Transjugular Intrahepatic Portosystemic Shunts

Advances and New Uses in Patients with Chronic Liver Disease

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KEYWORDS

• Transjugular intrahepatic portosystemic shunt • Portal hypertension • Ascites
• Varices • Portal vein thrombosis • Spontaneous portal systemic shunts
• Hepatorenal syndrome • Hepatopulmonary syndrome

KEY POINTS

- Transjugular intrahepatic portosystemic shunts have had significant advancements with the introduction of covered, controlled expansion stents resulting in improvement control of ascites and variceal bleeding.
- Transjugular intrahepatic portosystemic shunts are an effective treatment for portal vein thrombosis and can allow for recanalization of the portal vein to permit liver transplantation.
- Transjugular intrahepatic portosystemic shunts and embolization of spontaneous portal systemic shunts is an effective therapy for refractory hepatic encephalopathy.
- Transjugular intrahepatic portosystemic shunts for hepatopulmonary syndrome results in improvement in arterial oxygenation and patient symptoms; however, these results are not sustained after 3 months.
- Transjugular intrahepatic portosystemic shunts is an effective treatment of hepatorenal syndrome with improved mortality in a select patient group however this is not a primary indication for Transjugular intrahepatic portosystemic shunts based on limited data.

INTRODUCTION

Chronic liver disease is the most common cause for clinically significant portal hypertension. Portal hypertension is accompanied most often by the development of ascites and variceal bleeding.[1] These complications lead to significant morbidity and

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mortality among patients with cirrhosis. Since the introduction of transjugular intrahepatic portosystemic shunts (TIPS) in 1988, its use has been supported by clinical practice guidelines for the treatment of portal hypertensive complications.[2–5] Presently the primary indications for TIPS have been for the treatment of ascites refractory to medical management and bleeding gastrointestinal varices refractory to endoscopic therapies (**Table 1**).[3,5] Recently, there have been significant advances in TIPS stent technology as well as improvements in placement technique.[6–9] This has resulted in expanded use of TIPS beyond traditional indications supported by well-established guidelines. This article reviews the advances in TIPS and the evidence supporting emerging indications.

Table 1
Indications for TIPS

Indications for TIPS	Clinical Scenario
Traditional	
Esophageal varices	Bleeding refractory to endoscopic therapy
Gastric varices	Primary treatment of bleeding event
Ascites	Ascites refractory to diuretics
Hepatic hydrothorax	Hydrothorax refractory to diuretics
Budd-Chiari syndrome	Not responsive to anticoagulation
Novel	
Early management of ascites	Consideration after 2–3 large volume paracentesis
Before abdominal surgery	Decrease portal hypertension to permit safely performing surgery (ie, laparoscopic cholecystectomy)
Recanalization of portal vein thrombosis	Chronically occluded portal vein thrombosis with portal hypertensive complications and/or to facilitate liver transplant
Embolization of clinically significant spontaneous portosystemic shunts	Refractory hepatic encephalopathy from spontaneous portosystemic shunts
Treatment of hepatopulmonary syndrome	Treatment of moderate-severe hepatopulmonary syndrome
Treatment of hepatorenal syndrome	Treatment of hepatorenal syndrome refractory to medical therapy

PORTAL HYPERTENSION PHYSIOLOGY AND PLACEMENT

Portal Hypertension

Portal hypertension is characterized by an increase in the portal venous pressure in relation to the systemic pressure. This portosystemic gradient (PSG) leads to a pressure difference across the liver. This is typically driven by advanced fibrosis or cirrhosis but can also occur in the setting of portal vein thrombosis (PVT). TIPS placement effectively reduces portal pressure by creating a shunt from the portal venous system (portal vein), through the liver, to the systemic system (hepatic vein). This effectively reduces the PSG alleviating the increased hydrostatic pressure of the portal system. A normal PSG is 5 mm Hg or less. Clinically significant portal hypertension with formation of ascites and varices occurs when the PSG increases to greater than 10 mm Hg. Esophageal varices are at risk for bleeding with a PSG of greater than 12 mm Hg.

