

Transjugular intrahepatic portosystemic shunt – current status in 2011

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Abstract

This article overviews principles of portal hypertension and the role of implantation of a transjugular intrahepatic portosystemic shunt (TIPS) in its management. Since TIPS is available for over 30 years, technical achievements have been made and knowledge about indications, contraindications and patient selection has been improved. Recent studies and guidelines may lead to an increase in TIPS implantation rates. This review aims to commemorate the merits and demerits of TIPS in current clinical practice. (Acta gastroenterol. belg., 2011, 74, 553-559).

Key words : portal hypertension, variceal bleeding, refractory ascites, hydrothorax, Budd-Chiari syndrome.

Introduction

The history of TIPS

The first transjugular intrahepatic portosystemic shunt has been implanted in 1989 (1). Prior, surgical portosystemic shunts were the only comparable therapy to lower portal pressure. TIPS changed the management of portal hypertension. At first, TIPS was used for the management of variceal bleeding. Subsequent applications of TIPS included the control of refractory ascites and treatment of hepatic hydrothorax, Budd-Chiari syndrome, and veno-occlusive disease as well as attempts to improve the hepatorenal and the hepatopulmonary syndromes (2).

With increasing use of TIPS, risk factors for poor outcome have been identified : serum levels of creatinine, hyperbilirubinemia, hyponatremia, episodes of hepatic encephalopathy, advanced stage liver disease, salvage TIPS placement, and non-alcoholic cirrhosis Child-Pugh stage C (3-8). Of the complications associated with TIPS implantation, stenosis of the stent and occurrence of hepatic encephalopathy were the most frequent, although increasing experience led to reduction of complication-rates (7,9). In 2000, a new prognostic score for patients with end stage liver disease (MELD score) has been developed, using data of patients undergoing TIPS implantation (10). This score helped to identify risk factors for TIPS implantation as well as for patients with cirrhosis in general, since after a slight modification this score is nowadays used to rank patients for liver transplantation.

Since TIPS has become available, not only the spectrum of indications has been broadened and the knowl-

edge of risk-factors widened, but also interventional techniques could be improved and the stentgraft could be developed further. In 1999, a new ePTFE-covered stentgraft has become available which provides much higher patency rates and seems to be associated with higher survival-rates (11-13).

Parallel to the increasing use and further development of TIPS, also non-interventional therapies for portal hypertension changed : there are now effective pharmacologic and endoscopic treatments for the control of acutely bleeding varices as well as for primary and secondary prevention of bleeding from gastroesophageal varices (14,15). Until now, beside from studies evaluating TIPS for prevention of variceal bleeding or therapy of ascites, other indications for TIPS have not been subjected to controlled trials.

Background and Definitions

Portal hypertension

Portal hypertension is the most frequent complication of chronic liver disease. It is responsible for development of gastro-esophageal varices, ascites, hepatorenal syndrome, bacterial infections and hepatoc encephalopathy. These complications are the main causes for morbidity and mortality of chronic liver disease (14-17).

The normal portal pressure ranges between 1 mmHg und 5 mmHg. Pressures above this limit are classified as portal hypertension. Clinically, portal hypertension is "significant" at pressures above 10 mmHg, since at this threshold, varices and/or ascites develop. Variceal bleeding normally occurs at pressures above 12 mmHg. It is also known that patients with bleeding varices have a poorer prognosis at portal pressure levels above 20 mmHg (14,16).

According to the localisation of the pathology, portal hypertension is classified as prehepatic, intrahepatic, and posthepatic.

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Submission date : 10/08/2011
Acceptance date : 16/08/2011

Measurement of the portal pressure

Due to the anatomy of the portal venous system, measurement of portal pressure can only be performed indirectly: Via an internal jugular vein (in most cases the right, but also access via the left jugular vein or a femoral vein is possible), a hepatic vein is catheterised measuring the pressure wedged (by balloon occlusion) and unwedged. The difference between the two measured values is called "hepatic venous pressure gradient", which relates the portal pressure. HVPG-measurement is the gold standard for diagnosis, quantification and risk-stratification in portal hypertension (18).

Transjugular intrahepatic portosystemic shunt

Implantation of a transjugular intrahepatic portosystemic shunt (TIPS) is a highly effective interventional procedure resulting in decompression of the portal system by creation of a side-to-side portosystemic anastomosis (13,19). The minimal invasive procedure is usually performed in conscious sedation or in general anaesthesia.

