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TRANSJUGULAR INTRAHEPATIC PORTOSYSTEMIC SHUNT

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Abstract

Transjugular intrahepatic portosystemic shunt (TIPS) is an established procedure for the complications of portal hypertension. The largest body of evidence for its use has been supported for recurrent or refractory variceal bleeding and refractory ascites. Its use has also been advocated for acute variceal bleed, hepatic hydrothorax, and hepatorenal syndrome. With the replacement of bare metal stents with polytetrafluoroethylen (PTFE) covered stents, shunt patency has improved dramatically thus improving outcomes. Therefore, reassessment of its utility, management of its complications, and understanding of various TIPS techniques is important.

Keywords

Transjugular intrahepatic portosystemic shunt; esophageal varices; ascites; hepatic hydrothorax; hepatorenal syndrome; hepatopulmonary syndrome; venoocclusive disease; Budd-Chiari syndrome

Introduction

Portal hypertension is one of the major complications of cirrhosis. It results from increased intrahepatic resistance and increased splanchnic blood flow leading to a hyperdynamic circulatory state. The transjugular intrahepatic portosystemic shunt (TIPS) has been an established procedure in the treatment of the complications of portal hypertension including bleeding esophageal varices, refractory cirrhotic ascites, hepatic hydrothorax, hepatorenal and hepatopulmonary syndromes, and more recently, Budd-Chiari syndrome and veno-occlusive disease. However, despite these broad applications, refractory acute variceal hemorrhage and control of refractory cirrhotic ascites are the only two indications subjected to numerous controlled trials.

Conflicts of Interest: Dr. Sanyal: see attached document (page 35), Dr. Sydnor: none, Dr. Patidar: none

ARUN J SANYAL M.D.
CONFLICT OF INTEREST DISCLOSURE TABLE
JANUARY 2014 (based on incomes over last 24 months)
A: No interest
B: < $ 5000
C: $ 5001–10,000
D: $ 10,001–$50,000
E: $ 50,001–100,000
F: > $ 100,000

The TIPS procedure, first described by Rosch et. al[1] in 1979, is a percutaneous image

Company	Stock	Employment	Speaker	Consulting advisor	Research grants	Travel grants	Intellectual property	Royalties
Abbott	A	A	A	B	A	A	A	A
Exhalenz	A	A	A	A	A	A	A	A
Conatus	A	A	A	A	C****	A	A	A
Genentech	A	A	A	B^	A	A	A	A
GenFit	A	A	A	A*	A	A	A	A
Gilead	A	A	A	B	F	A	A	A
Echosens-Sandhill	A	A	A	A*	A^^	A	A	A
Ikaria	A	A	A	B	E	A	A	A
Immuron	A	A	A	A**	A	A	A	A
Intercept	A	A	A	A*	A	A	A	A
Merck	A	A	A	B	A	A	A	A
Norgine	A	A	A	B	A	A	A	A
Roche	A	A	A	B	A	A	A	A
Salix	A	A	A	C	E	A	A	A
Uptodate	A	A	A	A	A	A	A	C
Takeda	A	A	A	B	D	A	A	A
Astellas	A	A	A	A	D	A	A	A
Novartis	A	A	A	A***	E	A	A	A
Nimbus	A	A	A	B	A	A	A	A
Galectin	A	A	A	A***	E	A	A	A
Nitto Denko	A	A	A	B	A	A	A	A
Sequana	A	A	A	A*	A	A	A	A
Bristol Myers	A	A	A	B	A	A	A	A

^ I am consulting with Genentech re NASH and fibrosis.

^^ Echosens has provided a fibroscan machine for dedicated research use for NASH related studies via NIDDK NASH CRN

* I am a consultant but have divested myself- I have no financial conflict of interest

** I will be the PI of the Immuron upcoming trial for alcoholic hepatitis as part of NIAAA funded TREAT consortium. Immuron will provide drug and no additional funding.

*** have provided advice but not taken any personal remuneration

**** they will provide drug and lab costs for a NIAAA sponsored study of a caspase inhibitor for alcoholic hepatitis. I have no personal financial conflict of interest

Research grants listed above for Salix, Gilead and Exhalenz represent the site budgets for VCU clinical trials involving these companies and do not support me directly.

Research collaborations without any funding from the commercial entity: Regulus, CSL Behring, Ferring, Zora Lipidomics, and Metabolon

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guided procedure in which a tract or conduit is constructed within the liver between the systemic venous system and portal system with an intent for portal decompression (Figure 1)[2]. The most common conduit is between the right hepatic vein (HV) and the right portal vein (PV). Patency was originally achieved by bare metal stents. The advent of Polytetrafluoroethylen (PTFE) – covered stents in recent years has dramatically improved patency rates[3], and are preferred over bare metal stents[4].

In this section, we will review the indications, recommended patient selection, post-operative care, common complications and clinical outcomes related to the TIPS procedure. We also provide detailed stepwise technique to the TIPS procedure, as well as a description on advanced TIPS techniques.

Indications for TIPS Creation

TIPS reduces the portosystemic pressure gradient by shunting of blood from the PV to the HV. Its creation successfully reduces the portosytemic pressure gradient in over 90% of cases[5, 6, 7, 8, 9, 10, 11]. Indications for TIPS are summarized in Box 1.

Box 1

Indications for TIPS

INDICATION	References
Refractory or recurrent esophageal variceal hemorrhage*	4, 7–9, 24–31
Refractory Ascites*	57–62
Acute esophageal variceal bleeding	43,44
Hepatorenal syndrome (types 1 and 2)	81–84
Refractory bleeding gastric varices	46–50
Portal hypertensive gastropathy	52, 53
Hepatic hydrothorax	70, 72–77
Hepatopulmonary syndrome	78,79
Budd-Chiari syndrome	86–89
Hepatic Veno-occlusive disease	92–95

*Strongest evidence for TIPS based on controlled trials

Primary Prevention of Variceal Hemorrhage

The development of esophageal varices is a common complication of portal hypertension with subsequent hemorrhage representing a major cause of morbidity and mortality in patients with cirrhosis[12, 13]. The highest rate of development occurs in Child–Turcotte–Pugh (CTP) class B and C disease[14] with an increasing risk for hemorrhage occurring in larger varices (5% for small varices and 15% for large varices[15]), appearance of red-whale marks[11], and severity of disease (CTP class B and C). Currently beta blockers and endoscopic variceal ligation (EVL) are considered the best approach for the primary prevention for variceal hemorrhage. There are no trials to date comparing TIPS to other forms of therapy for prevention of variceal hemorrhage. Thus in the absence of evidence in

light of its risks (hepatic encephalopathy, procedural complications), TIPS is not indicated for primary prevention for variceal hemorrhage.