Evaluation for Transjugular Intrahepatic Portosystemic Shunt Candidacy

Recipients for TIPS should be formally evaluated by a gastroenterologist or hepatologist to determine if TIPS is appropriate and the benefits outweigh the risks. Liver transplantation candidacy is an important consideration because many traditional indications for TIPS (ascites, hepatic hydrothorax, and bleeding varices) are also indications for liver transplantation. If a patient is a candidate for liver transplantation, this evaluation should occur before the placement of the TIPS to ensure appropriate coordination with the transplantation center in the rare event TIPS leads to worsening hepatic function or liver failure. Considerations include the Model for End-stage Liver Disease (MELD) score, which prognosticates survival after TIPS. Recipients with MELD scores ranging from 6 to 14 generally are not impacted by TIPS, whereas MELD scores of greater than 19 have significantly decreased survival after TIPS, and placement of TIPS should be considered in conjunction with liver transplantation evaluation. Placement of a TIPS should also be performed by an Interventional Radiologist with sufficient expertise in the deployment of TIPS. Recipients should undergo cross-sectional imaging of the liver and portal system with intravenous contrast (either computed tomography or MRI) to assist with procedural planning. Liver ultrasound examination with Doppler imaging of the vessels is an alternative when contrasted cross-sectional imaging it contraindicated. Other pre-TIPS evaluation includes echocardiography to evaluate for underlying congestive heart failure and pulmonary heart failure to ensure cardiovascular reserve with the anticipated large volume of venous return to the heart after TIPS.

Contraindications and Considerations to Transjugular Intrahepatic Portosystemic Shunts

Absolute and relative contraindications to placement of a TIPS are listed in **Table 2**. Absolute contraindications include significant heart failure and/or severe pulmonary hypertension.[3] At the time of TIPS placement, there is a rapid increase in blood volume return to the right heart from portal system. This dynamic shift can result in severe acute decompensated heart failure and be an ongoing issue in those with baseline heart failure. Patients without heart failure but with severe volume overload and elevated right atrial pressures should ideally be adequately diuresed to a euvolemic state before TIPS placement to avoid triggering acute decompensated heart failure after TIPS. Similarly, significant valvular heart disease can result in cardiac decompensation after TIPS and these patients should be managed with the consultation of a cardiologist.[10] Other absolute contraindications to TIPS include ongoing bacteremia or uncontrolled infections because this could lead to seeding of the TIPS prosthesis and serve as a nidus for ongoing infection known as TIPSitis.[11]

Table 2
Absolute and relative contraindications to TIPS

Absolute	Relative
Congestive heart failure	Refractory hepatic encephalopathy
Severe pulmonary hypertension	End-stage liver disease (MELD >19)
Bacteremia/infection	Volume overloaded state
Biliary obstruction	Centrally located liver mass (hepatocellular carcinoma, metastatic disease)
Large liver cysts	Valvular heart disease

The most important relative contraindication to consider is the patient's history of hepatic encephalopathy (HE). HE arises from spontaneous portosystemic shunting (ie, varices or other intra-abdominal collateral veins) of blood combined with underlying hepatic dysfunction from chronic liver disease. Placement of a TIPS can further exacerbate HE owing to increased shunting of portal blood flow through the liver. Approximately 35% of patients experience transient HE after TIPS.[1,3] In some patients (<5%), HE can be refractory thereafter and require permanent occlusion of the TIPS. Thus, a patient with ongoing baseline HE that is not controlled with medical therapy is unlikely a TIPS candidate owing to risk of debilitating HE after TIPS.

Although the placement of a TIPS is a single procedure, there are considerations for its management thereafter. Recipients require monitoring of the TIPS stent with ultrasound doppler imaging at a minimum every 6 months to ensure patency.[3] If ultrasound examination suggests TIPS dysfunction or if there is clinical evidence to suggest occlusion, such as recurrent ascites, then a TIPS revision by interventional radiology is indicated.

