



# Transjugular Intrahepatic Portosystemic Shunt (TIPS)

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## ABSTRACT

Most of the morbidity associated with chronic liver disease results from the development of portal hypertension and its sequelae. Transjugular intrahepatic portosystemic shunt (TIPS) is a minimally invasive method of creating a portosystemic shunt that can effectively decompress the hypertensive portal circulation and treat its complications. Introduced more than a decade ago, the procedure is being increasingly used, and is rapidly becoming the procedure of choice in the treatment of uncontrolled and recurrent variceal bleeding, refractory ascites, hepatic hydrothorax, and Budd-Chiari syndrome. TIPS controls bleeding in almost 90% cases and palliates ascites in more than 80% cases. Whilst the efficacy is undeniable, there is concern over its durability, the risk of encephalopathy, and acceleration of liver failure. The recent introduction of PTFE-covered stents has improved the credibility of the shunt, matching the patency rates of surgical shunts, with far less morbidity and mortality. Encephalopathy can be effectively managed by either primarily electing a small-sized shunt or by reducing its size. It is crucial in selecting the appropriate patient for TIPS to prevent early TIPS-related mortality from accelerated liver failure, using scoring systems such as the MELD, APACHE II, and Child-Pugh grading. In its short history, the TIPS procedure has come a long way, and is evolving as a safer, more durable, and cost-effective alternative to its medical and surgical counterparts. The procedure is no longer being perceived as a temporary “bridge” to liver transplantation, and is becoming the replacement to surgical shunts in most centers where it is being practiced.

## INTRODUCTION

Portal hypertension is a significant problem affecting patients with liver disease throughout the world. In India especially, there is a predominant cirrhotic population, which is expected to rise with a perceived increase in the incidence of hepatitis B and hepatitis C virus-related infections. In addition, advent of high-quality imaging has facilitated better diagnosis of Budd-Chiari syndrome. Thus, there is predictably an overall increase in the incidence of chronic liver disease and portal hypertension being diagnosed and treated in India.

Whilst medical and endoscopic therapy is the mainstay in the treatment of these patients, the past few decades have witnessed a variety of fluoroscopy-guided percutaneous interventions being utilized in the management of patients with complications of portal hypertension viz. bleeding, ascites, and hydrothorax.

TIPS (transjugular intrahepatic portosystemic shunt) is one such radiological method used to decompress the portal venous system and involves creation of a conduit between the portal vein and hepatic vein within the liver substance. This conduit behaves just like a surgical porto-caval shunt, with far less morbidity and mortality, and has replaced the surgical shunt in most centres throughout the world.

## TECHNIQUE OF TIPS

TIPS are created in the interventional radiology suite, with facilities for high-resolution fluoroscopy, digital subtraction and continuous hemodynamic monitoring. Briefly, the procedure is as follows:

The jugular vein (usually right internal jugular) is catheterized, and a cannula advanced across the inferior vena cava into the hepatic vein. Through this cannula, a needle is passed, which is used to puncture the hepatic vein wall and traverse the liver parenchyma into the intrahepatic portal vein. The parenchymal tract created by the needle is dilated with a balloon and a stent deployed to maintain its patency.

The portal and hepatic vein pressures are measured before and after TIPS creation and the portosystemic gradient (PSG) calculated. This gradient provides a measure of the degree of portal hypertension and determines the end-point of the procedure. When treating patients, it is generally desirable to reduce the PSG to below 12-15 mm Hg.

## INDICATIONS FOR TIPS

Based on the available data, accepted indications for TIPS include:<sup>1</sup>

1. Acute variceal bleeding refractory to endoscopic and medical therapy
2. Recurrent variceal bleeding refractory to endoscopic or medical therapy
3. Refractory ascites
4. Hepatic hydrothorax
5. Budd-Chiari syndrome

Additional indications have been described in case reports and small case series. These newly described indications include hepatorenal syndrome, hepatopulmonary syndrome, and mesenteroportal vein thrombosis.

## CONTRAINDICATIONS TO TIPS

All forms of portal decompression (surgical or percutaneous) increase right atrial pressure, cardiac output and cardiac index. Similarly, they deprive the liver of a fraction of nutrient portal flow in order to achieve pressure reduction. Portosystemic shunts are contraindicated in patients who cannot tolerate these conditions. These include patients with heart failure, severe pre-existing hepatic encephalopathy, and severe hepatic failure.

Relative technical contraindications include (note that TIPS have been created in all these settings): polycystic liver disease, portal vein thrombosis with cavernomatous transformation, extensive primary or metastatic liver malignancy, and unrelieved biliary obstruction.

## RESULTS OF TIPS

### Overall results

The technical success is close to 100% in most series.<sup>2,3</sup> The mean PSG is decreased from 23-24 mm Hg before TIPS to 9.7-11 mm Hg after TIPS.

