New techniques in medicine

Current status of transjugular intrahepatic portosystemic shunts

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Summary

The use of the transjugular intrahepatic portosystemic shunt (TIPS) has emerged as an important nonoperative modality for variceal bleeding, intractable ascites, and for selected cases of hepatic venous obstruction. We believe that TIPS should be viewed as a 'bridge' to liver transplantation and should be carried out only in experienced centres. The adverse haemodynamic changes on the cardiopulmonary system after TIPS should be borne in mind. Prospective trials to evaluate the role of TIPS versus sclerotherapy in variceal bleeding will be watched with interest. There is, however, an urgent need to improve long-term results of TIPS as stent thrombosis and stenosis occur frequently. We advocate routine surveillance to detect these problems at an early stage.

Keywords: portal hypertension; transjugular intrahepatic portosystemic shunts; ascites; liver transplantation

Table 1 Severity of portal hypertension

Corrected sinusoidal pressure (mmHg)	Severity of portal hypertension
< 5	Normal
6-10	Mild
11-15	Moderate
>15	Severe

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The initial approach to patients with portal hypertension and its attendant complications of variceal bleeding, ascites, encephalopathy and hypersplenism is to conduct a thorough medical evaluation in order to establish a diagnosis and assess the underlying medical condition.¹ Resuscitation with fluid and blood products and admission to the intensive care unit are mandated for patients with acute variceal bleeding. The prognosis of patients with variceal bleeding depends on the underlying medical condition, the Child-Pugh score, and the aetiology of the liver disease.¹

Sclerotherapy may be initially successful at controlling bleeding in 90% of patients. However, bleeding recurs within the first year in up to 50% of patients.¹ Surgical shunts are very effective for variceal bleeding, however, this benefit is achieved at the price of a high operative morbidity and significant encephalopathy.²⁻⁶ Liver transplantation is an effective means of correcting portal hypertension but is impractical and unnecessary in most patients.⁷ The search for a better therapy for portal hypertension and variceal bleeding led to the development of a nonoperative portosystemic shunt (box 1). Box 2 gives the landmark events in the development of this procedure.⁸⁻¹⁴ The hope was that, because the transjugular intrahepatic portosystemic shunt (TIPS) could be inserted percutaneously without the need for open surgery, morbidity would be lower for TIPS than for surgical shunts. Furthermore, as the TIPS shunt diameter is smaller than the standard surgical shunt, it was anticipated that encephalopathy would be lower.¹⁴

TIPS is now offered to a wider range of patients, although patency rates in the medium- and long-term are still poor.¹⁵⁻¹⁷ Furthermore, some questions have been raised that TIPS may in fact delay definitive treatment, such as liver transplantation, because patients who are relatively stable stay for a longer time on the waiting list.

In this article we discuss the current status of TIPS. This procedure has become popular because other therapeutic options for the management of variceal haemorrhage have serious shortcomings.² Initially, TIPS was limited to a few specialist centres, but improved medical management of patients with portal hypertension and better radiological techniques have led to a wider application of this procedure.²⁻³

Technical considerations

A definitive diagnosis of portal hypertension is obtained by the direct measurement of portal venous pressure and portosystemic gradient. However, the diagnosis is commonly made endoscopically by visual identification of gastro-oesophageal varices. The risk of haemorrhage may be assessed by the size and appearance of the varix. Patients with portal hypertension may also be evaluated by sonography or arterial portography. Sonographic signs of portal hypertension include splenomegaly, ascites, and the presence of numerous small tortuous vessels suggestive of varices. Sonography is frequently used to assess the size, patency and direction of flow in the portal vein before the insertion of TIPS. It is also used for pre-operative assessment of patients before liver transplantation.

Arterial portography is used to clarify the anatomy of the portal vein if Doppler sonography is inconclusive. Arterial portography is accomplished by contrast injection into the splenic or superior mesenteric arteries. In patients with severe portal hypertension, arterial portography may not adequately display the portal venous anatomy because of the magnitude of portal flow diversion through varices or because of total reversal of flow in the portal vein.

