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Transjugular intrahepatic portosystemic shunt and liver transplantation

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Abstract Transjugular intrahepatic portosystemic stent shunting (TIPSS) appears to be an attractive, nonsurgical procedure to overcome complications of end-stage liver disease. During the period August 1992 to February 1995, 23 adults who had previously undergone TIPSS received liver transplants. These patients were compared to 36 cirrhotic patients, grafted during the same time period, in relation to the implantation technique, the intraoperative use of blood products, and the length of their hospital stay. These groups were comparable for previous right upper quadrant surgery, splanchnic vein modifications, and Child-Pugh classification. Liver transplantation was performed electively in all TIPSS patients. Ten patients (43.4 %) presented with a significant shunt stenosis at a median follow-up time of 4.5 months (range 2.5 to 30 months). At transplantation 8 of the 23 TIPSS patients (34.8 %) had specific TIPSS-related modifications i.e., extrahepatic portal vein aneurysm formation ($n = 2$), dislocation of the distal end of the stent into the inferior vena cava ($n = 4$) or into the main portal vein trunk ($n = 1$), bilioportal fistula ($n = 1$), and pronounced phlebitis of the inferior vena cava and hepatic veins due to redilation of shunt stenosis ($n = 4$). The intraoperative blood product requirement at transplantation was similar in the 23 TIPSS-patients and in the 36 cirrhotic patients who received transplants without the TIPSS procedure during the same time period [median 800 ml (range 0–20300 ml) vs median 620 ml (range 0–7600 ml), respectively]. There was also no difference between the two groups in length of hospital stay [median 18 days (range 0–34 days) vs median 19 days (range 0–66 days), respectively]. We conclude that TIPSS plays an important role in the management of life-threatening complications of end-stage liver disease arising in potential liver transplant candidates. TIPSS should be considered as a temporary, effective bridge to elective transplantation and not as a means to lower the blood product requirement at transplantation. Specific TIPSS-related modifications should be recognized early by the transplant surgeon in order to adapt the technique of graft implantation.

Key words TIPS, liver transplantation · Liver transplantation, TIPS · Portosystemic shunt, liver transplantation

Introduction

Due to the growing gap between the number of potential liver transplant recipients and the number of available liver donors, increasing numbers of patients with end-stage liver disease who are already on the waiting list are presenting with recurrent episodes of gastrointestinal bleeding, infected ascites, and renal failure [1, 2]. Transjugular intrahepatic portosystemic stent shunting (TIPSS) may be an attractive method for treating several of these complications and for buying time for potential liver transplant candidates awaiting elective transplantation [3, 21]. Decompression of the splanchnic venous system may also be a factor in reducing the operative complications of allograft implantation.

Materials and methods

During the period August 1992 to February 1995, 30 adult liver transplant candidates underwent a TIPSS procedure. Twenty-three of these patients actually received transplants. Three patients were removed from the waiting list because of resumed alcohol consumption ($n = 1$) or improvement in general condition ($n = 2$). Four patients died on the waiting list due to progressive liver failure ($n = 2$), cerebral bleeding ($n = 1$), and mucormycosis sepsis ($n = 1$) respectively 3, 14, 15, and 12 months after the procedure. Data on the transplanted patient population are summarized in Table 1.

Primary indications for TIPSS in the transplant recipients were variceal hemorrhage not controlled by balloon tamponade and/or sclerotherapy ($n = 12$), bleeding ileocaecal varices ($n = 1$), refractory ascites ($n = 6$), refractory pleural effusion ($n = 2$), ascites with hepatorenal syndrome ($n = 1$), and preoperative portal decompression after repeated biliary surgery ($n = 1$). At the time of the TIPSS procedure, two patients each had spontaneous bacterial peritonitis and active variceal bleeding.