Acute Variceal Bleeding

The use of TIPS in the setting of acute variceal hemorrhage is limited. In study by Monescillo et al, 116 cirrhotic patients were randomized within 24 hours of acute variceal hemorrhage to either receive endoscopic sclerotherapy or TIPS procedure based on HVPG of less than 20 or more respectively[16]. Patients who received early TIPS were found to have reduced treatment failure rates as well as better inhospital and 1-year survival. In a similar multi-center center study, comparing TIPS with PTFE-covered stents versus medical therapy with propranolol/nadolol and EVL, early use of TIPS (within 72 hours of randomization) was found have lower rates of re-bleeding with 3% in the early TIPS group and 45% in the pharmacotherapy plus EVL group[17]. Furthermore, survival at 1-year was significantly better in the TIPS group at 86% vs. 61 % in the pharmacotherapy plus EVL. The above studies suggest that if early risk stratification can be performed (via measurement of HVPG), early TIPS insertion could improve overall outcomes for patients who present with an acute variceal bleed.

Refractory Acute Variceal Bleeding

Combined treatment with EVL, prophylactic antibiotics, and vasoactive drugs is the suggested standard of care for the treatment for acute esophageal bleeding[12]. Patients who survive an initial episode of variceal hemorrhage are at a high risk for re-bleeding (over 60% at 1 year[18]). Factors that contribute to recurrent hemorrhage include severity of liver disease, severity of initial hemorrhage, presence of encephalopathy, impaired renal function, and increasing age[19, 20, 21, 22, 23]. In addition, patients with a hepatic venous pressure gradient (HVPG) greater than 20mm Hg are likely to have severe or recurrent bleeding, and are more likely to fail initial medical or endoscopic therapy[24].

Numerous randomized controlled trials have compared the use of TIPS with endoscopic therapy for refractory or recurrent variceal bleeding [4, 7, 8, 9, 25, 26, 27, 28, 29, 30, 31, 32]. The results of multiple meta-analysis (Table 1[33, 34, 35, 36]) of TIPS compared to various forms of endoscopic therapies has shown significant decrease in the risk of recurrent bleeding after the insertion of TIPS. Mortality rates were found to be similar between the endoscopy and TIPS groups, though the development of post-treatment hepatic encephalopathy (HE) was almost twofold in the TIPS group.

TIPS has also been compared to pharmacotherapy[37] for the prevention of recurrent variceal hemorrhage. In a prospective, randomized controlled trial, a total of 91 cirrhotic patients (CPT B and C) who survived their first variceal hemorrhage were randomized to receive TIPS (n of 47) or pharmacotherapy (n of 44, to receive propranolol plus isosorbide-5-mononitrate). With a mean follow up of 15 months, re-bleeding rates were 39% and 17% in the pharmacotherapy and TIPS groups respectively. Survival was the same in both groups (72%); however, the authors noted improved CPT class in pharmacotherapy group (72%) versus the TIPS group (45%).

Overall, many of the aforementioned trials included bare metal stents (versus PTFE-covered stents) and endoscopic therapy mostly consisted of sclerotherapy (versus EVL); thus the literature should be kept in perspective when analyzing primary and secondary outcomes. Amid the present use of PTFE covered stents, data regarding survival, patency rates, and the development of post-treatment HE seems to be improved[38, 39, 40, 41]. Furthermore, the results of a recent meta-analysis of six published controlled trials comparing clinical outcomes of TIPS with PTFE covered stents versus bare metals stents showed significant improvement of primary patency rates, significant reduction in the risk of developing HE, and a significant decrease in mortality[42].

Lastly, it is worth mentioning that TIPS has also been compared to surgical shunts in the management of recurrent variceal bleeding. In a meta-analysis including three prospective randomized trials and one retrospective case-controlled study, 30-day and 1-year survival were found to be the equivalent between the two groups[43], though the 2-year survival rate was significantly better in the surgical patients with an odds ratio (OR) of 2.5. Less frequent shunt failure was also significantly reduced in the surgical patients with an OR of 0.3. However, with the use of PTFE covered stents, the ease and efficacy of TIPS has made surgical shunts rare and there is limited expertise in the US to perform such shunts whereas TIPS is widely available.

Refractory Bleeding from Gastric Varices and Portal Hypertensive Gastropathy

Few studies have shown the efficacy of TIPS in refractory bleeding gastric varices[44454647]. In one series, 28 patients with gastric fundal varices unresponsive to vasoconstrictor therapy underwent emergent TIPS placement. Bleeding was controlled in most patients, comparable to the success rate for bleeding esophageal varices[45]. In another small series with 32 patients with refractory bleeding gastric varices, TIPS placement achieved homeostasis in 90% in those with active bleeding, and re-bleeding rates were 14%, 26%, and 31%, respectively at 1 month, 6 months, and 1 year[48]. In addition, TIPS has also been compared to glue therapy for bleeding gastric varices[4849]. In a prospective, randomized control trial comparing TIPS to cyanoacrylate therapy, TIPS was found to be more effective with less re-bleeding rates (11%) versus the cyanoacrylate group (38%)[47]. Both groups were also found to have similar survival rates and frequencies of complications. It is also important to note that another endovascular procedure, balloon-occluded retrograde transvenous obliteration for gastric varices (BRTO) has recently shown promising results for refractory bleeding from gastric varices[50].

Portal hypertensive gastropathy (PHG) is common in patients in portal hypertension and its prevalence parallels with severity of liver disease[51]. The diagnosis of PHG is made endoscopically with gastric mucosa having a “snakeskin” appearance of the fundus and body of the stomach. Though bleeding from PHG is uncommon, TIPS has been evaluated in several small studies[5253]. In these studies, there was 75–90% endoscopic improvement in PHG following TIPS, and one series demonstrated a decreased need for transfusions[52].

Refractory Ascites

Management of refractory ascites includes large volume paracentesis (LVP) and TIPS. The mechanism of action of how TIPS may improve ascites is through increased natriuresis via reductions in proximal tubular sodium reabsorption and in the RAAS[54]. There have been a total of six randomized controlled trials comparing LVP to TIPS (Table 2[55, 56, 57, 58, 59, 60]) involving 396 patients, of which 197 underwent TIPS. Findings from these studies have shown that TIPS improved control of ascites (range of 38–84%, mean of 64%) vs LVP (range 0–43%, mean of 24%). However, there were also increased rates of post TIPS HE (range of 23–77%, mean of 53%) with no effect on survival in four of the six studies. From the results of multiple meta-analysis[61, 62, 63, 64, 65], insertion of TIPS showed similar improvement of ascites, though survival benefit seemed to be inconclusive as 3 or the 5 meta-analysis did not show improved survival.