In cases where arterial portography is inconclusive, imaging of the portal system can be accomplished by direct portal catheterisation and the degree of portal hypertension can be estimated by 'wedged' hepatic pressure. In this

Treatment options for the control of variceal haemorrhage

- treatment of varices that have never bled (primary prophylaxis): beta-blockers and/or nitrates
- control of acute variceal bleeding: octreotide or vasopressin, endoscopic therapy (band ligation or sclerotherapy), balloon tamponade, TIPS, or surgery (devascularisation or emergent portocaval shunts)
- prevention of recurrent bleeding (secondary prophylaxis): pharmacological + endoscopic, TIPS, surgical shunts, or liver transplantation

Box 1

Landmark events in the development of TIPS

- 1969: Rosch *et al*⁸: experiments in dogs
 1977: Reich *et al*⁹: patency up to 42 days in the pig
 1979: Gutierrez *et al*¹⁰: increased patency with the use of balloon up to 1 year
 1983: Palmaz *et al*¹¹: use of expandable metal stent
 1989: Richter *et al*¹²: clinical use of the Palmaz stent
 1991: Zemmel *et al*¹³: first clinical series of TIPS
 1992: Ring *et al*¹⁴: clinical series using Wallstent

Box 2

technique, the free hepatic vein pressure is subtracted from the wedged pressure to yield the corrected sinusoidal pressure (table 1).

TIPS insertion creates a percutaneous transhepatic tract between the portal and hepatic veins, followed by the insertion of expandable metallic endoprosthesis to keep the tract open. Access to the portal vein is obtained by ultrasound or by fluoroscopy. The procedure avoids major surgery and anaesthesia, and is usually performed in 1–2 hours in experienced hands.

Indications for TIPS

Indications and contraindications for TIPS were established at a conference sponsored by the US National Digestive Diseases Advisory Board in 1994 (see box 3).¹⁷

GASTROINTESTINAL BLEEDING DUE TO PORTAL HYPERTENSION

TIPS can be used to treat a variety of bleeding complications seen in the patients with portal hypertension. Numerous clinical trials evaluating TIPS in the control of acute variceal bleeding have shown the efficacy of this procedure (table 2).^{18–26} A successfully placed TIPS stops bleeding from oesophageal, gastric or other ectopic varices in more than 90% of patients. However, recurrent bleeding due to TIPS occlusion can be high. Patients who have peptic ulcers, ulcers due to sclerotherapy or Mallory-Weiss tears cannot be treated with TIPS.

Higher APACHE II scores, aspiration pneumonia, and grade IV encephalopathy were predictive factors of mortality following TIPS placement.^{27–28} At our centre, patients with acute variceal bleeding refractory to medical and endoscopic therapy are managed according to the protocol recommended by Sanyal *et al*,²⁸ ie, they are intubated for airway protection and temporary control of variceal bleeding is achieved through balloon tamponade.

Several studies have compared TIPS to endoscopic therapy (sclerotherapy or variceal ligation) to prevent recurrent variceal bleeding. Although the risk of rebleeding was much lower in the TIPS group, there was no survival benefit and the rate of encephalopathy was significantly higher.^{29–33} TIPS is currently being compared to distal splenorenal shunt in the prevention of recurrent variceal bleeding in a multicentre study in North American centres. Patients with an initial episode of variceal bleeding should be offered medical and endoscopic management. In patients with uncontrolled acute variceal bleeding, a successfully placed TIPS controls bleeding in almost all cases. TIPS has no role in the management of varices that have not bled.

TIPS FOR THE MANAGEMENT OF REFRACTORY ASCITES AND HEPATIC HYDROTHORAX

The first-line treatment of ascites and hepatic hydrothorax in patients with liver cirrhosis is salt restriction and diuretic therapy. However, several patients become refractory to such a treatment and require repeated large-volume paracentesis and thoracentesis. Several clinical trials have shown the effectiveness of TIPS in controlling ascites (table 3).^{33–38} However, although TIPS can effectively control refractory ascites, the survival of these patients has not improved. A multicentre trial comparing TIPS with paracentesis for refractory ascites is currently underway in North America.