Right and left internal jugular veins were punctured percutaneously in 21 and 2 patients, respectively. A parallel stent was placed in one patient because of recurrent variceal bleeding due to almost total occlusion of the first TIPSS. Localization of right ($n = 19$) and left ($n = 5$) portal veins was done under external sonographic guidance with a metallic skin marker. Right ($n = 16$), middle ($n = 7$), and left ($n = 1$) hepatic veins were catheterized under fluoroscopic guidance. In order to facilitate venous catheterization, patients with tense ascites had large-volume paracentesis the evening before shunting.

Vein-to-vein puncture was carried out with a Colapinto needle; next, metallic stents of 8, 10, and 12 mm were placed in 5, 16, and 3 patients, respectively. Balloon-expandable Palmaz stents (Johnson & Johnson, Norderstedt, Germany) were used 23 times and a self-expandable Wall stent (Schneider, Minneapolis, Minn., USA) once.

The median portosystemic pressure of 15 mmHg (range 12–26 mmHg) gradient was reduced by 50 % (range 30–68 %). This reduction was aimed at maintainance of hepatopetal portal flow. In two actively bleeding patients, the hepatoportal shunt tract was dilated until disappearance of flow through coronary and esogastric veins at videoscopy.

All interventions were carried out, by the same, experienced interventional radiologist (P. G.) and were performed under local sedation, hyperhydration, selective bowel decontamination, and (short-term) systemic broad spectrum antibiotic therapy. Antibiotic therapy was prolonged only in the presence of infected ascites. No anticoagulation or antiaggregation therapy was used. Lactulose was given to all patients after TIPSS. In cases of TIPSS creation for refractory ascites or pleural effusion, diuretic therapy was continued as before. Median hospitalization time for TIPSS placement was 3 days (range 1–32 days).

Table 1 Patient characteristics of 23 liver transplant patients selected for TIPSS placement (*ABT*, aminopyrine breath test)

Gender (male/female)	9/14	
Median age (range)	51 years (29–67 years)	
Etiology of liver cirrhosis	• Hepatitis C	9
	• Cryptogenic	7
	• Hepatitis B	4
	• Alcoholic	2
	• Secondary biliary	1
Child-Pugh classification B/C	13/10	
Pre-TIPSS ABT value (median)[a]	0.42 % (range 0 %–0.85 %)	

[a] Normal value $\leq$ 2.8 %

All patients were followed up every 3 months with Doppler ultrasonography with flow and flow velocity measurement. Venographic examination of the shunt was performed if ultrasound examination was inconclusive or abnormal. Shunt stenosis was defined on the basis of flow velocity; if flow velocity doubled, the stenosis was considered to be significant. An aminopyrine breath test (ABT) was performed, as previously described [14], both before and after the TIPSS procedure in nine patients.

Early and late TIPSS complications were defined as those occurring within or after 1 week of TIPSS placement. The median delay between TIPSS and liver grafting was 6 months (range 1–30 months).

To evaluate the impact of TIPSS placement on intraoperative blood product use and on the length of hospital stay, 23 TIPSS patients were compared to 36 cirrhotic patients who did not undergo the TIPSS procedure but who did receive a first graft during the same time period. All transplant procedures were performed by four staff surgeons. The incidence of previous right upper quadrant surgery [3/23 TIPSS patients (13 %) vs 9/36 non-TIPSS patients (26 %); P = NS] and of splanchnic vein thrombosis [2/23 TIPSS patients (15.4 %) vs 7/36 non-TIPSS patients (19.4 %); P = NS] was similar in both groups. Both groups were also matched for gender (13 females and 10 males in the TIPSS group; 11 females and 25 males in the non-TIPSS group), age [52 (range 35–67) years in the TIPSS group vs 51 (range 16–68) years in the non-TIPSS group], and Child-Pugh status [13 (56.5 %) class B and 10 (43.5 %) class C in the TIPSS group vs 2 (5.5 %) class A, 14 (38.8 %) class B, and 20 (55.5 %) class C in the non-TIPSS group]. All patients were followed until death or for a minimum of 6 months post-transplantation.