Refractory Hepatic Hydrothorax

Hepatic hydrothrorax occurs in about 6–10% of patients with advanced cirrhosis[66]. The treatment of hepatic hydrothorax includes medical therapy, repeated thoracentesis, chest tube placement and diaphragmatic defect repair[67]. Refractory hepatic hydrothorax poses a significant therapeutic challenge and is limited to video-assisted thoracoscopic (VATS) and TIPS for those not who are not transplant candidates.

TIPS has been evaluated for refractory hepatic hydrothorax in numerous small non-controlled trials [70, 68, 69, 70, 71, 72, 73]. On the whole, 198 patients underwent TIPS with a response rate (both complete and partial) ranging from 59–82%. Survival, however, could not be reliably determined given that there were no control groups, and that most of the studies were retrospective studies. Nevertheless, 30-day mortality ranged from 5–25%, with 2 studies[74, 75] reporting a 1 year survival of 64% and 48% respectively. In summary, given its response rate, and limited therapeutic options, TIPS is an adequate management strategy for refractory hepatic hydrothorax.

Hepatopulmonary Syndrome

Hepatopulmonary syndrome (HPS) is complication of advanced cirrhosis and is due to the development of intrapulmonary vascular dilatation resulting in hypoxia[74]. There have been number of case reports and small series of studies evaluating TIPS in HPS[75, 76]. In one series, 7 patients with HPS underwent TIPS placement, of which only 1 patient had transient improvement in arterial oxygenation[78]. Thus, given the limited data available, TIPS insertion is currently not recommended for the HPS[3].

Hepatorenal Syndrome

There are two types of hepatorenal syndrome (HRS), type 1 and type 2, and its development confers a poor prognosis. Type 1 is a rapid, progressive decline in renal function (less than 2 weeks) and type 2 is characterized as gradual decline in renal function[77]. There have been 4 small studies (n of 61) evaluating the role of TIPS in HRS[78,79, 80, 81]. In these studies, TIPS insertion was found to improve renal function through enhanced glomerular filtration rates and renal plasma flow as well as via reductions in serum creatinine and plasma aldosterone levels. Because none of these studies were controlled, survival benefit cannot be fully

elucidated. In the largest series[82] 1 and 2 year survival rates were 20% for type 1, and 70% and 45% for type 2, respectively. In addition, TIPS may have a role in maintenance therapy in patients who initially respond to vasoconstrictor therapy[84] and as a bridge to liver transplantation[83].

Budd-Chiari Syndrome

The Budd-Chiari Syndrome (BCS) is caused by hepatic venous outflow obstruction or thrombosis hepatic veins or hepatic portion of the inferior vena cava (IVC) leading to a clinical constellation of liver injury, abdominal pain, and ascites[82]. There have been only a small number of studies evaluating the utility of TIPS for the management of BCS[83, 84, 85, 86]. In one of the larger series[89], 124 patients (of which included patients with severe BCS who did not respond to medical treatment and recanalization) underwent TIPS placement. Overall 5- year survival was 84% and transplant-free survival at 1 and 5 years after TIPS was 88% and 78% respectively.

From a technical aspect, creation of TIPS may be difficult if the hepatic veins are occluded. This can be overcome with a transcaval approach using ultrasound guidance through the caudate lobe with subsequent implantation of a covered stent[89]. Furthermore, a larger diameter of the shunt is recommended to allow for both decompression of sinusoidal and splanchnic beds[89]. A transmesenteric approach may also be performed in this situation, but this approach is limited to few centers[87].

Hepatic Veno-occlusive disease

Veno-occlusive disease (also known as sinusoidal obstruction syndrome) is usually seen after bone marrow transplantation[88]. The disease is similar to BCS, however, hepatic venous outflow obstruction occurs at the level of the hepatic venules and sinusoids. In a limited number of patients[89, 90, 91, 92], TIPS insertion had shown improvement in liver disease, although it did not improve survival. Given the limited data, the value of TIPS in veno-occlusive disease is unclear, and should be approached on a case by case basis.

Patient Selection and Pre-TIPS Evaluation

Patients who are being considered for a TIPS procedure should be under the care of a gastroenterologist or hepatologist with consultation from interventional radiology. Absolute and relative contraindications[3] are listed in Box 2. Absolute contraindications include heart failure, severe tricuspid regurgitation, severe pulmonary hypertension (mean pulmonary wedge pressure >45 mm Hg). Relative contraindications include anatomic issues that can complicate the creation of the shunt or reduce technical success (i.e. obstruction of hepatic veins, portal vein thrombosis, hepatic masses, hepatic cysts), severe coagulopathy, and HE. Even though TIPS can be created in the aforementioned situations, the risk, benefit, and difficulty with creating the shunt needs to be balanced with patient care and the clinical scenario. Examples of this include palliative treatment for HCC patients with refractory variceal bleeding, recanalization of occluded portal veins in patients with recurrent variceal bleeding, and treatment of patients with BCS and progressive liver failure. In addition,

patients with a history of HE are at an increased risk for exacerbation of HE after shunt creation[93] and they should be aware of this risk-benefit scenario

Box 2

Contraindications for TIPS

RELATIVE	**Absolute**
Hepatocellular Carcinoma, especially centrally located	Primary prevention of variceal bleeding
Obstruction of all hepatic veins	Congestive heart failure
Portal vein thrombosis	Severe tricuspid regurgitation
Moderate pulmonary hypertension	Severe pulmonary hypertension
Severe coagulopathy (international normalized ration >5)	Multiple hepatic cysts
Thrombocytopenia of <20,000 cells/cm^3	Uncontrolled systemic infection or sepsis
Hepatic encephalopathy	Unrelieved biliary obstruction

There have been numerous models created in predicting post-TIPS survival[94, 95, 96, 97, 98]. Among these, the modified Model for End-Stage Liver Disease score (MELD)[99] has proved to be superior to CPT score and Emory score[101]. A MELD score above 18 predicts a significantly higher mortality 3 months after TIPS as compared to a score of less than 18[99, 100]. In addition, mortality is also dependent on the original TIPS indication.

Like with any procedure, the TIPS procedure carries its risks and benefits, and a clear understanding of these risks and benefits must be understood and agreed upon by the patient. A detailed history and physical examination is required. In addition, pre-TIPS laboratory studies should be obtained 24 hours prior the procedure. These include serum electrolytes, complete blood count, coagulation studies, and liver and kidney function panel.

Cross-sectional imaging (liver ultrasound with Doppler, computer tomography, or magnetic resonance imaging) should be reviewed, and if not current (>1 month), a repeat study should be obtained to evaluate vascular patency and to look for hepatic masses or other pathology that may complicate the procedure. In patients who have suspected or known cardiac or pulmonary disease, an echocardiogram should be obtained to exclude diastolic/systolic dysfunction and pulmonary arterial hypertension because TIPS is known to increase central venous pressure, pulmonary capillary wedge pressure, and exacerbate known cardiac dysfunction[101]. In addition, a paracenetesis should be performed for refractory ascites prior the procedure in order to reduce the risk of peri-procedural bleeding. Furthermore, a thoracentesis may benefit patients with hepatic hydrothorax as it may improve respiratory function and assist with sedation.