Hepatic hydrothorax is a particularly difficult condition to treat by conservative management; patients refractory to such treatment may benefit from TIPS (table 3).^{39–43} TIPS has also been noted to facilitate the removal of chest tubes placed to treat hepatic hydrothorax.⁴¹

OTHER INDICATIONS FOR TIPS

TIPS has successfully been used to treat veno-occlusive disease following bone marrow transplantation, Budd-Chiari syndrome, and hepatorenal syndrome.^{44–49}

Table 2 Major clinical trials of TIPS in variceal bleeding

Author	Patients	Rebleeding (%)	1-year mortality (%)	Predictors of death
Rössle ¹⁸	61	15	10	NA
Rössle ¹⁹	100	11	15	NA
Jalan ²⁰	68	25	30	Hyponatremia, Child's C encephalopathy
Coldwell ²¹	96	NA	NA	Child's class
Sahagun ²²	100	20	29	Child's C
LaBerge ²³	90	18	40	Child's score >12
Stanley ²⁴	130	13	29	Child's C
Sanyal ²⁶	100	15	28	NA

NA: not available

National Digestive Diseases Advisory Board statement on TIPS (1994)

Accepted indications

- acute variceal bleeding that cannot be successfully controlled with medical treatment, including sclerotherapy
- recurrent variceal bleeding in patients who are refractory or intolerant to conventional medical management, including sclerotherapy and pharmacological therapy

Unproven but promising

- therapy for refractory ascites
- portal decompression for patients suffering from hepatic venous outflow obstruction (Budd-Chiari syndrome)

Unproven uses

- initial therapy of acute variceal haemorrhage
- initial therapy to prevent initial or recurrent variceal haemorrhage
- reduction of intra-operative morbidity during liver transplantation

Absolute contraindications

- right-sided heart failure with elevation of the central venous pressure
- polycystic liver disease
- severe hepatic failure

Relative contraindications

- active intrahepatic or systemic infection
- severe hepatic encephalopathy poorly controlled by medical therapy
- hypervascular hepatic tumours
- portal vein thrombosis

Box 3

Table 3 Major clinical trials of TIPS in refractory ascites (RA) and hepatic hydrothorax (HT)

Author	Indication	Patients	Response rate (%)	Mortality at 1 year (%)
Ochs ³³	RA	50	92	56
Najarian ³⁸	RA	50	62	58
Martinet ³⁷	RA	30	87	59
Gordon ⁴⁰	HT	24	80	54
Chalasani ⁴³	HT	26	77	44

Several studies have shown that TIPS can also be effective in hypertensive gastropathy or colopathy, stomal or other ectopic varices due to portal hypertension.⁴⁶⁻⁵⁰

Effect of TIPS on haemodynamics

Central venous pressure generally rises after TIPS, and heart failure has also been reported as a complication of the procedure. Linden *et al*⁶⁰ found that in the short- and medium-term, there was a decrease in the porto-atrial pressure associated with an increase in the mean pulmonary artery pressure and the right atrial pressure. The right ventricular end-diastolic volume remained unchanged, but systemic vascular resistance decreased while the pulmonary vascular resistance increased. Moreover, increased pulmonary pressure was present 1 month after insertion of TIPS. These data underscore the need for careful pre-TIPS evaluation as patients with poor ventricular function and those with pre-existing pulmonary hypertension may suffer from increased morbidity. Azoulay *et al*⁶¹ cautioned against worsening the hyperdynamic circulatory state which may lead to decompensation in patients with limited cardiac reserve. A similar experience was reported by Hadengue *et al*⁶² who reported a case of acute pulmonary oedema and myocardial infarction after TIPS placement.

TIPS and liver transplantation

Patients who undergo liver transplantation after the insertion of TIPS have been reported to have a number of advantages: decreased blood loss during surgery due to decrease in portal hypertension, avoidance of the need for veno-veno bypass during surgery resulting in a decrease in operative time, and preservation of renal function. However, these beneficial effects are under scrutiny.⁵³⁻⁵⁴ Misplaced TIPS did, however, result in difficult surgery in some cases. In cases where the upper end of the TIPS was inadvertently left above the diaphragm, placement of the vascular clamp on the superior vena cava was difficult and lead to thoracotomy. Similar difficulty may be encountered if the TIPS is too far down into the portal vein (personal experience). Care must be taken to ensure that the stent does not extend into the inferior vena cava or more than 1 cm into the main portal vein.