Advances in Transjugular Intrahepatic Portosystemic Shunt Stents and Procedural Technique

Until the early 2001, TIPS stents were exclusively bare metal or uncovered stents. These stents unfortunately had high rates failure characterized by stent thrombosis requiring multiple revisions for repeat dilations.[12] Polytetrafluoroethylene-covered stents, or covered stents were introduced in 2001 in the United States and now have entirely replaced bare metal stents in clinical use.[13] Covered stents are associated with lower rates of thrombosis and improved efficacy, as well as improved survival compare to traditional bare metal stents.[12] Covered stents were further improved in 2017 with the introduction of controlled expansion stents (Viatorr CX; W. L. Gore & Associates, Flagstaff, Ariz).[7] These covered, controlled expansion stents allow the operator to dilate the stent diameter to a fixed value of 8 mm. If necessary, then or at a future date, the stent could be further dilated to 10 mm to further decrease the PSG. Of note, noncontrolled expansion stents passively dilate over time to their nominal diameter regardless of initial dilation size. For example, a 10-mm diameter stent would continue to passively dilate even if was dilated to a diameter of 8 mm at the time of placement.[8,14] When compared with traditional covered stents, controlled expansion stents have been shown to result in significantly fewer admissions for ascites (6% vs 14%; $P = .006$) in the first 3 months as well as lower rates of HE when stents are dilated to 8 mm versus 10 mm (26.6% vs 43.2%) with a benefit seen up to 2 years after TIPS.[7,14]

Placement of TIPS has also greatly improved with the assistance of intravascular ultrasound-guided portal vein access. This technique involves the use of an intravascular ultrasound probe positioned in the inferior vena cava and allows for better visualization of the portal veins for guiding the operator.[15] Traditionally, the use of the ultrasound probe was limited to cases with challenging anatomy or hepatic masses. However, it has now gained widespread use because it significantly reduces the fluoroscopy time, volume of iodinated contrast, and overall procedure time.[6,16] This advancement has permitted placement of stents directly across the inferior vena cava into the portal veins when the hepatic veins are completely occluded such as in Budd-Chiari syndrome.[15,17,18] Similarly, in the setting of chronic PVT, placement of a TIPS via the hepatic vein approach to reestablish portal vein blood flow is technically challenging. Transhepatic and trans-splenic approach permits successful cannulation of the portal vein and placement of TIPS along with establishment of portal vein flow.[19–22]

EMERGING INDICATIONS FOR TRANSJUGULAR INTRAHEPATIC PORTOSYSTEMIC SHUNTS

Transjugular Intrahepatic Portosystemic Shunts for Early-Onset Ascites

Ascites that fails to respond to traditional diuretic therapy and dietary sodium restriction (<2 g/d) has been shown to be successfully treated with TIPS, with resolution of ascites approaching 60% to 80% compared with repeated large volume paracentesis (LVP).[3,5,23] Early randomized controlled trials (RCTs) of TIPS for ascites demonstrated these benefits with the use of primarily bare metal (uncovered) stents.[24–30] There were, however, conflicting data on the survival benefit of TIPS compared with LVP. These initial RCTs, using bare metal stents, were composed of heterogenous patient populations with a significant number of patients with decompensated liver disease (Child-Pugh C cirrhosis).[23,31–35] In the most recent multicenter RCT from 2017, the authors used covered stents (not newer controlled expansion stents) in patients with Child-Pugh Scores of less than 12 who were defined as having early ascites by needing 2 LVP within 3 weeks.[36] The authors compared TIPS (n = 29) with LVP with albumin infusions (n = 33).[36] They demonstrated a significant transplant free survival benefit of TIPS (93%) compared with LVP (52%) (P<.003) at 1 year. In multivariate analysis, the only factor associated with improved transplant-free survival was the placement of a TIPS. Among those receiving a TIPS, 52% did not require any further paracentesis compared with none in the LVP group. The average number of paracentesis after TIPS was only 1.0 $\pm$ 1.6 per patient in the TIPS group compared with 10.1 $\pm$ 7.0 per patient in the LVP group (P<.001). The rates of HE at 1 year were similar among the TIPS and LVP groups at 65%, whereas the number of days of hospitalization were significantly higher in the LVP group (35 $\pm$ 40) versus the TIPS group (17 $\pm$ 28) (P = .04).[36] These recent data suggest that patients with compensated cirrhosis (Childs-Pugh Score of <12) would benefit from placement of TIPS, both with improved transplant-free survival but also with decreased hospitalization without the added risk of increase HE. These findings, combined with early studies using bare metal stents, suggest that earlier intervention with TIPS at the onset of ascites before further hepatic decompensation likely confers a survival benefit along with improved quality of life from decreased paracentesis without added increase in rates of HE.