Conventional Technique

In the US the TIPS procedure is performed by interventional radiologists. The procedure is either performed under conscious sedation or under general anesthesia with endotracheal intubation[5]. The later is preferred by many for patient control and comfort due to the potentially prolonged nature of the procedure.

Hepatic Venous Access

A right internal jugular (IJ) approach is preferred as it allows a direct path to the IVC. Secondary options include left IJ vein[102] and femoral vein[103] approaches, but these are reserved for unusual anatomy or in cases of central venous occlusive disease. After the neck is cleaned and draped in a sterile fashion, IJ venous access is obtained via sonographic guidance. A catheter is then advanced beyond the right atrium into the HV under fluoroscopic guidance. The right HV is chosen whenever possible as it allows for an anterior inferior transhepatic puncture of the right portal vein, thus providing the safest approach for the TIPS. A wedged hepatic venogram is then obtained using carbon dioxide to demonstrate the portal venous anatomy (Figure 2).

Portal Venous Access and TIPS Insertion

There are several commercial sets available for portal puncture: Haskal (Cook Medical) and Ring (Cook Medical) transjugular intrahepatic access sets which both includes a 16-gauge modified Colapinto puncture needle; Rosch-Uchida transjugular liver access set (Cook Medical) which contains a 14-gauge needle; and Angiodynamic transjugular access set (Angiodynamics Medical) containing 14 and 21-gauge needles. After the CO2 portogram has been performed and a target identified, the needle (which is constrained in a hard inner sheath and softer 10 French outer sheath) is directed anteriorly and inferiorly from the right HV into the right PV (Figure 3). Once access is achieved, the needle is removed and a wire and catheter are advanced into the splenic or mesenteric vein. Portal venography (Figure 4) and pressure measurements are performed.

An angioplasty balloon is then used to dilate the tract (Figure 5), allowing for passage of the 10 French sheath into the PV. The PTFE-covered stent (Viatorr, W. L. Gore), which is the standard TIPS stent, is then deployed and post dilated to 8 mm. This is a unique stent because the caudal 2 cm, which resides in the PV, is uncovered, and the variable cranial length of the stent, which traverses the liver and HV, is covered by PTFE. After stent deployment and dilation, trans-TIPS portal venography (Figure 6) and pressure measurements are repeated. If the pressure remains higher than desired, the stent can be further dilated to 10 or 12 mm. A PPG less than 12 mmHg[3] should be achieved in patients with a history of bleeding esophageal varices and refractory ascites. However the optimal PPG for refractory ascites is still under much debate with some authors suggesting a PPG of less than 8mmHg[59]. In patients with pre-existing HE, a higher gradient may be appropriate to reduce post-TIPS HE[104], more data is needed to elucidate this.

Selective Embolization of Portosytemic Collaterals

At the discretion of the interventionalist, selective embolization of varices or other portosystemic collaterals can be performed after TIPS placement. This may benefit patients with a history of bleeding esophageal varices as embolization at the time of TIPS placement has been found to decrease the rate of recurrent esophageal bleeding (84% and 81% at 2 and 4 years respectively) vs TIPS alone (61% and 53% at 2 and 4 years respectively)[105]. Furthermore, selective embolization can also be performed in cases where the gradient is not reduced to less than 12 mmHg. There are a wide variety of embolic devices which can be used including coils and Amplatzer Vascular Plugs (St. Jude Medical).

Immediate Post-Procedural Management

After TIPS placement patients should be observed for a minimum of 12 hours in a hospital unit. Vital signs should be closely monitored for evidence of intraperitoneal hemorrhage. Post-TIPS laboratory values should be obtained including a complete blood count (to monitor for hemorrhage and infection), coagulation panel, and kidney and hepatic function tests. A liver sonogram with Doppler can be obtained a day after the shunt placement to evaluate for shunt patency.

Advanced and Alternative TIPS Techniques

Numerous options exist when difficult anatomy prohibits the right hepatic to right PV approach. These include a left hepatic to left portal approach or an IVC to right portal approach through the caudate lobe with or without the aid of transabdominal or intravascular ultrasound. The 'gunsight technique'[106] can be employed when success has not been achieved with traditional transvascular methods. This involves placement of a loop snare in the IVC from the IJ access and placement of a loop snare in the PV from a percutaneous approach. A needle is then advanced from a second percutaneous approach using lateral fluoroscopy through both loop snares into the IVC. A wire is passed through the needle into the IVC and snared from above, thus establishing systemic to portal access for placement of the shunt.

Occasionally, patients with PV thrombosis will present and require recanalization of the portal system. This can be achieved through a variety of techniques using a percutaneous or transhepatic approach in order to relieve the portal obstruction and facilitate flow through the shunt (Figure 7).

Complications

The most common complications following the TIPS procedure are listed in Table 3[2]. These complications can be divided into 3 major categories: technical related, portosystemic related and other unique complications.

Technical Access Related

Puncture of the liver capsule is common, occurring up to 30% of patients[109], though serious intraperitoneal bleeding is rare. Liver capsule puncture is likely in patients with a small liver, and when multiple needle punctures are required. Biliary puncture and fistula formation is also a rare complication, occurring with an incidence of less than 5%[107]. Fistula formation between the biliary and vascular systems could result in hemobilia, cholangitis, sepsis, and stent infection[1, 108]. If fistula formation occurs between a stent and the biliary system, early stent occlusion may ensue due to marked psuedointimal hyperplasia[109]. Fistulous communication may be decreased by employing controlled needle passage and number of needle punctures. Biliary diversion via internal or external drainage catheter may be used to address biliary-vascular fistulas, embolization can be performed in cases of hemobilia, and biliary-stent fistulas can be treated with placement of a PTFE covered stent to reline the hepatic parenchymal tract[109].

Hepatic infarction is a rare complication which can result from a reduction in sinusoidal flow. It can also occur secondary to stent compression of the hepatic artery. A low PPG after TIPS placement can increase the incidence of hepatic infarction. This problem can be treaded with placement of stents within the primary stent to reduce the shunt caliber.

Technical Stent Related

With the use of PTFE covered stents, thrombosis, occlusion, and stent migration are infrequently seen[2, 3]. Prior to the use of PTFE covered stents, the most common site for shunt stenosis was at the hepatic venous end. Mid-stent stenosis is thought to be secondary to pseudointimal hyperplasia within bare metal stents[110], with rates of stenosis ranging from 18–78%[3]. In a randomized control trial[111] comparing covered and bare metal stents, rates of primary patency in the covered and bare metal stent groups were 86% and 47% respectively at 1 year. At 2 years, patency rates were 80% and 19% for covered and bare metal stents respectively. In another large non-randomized series[112], primary patency rates were similar with 87% and 81% at 6 and 12 months respectively.

