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Liver Transplantation

Procedures and Management

PREFACE

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Transjugular Intrahepatic Portosystemic Shunt in the Treatment of Portal Hypertension

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The treatment of portal hypertension (PH) is an important problem in patients with end-stage liver disease (ESLD) who are candidates for orthotopic liver transplantation (OLTx). Variceal bleeding is a known major complication and the second leading cause of death after acute hepatic failure in portal hypertensive patients [1, 2]. The management of variceal bleeding in OLTx candidates should attempt to preserve the anatomy of the portal vein (PV). Previous reports have documented increased mortality and morbidity rates in patients with surgical porta-caval shunts undergoing OLTx [3, 4].

In recent years, endoscopic sclerotherapy has become the treatment of choice for acute variceal bleeding. Sclerotherapy is able to stop variceal bleeding in more than 90% of cases [5]. However, there is a high rate of rebleeding episodes after sclerotherapy [6-9].

An emergency portosystemic shunt is indicated in those 10-15% of patients in whom sclerotherapy has failed to stop variceal bleeding. Other indications for an emergent portosystemic shunt are bleeding from large gastric or intestinal varices or hemorrhage from portal hypertensive gastropathy (PHG) [6-10].

The high rate of mortality and morbidity and the lack of a significant improvement in the long-term survival of patients with PH coupled with the evolution of OLTx have greatly reduced the indications for surgical portosystemic shunting [11-13]. Therefore, much effort has been directed at developing an effective nonsurgical technique of portal decompression.

In 1969, Rosch et al. created a nonsurgical portosystemic shunt in dogs using a percutaneous transjugular approach. This technique is based on the close relationship between the hepatic vein (HV) and a main branch of the PV. These authors used a modified Colapinto needle advanced through a vascular catheter into a HV. The HV is punctured with the Colapinto needle which is then advanced through the hepatic tissue until the PV is cannulated. Finally, another catheter is inserted between the HV and the PV, thus creating an intrahepatic porta-caval shunt [14].

After this pioneering study, other investigators tried to create intrahepatic porta-caval shunts by resecting a cylinder of hepatic tissue [15] or using a cryostatic probe [16] for making a tunnel through the hepatic parenchyma.

In 1982, Colapinto et al., using a technique similar to that developed by Rosch, created a transjugular intrahepatic portosystemic shunt (TIPS) in a patient with massive variceal bleeding uncontrolled by balloon tamponade and too sick for surgical operation [17]. These authors created a TIPS by using a vascular balloon dilatation catheter, which was left expanded for 12 hours inside the hepatic tissue and then removed [17]. Subsequently, the same authors reported on 6 Child's class C patients who underwent a TIPS procedure according to the technique described above [18]. In this study, only a slight reduction of portal pressure was obtained and all the shunts eventually occluded due to closure of the liver tract. All patients died during a 6-month follow-up for causes related to ESLD [18].

In 1985, and in a subsequent study in 1986, Palmaz et al. made a significant improvement in the long-term patency of the intrahepatic shunt by using a new balloon expandable stainless steel vascular stent [19, 20]. This metal stent was used to keep the artificially created tract in the liver open. The first clinical application of Palmaz's stent was reported by Richter in 1990 [21]. Further clinical studies confirmed the efficacy of this new technique of portal decompression encouraging its larger clinical application in the treatment of PH [22].

INDICATIONS

Medical therapy, sclerotherapy and transhepatic embolization have all been shown to be useful in the treatment of variceal hemorrhage. However, the creation of a portosystemic shunt is associated with the lowest incidence of rebleeding episodes [6-8, 23-26]. In this way, TIPS is the result of a marriage between the surgical and angiographic experience in the treatment of PH, allowing for decompression the portal system without the risks related to a surgical procedure.

The most frequent indication to perform TIPS is acute variceal bleeding that cannot be stopped by sclerotherapy, in patients with poor general medical condition or ESLD that are ineligible for shunt surgery. However, it is important to stabilize the patients clinical condition before performing the TIPS. Most of such patients are Child's class B or C. It has been reported that emergency shunt operations in Child's class C patients carries a mortality as high as 40% to 100% [27-30].

