

Transjugular Intrahepatic Portosystemic Shunt: Current Indications, Patient Selection and Results

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ABSTRACT: **Background:** Inserting a transjugular intrahepatic portosystemic shunt by means of interventional radiology has become the procedure of choice for decompression of portal hypertension. The indications and criteria for patient selection have been expanded and refined accordingly.

Objectives: To review our experience with TIPS and analyze the results with emphasis on patient selection and indication (conventional vs. atypical).

Methods: In this retrospective analysis in a single center all cases were managed by a multidisciplinary team (comprising liver surgery and transplantation, hepatology, imaging, interventional radiology and intensive care).

Results: Between August 2003 and December 2009, 34 patients (mean age 51, range 27–76 years) were treated with TIPS. The cause of portal hypertension was cirrhosis (23 cases), hypercoagulability complicated by Budd-Chiari syndrome (n=6), and acute portal vein thrombosis (n=5). Clinical indications for TIPS included treatment or secondary prevention of variceal bleeding (10 cases), refractory ascites (n=18), mesenteric ischemia due to acute portal vein thrombosis (n=5), and acute liver failure (n=1). TIPS was urgent in 18 cases (53%) and elective in 16. Three deaths occurred following urgent TIPS. The overall related complication rate was 32%: transient encephalopathy (6 cases), ischemic hepatitis (n=2), acute renal failure (n=2) and bleeding (n=1). Long-term results of TIPS were defined as good in 25 cases (73%), fair in 4 (12%) and failure in 5 (15%). In three of five patients with mesenteric ischemia following acute portal vein thrombosis, surgery was obviated. Revision of TIPS due to stenosis or thrombosis was needed in 7 cases (20%).

Conclusions: TIPS is safe and effective. While its benefit for patients with portal hypertension is clear, the role of TIPS in treatment of portal-mesenteric venous thrombosis needs further evaluation. Patient selection, establishing the indication and performing TIPS should be done by a multidisciplinary dedicated team.

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KEY WORDS: transjugular intrahepatic portosystemic shunt (TIPS), portal hypertension, cirrhosis, Budd-Chiari syndrome, portal vein thrombosis

Transjugular intrahepatic portosystemic shunt is the formation of a low resistance conduit between a portal vein and a hepatic vein by deployment of an intrahepatic expandable stent. TIPS is performed percutaneously using interventional radiology techniques and equipment. TIPS leads to immediate decompression of portal hypertension. The first TIPS-like procedure was conducted by Palmaz in 1985 while the first clinical application was presented by Rossle et al. in 1989 [1]. Since then, TIPS gained popularity and has become the treatment of choice in many clinical scenarios in which portal hypertension or portal obstruction are the key pathophysiologies.

Established indications for TIPS include acute, non-controlled variceal bleeding, secondary prevention of bleeding (mainly from gastric and ectopic varices) and refractory ascites [2-5]. The uncertain role of TIPS in Budd-Chiari syndrome recently gained some support [5,6]. Rare, less conventional indications include acute portal vein thrombosis [7-10], hydrothorax, hepatopulmonary syndrome, hepatorenal syndrome (type 2), and prophylaxis of complications in cirrhotics who need major abdominal surgery [11,12].

The TIPS itself is considered safe and effective and has a low related mortality rate, particularly when performed electively. However, hemodynamically, TIPS is a non-selective side-to-side portocaval shunt, followed by partial or complete portal venous flow diversion from the liver. In cirrhotics, hepatic perfusion depends on the arterial buffer reserve, which is inversely correlated with the severity of cirrhosis [13,14]. Therefore, high MELD (model of end-stage liver disease) and Child-Pugh scores are risk factors of hepatic encephalopathy [15,16].

Absolute and relative contraindications to the insertion of TIPS are heart failure, severe pulmonary hypertension, severe liver failure, chronic recurrent encephalopathy, polycystic liver disease, severe obstructive arteriopathy, arterioportal fistula, liver abscess, central hepatocellular carcinoma and bile duct dilatation [4].

Long-term patency, the initial Achilles' heel of TIPS, improved considerably since the application of expanded

TIPS = transjugular intrahepatic portosystemic shunt

polytetrafluoroethylene-covered stent grafts and it is now comparable with that of surgical shunts [17,18].