Portosystemic Shunting Related

HE is the most frequent medical complication that usually occurs 2–3 weeks after TIPS insertion[113]. The pathophysiology of post-TIPS HE is complex, though mainly due to diverted portal flow away from the liver due to TIPS and into the arterial system[95,114] and decreased liver metabolic capacity. Frequency of new or worsening HE ranges from 10–44%[3], and factors associated with post-TIPS HE development include prior history of HE, increasing age, shunt caliber, high creatinine levels, low serum sodium concentration and liver dysfunction[95, 115]. Previously, studies with bare metal stents found an increased risk for the development of HE after TIPS insertion for ascites[57, 58, 59, 60, 61, 62]. Consequently, studies with covered stents found to have lower rates of HE after TIPS placement[113, 116]. A meta-analysis of further confirms this statement[33]. However, it should be mentioned that most of these studies were not designed to test post-TIPS HE. In addition, the methodology used to access for HE was highly variable and subjective based.

Prevention of post-TIPS HE include possibly having a higher PPG[106] (especially in patients with a high risk of HE), and treating precipitating factors prior to TIPS placement. Post-TIPS HE can be treated with standard therapy, and in refractory cases, the shunt can be reduced or occluded[95,116, 106117].

Unique Complications

Intravascular hemolysis and endotipsitis (infection of TIPS stent) are rare complications of TIPS[109, 118, 119] and infrequently occur with covered stents. If present, intravascular hemoloysis is usually self-limiting, resolving in 3–4 weeks. Endotipsitis presents with fever, abdominal pain, and laboratory evaluation reveals positive blood cultures and an elevated white blood cell count. Treatment is with prolonged antibiotics.

Post-TIPS Follow up and Maintenance

Recurrence of portal hypertension symptoms could indicate shunt dysfunction. Prompt sonogram with Doppler of the liver should be obtained to evaluate shunt velocity. Velocities of 50 cm/s or less or 250cm/s are associated with shunt dysfunction, with greater than 90% sensitivity and specificity[120]. If a patient is asymptomatic, sonogram with Doppler of the liver is usually performed within 4 weeks of placement and every 6 months to a year. The gold standard to evaluate shunt patency is portal venography. However this is reserved to evaluate shunt occlusion seen on sonogram as it is invasive and carries its own complications. If a bare metal stent was used, revision with a covered stent can be performed[120].

Future Considerations

The use of TIPS in the management of end stage liver disease has been refined and it is now an integral part of the treatment armamentarium for this condition. A key challenge that remains to be resolved is how to prevent further hepatic decompensation in those who already have some hyperbilirubinemia prior to TIPS. The impact of TIPS on the systemic microcirculatory dysfunction associated with cirrhosis also needs to be better understood. Although it is much less common than before, acute on chronic liver failure still occurs with TIPS and better methods to prevent this are needed. As expected, porta-systemic shunting increases the risk of infection and the role of selective gut decontamination or ways to improve intestinal barrier functions in preventing ACLF after TIPS are now needed. There have also been reports of an increased risk of HCC after TIPS. This needs to be definitively confirmed or refuted.

Conclusions

TIPS has become a valuable option in management for the complications of portal hypertension. The best available evidence for the use of TIPS includes refractory or recurrent esophageal variceal bleeding and refractory ascites. In addition, TIPS insertion could improve outcomes for patients who present with an acute variceal bleed, hepatic hydrothorax, and hepatorenal syndrome. With the use of covered stents, long term patency has dramatically improved, further advocating early use. The insertion of TIPS unfortunately comes with complications, with HE being one of the most common. A possible solution to this includes thorough selection of patients and careful attention to the final portosystemic gradient. Lastly, with advanced and alternative techniques, TIPS could play a larger role in the future treatment in patients with complications of portal hypertension.

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Key Points

- The largest body of evidence supports the use of TIPS in recurrent or refractory esophageal variceal bleeding followed by refractory ascites. Its use may also be beneficial for other conditions including hepatic hydrothorax, Budd-Chiari syndrome, Hepatorenal Syndrome, and Hepatopulmonary Syndrome.
- Contraindications for TIPS placement include systolic and diastolic cardiac disease, severe pulmonary hypertension, and primary prevention of variceal bleed.
- Numerous innovative supporting techniques have evolved over recent years to address problematic anatomy, improve the safety profile of the procedure, and to improve outcomes.

Outline

- Indications
- Patient Selection
- Conventional Technique
- Alternative and Advanced Techniques
- Complications
- Post-Tips Management
- Future Considerations and Conclusion

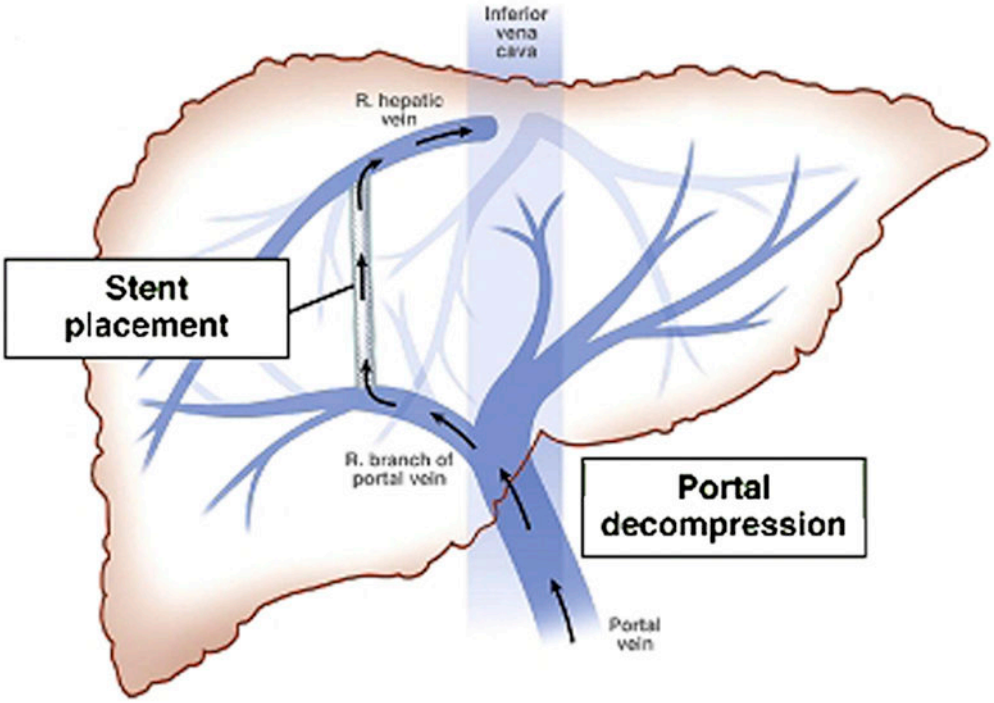

Figure 1. TIPS Procedure for Portal Decompression

Adapted from Bhogal HK, Sanyal AJ. Using transjugular intrahepatic portosystemic shunts for complications of cirrhosis. *Clin Gastroenterol Hepatol*. 2011;9(11):936-46, with permission