Recently, it has been suggested that TIPS be performed in patients not actively bleeding but who have undergone repeated sessions of sclerotherapy, or in patients that have experienced more than 2 episodes of bleeding during 14 days of observation [31, 32].

Less frequent indications for TIPS procedure are recurrent ascites resistant to medical therapy [33-40], hepatorenal syndrome or preoperative portal decompression [33, 34].

Possible contraindications for TIPS are hepatic tumor, large hepatic cyst or abscess, PV thrombosis and/or vena cava thrombosis. An absolute contraindication for TIPS is polycystic liver disease. In the presence of PV thrombosis, it may still be possible to perform TIPS if a large intrahepatic portal collateral is present [41].

There is no reported experience of TIPS in the literature on pediatric patients, most likely because the small diameter of the vessels in children make the procedure more difficult and may increase the risk of thrombosis of the shunt.

METHODS

Before a TIPS procedure, prophylactic broad-spectrum antibiotics should be given and severe coagulopathy, if present, should be corrected.

The first TIPS procedures were performed by using a combined transjugular and percutaneous transhepatic approach, but this technique was quickly abandoned because of the higher complication rate related to the transhepatic cannulation of the PV [21, 42, 43].

As experience has been gained, most TIPS procedures are completely performed with only a trans-

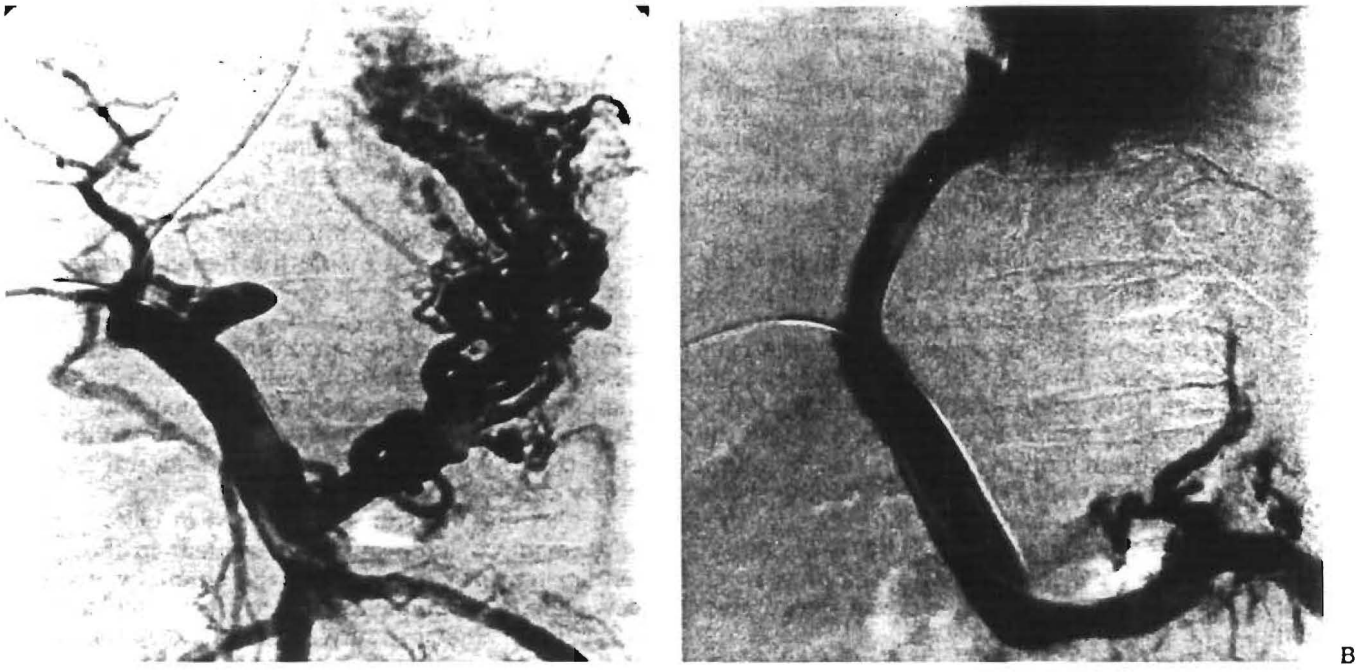

Fig. 3.1. *Transjugular intrahepatic portosystemic shunt using the Wallstent.*
A. Numerous gastroesophageal varices originating from the coronary vein are demonstrated on initial portogram following catheter placement into the portal vein. The portosystemic gradient was 33 mmHg.
B. Portogram performed following placement of Wallstent shows decompression of varices and excellent flow through the shunt into the inferior vena cava and right atrium. The portosystemic gradient was reduced to 14 mmHg.