Transjugular Intrahepatic Portosystemic Shunts for Treatment of Portal Vein Thrombosis

PVT can be acute or chronic and often occurs in the setting of cirrhosis. Among patients without cirrhosis and PVT, patients frequently have an hypercoagulable state such as in an inherited genetic mutation (ie, factor V Leiden or prothrombin mutations) or in the setting of a myeloproliferative disorder (ie, polycythemia vera).[37,38]

Acute portal vein thrombosis

Acute PVT is typically best managed with therapeutic anticoagulation; however, success rates are only 38% to 44% after at least 6 months of treatment.[37,39] The use of TIPS with portal vein thrombectomy or thrombolysis was shown to be successful with recanalization of the portal vein in 16 of 17 (94%) noncirrhotic patients with acute PVT. Subsequent portal vein patency was 88% at 2 years.[40]

Chronic portal vein thrombosis

Among patients with chronic PVT, the occluded portal vein undergoes cavernous transformation, which leads to the formation of vascular channels. Yet, this transformation is often insufficient to decompress the portal system, and gastroesophageal varices can form with clinically significant bleeding.[41] Treatment of chronic PVT with

therapeutic anticoagulation is also fairly unsuccessful with resolution rates of less than 5%, and associated variceal bleeding rates of greater than 50%.[41–43] Aside from variceal bleeding, the presence of chronic PVT has frequently been a contraindication to liver transplantation, given the inadequacy of the native portal vein for anastomosis to the recipient portal vein.[44] Using transhepatic and trans-splenic access as described elsewhere in this article, a TIPS can be placed and allow recanalization of the portal vein, a technique described as a TIPS portal vein reconstruction.[19] Rates of successful recanalization of the portal vein have historically ranged from 57% to 84% (**Table 3**). In the most recent report, among patients listed for liver transplantation at a single center, TIPS portal vein reconstruction was technically successful in 98% of patients, with 39% undergoing successful liver transplantation without subsequent PVT or portal vein complications after transplantation.[45]

Table 3
Reports of TIPS for the treatment and recanalization of chronic PVT

Author, Year	Study Period	Portal Vein Recanalization	Duration of Follow-up	Portal Vein Patency Rate
Luca et al,[46] 2011	2003–2010	57% (40/70)	20.7 mo	95% (38/40)
Qi et al,[47] 2015	2009–2011	84% (43/51)	40.07 mo	76% (33/43)
Han et al,[48] 2011	2001–2008	75% (43/57)	24 mo	68% (29/43)
Thornberg et al,[45] 2015	2009–2015	98% (60/61)	19.2 mo	92% (50/60)

Transjugular Intrahepatic Portosystemic Shunts for the Treatment of Spontaneous Portosystemic Shunts

HE in cirrhosis often occurs in two situations, episodic HE or refractory HE. Episodic HE is thought to be related to an acute precipitant, such as infection or gastrointestinal bleeding, whereas refractory HE is characterized by ongoing mental disturbance, typically with continuously elevated ammonia levels but without precipitating triggers. Medical therapy of refractory encephalopathy is often ineffective.[49] Refractory encephalopathy is thought to be related to spontaneous portosystemic shunts that divert substantial portal blood flow away from the liver and result in poor hepatic clearance of toxins. Shunting can occur via small collaterals; however, large shunts may be present that can be detected on cross-sectional imaging. Large spontaneous portosystemic shunts typically include mesoentericorenal or mesoentericocaval shunts and can occur in the setting of relatively preserved hepatic synthetic function. This preserved hepatic function results in low MELD scores; hence, patients often have low priority for liver transplantation despite debilitating HE. These spontaneous portosystemic shunts are estimated to contribute to shunting and persistent HE in 46% to 70% of cases.[50–52] As such, these spontaneous portosystemic shunts have been a therapeutic target for embolization and treatment of refractory HE. The use of TIPS grants access into the portal system and easily permits both embolization of culprit shunts and offers portal decompression through the TIPS to prevent future spontaneous portosystemic shunt formation through reduction in the PSG. The published evidence on the embolization of spontaneous portosystemic shunts for treatment of HE has been limited to small case reports with varying approaches at embolization and varying use of TIPS.[53] The largest retrospective multicenter case series to date using TIPS to embolize spontaneous