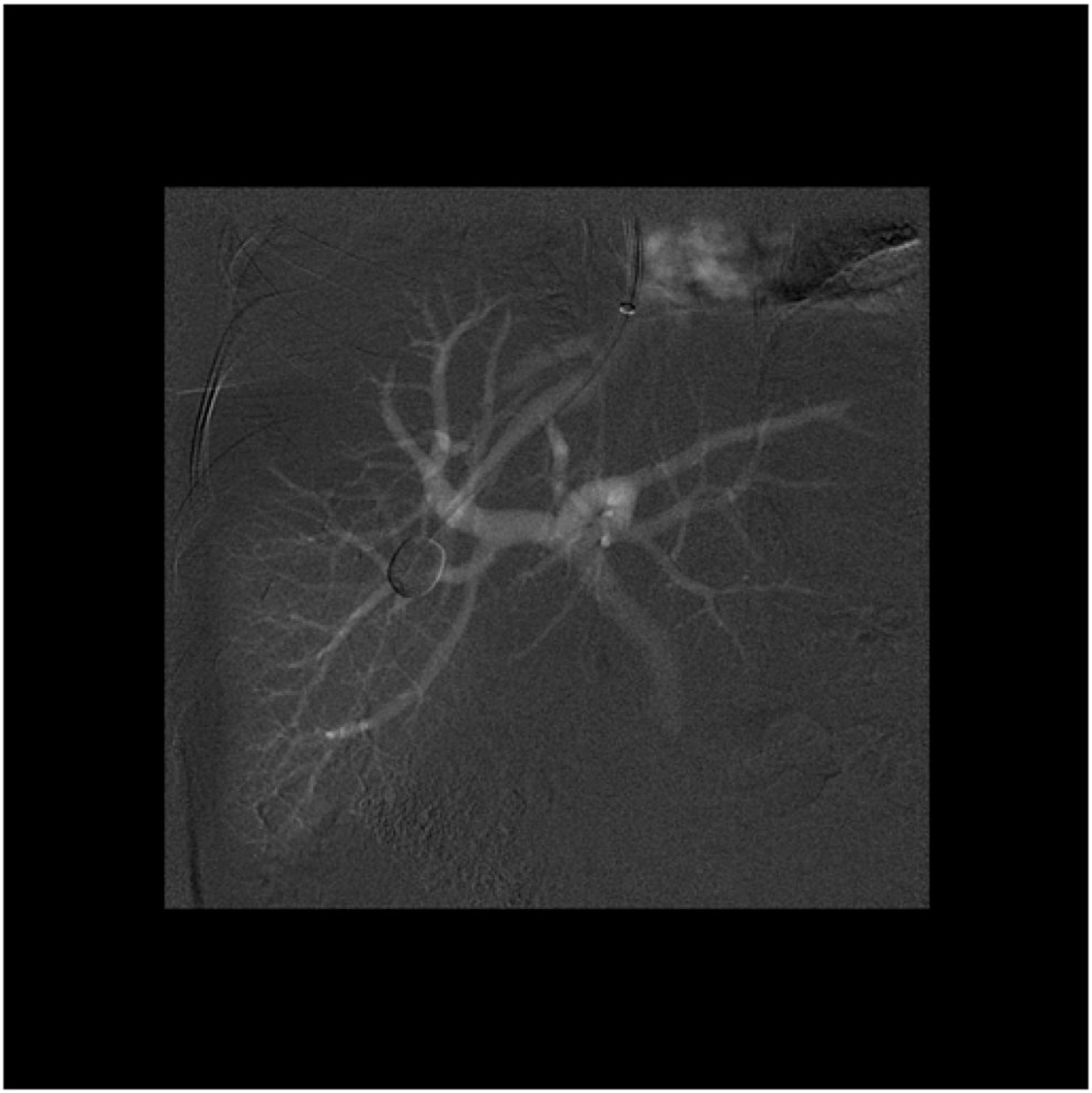

Figure 2.
Wedged hepatic venogram using an occlusion balloon from the right hepatic vein demonstrating normal portal venous anatomy.

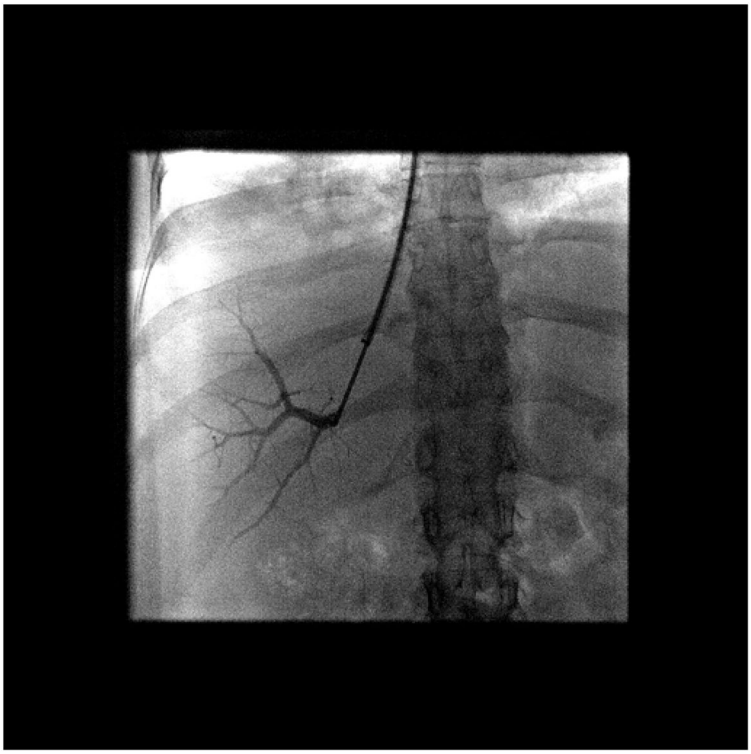

Figure 3.
Injection of contrast confirming placement of needle in a branch of the right portal vein.