Results

TIPSS-related modifications before transplantation

Two of the 23 patients (13 %) had intra-abdominal ($n = 1$) and intrathoracic ($n = 1$) bleeding related to the procedure (Table 2). The latter patient also developed

Table 2 TIPSS-Related complications in 23 liver transplant patients (*IVC*, inferior vena cava; *PV*, portal vein)

Early (< 1 week)	Bleeding	2 (8.7 %)
	Thoracic 1[a]	
	Abdominal 1	
	Bilioportal fistula[a]	1 (4.3 %)
Late (> 1 week)	Shunt stenosis	10 (43.4 %)
	Inflammation of hepatic veins and/or IVC	4[b] (17.4 %)
	Stent dislocation into IVC	4 (17.4 %)
	PV aneurysm	2 (8.7 %)
	Stent dislocation into PV	1 (4.3 %)

[a] Same patient
[b] All four patients had balloon dilation of shunt stenosis

pronounced hyperbilirubinemia due to bilioportal fistula. One of the 13 treated patients experienced recurrent bleeding from varices. The first shunt, between the right hepatic and portal veins, was almost occluded. A parallel TIPSS had to be performed urgently, 2.5 months after the first TIPSS, between the middle hepatic and left portal veins. In all six patients treated for refractory ascites, the ascites either resolved completely or its treatment with diuretics and salt restriction became easier. TIPSS was particularly effective in untractable massive right pleural effusion ($n = 2$), in one patient with gastrointestinal bleeding due to ileocaecal varices who did not undergo surgery and in one patient with well-defined hepatorenal syndrome [10].

Encephalopathy worsened in 3 out of the 23 patients (13 %) but improved in 2 patients (8.7 %) due to cessation of gastrointestinal bleeding. Ten patients (43.4 %) developed a shunt stenosis at a median follow-up time of 4.5 months (range 2.5–30 months). Hemodynamically significant stenoses resulted in the (re)appearance of ascites or pleural effusion in six patients and in rebleeding in one patient. In three patients dilatation of the significantly stenosed shunt was performed prophylactically. In all but one case, the shunt stenosis was localized on the hepatic venous side. One patient presented with a stenosis due to pronounced diffuse intimal hyperplasia. Six shunts were dilated 4, 4, 4, 5, 7, and 25 months post-TIPSS. In two patients, an additional stent was positioned into the same hepatoportal tract 2.5 and 5 months after the first TIPSS placement. One patient, as already mentioned, needed a parallel TIPSS. One other patient was not treated because of persistent, pronounced encephalopathy.

Three patients (13 %) improved their Child-Pugh status (from class C to B) following TIPSS because of disappearance of ascites. In contrast, four patients (17.4 %) downgraded their status (from B to C) as a consequence of new-onset ($n = 2$) or worsening encephalopathy ($n = 1$) and an increase in bilirubinemia ($n = 1$).

None of nine patients tested had an improved ABT score after TIPSS [median 0.42 % (range 0 %–0.85 % before TIPSS) vs median 0.34 % (range 0.02–0.55 % following TIPSS)]. Liver transplantation was electively performed in all 23 TIPSS patients.

TIPSS-related modifications at liver transplantation

Collateral venous pathways (e.g., coronary vein and recanalized large umbilical veins) persisted at surgery in all patients, reflecting the lowest possible pressure gradient reduction obtained at TIPSS creation. Eight of the 23 transplanted TIPSS patients (34.8 %) had to have modification of the transplant procedure as a result of local complications caused by the stent. Four of seven patients (17.6 %) who presented with severe inflammatory changes in the hepatic veins and/or suprahepatic inferior vena cava (IVC) had had balloon dilation of a shunt stenosis due to intimal hyperplasia.

On four occasions (17.4 %), there was dislocation of the stent from the hepatic vein into the suprahepatic vena cava (Fig. 1). The metallic fibers were removed in three patients, but in the fourth patient the fibers could not be removed so they were fixed to the venous wall. In all cases, the hepatic venous wall was severely inflammed. In one patient (3.1 %), the proximal end of the stent had been displaced into the main portal vein (PV) trunk. The prosthesis could be dissected free of the thin-walled venous vessel wall without problems.