jugular approach under fluoroscopy; doppler ultrasound may be useful for PV localization [32, 41, 43, 44].

A 5 F slightly curved catheter is coaxially guided through a 7 F outer teflon catheter and passed to the suprahepatic inferior vena cava (IVC) via an internal jugular venous puncture site. The 5 F catheter is advanced into the right HV and a hepatic venogram is obtained. If the HV appears suitable for a TIPS, the 5 F catheter is then removed and the 7 F teflon catheter is advanced into the HV; passage over a guide wire may be required to avoid kinking. A 16-G Ross modified Colapinto needle is then advanced through the 7 F teflon catheter into the HV. The HV puncture site is selected approximately 2 cm beyond the junction of the HV and IVC. Generally, the needle tip is rotated to an anterior direction. The needle is advanced through the hepatic parenchyma until a PV branch, usually the right, is entered. The PV access is confirmed by blood aspiration and visualization of the portal system by injection of water soluble contrast. Investigators have suggested that real time ultrasound can be useful in decreasing the number of attempts of PV puncture [32, 43, 44]. However, other investigators consider real time ultrasound guidance unhelpful, with fluoroscopy more than sufficient to achieve PV cannulation [41].

Once the PV is entered, a guide wire is advanced into the PV. The needle is then removed and a 5 F catheter is advanced into the PV over the guide wire. The venous pressure gradient between the PV and supra hepatic IVC or right atrium is measured and a portal venogram is performed to demonstrate the anatomy of the portal venous system (Fig. 3.1 A). The 5 F catheter and the 7 F teflon catheter are exchanged for a 35 cm 9 or 10 F sheath which is passed to the HV. This exchange is performed over a heavy duty guide wire. A 10 mm balloon is then passed through the sheath into the liver tract. After balloon dilatation of the hepatic parenchymal tract, the balloon is removed. Finally, an expandable metal stent is placed in the liver tract between the HV and the PV. Since a functional portosystemic shunt has been created, a vascular catheter is inserted into the portal system to demonstrate a decreased portosystemic gradient, the shunt flow and the status of varices (Fig. 3.1 B). If the reduction in portal pressure is not considered adequate to achieve good portal decompression, it is possible to expand the intrahepatic shunt from 8 to 12 mm in diameter, if a Palmaz stent has been used.

The placement of a second shunt in a different position can be an alternative technique to enlargement of the shunt previously described, if the intrahepatic shunt has been created with a Wallstent. Because of its design, Wallstent cannot be enlarged beyond 10 mm.

WORLDWIDE EXPERIENCE

Until recently, only a limited number of TIPS cases has been reported in the international literature.

As discussed above, Colapinto et al. reported the results of 6 patients who underwent TIPS. These authors demonstrated variceal obliteration and obtained a portal pressure reduction of 10-15 mmHg, with a 70% rate of rebleeding episodes and 100% mortality rate during a 6-month follow-up [18].

In 1989, Rossle et al. published their results in 10 patients who underwent TIPS. They obtained a significant reduction in the portal pressure without rebleeding episodes during a 3-9 months follow-up [45].

In 1990, Roberts et al. performed a TIPS procedure by using a percutaneous transjugular and percutaneous transhepatic approach in a liver transplant candidate with acute variceal bleeding. The creation of the intrahepatic portosystemic shunt was followed by an immediate cessation of variceal bleeding. In spite of a recurrent hemorrhage, the patient underwent successful OLTx [46].