portosystemic shunts to treat refractory HE involved 37 cirrhotic patients, excluding patients with Child-Pugh C (>13).[54] Refractory HE was defined as at least 2 hospital admissions for HE (grade 2 or higher based on the West Haven classification) despite at least 30 days of maximal medical therapy (daily lactulose with or without an oral antibiotic). The average MELD score among TIPS recipients was 13. Within the first 100 days after TIPS and embolization, 59.4% of patients (22/37) remained free of HE. Eighteen patients (48.6% overall) remained free of any HE for the duration of follow-up (mean, 697 $\pm$ 157 days). After embolization of the spontaneous portosystemic shunts, there was a significant decrease in the severity of HE and, when it did recur, in the number of hospitalizations and length of stay (**Fig. 1**). Four patients (11%) required repeat embolization based on recurrence of HE. In multivariate analysis, the MELD score was found to be the most predictive of post-TIPS HE with a cutoff score of 11, yielding the highest discrimination (sensitivity of 68.4% and specificity of 77.6%) for recurrent HE.

Transjugular Intrahepatic Portosystemic Shunts to Facilitate an Abdominal Surgery

Extrahepatic intra-abdominal surgery in the setting of cirrhosis and portal hypertension has been associated with a significant risk for postoperative mortality (10%–76%) and postoperative complications, including intraoperative bleeding related to portal hypertension, persistent ascites, and even hepatic decompensation manifest by liver failure.[55–57] The Child-Pugh score is a well-validated tool to predict postoperative mortality after abdominal surgery in patients with cirrhosis.[56,58] Although patients with Child-Pugh C cirrhosis have the worst prognosis, patients with Child-Pugh score A and B are at risk for poor postoperative outcomes. Intraoperative bleeding related to portal hypertension is often problematic. Ascites in the postoperative period can prohibit surgical wound healing and result in abdominal wound infections and even dehiscence.[59,60] The placement of a surgical drain to permit drainage of ascites is not ideal, given risk for bacterial peritonitis along with the likelihood of continued drainage. Placement of a preoperative TIPS to effectively reduce the portal pressure gradient and decrease intraoperative bleeding complications, as well as prevent postoperative ascites, is appealing. There have been multiple reports of success in using TIPS to facilitate abdominal surgery; however, there are no RCTs.[61–66] One group within the context of a case-controlled retrospective study examined 18 patients with cirrhosis who underwent a TIPS compared with 17 historical controls matched on age, etiology of cirrhosis, indication for surgery, and type of surgery to assess potential survival differences.[67] No significant differences in survival were observed at 1 month (83% vs 88%) or 1 year (54% vs 63%), although the Child-Pugh score was higher in the TIPS group compared with the control group (7.7 vs 6.2; $P<.05$). A subsequent larger study assessed 66 preoperative TIPS recipients compared with 68 non-TIPS operative patients across 4 institutions.[68] The groups were matched on etiology of cirrhosis and surgical procedures, and the categories of Child-Pugh score (6 vs 6) and MELD scores (11 vs 11) were similar among the 2 groups. The preoperative TIPS group had lower intraoperative RBC transfusions (8 vs 1; $P = .015$) and lower rates of postoperative ascites (20.4% vs 38.2%; $P = .012$); however, the 30-day and 90-day postoperative mortality rates were similar (1.8% vs 3% [$P = .355$] and 7.5% vs 7.8% [$P = .644$], respectively). Yet, although no difference in survival was observed, survival rates in both groups outperformed traditional mortality estimates after extrahepatic intra-abdominal surgery, suggesting the control group patients perhaps were otherwise optimal candidate for surgery resulting in improved survival rates (**Table 4**).