Two patients (8.7 %) had developed a thin-walled extrahepatic, PV pseudoaneurysm caused by erosion of the intima by the proximal end of the Palmaz stent (Fig. 2). In order to avoid bleeding at the beginning of transplantation, the hepatic hilum was approached only after completely freeing the hepatic parenchyma from the retrohepatic IVC. In one patient (3.1 %), analysis of the hepatectomy specimen showed a (preoperatively unproven) bilioportal fistula that was responsible for pronounced jaundice. This finding did not, however, influence the implantation technique.

In all patients the liver was implanted using the piggyback (PB) method with preservation of the recipient IVC [1, 20]. In 17 TIPSS patients and 33 non-TIPSS patients, allograft implantation was performed using PB with laterolateral cavocavostomy under lateral and partial clamping of the recipient IVC [1]. With the latter method there is a single anastomosis between the posterior surface of the donor IVC and the anterior surface of the recipient IVC. This technique was useful when there were phlebitic changes in the hepatic veins and when dislocation of the metallic stent into the IVC had occurred. Venovenous bypass was used in two patients only: one with severe impairment of cardiac ejection and one who developed severe hypotension on clamping the IVC and PV.

The median intraoperative blood transfusion requirement at transplantation in the 23 TIPSS patients

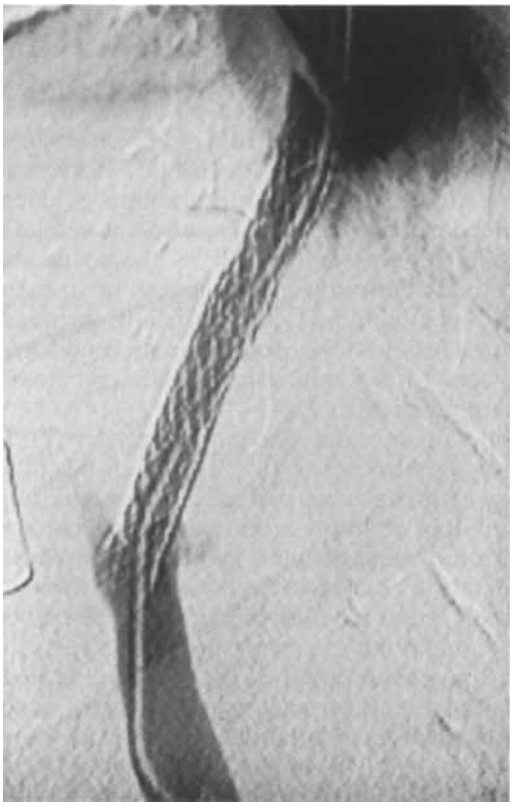

Fig. 1 Venogram showing localization of caval end of TIPSS at the level of the hepatic vein to be transected during the transplant procedure

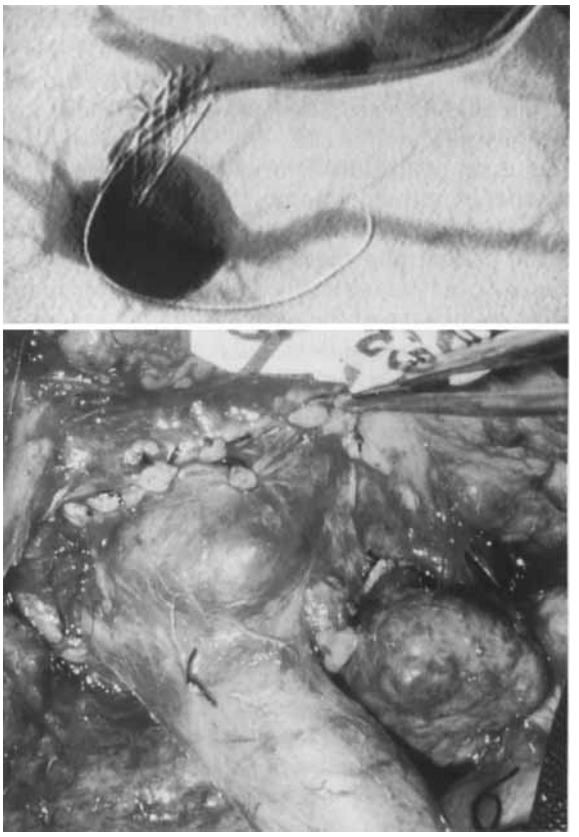

Fig. 2 Angiographic and intraoperative view of extrahepatic portal vein aneurysm caused by the portal TIPSS end