TIPS and portosystemic encephalopathy

The major side-effect of a successfully placed TIPS is encephalopathy, which is clinically manifest in approximately 25% of new cases.⁵⁵⁻⁵⁹ The symptoms are generally mild and can readily be managed with dietary protein restriction and lactulose therapy. In less than 5% of patients, uncontrolled encephalopathy poses a major clinical problem. The common manifestations vary from mild sensory disturbances to deep coma, acute recurrent episodes of confusion, and obtundation which may be precipitated by gastrointestinal bleeding and electrolyte disturbances. However, the chronic encephalopathic state seen after surgical shunts is generally not seen after TIPS. It has also been noted that patients with TIPS having larger diameters were at a greater risk of developing encephalopathy.

Sanyal *et al*⁶⁵ prospectively compared the outcome of portosystemic encephalopathy in 30 patients undergoing TIPS versus 25 patients undergoing sclerotherapy. They found that mental status and asterixis scores worsened significantly in the first month after TIPS; increasing age, medical history of encephalopathy, and trail scores for part B greater than 100 s were predictors of portosystemic encephalopathy after TIPS placement.

Other complications of TIPS

Procedure-related morbidity from TIPS occurs in up to 10% of cases. These include self-limited intraperitoneal haemorrhage (1–6%), haemobilia (1–4%), sepsis, transient oliguric renal failure, and atrial arrhythmia. Increases in serum bilirubin, transaminases, prothrombin time and ammonia, that peak within the first week after TIPS and subsequently resolve, occur in 10–20% of patients. Stent migration or marked stent misplacement have been encountered occasionally during the course of TIPS procedures.⁵⁷ Recently, attention has been drawn to a unique complication of TIPS, ie, haemolysis, first described by Sanyal *et al* and later by other investigators.^{60–62} They ascribed this syndrome to trauma due to 'naked stent'. In a series of 100 cirrhotics of whom 60 underwent TIPS placement, 12% developed haemolysis as defined by a decrease in haemoglobin by 2 g/dl. In another study, the mean serum haptoglobin was significantly lower in the patent TIPS group than in controls. Overt haemolysis was not observed in these reports and it was rarely clinically severe.

With the currently available data, TIPS appears to be competitive with both sclerotherapy and surgery in the management of recurrent variceal bleeding. The reported rate of rebleeding varies from 7–31% following TIPS; lower than the rate achieved with sclerotherapy but higher than that following surgical shunting. This is because the primary patency rate for surgical shunts is superior to TIPS. Furthermore, most surgeons ligate the coronary vein at the time of creation of the surgical shunt. Procedure-related morbidity and mortality appears to be lower for TIPS than for conventional surgical shunts.

Thirty-day mortality is variable and appears to be related to the underlying condition of the patient rather than the morbidity of the procedure itself, which varies from 3–15%. Very few direct procedure-related deaths have been reported. Procedural deaths from intraperitoneal haemorrhage occur in less than 3% of patients, even when the liver capsule is traversed during the procedure. Death from hepatic failure has been observed in 3–7% of patients in the acute post-procedural period (first 30 days). Diminished hepatic perfusion from diversion of portal venous blood and lack of hepatic arterial blood flow has been a suspected contributory factor.

TIPS stenosis and surveillance

Although procedure-related morbidity and mortality appear to be lower for TIPS than for conventional surgical shunts, poor shunt patency has emerged as a major problem commonly due to stent stenosis. Sanyal *et al*¹⁶ noted that 58% of the patients had recurrent portal hypertension at 6 months following TIPS (stent stenosis 51%, thrombosis 5%, retraction 2%). There are two main patterns of stenosis: a diffuse or focal stenoses at the hepatic venous end and diffuse intra-shunt neo-intima formation. In their study, all patients with TIPS required at least one revision of the stent when followed for at least 3 years. The high frequency of shunt occlusion calls for close surveillance by Doppler ultrasonography or angiography. At our centre, we use Doppler ultrasonography for surveillance of TIPS patency (day 1, months 3 and 6, then every 6 months).

Indiana University experience

We recently analysed the variables that predict survival in cirrhotics undergoing TIPS at our institution. We retrospectively analysed 75 patients undergoing TIPS between 1/94 to 3/97. The indications for TIPS were variceal haemorrhage in 66%, ascites in 26%, and hydrothorax in 7% of patients. The 30-, 180-, and 360-day survival was 84%, 65%, and 55%, respectively. Using a Cox's proportional model, we found that the most significant predictors of death were bilirubin > 3 mg/dl, albumin < 2.5 mg/dl and Child's class C.

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