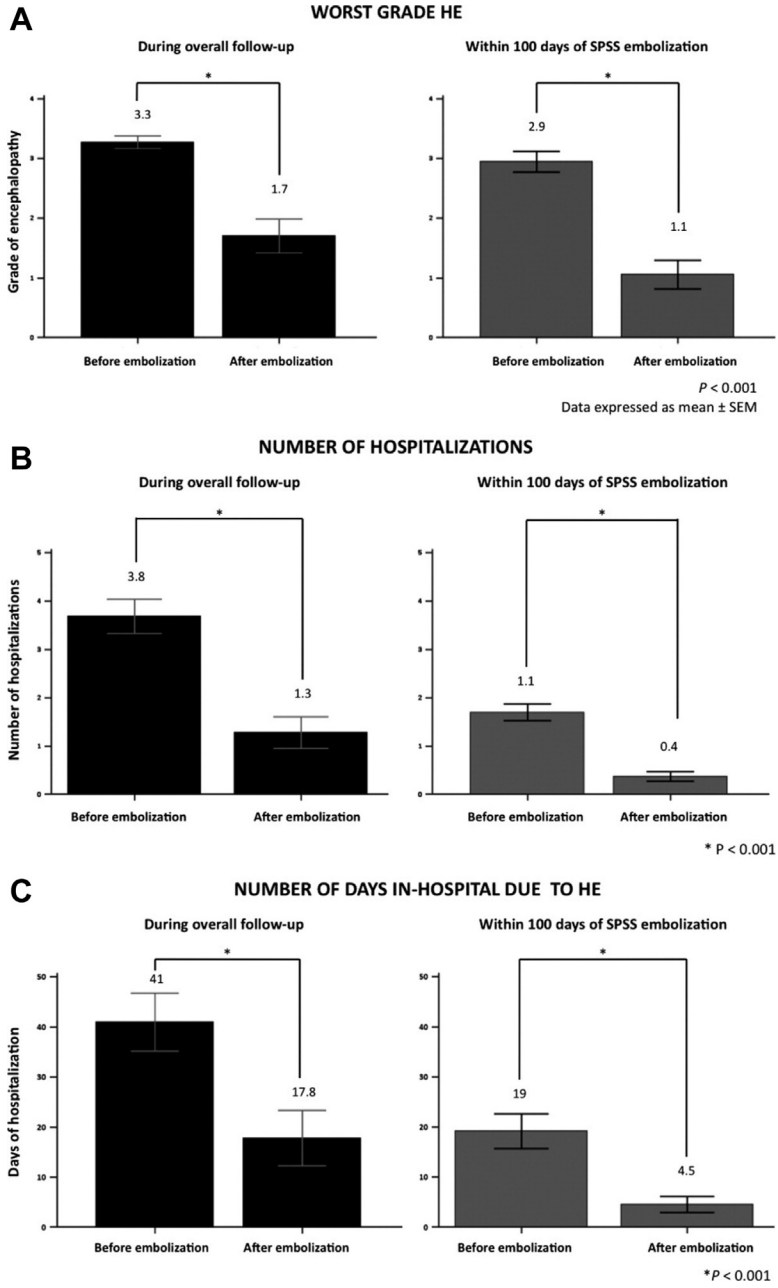

Fig. 1. Short- and long-term changes before versus after embolization in terms of the most severe grade of HE (*A*), number of hospitalizations (*B*), and days spent in the hospital (*C*) because of HE. SEM, standard error of the mean. (*From* Laleman W, Simon-Talero M, Maleux G, et al. Embolization of large spontaneous portosystemic shunts for refractory hepatic encephalopathy: a multicenter survey on safety and efficacy. *Hepatology*. 2013;57(6):2448-2457; with permission.)