was similar to that required in the 36 cirrhotic patients who received transplants during the same time period without previous TIPSS [800 ml (range 0–20300 ml) vs 620 ml (range 0–7600 ml), respectively]. There was also no difference between the two groups to length of hospital stay [median 18 days (range 0–34 days) vs 19 days (range 0–66 days), respectively].

Three TIPSS patients (13 %) and two non-TIPSS patients (5.5 %) died during the early (< 3 months) post-transplant period. The first patient, who had mural PV thrombosis at the time of the TIPSS, had thrombosed all three splanchnic veins at transplantation; venous graft revascularization was performed using a free iliac venous graft between a recipient jejunal vein and the donor portal vein. The patient died some hours following transplantation due to primary graft nonfunction that caused hemodynamic instability and coagulopathy. A second patient died of cerebral aspergilloma related to graft-versus-host disease following compatible, but mismatched (0 to B blood group), liver grafting. The third patient, transplanted because of secondary biliary cirrhosis, died of multiorgan failure following retransplantation; the latter was performed after the first liver graft failed as a result of hyperacute rejection in the presence of a 100 % positive crossmatch. This case was particularly difficult due to previous biliary surgery that had caused a frozen right upper quadrant. Despite the presence of a duodenal fistula to the gallbladder fossa and perihepatic abscess cavities, the hepatectomy was performed without major blood loss.

Both non-TIPSS patients died of poor graft function.

Discussion

The major problem in liver transplantation is the increasing shortage of available donor organs, resulting in a rising incidence of (lethal) complications such as bleeding, infected ascites, or renal insufficiency in patients waiting for a graft [2]. Uncontrollable hemorrhage and/or intractable ascites related to portal hypertension can be treated by selective or nonselective surgical portosystemic shunting [3, 21]. Although differences in post-transplant morbidity and mortality between patients with and without previous portal hypertension surgery have become less pronounced, such interventions render the transplant procedure technically more difficult [2, 6, 8, 12]. Moreover, portosystemic surgery

requires general anesthesia, and mortality remains high in Child-Pugh group C liver disease and in urgently treated patients [16, 21]. Without portosystemic decompression, repeated endoscopies, paracenteses, and intensive care admissions are the rule.

Treatment of advanced portal hypertension using the percutaneous intrahepatic portosystemic shunt, developed by Rösch in 1969, is an attractive alternative for both the patient and the transplant surgeon [18]. This procedure can be done easily and safely under sedation; it allows calibration of the portosystemic shunt, possibly preserving hepatopetal flow, and it avoids difficult situations encountered at transplantation due to previous portal hypertension surgery [6, 8, 11, 12].

The rationale for the use of this interventional radiological procedure as a bridge to transplantation is sound [11, 17]. The major advantage of successful TIPSS is that elective transplantation becomes possible even in end-stage liver disease patients who have life-threatening complications related to refractory ascites and repeated gastrointestinal bleeding [4, 7]. TIPSS is of particular interest in the treatment of "thoracic ascites" and of gastrointestinal bleeding of unknown origin, as well as in patients whose source of bleeding is inaccessible to tamponade, or to sclerotherapy, or who have recurrent bleeding after adequate therapy [13, 19].

TIPSS also allows for better psychosocial evaluation of a potential liver transplant candidate, which is extremely important when dealing with patients with alcoholic cirrhosis or those suddenly confronted with the therapeutic option of transplantation due to the occurrence of a severe complication of their "stable" liver disease [15].