After placing a sheath into the right internal jugular vein (this is the typical access, although the left jugular vein or a femoral vein can also be used), a special needle is advanced from a liver vein into an intrahepatic branch of the portal vein. Then a self expanding covered stent-graft is placed into the parenchymal channel. The diameter of the stent determines the target portal pressure. TIPS placement is usually performed by an interventional radiologist or a special trained hepatologist. Success-rates and complication rates highly correlate with the expertise and number of implantations. Therefore, TIPS implantation should only be performed in specialised centers.

The success-rate is above 90% (19,9). The target pressure depends on the indication for TIPS placement and patients characteristics: For prevention of rebleeding, 12 mmHg is an effective target pressure, although a reduction of portal pressure by 50% is also effective in cases when the pressure of 12 mmHg cannot or should not be reached (20,21). For therapy of ascites, pressure is considered to be optimal below 12 mmHg (maybe 8 mmHg), but data regarding this threshold are limited (22).

Fatal complications are rare and occur in about 1,7% of cases (19).

Current standard of care is TIPS-placement using ePTFE-covered stentgrafts, since complication rates are lower and outcome is better than in bare metal stents (19).

Patient selection for TIPS implantation is crucial. Prior to TIPS, several investigations need to be performed to assess risk and benefit for the patients. Basic parameters before TIPS placement can be found in table 1.

A standard report for the TIPS-procedure can be found in table 2.

Indications for TIPS

TIPS for variceal bleeding

In portal hypertension, first line treatment of acute variceal bleeding should always consist of vasoactive therapy, antibiotic prophylaxis/therapy, and endoscopic therapy (15).

Salvage TIPS in acute variceal hemorrhage

TIPS-implantation for acute variceal bleeding refractory to medical and endoscopic therapy ("salvage TIPS") is nowadays a rare indication. It should be considered in case of failure of optimal medical therapy and at least 2 attempts of endoscopic therapy (15,23).

According to a recent consensus statement, failure is defined by one of the following criteria (19):

- Fresh hematemesis or aspiration of ≥ 100 mL of fresh blood via a nasogastric tube ≥ 2 hours after the start of the specific drug treatment or therapeutic endoscopy.
- Development of hypovolemic shock.
- 3 g drop in hemoglobin (or a 9 percent drop in hematocrit) within any 24 hours period if no transfusion is administered.

In addition, any bleeding occurring 48 hours after the initial admission for variceal hemorrhage after a 24 hours or more bleed-free period is considered to represent rebleeding.

In case of placement of a salvage TIPS, some patients receive either a balloon-tamponade (24) or a self expanding esophageal metal stent (DANIS stent) as a bridge to TIPS-placement (25). The latter has the advantage that it can be left in the oesophagus for 7 days, allowing to transfer the patient to a center where TIPS implantations are performed or allowing to organise a TIPS-procedure.

In the majority of patients, salvage TIPS is effective in controlling oesophageal and gastric variceal bleeding refractory to medical and endoscopic therapy (26-28). Despite that, patients undergoing salvage TIPS have a poorer prognosis than patients who respond to medical/endoscopic therapy or than patients undergoing elective TIPS placement (2,24,26).

A-la-carte -TIPS & Early TIPS

One study showed that patients with a HVPG > 20 mmHg may have a benefit regarding rebleeding and survival if a TIPS was placed within 24h of admission due to variceal bleeding (29).

A more recent study showed that in patients with Child Pugh Class C (< 14) and in patients with Child Pugh class B (patients with class B had active bleeding at the time of endoscopy), medical and endoscopic standard-therapy in combination with TIPS implantation within 72h of admission was associated with a reduction of treatment failure and mortality compared to standard-therapy without TIPS-placement (30).

These 2 studies shed a new light on the use of TIPS in patients with advanced liver disease and variceal bleeding. This led to a recent recommendation to implant a TIPS within 72 h (ideally < 24 h) in patients at high-risk of treatment failure (e.g. Child-Pugh class C < 14 points or Child class B with active bleeding) after initial pharmacological and endoscopic therapy (19). Based on the study of Monescillo (29), measurement of HVPG within 24 hours after admission for variceal bleeding and implantation of a TIPS in patients with HVPG > 20 mmHg also seems to be a valid approach.

Based on the recent recommendation of the Baveno V conference (15), TIPS will have a renaissance regarding its use in the management of variceal bleeding. It can be expected that some hospitals will increase their capacities for TIPS placement, although it should be noted that in many hospitals with an endoscopy unit it will never be feasible to place a TIPS 24-72 hours after admission. In such cases, close cooperations with specialised centers to transfer the patients for TIPS implantations are desirable.