Richter et al. reported on 24 cirrhotic patients in which a surgical shunt was not indicated and who therefore underwent TIPS. A successful TIPS was obtained in 75% of cases with a 43% drop in the mean portal pressure. The 30-days mortality rate was 11% and in only 1 patient was death related to a technical problem during the TIPS procedure. During a 2-year follow-up these authors reported a 50% total mortality rate [43].

Zemel et al. performed TIPS in 8 patients and obtained a drop in the average portal pressure from 36 to 11 mmHg. In 5 cases an 8 mm stent was used, in 2 cases a 10 mm stent and in 1 case a 12 mm stent. Upper endoscopy was performed two weeks after TIPS in all patients and showed universal variceal decompression. One patient rebleed from rectal varices. This patient was treated by increasing the shunt size from 8 to 12 mm. There was no other episode of rebleeding or patient death during a follow-up ranging from 1 to 9 months [31].

Recently, larger series of TIPS have been reported, as proof that this technique of portal decompression is gaining increasing acceptance.

Althaus et al. reported on 62 patients who underwent TIPS. Indications included active bleeding from esophagogastric varices and intractable ascites. Only 14% of patients experienced rebleeding episodes due to thrombosis of the shunt. The most significant complications were hepatic encephalopathy (13%) and hepatic trauma (7%) [47].

Barton et al. have published a series of 60 patients with recurrent variceal bleeding treated with TIPS. The mean PV pressure drop was from 38.5 to 23.8 mmHg. The rebleeding rate was 20%. The mortality rate during a mean follow-up period of 6.5 months was 21.6%. In this study, they compared the Gianturco-Rosch Z stent with the Wallstent and did not find any significant difference between the two stents [48].

Zemel et al. reported on 55 TIPS patients with a follow-up of 2-24 months (mean 7.6 months). The percentage of thrombosis or stenosis of the shunt, including HV stenosis, was 11%. The mortality rate was 11% and mild encephalopathy, easily controlled with medical therapy, was observed in 9% of cases. Ascites disappeared in 95% of patients [49].

LaBerge et al. reported on 100 TIPS patients. Ninety-four of these were done for active variceal bleeding, 3 for recurrent ascites, 2 for hepato-renal syndrome and 1 for preoperative portal decompression before OLTx. The technical success rate was 96%. After TIPS they observed a 35% drop in the portal pressure. Shunt stenosis or obstruction occurred in 15.6%. During a 6-month follow-up the incidence of rebleeding episodes and mortality was 10.4% and 27%, respectively [36].

Savin et al. reported their experience in 42 TIPS patients; 22 were classified as Child B and 16 as Child C. The indication for TIPS was active variceal bleeding in 96% of cases and recurrent ascites resistant to medical therapy. After TIPS they observed a drop in the mean portosystemic pressure gradient from 17 to 7 mmHg. Recurrent hemorrhage was observed in 14% of the cases and the incidence of encephalopathy was 13% [38].

Richter et al. reported their results on 120 patients who underwent TIPS during a 5-year period. The mean portosystemic pressure gradient reduction was from 29 to 12 mmHg. The stenosis rate was 12.3%, mainly localized at the level of the HV. The survival rate at 30 days, 1 year, and 3 years was 94.7%, 68%, and 42%, respectively [50].

Zajko et al. from our Institution reported their experience using TIPS in 45 patients (Child class: A = 10, B = 26, C = 9). Indications included variceal bleeding in 44 and intractable ascites in 1. Palmaz stents were used in the first 21 patients and Wallstents in the last 24. Routine follow-up portal venography was performed at 3, 6 and 12 months post TIPS. Successful TIPS was obtained in 100% of cases with a drop in the average portosystemic gradient from 27 to 11 mmHg. Thirty-day mortality was 6.7%. With a mean follow-up of 8 months, variceal bleeding occurred in 6.7%; 13 patients underwent OLTx. The most significant problem reported by these authors was stenosis of the HV occurring in 36% of cases. Stenosis of the shunt due to pseudointimal hyperplasia within the stent occurred in 7%. Most cases of HV stenosis occurred in shunts created with the Palmaz stent. Most of these patients were asymptomatic with the stenoses detected during routine shunt follow-up portal venography or Doppler ultrasound. HV stenosis was treated with shunt revision using the Wallstent, balloon angioplasty, or both [51].