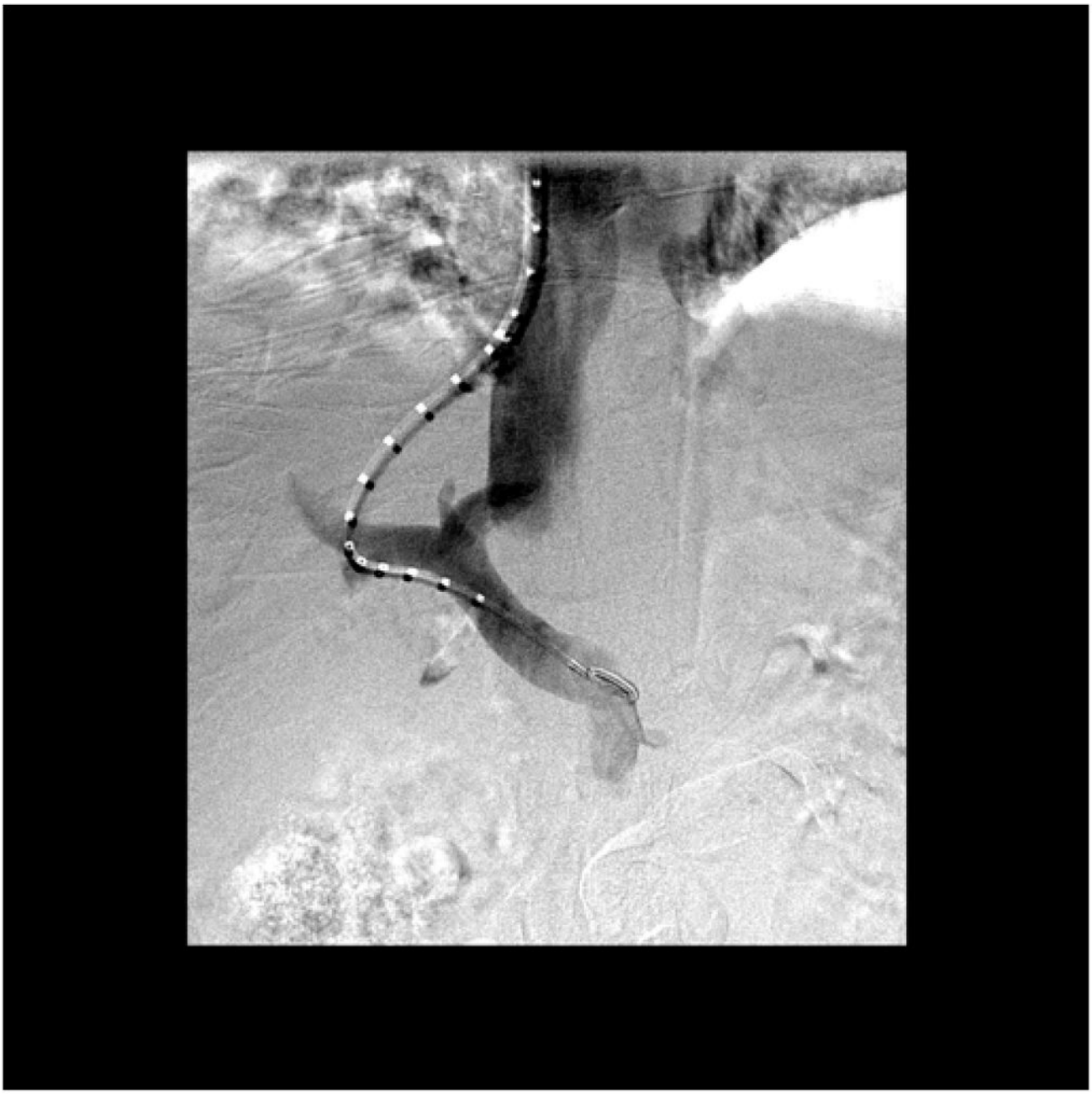

Figure 4.
Simultaneous injection of contrast through a marker pigtail catheter in the portal vein and sheath in the right hepatic vein demonstrating appropriate anatomy.

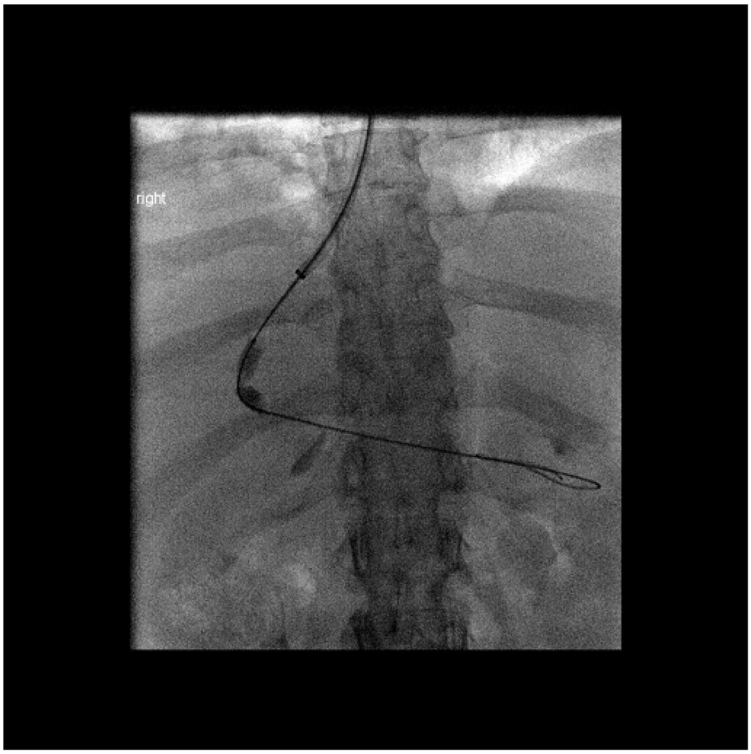

Figure 5.
Angioplasty balloon dilating the transhepatic tract to 8 mm prior to stent placement.

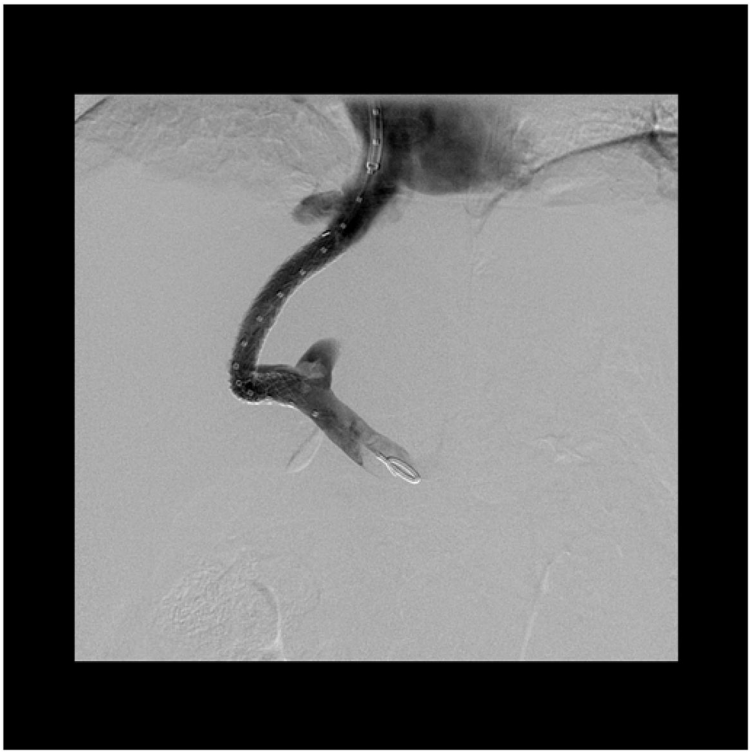

Figure 6.
Completion venogram through the pigtail catheter demonstrating appropriate flow from the portal vein through the TIPS shunt into the right hepatic vein and right atrium.