PATIENTS AND METHODS

We review our experience with TIPS and analyze the results with emphasis on patient selection and indication (conventional vs. atypical). The study was conducted in a tertiary referral center for patients with acute and chronic end-stage liver disease, portal hypertension and related complications. The center has the capability of performing all interventional radiology and surgical procedures, including TIPS and liver transplantation. Patient care and management were provided by a multidisciplinary dedicated team, comprising liver surgery, transplantation, hepatology, imaging, interventional radiology and intensive care physicians.

In this retrospective review of all TIPS procedures, performed in a single institution and by the same team, we defined results as good, fair, or failure, according to long-term outcome (achievement of the defined goal). We evaluated contributory factors such as age, etiology, clinical indication, urgency, severity of ESLD, and change in hepatic veins-portal gradient.

PATIENT SELECTION AND INDICATIONS

There were three main groups of patients and indications:

- Established indications: Patients with cirrhosis and portal hypertension, complicated by gastrointestinal bleeding or intractable ascites.
- Optional indications: Chronic and acute Budd-Chiari syndrome, complicated by impaired liver function or tense ascites.
- Atypical indication: Acute portal vein thrombosis, primary or secondary to Budd-Chiari syndrome.

TECHNIQUE

TIPS was performed under general anesthesia or conscious sedation according to patients' condition and characteristics. Internal jugular access was obtained with ultrasound guidance. In Budd-Chiari syndrome, the left internal jugular approach was preferred [6]. Following the selection of a hepatic vein or hepatic vein stump, under digital subtraction fluoroscopy, the TIPS set needle was advanced into the portal system. The needle was then exchanged with a calibrated catheter and a portogram with pressure measurements was performed.

The stent type (bare metal or stent graft) and its diameter (8–10 mm) were selected according to the indication and the desired Δ HVPG. Post-deployment dilatation was performed with 8–10 mm balloons to reduce HVPG to below 10 mmHg

ESLD = end-stage liver disease

Δ HVPG = hepatic veins-portal gradient

for bleeding prevention or below 12 mmHg for ascites [4]. In patients with acute variceal bleeding, the left gastric vein was embolized via the TIPS using 95% ethanol and/or coils.

In cases of acute portal vein thrombosis, the TIPS served initially as an access and finally as an outflow to the portomesenteric system. Dec clotting was based on local thrombolysis (infusion of urokinase over 24–48 hours) and mechanical thrombectomy with various devices [7–11].

POST-PROCEDURE

Patients were observed in the surgical intensive care unit following urgent TIPS or in the surgical department following elective procedures. Immediate follow-up was clinical and laboratory. Routine Doppler sonography was done to assess patency.

Patients were followed in the transplant clinic if they were listed for transplantation, in the liver surgery clinic if the indication was portal vein thrombosis, or by the hepatologists in cases of cirrhosis or Budd-Chiari syndrome. Defined outcome measures included survival, resolution of ascites, disappearance of varices or portal gastropathy per endoscopy, or resolution of mesenteric ischemia obviating surgery.

RESULTS

Between August 2003 and December 2009 a total of 34 patients (mean age 51 years, range 27–76) were treated with TIPS. Complete data could be obtained for 31. Mean follow-up was 37.3 months (range 2–76).

ETIOLOGY AND SEVERITY OF LIVER DISEASE

Liver cirrhosis was the cause of portal hypertension in 23 cases, sub-acute Budd-Chiari syndrome in 5, acute Budd-Chiari in 1 and primary portal vein thrombosis in 5 [Table 1]. Severity of cirrhosis as defined by Child-Pugh score was: Class A in 39%,

Table 1. Etiologies, clinical indications and results of TIPS procedures

Etiology		Long-term results		
		Good	Fair	Failure
Cirrhosis (n=23)	Bleeding, acute or urgent prevention (n=10)	8		2*
	Intractable ascites (n=13)	10	3	
Budd-Chiari syndrome (n=6)	Acute liver failure (n=1)			1*
	Intractable ascites (n=3)	3		
	Secondary portal vein thrombosis (n=2)	2		
Primary portal vein thrombosis (n=5)	Acute mesenteric ischemia (n=5)	2	1	2
Total n (%)		25 (73%)	4 (12%)	5 (15%)

*Death

B in 52% and C in 9%. Mean MELD score (model of end-stage liver disease) score was 13.4 (range 7–23).