COMPLICATIONS

Because of limited reported experience, it is difficult to determine the exact incidence of complications related to the TIPS procedure. The different techniques used and personal experience play an important role in determining the nature and incidence of complications observed.

The most frequent complications after TIPS are thrombosis or stenosis of the shunt or HV (Fig. 3.2 A), the development of hepatic encephalopathy and recurrent hemorrhage (Table. 3.1).

The incidence of shunt thrombosis or stenosis including HV stenosis ranges from 10 to 66% [35, 36, 38, 47-49, 51, 54, 55] and is the main cause of rebleeding episodes. However, most cases of shunt stenoses are detected on routine follow-up portal venography during the first 6 months (unpublished data). Pseudointimal hyperplasia is the main factor causing shunt obstruction [32, 51-53, 55]. Doppler ultrasound may be useful in determining shunt patency. It has been reported that a blood flow velocity through the shunt >60 cm/sec or <50 cm/sec is an index of shunt patency or outflow stenosis, respectively [56]. Thromboses or stenoses of the shunt are generally treated by balloon dilatation and/or by placement of additional stents (Fig. 3.2 B) [31, 36, 41, 48, 49, 51, 54, 57]. In other cases it may be necessary to establish a new intrahepatic shunt [36, 49, 53, 58].

As with all portosystemic shunts, TIPS can also cause hepatic encephalopathy [36, 38, 47,49]. Some investigators reported a 13% incidence of encephalopathy after TIPS. This result is similar to that reported after portosystemic shunt performed with a small size graft of 8-10 mm in diameter [59, 60]. In general, this kind of encephalopathy responds well to the medical therapy permitting a good quality of life [57, 59-61].

Regardless of the kind of stent used (Palmaz, Wallstent, etc.), migration of the stent into the pulmonary artery or right atrium has been reported [31, 57, 62].

Tab. 3.1. *Worldwide experience.*

Authors	Thrombosis/ stenoses (%)	Encephalopathy (%)	Bleeding recurrence (%)	Mortality (%)	Follow-up (months)	N. of patients
Althaus [47]	14	13	14	0	—	62
Barton [48]	15	—	20	21,60	1-26	60
LaBerge [36]	15,60	17,70	10,40	27	2-24	100
Maynar [54]	19,50	—	19,50	12	1-12	41
Richter [50]	12,30	—	—	58	0-60	120
Savin [38]	14	13	14	0	—	42
Saxon [52]	66	—	19	—	2-24	21
Zajko [57]	36	—	6,70	6,70	1-12	45
Zemel [49]	11	9,10	5,5	11	2-24	55