Procedural mortality is <1%, which is much less than the surgical portosystemic shunts. The 30-day mortality ranges from 3-44%, almost entirely attributable to patient selection and their pre-TIPS condition. Most mortality is from worsening liver function, sepsis or multiorgan failure. This rate is minimized by appropriate case selection; elective patients with compensated liver function respond much better than patients with severe hepatic decompensation. Various parameters have been used in identifying such patients, such as the Acute Physiology And Chronic Health Evaluation (APACHE II) score, serum bilirubin levels, modified Child-Pugh score and Model for End-stage Liver Disease (MELD) score.<sup>4-7</sup> Using these scoring systems, it is possible to identify a sub-group of high-risk cirrhotic patients that are likely to have a poor outcome from a TIPS procedure.

### Control of bleeding

TIPS can control active or recurrent variceal bleeding in 81-96% of patients. In several randomised clinical trials comparing TIPS to endoscopic therapies (ET), the mean rate of variceal rebleeding after TIPS was 32% lower than that of endoscopic therapy; mean rates of rebleeding for TIPS and ET were 17% (range 9-24%) and 49% (range 24-66%), respectively, while encephalopathy rates were understandably higher in the TIPS group: 33% versus 17% for ET.<sup>8</sup> Average mortality at one year proved indistinguishable in both groups (approximately 23%), although one series by Garcia-Villareal demonstrated one- and two-year actuarial

survival benefits for TIPS patients.<sup>9</sup> Interestingly, nearly 20% of cases undergoing ET had to be salvaged by TIPS, and it could be argued that survival benefit with primary TIPS might have been more evident if the concomitant morbidity of failed endoscopic patients had not been included in the TIPS groups.

In nearly all cases, rebleeding after TIPS was directly related to shunt stenosis or occlusion. It is conceivable that if the obstacle of TIPS patency were reduced, the rates of TIPS-related rebleeding would be lower, as would patient morbidity from interim episodes of bleeding.

### Control of ascites

The literature evaluation using TIPS for the treatment of refractory or recurrent ascites is less well developed, although this has become the predominant indication of TIPS in most hospital practices. An important randomised trial was published by Rossle et al, in which 60 patients underwent repeated large volume paracentesis versus TIPS.<sup>10</sup> At 3 months, 61% of the TIPS patients were free of ascites compared with 18% in the paracentesis group. Interestingly, encephalopathy rates were similar in both groups. In addition, survival without liver transplantation was statistically better in the TIPS group at both one and two years (69% and 58% TIPS versus 52% and 32% paracentesis). Their findings suggest that patients meeting the profiles of those reported should undergo TIPS rather than repeated paracentesis because of better treatment outcomes and survival.

These authors also documented improvements in creatinine in their patients, findings that several groups have previously described in careful analyses of the haemodynamic, physiologic, and hormonal effects of TIPS. It appears that TIPS can profoundly affect the hepatorenal axis by improving renal blood flow, glomerular filtration rates, and sodium handling, and by correcting the hyperaldosteronaemic and hyperadrenergic states in cirrhotic patients with refractory ascites. These finding have, in part, spurred the use of TIPS in patients with hepatorenal syndrome, and improving their survival which is otherwise abysmal.<sup>11</sup>

### Budd-Chiari syndrome

Budd-Chiari syndrome results from obstruction to the venous outflow from the liver. Most of the cases in India are due to membranous obstruction of the inferior vena cava and/or hepatic veins, which are best managed by angioplasty and stenting of the occluded vessel. At times, however, the hepatic vein thrombosis is very extensive, precluding angioplasty. In such cases, TIPS is proving to be effective at reversing hepatic congestion, reducing the stimulus to hepatocyte necrosis, and retarding the progression to cirrhosis.<sup>12</sup> TIPS mimics the decompressive effect of a mesoatrial shunt, because its outflow is always cephalad of the narrowed portion of the inferior vena cava, obviating some of causes of failure of surgical mesocaval shunts that decompress portal blood into a hypertensive, infrahepatic inferior vena cava.

Creating TIPS in BCS patients can be technically challenging because of hepatic vein thromboses, enlarged swollen livers, and hypercoagulability that causes acute shunt thrombus formation. We have followed BCS patients who had undergone TIPS with

shunt venograms and liver function tests and have confirmed maintenance of reduced portal venous pressures, absence of ascites, and most importantly, sustained improvement in the liver function.<sup>13</sup>

## SHUNT PATENCY: THE ACHILLES' HEEL OF TIPS

Despite the adoption of TIPS at academic and private hospitals worldwide, the procedure remains clouded by the unpredictable durability of the shunt. Shunt malfunction, secondary to shunt stenosis or occlusion, is the commonest cause of recurrent portal hypertension in patients that have undergone TIPS.<sup>14</sup> A complex process of pseudointimal proliferation, by which a layer of tissue migrates through the stent interstices and reduces or occludes the shunt lumen and causes shunt stenosis. The mechanism of this proliferation is poorly understood, and is probably related to bile seepage into the TIPS.