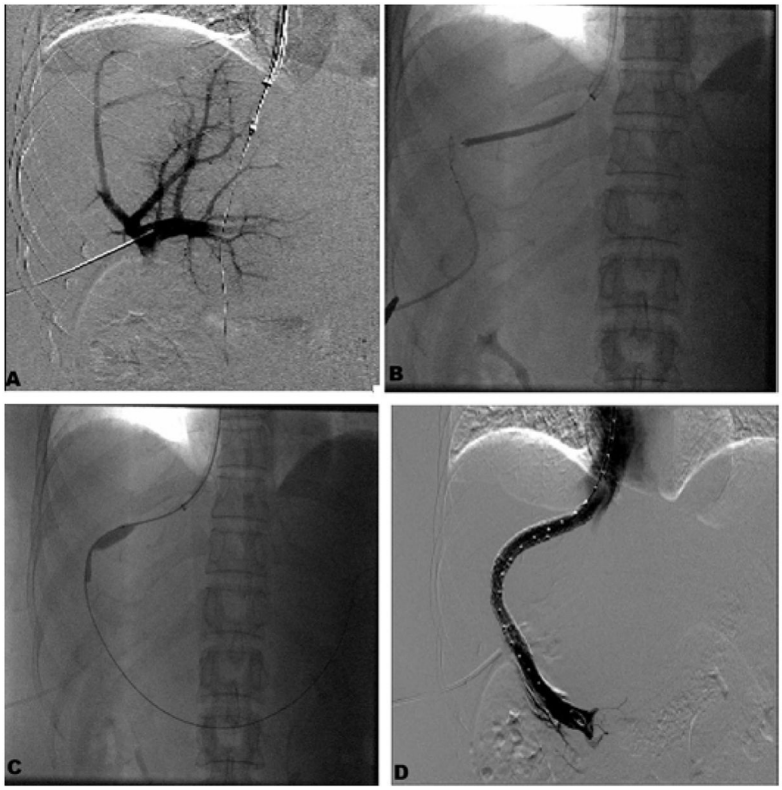

Figure 7. TIPS Procedure with 'Gunsight Technique'

A: Intravascular US has been placed in the IVC and percutaneous access into the portal system has been obtained and confirmed with an injection of contrast through the needle.

B: After puncturing through loopsnares in the right portal vein and IVC from a second percutaneous access, the wire was pulled through the IVC sheath and the tract between the two sheaths is being angioplastied with a small diameter balloon.

C: The wire was pulled into the portal vein and advanced into the splenic vein from above and the tract is now being dilated to 8mm.

D: Completion venogram through the pigtail catheter demonstrating appropriate flow from the portal vein through the TIPS shunt into the right hepatic vein and right atrium.

Table 1

TIPS versus Endoscopic Treatment in Secondary Prophylaxis for Vacriceal Bleeding: Results from Multiple Meta-Analysis.

Study Findings	References			
	Luca et al., 1999[32]	Papatheodoridis et. al, 1999[33]	Burroughs and Vangeli, 2002[34]	Zheng et al, 2008[35]
No. of Pts	750	811	948	883
No. of Randomized Trials	11	11	13	12
No. of TIPS	372	403	472	440
No. Endoscopic Therapies	378	408	476	443
Recurrent Bleeding				
TIPS, no. (%)	81 (21)	76 (18.9)	88 (18.6)	86 (19)
Endoscopic Therapy, no. (%)	196 (52)	190 (46.6)	210 (44.1)	194 (43.8)
NNT with TIPS	3.3	4	4	Not Reported
Post-Treatment Encephalopthy				
TIPS, no. (%)	119 (35)	126 (34.0)	134 (28.4)	148 (33.6)
Endoscopic Therapy, no. (%)	65 (19)	70 (18.7)	83 (17.3)	86 (19.4)
Mortality				
TIPS, no. (%)	109 (28)	110 (27.3)	130 (27.5)	111 (25.2)
Endoscopic Therapy, no. (%)	98 (26)	108 (26.5)	118 (24.8)	98 (22.1)

NNT – Number Needed to Treat

TIPS, transjugular intrahepatic portosystemic shunt

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Table 2

TIPS versus Large Volume Paracentesis in Treatment for Refractory Ascites

Study Findings	**References**					
	Lebrec et al[57]	**Rossle et al[58]**	**Gines et al[59]**	**Sanyal et al[60]**	**Salnero et al[61]**	**Narahara et al[62]**
No. of pts	25	66	70	109	66	60
No. of TIPS pts	13	29	35	52	33	30
No. of LVP pts	12	31	35	57	33	30
Improvement of ascites						
TIPS no. (%)	5 (38)	16 (84)	18 (51)	30 (53)	26 (79)**	24 (80)
LVP no. (%)	0 (0)	9 (43)	6 (17)	9 (16)	14 (42)**	8 (27)
Survival						
TIPS %	29*	58*	26*	26	59*	64*
LVP %	56*	32*	30*	30	29*	35*
Post-Treatment Encephalopathy						
TIPS no. (%)	3 (23)	15 (51)	27 (77)	22 (39)	20 (61)	20 (66)
LVP % no. (%)	0 (0)	11 (35)	23 (66)	13 (23)	13 (39)	5 (17)

* Transplant-free survival after two years

** Defined as treatment failure, which was defined as when a patient received at least 4 LVP within 1 month for episodes of recurrent tense ascites.

TIPS, tranjugular intrahepatic portosystemic shunt

LVP, large volume paracentesis

Table 3

Complications from TIPS

Technical complications
Related to access
Capsule puncture
Intraperitoneal bleed
Hepatic infarction
Fistula
Hemobilia
Related to the stent
Thrombosis
Occlusion
Stent migration
Sepsis
Related to portosystemic shunting
Hepatic encephalopathy
Hemodynamic consequences
Sepsis
Unique complications
Intravascular hemolysis
Endotipsitis

From Bhogal HK, Sanyal AJ. Using transjugular intrahepatic portosystemic shunts for complications of cirrhosis. *Clin Gastroenterol Hepatol*. 2011;9(11):936–46, with permission.