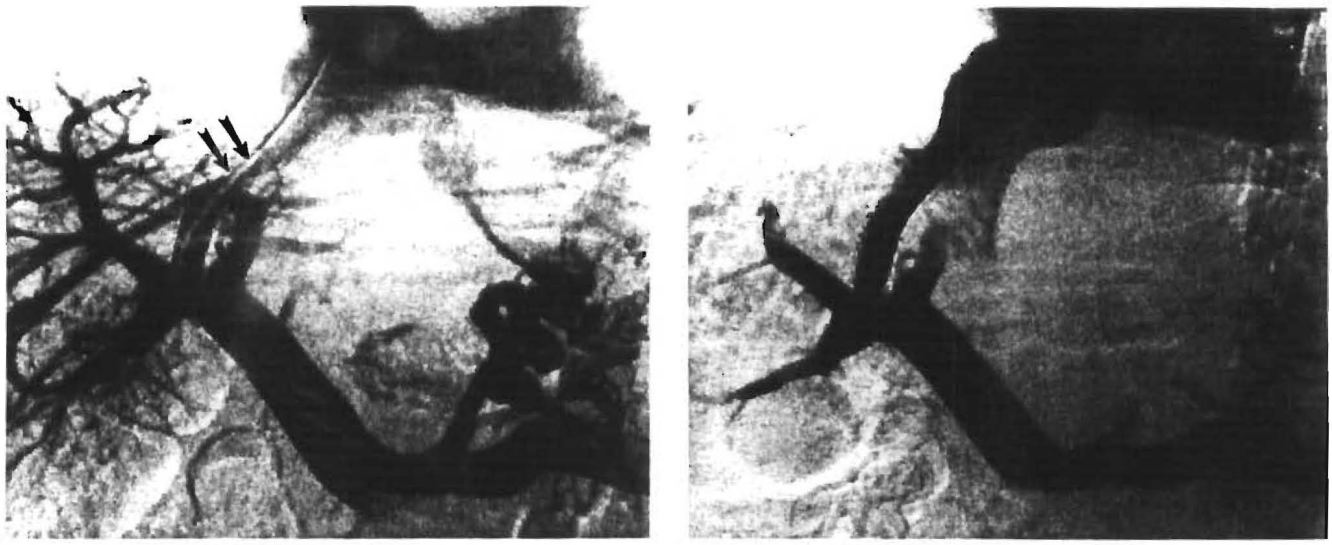

Fig. 3.2. *Shunt malfunction caused by outflow stenosis of the hepatic vein treated by shunt revision with a Wallstent.*
A. Severe stenosis of the hepatic vein (arrows) at the level of venous outflow from the shunt. In this patient, the initial shunt was created with a Palmaz stent. The outflow stenosis has resulted in recurrence of gastroesophageal varices and marked increase in intrahepatic portal vein flow. The portosystemic gradient was 20 mmHg.
B. Following shunt revision, portography shows complete decompression of varices, a marked reduction in intrahepatic flow, and excellent flow through shunt into the inferior vena cava. Shunt revision was performed through the previous Palmaz stent and across the hepatic vein stenosis. The hepatic venous outflow is now widely patent and the portosystemic gradient was reduced to 6 mmHg.

This complication can be treated by removing the stent with an angiographic catheter (in the case of a Wallstent) [31, 62]. A Palmaz stent may have to be moved and expanded in the pulmonary artery or the IVC. Although there are no studies that demonstrate the superiority of one stent over another, some investigators believe that the Wallstent is less frequently involved in migration phenomenon because of its higher elasticity [62].

Less common complications of TIPS include intraperitoneal hemorrhage [35, 63], hemobilia [35, 53], puncture of the gallbladder or colon [35], acute renal failure [53, 64], thrombosis of PV or jugular vein [61], sepsis [57, 63], acute respiratory distress [61], hepatic trauma and myocardial ischemia [38, 47].

DISCUSSION

TIPS induces hemodynamic changes very similar to those obtained after a surgical portosystemic shunt using synthetic grafts of different diameter (8-12 mm). Clinical results are also similar, particularly when comparing the incidence of shunt obstruction, the percentage of rebleeding episodes and the frequency of portosystemic encephalopathy [59, 60, 65, 66]. However, TIPS has several advantages over a surgical portosystemic shunt. With TIPS the patient does not undergo the stress and the risk of an operation and it may be possible to modify the size of the shunt according to the individual hemodynamic characteristics [21, 22, 43, 67]. Because of its moderate invasive nature, TIPS is mainly indicated in those Child's C patients at increased risk for surgery [43], where the mortality rate after surgical portosystemic shunt has been reported to range from 40 to 100% [27].

The main technical progress responsible for TIPS larger clinical use are the introduction of balloon expandable (Palmaz) [19, 20, 68] and self-expanding (Wallstent) [32, 69] metallic vascular stents, more rigid needles (that allow a better angle of puncture and easier perforation of the hepatic tissue) and the use of high definition Doppler ultrasound for PV localization [44, 56, 70].

The Palmaz stent and Wallstent are the most widely used stents. Advantages of the Palmaz stent include flexibility in the size and, therefore, the ability to regulate the hemodynamic effect of the shunt as documented by pressure gradients; in addition a relatively precise positioning is possible. Disadvantages of this stent include the larger-size sheath necessary for introduction and its lack of longitudinal flexibility, which sometimes makes insertion more difficult than with other types of devices [57]. Also because of its rigidity, a relatively central puncture of the main right or left PV is necessary. Advantages of the Wallstent include the use of a somewhat smaller delivery system and the ability to puncture any PV branch because of the inherent flexibility of the stent. Disadvantages include less precise positioning due to the significant shortening of the stent after deployments and limitation in the fixed outer diameter of 10 mm, which may theoretically necessitate additional shunts in some patients [57].