Most centres performing TIPS have a surveillance program for early detection of shunt malfunction, using colour Doppler and/or venography. A secondary outpatient intervention, such as angioplasty and stent placement, is used to maintain shunt patency when stenosis of the TIPS is detected. When revision of the TIPS is not successful, a new, parallel shunt may be created. Overall the primary patency rate for TIPS is 25-66% at 1 year and 5-32% at 2 years. The secondary intervention can raise the patency rate to up to 87% at 3 years.

### Improving TIPS patency using stent-grafts

Unpredictable and poor TIPS patency rates have spurred a lot of research into improving shunt patency. Several animal studies and human trials have shown remarkable abilities of polytetrafluoroethylene (PTFE) lined stents to prolong TIPS patency, by preventing proliferation of tissue within the stent lumen, and by protecting the shunt from seeping bile.

At present, only one such commercially manufactured TIPS device using PTFE is available (Viatorr TIPS endoprosthesis, W. L. Gore and Associates), which has been in clinical use since 4 years. When compared with the regular uncovered stent, the PTFE-covered devices dramatically decrease the rate of shunt dysfunction (13% versus 44% at a median of 300-day follow up).<sup>15</sup> Expectedly, this is associated with a reduction of clinical relapses and the number of reinterventions. Also, there is a trend toward better 1-year and 2-year survival in the PTFE group, although not statistically significant. Many prospective studies have established the supremacy of stent-grafts; according to the largest published study by Hausegger et al, involving 71 patients, primary and secondary patency rates of 81% and 100% respectively, were achieved with the new TIPS device at 1 year.<sup>16</sup> The patency improves further if the device is positioned accurately, covering the entire parenchymal tract and the hepatic vein through its junction with the IVC; restenosis rates drop to <5% in such cases. The clinical results have also been equally impressive, with a 30-day mortality of 10% and an overall mortality rate of 28% (mean follow up, 16 months). Given the compelling data from this study and various others published this year, it would clearly define a trend of using the stent-grafts in the vast majority of TIPS.

## COMPLICATIONS OF TIPS

Major procedural complications are rare, occurring in less than 1% of cases. These include hepatic laceration, hepatic arterial injury, haemoperitoneum from extrahepatic portal vein puncture, and inadvertent intra-abdominal organ injury.

Complications could also result from portosystemic shunting, and may appear immediately or as a delayed event following TIPS. The important shunt-related complications included liver failure and hepatic encephalopathy.

Liver failure is one of the leading causes of death in patients undergoing TIPS. After TIPS insertion, there is significant portal flow diversion and the liver relies on the hepatic arterial supply for survival. In some cases, the hepatic arterial flow may not be sufficient to provide enough blood to the liver, and hepatic failure ensues. Careful selection of patients for TIPS using the APACHE II, modified Child-Pugh, and MELD scores is critical in avoiding this complication.

As with surgical shunts, hepatic encephalopathy is fairly common after TIPS, occurring in 3-75% patients (usually 15-30%) in different series. Most cases are mild and well controlled with medical management. Refractory encephalopathy can develop in 3-7% of patients, requiring either implantation of a "reducing stent" or alternatively, occlusion of the shunt.<sup>17</sup>

Choosing a smaller calibre shunt is another concept that is rapidly evolving to prevent TIPS-related encephalopathy. There is an ongoing prospective trial comparing the efficacy and encephalopathy rates of 8mm stent-grafts versus the standard 10mm stent-grafts. This trial is based on the success of 8mm grafts used in surgical meso-caval shunts and its results are eagerly awaited.

## INDIAN EXPERIENCE WITH TIPS<sup>18</sup>

Despite the high incidence of cirrhosis, there is resistance from hepatologists and gastroenterologists throughout the country in offering the TIPS procedure to their patients. Various reasons have been cited. Most of the times, this has been attributed to the poor durability of the shunt. Enforcing a surveillance program for ensuring long-term shunt patency is often difficult; many patients failing to comply especially if they do not have easy access for Doppler and venography. The use of stent-grafts has improved the confidence of physicians in TIPS, as the shunt patency is significantly improved and there is no need of any shunt surveillance. We are now electively performing TIPS in patients with Child-A cirrhosis, Budd-Chiari syndrome and at times, non-cirrhotic portal fibrosis, a group that would otherwise be considered suitable for a surgical shunt.

Another mitigating factor is the cost of the procedure, often perceived as being prohibitively high. However, the cumulative expenditure involved in multiple sclerotherapy sessions or repeated paracentesis often becomes costlier than the TIPS procedure itself. In addition to being cost-effective, TIPS provides a vastly improved quality of life, whereby the patient does not need multiple hospitalisations, transfusions and drugs. It is however, important to choose the appropriate cases; poor selection of cases causes disrepute to the procedure, and can end a fledgling TIPS program.

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