TIPS for prevention of variceal rebleeding

According to current guidelines, common strategies are that all patients with portal hypertension who experienced an episode of variceal bleeding should either receive pharmacologic prophylaxis with non-selective beta blockers, or undergo repeat endoscopy sessions with therapy of varices, or receive a combination of both (15).

Unfortunately, this strategy is not successful in all patients. In patients experiencing an episode of rebleeding despite optimal pharmacologic and/or endoscopic prophylaxis, TIPS implantation is a good and effective therapy. This has been incorporated into the recent Baveno-V recommendation (15).

Several studies comparing TIPS with endoscopic therapy (plus/minus pharmacological prophylaxis) have been performed (31-36). Although patients with TIPS had lower rates of rebleeding episodes, TIPS implantation had no effect on survival in these studies. This finding and the complications associated with TIPS are the main reason why TIPS is currently not considered as first line therapy in prevention of rebleeding.

It should be noted, that the more recent studies of Monescillo and Garcia-Pagán mentioned above showed a survival benefit in selected patients (29,30).

TIPS for treatment of refractory ascites

TIPS is a good and effective therapy for patients with ascites, in whom medical therapy is not effective. Ascites is classified as “refractory” if it cannot be mobilized by low sodium diet and maximal doses of diuretics (400 mg spironolactone and 160 mg furosemide per day) (37).

Several studies have been performed comparing TIPS to large volume paracentesis and several meta-analyses of these studies have been published (22,38-44). These studies and analyses are difficult to interpret, since in the

course of time, many achievements regarding technical aspects (e.g. use of a covered stentgraft instead of a bare metal stent) and patient selection have been made (45). Taking these factors into account, it can be subsumed that TIPS for refractory ascites seems to be more effective than repeated large volume paracentesis with regard to control of ascites and – in well selected patients - survival.

TIPS for portal vein thrombosis

TIPS-implantation is feasible in most patients with cirrhosis and non-tumoral portal vein thrombosis (46,47). In these patients, recent studies indicate that TIPS implantation is highly effective in decreasing the extent of thrombosis. In addition, reported survival-rates after TIPS-placement were good (46,48). Therefore, TIPS seems to be a good treatment option in these patients, although no general recommendations or consensus-statements have been published until yet.

TIPS for Budd Chiari syndrome (BCS)

BCS is a rare disease. Therefore, controlled studies comparing therapies for patients with BCS are not available. In BCS, therapy and prognosis depend on several factors such as severity of liver disease, etiology of BCS and response to anticoagulation (19,49-52).

According to the few published studies and current guidelines, TIPS is a good and effective therapy for patients who do not respond to anticoagulation. Patients with advanced disease should be evaluated for liver transplantation, but may undergo TIPS placement as a bridge to transplantation (19).

In patients with BCS, TIPS implantation is more difficult and associated with higher complication rates than in other indication. Therefore implantation should be performed in centers with high experience (19,49,52).

Hepatic hydrothorax

Development of a hepatic hydrothorax is a sign of advanced liver disease and a poor prognosis. Only a few small studies have been published evaluating the effect of TIPS for this indication (53-55).

In these small series, TIPS could reduce the need of thoracocentesis ; the effect on survival could not be evaluated in these investigations. Since the therapeutic alternatives are poor in these patients, TIPS is an effective and important therapy for hepatic hydrothorax (19).

Other effects of TIPS

TIPS also have beneficial effects on renal function, by lowering plasma creatinine levels and increasing sodium excretion (45). TIPS can also improve renal function in hepatorenal syndrome type 1 & 2, but data are limited for this indication (56,57).

TIPS implantation has also been shown to improve quality of life and nutritional status (58,59).

Conclusion

In selected patients and indications, TIPS is a very effective and safe therapy of complications of portal hypertension. Recent studies widened the indications for TIPS and ongoing studies may also lead to an increase in the use of TIPS in clinical practise, both hopefully leading to an increase in quality of life and survival of patients with portal hypertension.

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Appendix

Aside from examinations according to the individual patient, the data of the table above should be ascertained in every patient undergoing TIPS :

Laboratory parameters

In patients with clinically stable conditions, laboratory parameters should be obtained within 3 days before TIPS-implantation, including complete red and white blood counts, coagulation parameters (Normotest or prothrombin time, thrombin time, and INR), serum levels of albumin (g/l), bilirubin (mg/dl), creatinine (mg/dl), and C-reactive protein (mg/dl). These parameters are either needed to clarify the etiology or indication for TIPS, to determine the risk of the interventional-radiologic procedure itself or to evaluate the probability of survival after TIPS-implantation. Severe anemia or severe coagulation disorders should be carefully evaluated and other etiologies aside from liver disease should be excluded. Serum levels of bilirubin > 5 mg/dl as well as laboratory signs of inflammation are considered as contraindications for TIPS-placement, at least in the elective setting. The significance of impaired renal function with elevated levels of serum creatinine should be considered in context with other known risk-factors or risk scores.

