vascular plug or balloon occlusion.<sup>51-53</sup> CARTO may either be performed by deploying coils and Gelfoam slurry through a microcatheter (CARTO 1 Procedure) (**►Fig. 9**) or by deploying coils following successful shunt stasis from occlusion balloon (CARTO 2 Procedure) (**►Fig. 10**).<sup>51</sup> As compared with BRTO and PARTO, clinical data<sup>49,51-53</sup> has suggested CARTO as a safer alternative for shunt occlusion with comparable treatment efficacy. Limitations of CARTO include high procedure costs for cases that require multiple detachable coils.<sup>51</sup> The approximate average time to procedure completion in BRTO, PARTO, and CARTO ranges from 8 to 10 hours, 2 to 3 hours, and 30 minutes to 1 hour, respectively, as per multiple studies.<sup>54</sup> The overall reported technical success rates for CARTO and PARTO from three recent large studies were 100% with 49 to 92% of patients having clinically significant improvement from HE during the follow-up period at 6 to 27 months.<sup>7,46,55</sup>

Similar to BRTO, when the varix or shunt is embolized in an antegrade fashion, that is, in the direction of the inflow veins, the technique is termed as balloon antegrade transvenous obliteration (BATO). These can be either performed via a preexisting TIPS called as trans-TIPS BATO (**►Fig. 11**) or transhepatic.<sup>51</sup> In general, BATO (specifically percutaneous transhepatic obliteration) is considered as an adjunct or alternative to BRTO when BRTO fails completely or partially in obliterating the gastric variceal system. As an adjunct to BRTO, BATO increases the technical success rates and decreases the overall risk of sclerosant leak.<sup>51</sup> A combined technique with BATO and CARTO/PARTO termed retrograde-antegrade accelerated trap obliteration where both the inflow and outflow veins are embolized simultaneously with coils or plugs has been described for obliteration of bleeding gastric varices with promising results.<sup>56</sup> However, there is currently no study comparing the clinical efficacy of antegrade versus retrograde embolization techniques in the management of rHE.

Overall, studies have reported very few major adverse effects related to shunt embolization. The recurrence of symptomatic portal hypertension (varices and ascites) was seen in all series (**►Table 2**).<sup>7,18,46,55,57</sup> The most reported adverse event was worsening esophageal varices (19–46%) with rebleeding complications around 10%.<sup>51</sup> Newly developed or increased amount of ascites was noted in 9.5 to 33% of studies with a



**Fig. 9** Coil-assisted transvenous obliteration: A 68-year-old woman S/P transjugular intrahepatic portosystemic shunt (TIPS) for refractory ascites complicated by intermittent hepatic encephalopathy. (A) Trans-TIPS venogram showing filling of the large paraumbilical varix, (B) coils deployed into the varix, and (C) postembolization portal venogram demonstrating patent TIPS with central portal vein perfusion and thrombosed paraumbilical varix.



**Fig. 10** Coil-assisted retrograde transvenous obliteration: A 40-year-old male with alcoholic cirrhosis and intermittent hepatic encephalopathy. (A) Balloon-occluded venogram showing filling of the gastric varix, (B) sclerosant being injected into the varix, and (C) after coil embolization through the balloon catheter.



pooled percentage of 18.3%. Rare complication may include hemoperitoneum, hemobilia, bacterial cholangitis, spontaneous bacterial peritonitis, capsular bleeding, and portal vein thrombosis. Balloon rupture in BRTO procedures may expose patients to sclerosing agents that have been associated with hemolysis, renal failure, cardiogenic shock, and disseminated intravascular coagulation.<sup>31,50,51</sup>

Combination of TIPS and retrograde transvenous obliteration in the management of gastric variceal bleeding has been shown to have higher clinical efficacy<sup>58</sup> however, there is lack

of data regarding combination therapy for the management of rHE. As the diameter of a TIPS shunt can be calibrated to meet the goal, we propose embolizing a significant diameter spontaneous shunt prior to TIPS reduction for the management of rHE.