Table 4
Preoperative TIPS before abdominal surgery

Author, Year	Number of Patients	Abdominal Surgery	Child-Pugh Score	Time from TIPS to Surgery (Range)	Pre-TIPS PSG Post-TIPS PSG (mm Hg)	Surgical/TIPS Complications	Postoperative Mortality, n (%)
Azoulay et al,[61] 2001	7	Tumor resection AAA repair Hartmann's reversal	A–C	1–5 mo	18 ± 5 9 ± 5	1 liver failure 1 postoperative ascites	1 (17%)
Grübel et al,[62] 2002	2	Colectomy Nephrectomy	C	3–8 wk	17–26 8–14	None	0 (0%)
Gil et al,[63] 2004	3	Tumor resection	A–B	14–45 d	20–28 6–7	1 encephalopathy 1 CHF	0 (0%)
Schlenker et al,[64] 2009	7	Abdominal and pelvic resection	A–B	1–32 d	9–22 3–10	1 postoperative ascites 2 encephalopathy 1 liver failure	1 (17%)
Kim et al[65]	6	AVR Colectomy	A–C	6–46 d	Not reported	1 renal failure 3 encephalopathy	0 (0%)
Menahem et at,[66] 2015	8	Colon resections	A–C	1–9 wk	15.5 ± 2.9 7.5 ± 1.9	1 bacterial peritonitis 1 encephalopathy 3 ascites 1 hemorrhage 3 liver failure	2 (25%)

Abbreviations: AAA, abdominal aortic aneurysm; AVR, aortic valve replacement; CHF, congestive heart failure.

Adapted from Philip M, Thornburg B. Preoperative Transjugular Intrahepatic Portosystemic Shunt Placement for Extrahepatic Abdominal Surgery. In: *Seminars in Interventional Radiology*. Vol 35. Thieme Medical Publishers; 2018:203-205; with permission.

Transjugular Intrahepatic Portosystemic Shunts for Hepatopulmonary Syndrome

Hepatopulmonary syndrome (HPS) is a disorder of pulmonary oxygenation that occurs in the setting of portal hypertension with or without cirrhosis with a severity that is independent of the severity of underlying liver disease.[69,70] The pathophysiology of HPS consists of inappropriate vasodilation of the pulmonary capillaries that results in a ventilation–perfusion mismatch from increased shunting of pulmonary blood flow, leading to a decrease in arterial oxygen tension. The inappropriate vasodilation is suspected to relate to an increased release of nitric oxide from the pulmonary endothelium in combination with genetic polymorphisms associated with proinflammatory mediators released by circulating macrophage in response to portal hypertension.[71,72] Unfortunately, there is no proven medical therapy for HPS, and treatment is supportive with oxygen supplementation.[73] Prompt referral for liver transplantation evaluation is recommended because transplantation ameliorates the problem.[73] TIPS has been assessed as a potential treatment of HPS within the context of 11 case reports and series. A meta-analysis of the reports of 12 patients who underwent TIPS for the treatment of HPS reported on a mean duration of follow-up of 9.3 months.[74] Improvement in arterial oxygenation was observed in 9 patients immediately after TIPS; however, this finding was not sustained in 2 patients. Of the remaining 3 patients, 2 remained unchanged after TIPS and 1 had worsening oxygenation 4 months after TIPS. Interestingly, 1 patient had recurrence of subjective pulmonary symptoms in the setting of TIPS stenosis that resolved with TIPS revision. The same authors published a follow-up report among TIPS recipients at their institution over a 1-year period.[75] They identified 23 TIPS recipients meeting the diagnostic criteria for HPS who were undergoing TIPS for another indication, such as variceal bleeding, ascites, or Budd-Chiari syndrome. Of the 23 patients with HPS, dyspnea was reported in 5 patients. After TIPS, 4 of 5 patients (80%) reported improvement in dyspnea immediately after TIPS. However, 50% reported return of dyspnea after 3 months. Improvements in measured arterial oxygen tension were also observed at 1 month after TIPS, but this improvement was not sustained at 3 months. These data combined with previous case reports suggest that TIPS may have a role for transient improvement in symptoms and oxygenation in HPS, with success in 75% to 80% of patients. However, improvement is not sustained after 3 months. Until additional data are available, there is no definitive role for TIPS placement in the setting of HPS at present.