Etiology of liver disease

The etiology of liver disease should be specified in every report. In case of obscurity, a hepatologist should be consulted and optionally, a transjugular liver biopsy during the TIPS-procedure should be performed.

Ascites

Ascites needs to be graded according to the Child-Pugh classification by clinical examination or ultrasound (1 : no ascites, 2 : resolution of ascites within 1 week by sodium restriction and diuretic therapy, 3 : tense ascites, unresponsive to 1 week treatment). "Ascites refractory to therapy" is defined as recurrence of ascites after complete paracentesis despite maximal daily sodium restriction of 2 g and maximal diuretic therapy (400 mg spironolactone and 160 mg furosemide per day). In all patients with ascites, a paracentesis should be performed examining the fluid by microscopy and inoculating it directly into blood culture bottles. An ascitic neutrophil count of ≥ 250 polymorphonuclear cells/mm³ is diagnostic for SPB (37). SBP should be treated before TIPS is considered since ascites might become responsive to medical therapy once SBP has resolved. The serum-ascites albumin gradient should be evaluated.

Hepatic encephalopathy (HE)

Presence of clinically manifest encephalopathy as well as of minimal encephalopathy is a contraindication for TIPS. To detect minimal encephalopathy, a standardized battery of tests (number connection tests A and B, line-tracing test, serial-dotting test, and digit-symbol test) should be performed.

Radiologic examinations

Performing an echocardiography to detect pulmonary hypertension and insufficiency of the right ventricle is mandatory. To profile anatomical structures and to detect portal vein thrombosis or hepatocellular carcinoma, a triphasic computed

Table 1. — Data needed prior to TIPS implantation

Laboratory parameters	Clinical Parameters	Radiologic examinations	Prognostic scores
Red and white blood counts	Etiology of liver disease	Echocardiography	Child-Pugh Score
Coagulation parameters - Normotest, - Thrombin time, - INR	Ascites according to Child-Pugh classification	CT (triphasic)	
Bilirubin	Test for hepatic encephalopathy		
Albumin	Optional : oesophago-gastroduodenoscopy		
Creatinine			
CRP			
Paracentesis (in patients undergoing TIPS for refractory ascites)			
Optional : analysis of 24 hours urine collection (alternatively 8 hours collection)			

tomography of the liver (in patients with impaired renal function a MRI should be performed.

Prognostic scores

The Child-Pugh score was shown to be a good predictor of survival in patients undergoing TIPS (3). Therefore, this score should be performed, including the number connection test.

Further facultative examinations and tests

Analysis of the urine collected within 24 hours including creatinine-clearance (optionally analysis of urine collected within 8 hours) and performance of an oesophagogastroduo-

denoscopy (if not already performed during an episode of variceal bleeding within the preceeding 4 weeks) are recommended.

The number of stentgrafts used, their length, diameters, and the grade of dilatation should be specified. Venous pressures should be measured before TIPS-placement in the inferior caval vein and in the hepatic vein (unwedged and in wedge position) and the portal pressure gradient should be calculated. Alternatively to the (indirect) wedge-measurements, direct portal pressure measurements during the TIPS-procedure (pressure in the portal vein after puncture vs. the pressure in the hepatic vein) could be obtained.

Table 2. — **Example for a standardised report for the TIPS procedure**

Every report of a TIPS procedure should contain basic patient characteristics (etiology of liver disease, indication for TIPS, weight and height of the patient), pressure measurements, specifications of the stent, and the medications administered during the TIPS procedure :

Etiology of liver disease	alcoholic, virus-related, etc.	
Indication for TIPS	acute refractory variceal bleeding, refractory ascites, prevention of rebleeding, etc.	
Venous pressure before implantation	inferior caval vein	
	hepatic vein (unwedged and in wedge position) OR	portal pressure measured directly vs. hepatic vein pressure
Venous pressure after implantation	hepatic vein unwedged	
	hepatic vein in wedge position	
Stent	model	
	length	
	number of stents implanted	
	diameter of the stents	
	grade of dilatation of the stents	
Medication during TIPS placement		