CLINICAL INDICATION

Standard ("established") clinical indications included bleeding (acute or early prevention of rebleeding) in 10 cases and intractable ascites (failure of diuretics and large volume paracentesis) in 16 cases (13 in cirrhosis and 3 in Budd-Chiari syndrome). In one case of acute Budd-Chiari syndrome, the indication was acute liver necrosis and failure, and in two cases the indication was secondary symptomatic portal vein thrombosis. Less common ("atypical") indication was an attempt to overcome mesenteric ischemia due to acute primary portomesenteric venous thrombosis [Table 1]. TIPS was urgent in 18 cases and elective in 16.

TECHNIQUE

Precise anatomic data were available in 31 cases. Most TIPS were located between the right hepatic veins (outflow) (19 cases) and the right portal vein (inflow) (n=25). Other outflow sites were the middle (n=10) and left (n=2) hepatic veins and inflow sites, the left portal vein (n=3) and the main portal vein (n=3). The first six TIPS were created with bare metal stents and the rest with ePTFE covered stent-grafts.

ADDITIONAL PROCEDURES

Transjugular liver biopsies were done in four patients, left gastric vein embolization in six, mechanical thrombectomy in seven and local portomesenteric thrombolysis in five patients.

PATENCY

The immediate technical success rate was 97%. However, in 16 cases (47%) there was a need for re-intervention: planned second thrombectomy in 5, suspected dysfunction by ultrasound Doppler in 5 and late stenosis or thrombosis in 7 (20%). Risk factors for late dysfunction were type (metal stent vs. stent graft, 50% vs. 14%, respectively) and etiology (hypercoagulation vs. cirrhosis, 27% vs. 17%, respectively).

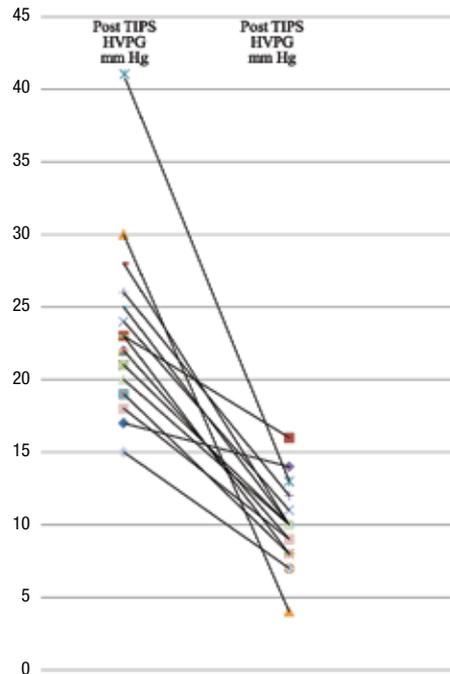
HEMODYNAMIC RESULTS

In 15 patients with cirrhosis, we could recall pre- and post-TIPS hepatic veins-portal gradient, while in 5 others, only the ΔHVPG was documented. The mean HVPG was 21.8 mmHg pre-TIPS (range 15–41) and it decreased to 13 mmHg post-TIPS (range 3–29) [Figure 1].

MORBIDITY AND MORTALITY

There were three deaths following urgent TIPS. One was due to fulminant liver failure secondary to acute Budd-Chiari

Figure 1. Hepatic vein: portal gradient before and after TIPS (ΔHVPG, mmHg)



syndrome; one occurred following ongoing variceal bleeding due to open but ineffective TIPS, and one was due to sepsis following successful control of massive bleeding. Eleven patients (32%) developed serious complications, including transient hepatic encephalopathy (6 cases), ischemic hepatitis (n=2), acute renal failure (n=2), and bleeding (n=1). Bleeding occurred following an attempt to treat portal vein thrombosis, causing hemorrhagic shock which mandated urgent laparotomy.