Transjugular Intrahepatic Portosystemic Shunts for the Hepatorenal Syndrome

The hepatorenal syndrome (HRS) has long been thought to be a form of functional renal failure that occurs in the setting of intense renal vasoconstriction among patients with cirrhosis or acute liver failure.[76] More recently, that concept has been challenged by emerging data suggesting HRS is likely multifactorial with a contribution from proinflammatory cytokines resulting in cellular changes at the renal tubular level that result in decreases in the glomerular filtration rate.[5,77] Nonetheless, the current mainstay of treatment for HRS has been volume expansion of the intravascular space, and splanchnic and arterial vasoconstrictors in an effort to increase renal perfusion. Placement of a TIPS has the potential to redistribute portal blood volume to the systemic circulation, thereby increasing renal perfusion and decreasing the effects of the renin–angiotensin–aldosterone system.[78] TIPS has been assessed for the treatment of HRS; however, the reports are few owing to the unique patient profile who would benefit from a TIPS. The largest prospective study using TIPS for the treatment of HRS among nonliver transplantation candidates involved 31 patients. Patients with documented HRS unresponsive to standard volume-expanding medical therapy

received TIPS on average 3.4 weeks after the onset of renal insufficiency. The average portal to systemic gradient pressures decreased from 21 to 13 mm Hg after TIPS. Table 5 demonstrates baseline laboratory parameters including renal function and urine volume. There was a significant improvement in serum creatinine, the glomerular filtration rate, and urine output after TIPS.

Of the 31 patients, 4 of 7 on hemodialysis before TIPS were able to stop dialysis following return of renal recovery. After TIPS, survival at 3, 6, and 12 months was 81%, 71%, and 48% respectively, a dramatic improvement compared with historical reports of 10% survival at 3 months after the onset of HRS. The greatest survival benefit was seen among patients with type 2 HRS and those who had resolution of ascites with TIPS. Of note, improved renal function among non-HRS patients undergoing TIPS for refractory ascites have also been reported.[23] Despite these promising results, further RCTs have not been conducted among patients with HRS. In lieu of additional data, there is as of yet not a defined role for TIPS in the setting of HRS.

Table 5
Liver and renal function after TIPS

Characteristic (Mean)	Baseline (n = 31)	Week 1 (n = 30)	Week 2 (n = 30)	Week 4 (n = 29)	*P* value
Child-Pugh score	9.5	9.4	9.3	8.8	NS
Bilirubin (mg/dL)	3.1	4.4	4.1	3.2	NS
Albumin (g/dL)	2.9	2.9	3.4*	3.3	*<.05
Serum creatinine (mg/mL)	2.3	1.7	1.6	1.5	<.01
Creatinine clearance (mL/min)	18	42	48	44	<.001
Urine volume (mL/24 h)	544	788	1041	1248	<.05

Values displayed are averages and *P* values represent comparison with baseline values.
* Week 2 compared to Baseline.
Adapted from Brensing KA, Textor J, Perz J, et al. Long term outcome after transjugular intrahepatic portosystemic stent-shunt in non-transplant cirrhotics with hepatorenal syndrome: a phase II study. https://doi.org/10.1136/gut.47.2.288; with permission.

SUMMARY

TIPS has been an established treatment for portal hypertensive complications, including refractory ascites and variceal bleeding. Advancements in TIPS stent technology and improvements in technique of placement have led to novel indications for TIPS beyond traditional guideline-supported indications. These emerging indications include the treatment of chronic PVT and the use of TIPS before abdominal surgery to alleviate portal hypertensive complications. The use of TIPS can also facilitate the embolization of large portal systemic shunts to alleviate refractory HE owing to excessive portal shunting. Along with these novel indications and expanded use, additional data are awaited to determine if TIPS for other indications such as HPS and HRS is safe and effective. Despite these advances, TIPS remains an invasive procedure with risks for complications, hence the evaluation and decision to place a TIPS should be made in conjunction with an experienced gastroenterologist/hepatologist and performed at a center with expertise to ensure a successful patient outcome.

DISCLOSURE

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