After the intrahepatic portosystemic shunt is made, the pressure gradient between the PV and the HV is measured to determine the efficacy of the shunt. Investigators have observed that rebleeding episodes are unlikely if the portosystemic gradient is <12 mmHg [71, 72]. However, others have reported that the percentage decrease in the portosystemic gradient is a more important predictive factor than the absolute final gradient [73].

If portal decompression is not adequate following TIPS, it may be possible to increase the shunt size (in the case of a Palmaz stent shunt) until a diameter of 10-12 mm or perform transcatheter variceal embolization [21, 31, 32, 43]. If TIPS has been created with a Wallstent, variceal embolization or an additional shunt may be performed [55, 58].

Recently, it has been reported that 77% of patients with an intrahepatic shunt of 8 mm in diameter required variceal embolization; however, this procedure was performed in only 36% of patients with an intrahepatic shunt of 10 mm in diameter [33].

It has been suggested that TIPS, as with other portosystemic shunts, can result in deterioration of liver function, mainly in those patients undergoing an emergent TIPS or those with Child's C liver disease [74]. Recently, however, no deterioration of liver function after TIPS has been reported during a 6-month follow-up [75]. The incidence of hepatic encephalopathy has been reported to range from 0 to 35% [36-38, 40, 47, 49, 57, 75]. This wide range of results can be due to different groups of patients included in the studies, to the size of the intrahepatic shunt, and to different follow-up periods.

In studies citing disproportionately low incidence of hepatic encephalopathy, the question of inadequate follow-up must be raised. The disappearance of intractable ascites has been observed in 70-100% of the patients undergoing TIPS [31, 37, 40, 48, 49, 55, 57]. Therefore, an increased number of patients have undergone TIPS where the main indication was ascites resistant to medical therapy, periodic paracentesis, and peritoneal venous shunts [36, 37, 39, 40, 47, 53].

The incidence of rebleeding episodes following TIPS has been reported to range from 11 to 20% on long-term follow-up (20-26 months) [35, 48]. For surgical portosystemic shunts, as for TIPS, rebleeding episodes are mainly secondary to shunt obstruction or to HV outflow problems [35, 36, 38, 47-49, 51, 54].

Recently, Richter et al. [50] and LaBerge et al. [36] reported a short-term (30 days) mortality rate of 5.3% and 13%, respectively. For the long-term (3 years 50; 20 months 36) mortality was of 58% and 27%, respectively. Most of those patients were classified as Child B or C, patients in whom emergent surgical porta-caval shunt was not indicated because of the extremely high operative risk.

An increasing number of liver transplant programs are using TIPS as the technique of choice for portal decompression. Portal hypertensive patients undergoing a porta-caval shunt have an increased operative risk, mainly related to the presence of adhesions and stenosis or thrombosis of the PV. Such complications significantly enhance the technical difficulty during OLTx [12, 13]. In patients with TIPS, the stent can be easily removed with the liver during OLTx.

For these reasons, in the last years, at our Institution we have performed only a limited number of surgical portosystemic shunts despite the high number of OLTx performed [12, 13].

CONCLUSIONS

TIPS is an exciting new interventional radiologic technique for the treatment of PH, which should only be performed in an angiographic suite where high resolution fluoroscopy and digital angiography are available, as well as experts trained in interventional radiological techniques. In addition, TIPS should be performed in hospitals where an experienced surgical team in hepatobiliary surgery is available.

Despite its new clinical introduction, TIPS is a safe and effective technique of portal decompression, mainly useful in that group of patients with acute variceal bleeding or in patients with recurrent bleeding unresponsive to sclerotherapy.

Therefore, TIPS can replace the emergent surgical portosystemic shunt.

With increased clinical experience, it may replace the elective surgical portosystemic shunt in well selected cases.

TIPS plays an important role in the management of portal hypertensive related bleeding in OLTx candidates, permitting a "bridge effect" in avoiding further bleeding episodes while a suitable donor becomes available.

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