LONG-TERM CLINICAL OUTCOME

Results were defined as good in 26 cases (73%), fair in 4 (12%) and failure in 5 (15%) [Table 1]. Failures included three deaths and two cases in which bowel resection due to mesenteric venous ischemia was not prevented. However, it is not clear if the extent of resection was influenced by the TIPS. Positive predictors of success were etiology (cirrhosis and chronic Budd-Chiari syndrome vs. acute Budd-Chiari syndrome and acute portal vein thrombosis: 91% and 100% vs. 0% and 60%, respectively) and setting (elective vs. urgent: 100% vs. 72%).

TIPS AS A BRIDGE TO LIVER TRANSPLANTATION

TIPS was performed in four patients awaiting liver transplantation. Two underwent successful transplants, 8 and 11 months later, and two are stable and listed.

ePTFE = expanded polytetrafluoroethylene

DISCUSSION

The current data regarding TIPS, categorized systematically by the hierarchy of evidence-based medicine and translated into practical guidelines, was summarized by Boyer and Haskal for the American Association for the Study of the Liver [4] and was updated recently [5].

TIPS TO TREAT OR PREVENT BLEEDING

Variceal bleeding is a major cause of death among cirrhotic patients and correlates with portal hypertension [19]. Many studies demonstrated high efficacy of TIPS in the control of acute massive bleeding and in prevention of rebleeding [4]. In a randomized controlled study, TIPS was more effective than medical treatment in secondary prevention but this was not translated to survival benefit [20]. Based on current data, TIPS should not be the first line of treatment or prophylaxis but should be reserved for failures. Different prioritization should be considered when the bleeding source is portal gastropathy or atypical varices, which are less amenable to endoscopic eradication [4].

TIPS AND REFRACTORY ASCITES

Refractory ascites reflects severe portal hypertension and advanced hepatic synthetic insufficiency and is associated with poor outcome. While the efficacy of TIPS to treat refractory ascites was demonstrated in many non-controlled studies (response rate 38–79%) [4], its status compared to repetitive large volume paracentesis and peritoneal-venous shunts is less clear [4,21]. Moreover, it is associated with a higher incidence of hepatic encephalopathy and its net effect on overall survival is questionable. Data from randomized controlled studies are contradictory [4]. Reasonable indications for TIPS include a need for frequent (more than once weekly) large volume paracentesis, intolerance to large volume paracentesis (renal insufficiency), hydrothorax, umbilical hernia, or type 2 hepatorenal syndrome [4,22].

TIPS FOR BUDD-CHIARI SYNDROME

The role of TIPS in Budd-Chiari syndrome is less well defined [4,5]. A recent large collective retrospective series demonstrated effectiveness and improved transplant-free survival following TIPS [6]. Our experience with chronic or sub-acute Budd-Chiari syndrome complies with this conclusion. Moreover, TIPS was applied successfully in two cases complicated by acute portal vein thrombosis [7]. The role of TIPS to bridge or avoid urgent transplantation in the face of acute liver failure in Budd-Chiari syndrome is not evident.

TIPS AND PORTOMESENTERIC THROMBOSIS

A suggested but unproven indication for TIPS is treatment of acute portal vein thrombosis [7-10]. We applied a trans-

TIPS approach in seven cases. In two, which presented with hepatic ischemia, PVT was a complication of Budd-Chiari syndrome; and in five, acute PVT was primary and associated clinically with mesenteric ischemia. The effect of TIPS and local thrombolysis on the natural course is uncertain; although in three cases ischemia subsided without a need for bowel resection. This application of TIPS in acute PVT mandates further careful evaluation [23].

TIPS IN ISRAEL

In a previous study we reported the poor outcome of patients with end-stage liver disease in Israel, which could not be solely attributed to organ scarcity [24]. Reasonable and timely referral to TIPS may improve survival of both non-transplant and transplant candidates. As in other medical and surgical issues, the relation between volume, experience and outcome was demonstrated for TIPS as well [4]. It is therefore recommended that TIPS be offered only in referral centers with the appropriate expertise, including liver transplantation [4].

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PVT = portal vein thrombosis

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