Despite spectacular clinical improvement in some patients, TIPSS should remain essentially a bridge to transplantation in end-stage liver disease patients who have been selected as potential candidates and who have severe complications of their disease. This approach is corroborated by the fact that liver function itself does not improve following TIPSS, as reflected in the causes of mortality of patients on the waiting list who were not grafted in time, in the lack of improvement in the Child-Pugh score and the aminopyrine breath test (in a small number of patients in our series), and in the fact that the incidence of early and late shunt-related complications is fairly high [7, 11, 13, 19]. Shunt stenosis, with eventual progression to occlusion, has been reported in up to 30 % of patients despite short follow-up periods [13, 19]. The TIPSS must be reviewed every 3–4 months by Doppler sonography and venography, if the ultrasound is abnormal or difficult to interpret. Venography performed under local anesthesia allows dilatation, thrombolysis, or placement of an additional stent during a single session [11, 13, 19]. New-onset or worsening encephalopathy is reported in up to 25 % of patients [13, 19]. This complication can be managed by dietary manipulation and lactulose starting from the time of TIPSS placement onwards. Narrowing of the shunt channel by the introduction of an additional endoluminal stent is another possible way to treat the encephalopathy [13]. The risk of encephalopathy should, however, not deter the use of TIPSS as a treatment for life-treatening complications, e.g., uncontrollable bleeding, in a potential transplant candidate. In contrast to others, we feel TIPSS should not be performed to facilitate transplant surgery or to reduce intraoperative blood loss [5]. In our study, intraoperative blood transfusion during transplantation and length of hospital stay were similar in TIPSS and non-TIPSS transplant recipients.

Preoperative portal decompression by TIPSS for blood-saving purposes is, in our opinion, justified only in patients who have had repeated hepatobiliary surgery (e.g., multiple attempts at bile duct repair or reoperations after portoenterostomy) and in patients who need to be regrafted because of cirrhosis due to viral allograft reinfection; these are both conditions which, in our experience, make the transplant procedure very difficult. The feasibility and usefulness of TIPSS in the treatment of portal hypertension occurring after liver transplantation have been demonstrated already at our institution [9].

One must bear in mind that TIPSS material is costly and that the procedure itself may cause specific vascular changes. Hepatic veins and IVC can show phlebitic changes, especially after balloon dilation of shunt stenosis. The proximal end of the stent may also cause intimal damage, leading to the formation of extrahepatic PV aneurysm. In these cases, complete dissection of the liver hilum is best postponed until the liver parenchyma and retrohepatic IVC are separated completely. This surgical strategy avoids the need for early, and thus prolonged, PV occlusion due to an inadvertent lesion of the PV aneurysm at the beginning of recipient hepatectomy.

Dislocation of the distal end of the stent at the level of the division of the hepatic veins must be recognized in order to allow correct IVC clamping. The presence of metallic stent fibers may cause bleeding or air embolism due to incomplete IVC occlusion by the vascular clamp and also rupture of the suprahepatic IVC during the transplant procedure [5]. In cases of severe inflammation in the hepatic veins, piggyback liver transplantation with laterolateral cavocavoplasty is a convenient method of graft implantation [1].

In cases of migration of the stent into the main portal trunk, the PV should be dissected to the splenomesenteric confluence in order to allow PV clamping at an intact level. Flush transection of the PV to the liver parenchyma will then allow dissection and removal of fibers in a dry operating field.

We conclude that transjugular intrahepatic portosystemic shunting is an effective, reliable, nonsurgical pro-

cedure for the treatment of liver transplant candidates or patients presenting with life-threatening complications of their liver disease. The major advantage of TIPPS with regard to liver transplantation is that it allows for more elective procedures in such patients. Since there is always a chance of early or late complications, the decision to create a TIPSS should be made only after multidisciplinary discussion between hepatologist, interventional radiologist, and transplant surgeon. One must always bear in mind that incorrect TIPSS placement or inadequate application of the TIPSS technique could compromise later transplant surgery.

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