## Conclusion

Treatment refractory HE, though uncommon, often requires invasive endovascular therapy. Careful patient selection for elective creation of portosystemic shunt still remains the key

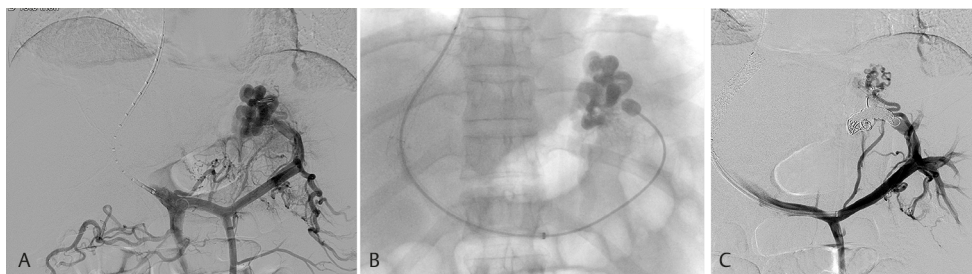
**Table 2** Major studies on shunt embolization for recurrent or rHE

Author/country/year	Patients (n/n) <sup>a</sup>  Study type	Techniques utilized	Technical success rate (%)  Follow-up period	Long-term outcomes	Major complication  PHT clinical events and complications	Unique findings
Philips et al/India/2017 <sup>18</sup>	21/21 Retrospective, single center	BRTO, CARTO, PARTO, Gelfoam, surgical shunt occlusion	95.2 1–9 months	71% showed no overt HE at 9 months	One death due to hemoperitoneum and multiple organ failure AVB in one, new-onset ascites in two	Largest single-center series, CTP >11 as the cutoff for excluding patients from shunt embolization, first to demonstrate amelioration of cirrhosis-associated Parkinson disease with shunt embolization
Lynn et al/USA/2016 <sup>55</sup>	18/20 Retrospective, single center	CARTO, PARTO	100 Median 12 months	92% showed no overt HE at 6–12 months	Hemobilia and bacterial cholangitis in one Ascites in six patients	Inclusion of patients with prior liver transplantation
An et al/Korea/2014 <sup>46</sup>	17/17 Retrospective, single center	CARTO, PARTO, Gelfoam	100 Median 19 months	60% showed no overt HE at 24 months	None Ascites in three patients	Presence of a matched control group, increase in liver volume post-shunt embolization, MELD ≥ 15, and baseline presence of hepatocellular carcinoma predicted mortality at the end of 1 year
Naeshiro et al/Japan/2014 <sup>56</sup>	14/14 Retrospective, single center	BRTO, CARTO	92.9 Median 27 months	93% showed no overt HE at 27 months	None None	Suggested CTP ≤ 10 as the cut-off for selection for shunt embolization to prevent postprocedural complications, suggested splenectomy or splenic artery embolization postshunt embolization to prevent worsening of PHT complications
Laleman et al/Europe/2013 <sup>7</sup>	37/37 Retrospective, multiple center	CARTO, PARTO	100 Mean 697 days	49% showed no overt HE at 24 months	Capsular bleeding Ascites in six patients, spontaneous bacterial peritonitis in two, portal vein thrombosis in four patients	Multicenter study, MELD ≥ 11, higher risk of recurrence of HE

Abbreviations: AvB, acute variceal bleeding; BRTO, balloon-assisted retrograde transvenous occlusion; CARTO, coil-assisted retrograde transvenous occlusion; CTP, Child–Pugh–Turcotte score; MELD, model for end-stage liver disease; PARTO, plug-assisted retrograde transvenous occlusion; PHT, portal hypertension; rHE, refractory hepatic encephalopathy.

Source: Modified from Philips CA, Rajesh S, Augustine P, Padsalgi G, Ahamed R. Portosystemic shunts and refractory hepatic encephalopathy: patient selection and current options. *Hepat Med* 2019;11:23–34.

<sup>a</sup>Data shown as number of patients who completed a minimum of 1 month follow-up/total number of patients in the study.



**Fig. 11** Trans- TIPS balloon antegrade transvenous obliteration: A 64-year-old gentleman with alcoholic cirrhosis with associated ascites and recurrent variceal bleeding despite banding/clipping and medical therapy. (A) Trans-TIPS venogram showing retrograde flow within an enlarged/dilated splenic vein with filling of multiple splenic and gastric varices, (B) sclerosant being injected into the varix with balloon-occlusion, and (C) multiple coils were then deployed for embolization.

for prevention of post-TIPS HE. Endovascular techniques such as TIPS reduction or occlusion, BRTQ, PARTO, and CARTO are safe and efficacious in patients with good liver function. Patients with high MELD score or poor liver function with HE have guarded outcomes from these interventions. TIPS reduction/occlusion and SPSS embolization can exaggerate portal hypertension.

#### Conflict of Interest

A.M.D. reports personal fees from Boston Scientific, personal fees from Johnson and Johnson Ethicon, unrelated to the submitted work. S.T. reports grants from National Institutes of Health, during the conduct of the study, unrelated to the submitted work.

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